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Gaps in Optimal Care for Acute Myeloid Leukemia among Adults in their Communities and a Proposal for Future Care Model

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Abstract

Despite significant diagnostic and therapeutic advances in Acute Myeloid Leukemia (AML) and Myelodysplastic Syndrome (MDS) over the past two decades, a substantial proportion of US patients continue to face systemic barriers that prevent care optimization. This review examines four domains where these disparities are most pronounced: precision at diagnosis using molecular testing, germline genetic counseling, clinical trial enrollment, and allogeneic hematopoietic stem cell transplantation (HSCT). We quantify current gaps in these domains, appraise previous and current efforts to bridge the gaps, ending with a proposed path forward. We highlight that patients in community settings are 14% less likely to undergo molecular testing compared to those at academic institutions, directly limiting risk stratification and access to targeted therapies. Fewer than 20% of patients meeting criteria for germline genetic counseling receive it. Clinical trial enrollment remains critically low, with enrollment incidence ratios as low as 0.28 among certain minority populations, reflecting both structural access barriers and the limited effectiveness of existing federal diversity mandates. Allogeneic HSCT rates remain disproportionately low among older, frail, and socioeconomically disadvantaged patients. Various solutions are explored across each domain, with a central theme of reducing systemic burden, expanding community-based support, and building more integrated care infrastructure. The compounding effect of these deficits continues to drive gaps in AML and MDS care; addressing these gaps is essential to achieving equitable outcomes.

Take Home Messages

1. We highlight diagnostic gaps for patients with AML and MDS based on patient setting. Using hub and spoke network models, patient navigation and cross institutional tumor board access we propose to overcome these gaps.
2. We discuss gaps in access to clinical trials for management of AML and MDS as well as allogeneic HSCT. Using expansion in telehealth services, decentralized clinical trial delivery and mimicking "count me in" initiatives we provide a framework to close these gaps in patient care.

Introduction

About 30,000- 35,000 patients each year in the United States are diagnosed with acute myeloid leukemia (AML, N 22,000) and high grade myelodysplastic syndromes (MDS, N 10,000-15,000) among adults.[1,2] It is considered a rare diagnosis with a worldwide increase in incidence and has a 50% mortality within first year of diagnosis.[1] While patients with a diagnosis of acute leukemias live across all parts of the US, only the NCI designated cancer centers, comprehensive cancer programs and other large community-based programs have the required subspecialists to manage this aggressive cancer expeditiously. The growing adoption of non-intensive strategies and targeted therapies in AML has led to an increasing number of patients managed in their community setting.[3] A recent stakeholder meeting held to address challenges faced by community-based AML management identified access to advanced diagnostics, clinical trials, timely blood transfusions and financial toxicity as significant barriers in optimal care for acute leukemias.[3]

This review examines four critical domains in which gaps between evidence-based recommendations and real-world practice are most pronounced: (1) molecular testing at diagnosis, (2) utilization of genetic counseling services, (3) access to clinical trials, and (4) hematopoietic stem cell transplants (HSCT). For each domain, we characterize the current evidence, identify the systemic barriers driving underutilization, and propose implementation strategies aimed at closing the gap between guideline intent and clinical practice.

I: Molecular Testing at Diagnosis

Genomic characterization at diagnosis is foundational to the management of AML and MDS.[4,5] Mutational profiling informs risk stratification, shapes treatment selection, response to therapy and guides post-remission disease curative strategies including the decision to pursue allogeneic HSCT.[4,5] Both the 2022 European Leukemia Net (ELN)[6] recommendations and the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[7] stipulate comprehensive cytogenetic and molecular testing for all newly diagnosed AML patients. A rapid elucidation of the molecular architecture of AML and MDS through Next Generation Sequencing (NGS) leads to increased accuracy in diagnosis, provides clues to disease origins and targets for precise treatments. For example, presence of mutations in genes such as NPM1 even at low blast percentage calls for AML as the diagnosis,[4] targeting mutations such as FLT3,[8] has been shown to have greater efficacy than the traditional chemotherapy regimen alone.[9,10] There is also emerging data for targeting treatments towards mutated IDH1 which has been shown to prolong event free survival and KMT2A which has been shown to induce high remission rates.[11,12] It has been now well established that for select non-proliferative AML, patients can safely wait for molecular tests to result before treatment initiation.[13,14]

Gaps in molecular testing

A consistent gap exists in the application of NGS at diagnosis of AML and MDS based on care setting. Patients with AML are more likely to undergo molecular testing in comparison to those with MDS,[15] and patients at academic centers were more likely to receive molecular testing than those in community settings (84.3% vs 70.2%, $P < .001$, Table 1).[16,17] The percentage of genomic testing performed overall has increased over the years, with the magnitude of improvement being considerably greater at community and government sites than at academic centers.[17] More than half of patients are diagnosed in the community,[18] yet despite this improvement in testing, 1 in 7 community-based patients still do not receive suitable testing. In a retrospective cohort of patients, it was shown unin-

*Table 1: Ancillary testing by academic versus community/government sites[17]. AML, acute myeloid leukaemia; FISH, fluorescence in situ hybridisation; NS, not significant. *Academic versus community/government sites. Table extracted from Pollyea D et al article[17]*

n (%)	**All patients with AML (N = 565)**	**Academic sites (n = 229)**	**Community/ government sites (n = 336)**	***P* value***
Conventional karyotype testing	N = 565	n = 229	n = 336	
Yes	539 (95.4)	220 (96.1)	319 (94.9)	NS
No	26 (4.6)	9 (3.9)	17 (5.1)	
Flow cytometry performed	N = 565	n = 229	n = 336	
Yes	558 (98.8)	225 (98.3)	333 (99.1)	NS
No	7 (1.2)	4 (1.7)	3 (0.9)	
FISH analysis	n = 564	n = 229	n = 335	
Yes	427 (75.7)	171 (74.7)	256 (76.4)	NS
No	137 (24.3)	58 (25.3)	79 (23.6)	
Molecular genetic testing	N = 565	n = 229	n = 336	
Yes	429 (75.9)	193 (84.3)	196 (70.2)	0.0001
No	136 (24.1)	36 (15.7)	100 (29.8)	

sured patients were less likely to receive targeted therapy compared to privately insured (0% vs. 16.8%, p=0.01), demonstrating inequities in treatment directly related to molecular testing (71% vs. 91%, p<0.05).[19]

It is worth noting that an increasing number of academic centers, particularly those with dedicated hematopathology programs, now have the capability to perform molecular testing including NGS in-house,[20] whereas community, government, and safety-net institutions tend to outsource testing to commercial reference laboratories that can incur longer turnaround times measured in weeks,[21] exceeding the timelines recommended by the ELN 2022 guidelines and International Consensus Classification — most critically, FLT3 status within 72 hours of diagnosis.[6,22] As a result, molecular tests often result after treatment has been initiated, a documented scenario in oncology settings,[23] which undermines the premise of molecularly-guided therapy selection in AML and MDS. Another related barrier facing non-academic centers is the lack of standardization across commercial laboratory platforms. Variability in gene panels and reporting formats, make it difficult for community institutions to deliver consistent, high-quality molecular profiling to their patients.[24] Finally, while the Centers for Medicare and Medicaid Services issued a National Coverage Determination in 2018 establishing coverage for FDA-approved NGS companion diagnostics,[25] implementation has remained uneven across Medicare Advantage plans and local coverage determinations. The full effect of expanded coverage on real-world testing rates among Medicare-enrolled AML patients has yet to be comprehensively characterized, and ongoing coverage gaps remain a barrier to access for this population.

Appraisal Of Efforts to Mitigate Testing Gaps

A dedicated molecular pathology infrastructure enables a quality-based care model. At institutions such as University of Wisconsin Health, direct collaboration between pathologists and oncologists through precision medicine molecular tumor boards allows NGS results to be interpreted in real time alongside clinical context,[26-28] rather than arriving as a standalone report from an external laboratory. Data from a Wisconsin-based study spanning 2010 to 2021 demonstrated that among patients treated at an academic center, molecular testing rates did not differ by area deprivation index,[19] but did dif-

fer by insurance status; supporting the conclusion that care setting is the primary driver of testing disparities, and that proximity or collaborative care with academic infrastructure can partially mitigate the effect of socioeconomic disadvantage. The PETHEMA group in Spain, established a nationwide network of seven laboratories with an aim of centralizing and standardizing NGS analysis for AML patients. Following harmonization of gene selection and reporting criteria across participating sites, concordance between centers rose from 60.98% to 85.57%,[29] despite the use of differing diagnostic platforms across institutions. This collaborative network model has since been extended to other molecular tests including conventional and quantitative real-time PCR. Treatment at academic centers has been consistently associated with higher rates of guideline-concordant molecular testing in AML and this model enables such care across geographic barriers.

Proposed Solutions

Access to NGS testing is now widespread across the US; the persistent gaps in its use are therefore more likely explained by other factors. One is variation in clinical suspicion for AML or MDS during initial workup for cytopenias, which some ordering-criteria frameworks treat as a primary gatekeeping factor.[30] Another is cost and reimbursement, which physician surveys consistently rank among the top concerns limiting routine NGS use.[31] Increasing awareness of strategies such as extracting and holding DNA until morphology results, might increase the testing rate. Similarly, greater awareness is needed that time to AML or MDS treatment can safely be extended, when clinically appropriate, to allow molecular testing results to return and inform inclusion of targeted therapies in the treatment regimen.[13,14]

Improving patient connectivity to academic institutions, rather than simply to reference laboratories, through oncology nurse and broader patient navigation programs may represent one of the most actionable strategies for closing the molecular testing gap, particularly for patients in underserved or geographically remote communities. Structured navigation models have demonstrated efficacy in improving care access for patients with chronic conditions such as diabetes,[32] and similar frameworks applied to AML diagnosis and referral pathways warrant prospective evaluation. Lastly, with AML impacting predominantly Medicare-eligible population, advocacy to ensure coverage for expanded molecular testing is a key step.

II: Access to Germline Testing and Genetic Counselling

AML and MDS are considered rare under the age of 45 years, as myeloid malignancies are diseases of aging.[33] For MDS, approximately 90% of cases are diagnosed in adults over the age of 60 years, with only 6% diagnosed in those younger than 50 years.[33,34] Etiology was difficult to ascertain at an individual level until recently. Prior exposure to chemotherapy and environmental toxins such as benzene are discussed to be known risk factors. With application of NGS, several germline genetic underpinnings have been discovered.[33,34] Current guidelines recommend genetic counselling for most AML or MDS patients, specifically for those with characteristics listed in Table 2. For germline testing, skin punch biopsy or hair follicle is the preferred tissue type.[35] As the tumor sample is blood, it is key to use non-hematological sources, such as fibroblasts from skin biopsy or hair follicle bulb to obtain a specimen free of blood contamination. DDX41 constitutes the most common germline cause of cancer predisposition for patients with AML or MDS among adults (4%), with an additional 1% having other established germline genetic alterations.[36,37] Median age of patients with DDX41 cancer predisposition is 68 years.[36,37] Discovery of this gene in adults with myeloid malignancies defied the historic thought process that germline predisposition was coupled with syndromic features and a younger age of onset.

Gaps in germline testing

A comprehensive assessment and management of these patients include a multidisciplinary approach with hematologists, genetic counselors, hematopathologists and HSCT teams working in synchrony to avoid any undue delays.[35] Most patients are diagnosed and managed initially in their community and are subsequently referred to academic centers for HSCT.[3] Germline testing is then initiated when any of Table 2 criteria are identified. This creates a 4–8-week delay to HSCT, especially if a related donor is considered as primary donor source. Even when treated in academic centers, among all patients with myeloid disease, only 20%

Table 2: Indication and Barriers for Germline Testing[7,35]

Indications for Germline Testing & Counseling
AML diagnosed before the age of 50 years
MDS at any age
Bone marrow failure or germline condition suspected or diagnosed at any age
Related stem cell donor
Hypoplastic MDS or aplastic anemia
Personal history of at least two cancers (one of which is a blood cancer)
Positive family history of cancer*
Identification of a variant that could be a germline cancer risk allele
*defined as ≥1 person with blood cancer within two generations
Barriers to Germline Testing in AML and MDS
Lack of workforce: Genetic counselors with specialty in hematology
Difficulty obtaining skin biopsy
Utilizing a limited panel of genes in germline testing & need for collaborative efforts
Lower awareness among providers on hereditary predisposition in AML and MDS
Turnaround time of germline testing results
Insurance reimbursement and added costs
Limited comprehensive CLIA certified germline testing panels

of the patients ultimately underwent genetic counseling.[26]

The most common reasons for not getting counseling were critical illness, prolonged hospital stays, and early deaths among patients with AML and MDS.[26] Lack of access to genetic counselors in community settings, need for obtaining skin biopsy for growing fibroblasts, and other reasons outlined in Table 2 are potential causes for low integration of germline testing in these diseases.

Appraisal of Efforts for Increasing Germline Testing

At academic centers such as the University of Iowa, initiating an inpatient consult for genetics counseling reduced consult to result time to 53 days, much shorter than the 96 days reported with outpatient-based referral.[38] Such institutional policies, when adopted as standardized guidelines and supported by payers, can overcome this barrier.

Proposed Solutions

Further audits and data acquisition should be undertaken to highlight the germline testing gaps; an approach shown to increase guideline-concordant referral rates when implemented as a structured quality-improvement effort.[39] These identified issues can also then be escalated to patient advocacy groups and incorporated into healthcare education, particularly for community oncology providers. Expanding the genetic counseling workforce with hematology-specific expertise would address a key care gap for AML and MDS patients, for whom current referral-to-result timelines—as stated above—may be incompatible with the urgency of decision-making. Virtual infrastructure offers one way to close this timeline gap: with the use of technology and virtual meetings, molecular tumor boards can and should be made accessible to community providers, facilitating case discussions with genetic counselors and bioinformaticians as a strategy to circumvent local access gaps.[40]

III: Access to Clinical Trials

Gaps in clinical trial access

Clinical trials are central to therapeutic progress in oncology, yet participation remains markedly unequal. Pediatric oncology—where trial enrollment has historically exceeded 50%— illustrates this relationship: population-level analyses have shown that age groups with higher trial participation rates have experienced correspondingly faster gains in survival.[41] While this pattern is correlational rather than causal, the sustained decline in childhood cancer mortality underscores the importance of sustained investment in clinical trial infrastructure as a meaningful lever for improving outcomes. In contrast, only 7.1% of US adults with cancer participated in treatment trials during 2013–2017, ranging from 4.1% at community cancer programs to 21.6% at NCI-designated comprehensive cancer centers.[42] These disparities are particularly consequential in AML and MDS because patients are predominantly older, may be medically frail, and often require diagnostic and treatment decisions within days.[34,43] Geographic analyses based on ClinicalTrials.gov show that active acute leukemia trials remain concentrated at academic centers in major metropolitan areas.[45] Geographic distance represents one of the most consequential barriers to trial access, particularly for older patients, in whom travel burden compounds transportation difficulties, caregiver dependence, and functional limitations.[45-47] However, the reported 619 studies reflect trial availability at a single point in time rather than the number realistically accessible to an individual patient, since the search spanned multiple leukemia subtypes, enrollment statuses, and study sites.[48] Access is also inequitable after patients reach a trial center. In a 2025 systematic review of randomized AML trials, only 23.3% reported race or ethnicity; among reporting trials, Black, Hispanic, and American Indian/Alaska Native patients constituted 4.7%, 3.4%, and 0.5% of participants, respectively.[49] Hispanic and Asian patients were substantially underrepresented relative to US AML incidence, whereas White patients were overrepresented.[49] Similarly, an analysis of US AML trials conducted from 2002–2017 found significantly lower incidence-adjusted enrollment among non-Hispanic Black, Native American, Asian, and Hispanic patients than among non-Hispanic White patients.[50] Collectively, these data show that the access gap is not limited to the location of trial sites but extends across demographic reporting, eligibility determination, referral, and enrollment after arrival at a trial center.

Past efforts have improved the visibility of disparities but have produced limited evidence of improvement in enrollment itself. Federal requirements and guidance promoting demographic reporting and broader inclusion increased the proportion of leukemia trials reporting race; however, Hantel et al. found that despite this, relative enrollment of Black and Hispanic patients declined after reporting requirements were introduced.[50] Reporting mandates are therefore necessary for accountability but insufficient when they are not paired with operational changes in how patients are identified, referred, and supported.

Appraisal of Past Efforts to Expand Clinical Trial Enrolment

Community-based trial delivery has stronger disease-specific support. In an analysis of 1,170 older adults enrolled in two Alliance AML CALGB trials, the reports of grade ≥3 adverse events, one-month mortality, and adjusted overall survival did not differ significantly between selected NCORP-supported community and academic centers.[18] Although these trials enrolled patients receiving intensive chemotherapy and may not represent all patients with AML, they demonstrate that complex AML trials can be conducted safely outside academic centers when community investigators, even with high patient volumes, are given access to investigational drug pharmacy for study and a hospital where patients enrolled on clinical trials can be monitored.[18] To reduce reliance on physician-initiated referral, addressing a documented bottleneck in which physician preference or inaction limits trial participation, the United Kingdom's NHS 'Count Me In' initiative offers a patient-driven model that could be adapted to address this gap. By documenting research preferences at initial clinical consultations, with patients automatically contactable about eligible trials unless they actively opted out, the number of patients reachable or eligible for research increased by 637% within 12 months and significantly diversified the enrolled cohort.[51] This patient-led opt-in/opt-out approach was applied to mental-health studies, thus its application to AML/MDS remains a promising hypothesis and can be an interesting way to approach cancer clinical trials.

Current efforts to reduce the gap

Ongoing initiatives increasingly address the structural mechanisms underlying exclusion. The NCORP network provides an established framework for bringing NCI-supported studies into community settings, while FDA and ASCO–Friends of Cancer Research recommendations encourage eligibility criteria that are justified by treatment-specific safety considerations rather than historical convention.[52,53] The potential impact of eligibility reform is substantial: in a multicenter analysis applying criteria from 190 frontline AML trials to 2,226 patients with newly diagnosed AML, replacing conventional trial criteria with safety-based alternatives increased median modeled eligibility from 47.9% to 84.2% and reduced differences in eligibility among racial and ethnic groups.[52] Liberalizing trial criteria based on age cutoffs, FDA prescribing labels, adverse event data from earlier phase trials, drug metabolism and, drug interactions instead of traditional criteria such as age limits, previous malignancy history, specific unrelated organ disease exclusions increased the weighted median eligibility for clinical trials from 48.2% to 91.4% of patients.[52] Trial criteria should therefore be retained only when supported by biologic rationale or observed toxicity. However, broader eligibility will not resolve disparities if eligible patients are never offered a trial. An analysis of NCI-designated comprehensive cancer centers found that a substantial proportion of racial and ethnic inequities occurred after patients had already accessed centers with acute leukemia trials, indicating that navigation, screening, clinician offering, and patient-level support require attention alongside geographic expansion.[54] Ongoing efforts should therefore evaluate the complete enrollment pathway—from residence and referral to eligibility, offer, consent, and treatment—rather than using aggregate enrollment as the sole measure of equity.

Proposed Solutions

A high-yield next step would be to combine automatic trial identification that relies less on physician choice and more on a system-based approach, with a decentralized trial (DCT) delivery at community centers. At diagnosis, electronic health record systems should generate an opt-out trial-screening request using age, diagnosis, molecular findings, organ function, and distance from an enrolling site; a centralized leukemia trial navigator could then provide the treating physician and patient with a matched-trial assessment within a target period. Regional hub-and-spoke networks should allow academic centers to retain responsibility for protocol oversight and investigational therapy while community partners perform protocol-permitted laboratory testing, transfusions, toxicity monitoring etc. DCT elements permitted under FDA guidance, including telehealth, in-home nursing and digital health tools should be integrated into future AML and MDS protocols.[55]

Sponsors should budget prospectively for transportation, temporary lodging, dependent care, interpreter services, and digital access, because opening a trial geographically does not make it accessible when participation transfers substantial financial and logistical costs to patients. Each trial and cancer center should also report the proportions of potentially eligible patients who were screened, offered enrollment, declined, or were excluded—stratified by age, race and ethnicity, insurance, rurality, and travel distance—and compare enrollment with the demographic and disease burden of its catchment area.

Finally, partnerships with federally qualified health centers, community health workers, tribal health organizations, and minority-serving advocacy groups should begin during protocol design rather than after poor accrual is recognized. Indigenous health partnerships at trial sites have been associated with higher-than-expected Native American enrollment relative to national incidence (OR 1.91),[56] suggesting this model could be extended to other underrepresented groups. These partners could review consent materials, identify locally important barriers, participate in site selection, and establish referral pathways before activation. Together, automated screening, safety-based eligibility criteria, community trial infrastructure, and funded navigation are likely to have greater impact than awareness campaigns or reporting requirements implemented in isolation.

IV. Access to Hematopoietic Stem Cell Transplant (HSCT)

Quantifying gaps in HSCT access

Allogeneic HSCT remains the only curative treatment for intermediate and high-risk AML and MDS, with the graft-versus-leukemia effect producing superior long-term outcomes compared to chemotherapy.[57-59] Over the last 20 years, multiple studies have reported persistent disparities in HSCT utilization across race, social support, treatment setting, and financial status.

HSCT rates in a US Representative Population: Dating back to 1997, Mitchell JM et al. identified that Black leukemia patients were 51% to 53% as likely as white patients to undergo HSCT.[60] A more recent cohort study of 136,280 transplant patients using CIBMTR and SEER data reached a similar conclusion two decades later, despite increased HSCT volume overall: rates of HSCT for AML and MDS remained lower in non-Hispanic Black patients. The data revealed that between 2017 and 2018, Black patients received allogeneic HSCT at just over half the rate of White patients in AML (42% less) and less than half the rate in MDS (60% less).[61] Bashey et al., examining barriers to HSCT through the Northside Hospital transplant and leukemia database, found lack of caregiver support was the most frequently documented disqualifying factor among Black patients compared to White patients (37% vs 11%, P = 0.002).[62] This points to caregiver infrastructure — alongside structural racism, poverty, and unequal access — as an upstream mechanism underlying the disparity, rather than race itself. *(See figure 2)*

Chronological age and care-giver limitations: Lack of social support is not confined to racial and ethnic minority communities. Nineteen percent of all patients in the Bashey et al. study who did not proceed to HSCT cited caregiver issues as a reason.[62] A qualitative study of HSCT recipients at Dana-Farber Cancer Institute (36% with an AML diagnosis) found that 74% identified significant deficits in social support as an unmet need — even within a predominantly White, relatively resourced cohort.[63] This suggests the support burden itself is near-universal in intensity, but unequally distributed in its consequences, with non-White and socially isolated patients carrying a structurally compounded disadvantage. Despite an increase in various donor options, **older age** continues to present a distinct challenge in the context of HSCT. Retrospective analyses have shown that age is not independently associated with worse HSCT outcomes.[64,65] Yet, chronological age remains a widely cited consideration in HSCT decision making, noted as the most common reason for non-eligibility at community/government sites specifically (71.5%),[66] with marked variation in practice across treating physicians and centers.[64,66,67] As recipients age, HLA-matched related donors, such as siblings tend to be similarly aged, raising concerns about graft quality and immunological fitness.

Treatment setting, financial and insurance status compound these barriers. Analysis of the Connect® Myeloid Disease Registry found that patients managed at community or government centers were significantly less likely to be considered for HSCT than those at academic centers (28% vs 44%; p<0.001).[66] Financial and insurance status independently shape both access and outcomes. Integrated CIBMTR and SEER data show that each 10% increase in the proportion of residents below the poverty line is associated with a 14% reduction in HSCT rates (ERR 0.86, p < 0.01).[68] Patients with non-public insurance were more likely to receive HSCT than those with public insurance (69.5% vs 30.4%, p < 0.001),[69] and many low-income patients fall above Medicaid eligibility thresholds while remaining unable to afford alternative coverage or the indirect costs HSCT imposes regardless of insurance type.[68] Insurance status also shapes post-transplant outcomes: one multivariable analysis found that lacking insurance was associated with significantly worse overall survival (HR 1.49, 95% CI 1.05–2.12) and relapse-free survival (HR 1.41, 95% CI 1.00–1.98).[70]

Taken together, these findings underscore that transplant access is not determined by clinical eligibility alone, but is profoundly shaped by race, age, social infrastructure, and finances.

Appraisal of Past Efforts to Reduce the Gaps in HSCT Access

Several interventions targeting these specific barriers have been tested, with mixed but informative results. On the donor-availability barrier, a meta-analysis comparing matched unrelated donors (MUDs) and age-matched related donors or haploidentical donors found no significant difference in overall survival, progression-free survival, or non-relapse mortality.[71] Kim et al. addressed this directly for older adults in an analysis of 499 patients aged 60 years or older with AML or MDS undergo-

ing allogeneic HSCT at Dana-Farber Cancer Institute, comparing outcomes between older matched related donors (MRD) and younger MUDs. Four-year PFS was equivalent between groups (40% MRD vs 41% MUD; p=0.79), as was OS (50% vs 44%; p=0.15), with no significant difference in non-relapse mortality, relapse, or acute graft-versus-host disease.[72] While advanced age remains a widespread justification for non-referral,[64,65] these outcomes confirm that alternative donor sources can be leveraged to effectively eliminate the donor availability bottleneck in older adults, without meaningful penalty to transplant-related outcomes. Ultimately, these findings highlight that current referral practices lag the clinical evidence.

On the treatment-setting barrier, a single-center study of AML in rural Appalachia offers a useful counter-case to the Connect Registry findings above with the utilization of their well-integrated rural cancer program.[73] Forty-two percent of the cohort resided rurally at diagnosis, yet the study demonstrated equivalent overall survival and equivalent rates of allogeneic HSCT between rural and urban patients — attributed to intensive telehealth integration, patient education, and structured collaboration with local oncology practices.[73] This result indicates that geographic disadvantage, like caregiver unavailability, can function as a modifiable barrier when supported by deliberate infrastructure, rather than a fixed structural limit on access.

Ongoing efforts to reduce the gap

The multidimensional barriers observed — spanning family frailty, race, social infrastructure, donor availability, insurance, and finances — are being directly addressed by NMDP's "ACCESS" and "Donor For All" initiatives.[74,75] The ACCESS initiative, in collaboration with the American Society of Transplant and Cellular Therapy (ASTCT), focuses on providing equal access and overcoming poverty-, race-, and ethnicity-based inequality in HSCT and cellular therapy, working with both patients and physicians to close knowledge gaps and streamline complex care. It represents the most comprehensive institutional response to HSCT access disparities currently in operation. Prior to ACCESS, NMDP conducted survey-based research identifying Medicaid coverage gaps as a discrete barrier to transplant access, and in collaboration with ASTCT, is now developing reference guidelines for insurance providers alongside targeted advocacy in high-need demographic areas.[74]

NMDP's Donor for All initiative operates at both the scientific and structural level, expanding donor accessibility regardless of whether a fully HLA-matched donor is available. This is of particular significance for Black and Hispanic patients, for whom the probability of finding a fully matched unrelated donor on existing registries is approximately 29% and 46%, respectively, compared to 79% for White patients.[75] Through CIBMTR, the joint research collaboration between NMDP and the Medical College of Wisconsin, NMDP has sponsored the sequential 15-mismatched unrelated donor (MMUD), ACCESS, and OPTIMIZE clinical trials. These have established that MMUD HSCT with post-transplant cyclophosphamide (PTCy) prophylaxis produces outcomes comparable to fully matched transplants, with a relatively low risk of GVHD (≤10.3%).[75,76] Modelling data suggest that wider adoption of MMUD transplantation could increase donor match availability for Black patients from 29% to as high as 84%[75] a transformative expansion of the transplant-eligible pool for minority populations, with match rates for non-Hispanic White patients also predicted to reach 99%.[75] This evidence base — spanning haploidentical and MUD alternatives — continues to support expanding donor eligibility independent of recipient age or ethnic background.[71,75-77]

Proposed solutions

Of the four barrier types outlined above, expansion of MMUD transplantation represents one of the most effective actionable levers, narrowing the racial disparity in HSCT access (29% to 84% donor availability for Black patients),[75] and potentially improving donor availability and quality for older patients.

A single-center analysis at Memorial Sloan Kettering (MSK) found that while MMUD grafts comprised only 8% of allogeneic HSCT for acute leukemia overall (vs. 54% MUD and 20% MRD),[78] patients of non-European ancestry used mismatched grafts at more than three times the rate of White patients (50% vs 16%),[78] reflecting both the disparity in fully-matched donor availability described above and MSK's capacity, as an early PTCy adopter and Blood and Marrow Transplant

Clinical Trials Network trial site (BMT CTN), to pursue mismatched options routinely. Nationally, MMUD uptake has lagged: CIBMTR data show MMUD comprised only 6% of allogeneic HSCT through 2020, rising to 12% by 2023, an increase concentrated largely among investigational centers participating in trials such as BMT CTN 1702 rather than diffusing broadly across community practice.[79]

This gap is not primarily one of donor-database access, as NMDP's registry and search infrastructure are already available nationwide, but of center-level capacity to act on mismatched search results: HLA expertise, transplant coordinator bandwidth, and clinical comfort managing PTCy-based MMUD protocols. Bridging this gap will likely require deliberate capacity-building at smaller and community-based programs, such as expanded use of existing NMDP Search Strategy Advice services, dedicated transplant coordinator support for mismatched-donor workups, and structured mentorship or hub-and-spoke partnerships with high-volume MMUD centers like MSK — modelled on the same infrastructure-driven approach that closed the rural-urban gap in the Appalachia telehealth study above.

Caregiver-navigation models, while still lacking randomized outcome data, are promising and deserve prioritization. They address the most frequently cited disqualifying factor for HSCT in racial minorities[62,63] and are actionable at the point of referral — whereas MMUD expansion, though transformative, operates on a longer timeline. The most concrete national effort toward this goal is the NMDP/PCORI "Reimagining Caregiving Together" initiative, which convenes patients, social workers, clinicians, and payers to define safe post-allogeneic HSCT care standards and build a comparative-effectiveness research agenda for alternative post-HSCT models; pre/post workshop surveys showed a significant decrease in perceived need for a 24/7 caregiver following structured discussion, suggesting the requirement is partly cultural rather than strictly clinical.[80]

Restructuring caregiver requirements, rather than treating them as fixed, is a comparably high-yield and more immediately deployable next step. A 2025 ASTCT review of the caregiver paradigm catalogues emerging alternatives to the traditional 24/7 in-person requirement, including remote patient monitoring as a partial substitute for continuous observation, community-based non-family caregiving partnerships, policy interventions such as paid family/medical leave and Medicaid-covered home support, and enhanced screening to distinguish patients who genuinely require continuous support from those who need only intermittent coverage.[81] Notably, the review is explicit that evidence supporting the traditional requirement itself is inconclusive, and calls for evidence-based, patient-centered models that do not exclude patients from transplant on caregiver status alone.[81]

Conclusion

This review highlights the additive effects of system and patient level frailties in the context of aggressive malignancies such as AML and MDS, where underserved patients bear a disproportionate burden of vulnerability. These issues, if left unaddressed, ultimately continue to widen the deficit in access to quality care. Improvements in cancer care require coordinated action across national policy, healthcare institutions, clinical trial design, provider education, and patient or community support systems to address current barriers (see figure 2). Without deliberate investment into infrastructure deficiencies, insurance expansion programs, development of complex care-navigation, standardized testing and treatment protocols, as well as sustained resources and funding into the underserved communities – the most vulnerable will continue to bear the greatest burden of these illnesses. Advocacy for blood cancer patients in these vulnerable communities is now, more than ever, a critical mission of state and federal health officials.

Conflict(s) of Interest

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Declaration of AI Use

AI tools were used for queries generated by authors; the AI generated data was further substantiated with original studies, ideas developed and edited by authors. Generative AI - ChatGPT 5.6 Luna was used to update and format figure 2. The contents of the figure were derived from the prospective implementation points identified in the paper, and AI was used to adapt those points to the original figure. authors created.

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