

ASH Studies Uncover Drivers of Health Disparities and Opportunities to Enhance Equity

Studies underscore continuing role of demographic factors and comorbidities in blood cancer treatment and research.

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Four studies presented during the 65th American Society of Hematology (ASH) Annual Meeting and Exposition examine how demographics and other characteristics of patients and researchers play into inequities in health outcomes in the context of blood cancers. Several of the studies suggest opportunities to proactively address these issues and potentially improve health equity.

“Increasingly, researchers are looking beyond the question of ‘What is the best treatment?’ and asking, ‘Is this treatment the best for every person with this disease?’” said Alison R. Walker, MD, MPH, MBA, of Moffitt Cancer Center and chair of ASH’s Committee on Diversity, Equity, and Inclusion (DEI). “We need to take into consideration social determinants of health and other factors that contribute to differences in outcomes or treatment response in order for all patients to be able to actualize optimal health.”

The studies shed new light on continuing disparities in clinical health care and outcomes as well as in biomedical research fields, issues that ASH has prioritized with a variety of [DEI initiatives](#).

In the first study, researchers tracked how genetic markers and racial background interact to explain why certain treatment regimens for acute myeloid leukemia (AML) – an aggressive form of blood cancer in which the body produces abnormal white blood cells – are associated with poorer outcomes in some racial groups. The results provide evidence that testing for a panel of genetic markers could help close this gap by informing treatment decisions.

The second study shows females are much less likely to lead active R01 grants that relate to classical (non-malignant) hematology topics compared with males. The study calls attention to the need to close the gender gap and create academic environments where more female hematologists are successful in submitting and receiving this level of external funding.

The third study quantifies the differences in outcomes from multiple myeloma treatments in real-

world settings compared to clinical trials, suggesting a need to better understand and address factors that may undermine treatment access or effectiveness.

In the fourth study, researchers found that people with psychiatric or substance use disorders had significantly worse outcomes from AML treatments involving venetoclax combinations compared with those who did not have such disorders. The findings point to potential opportunities to better support patients with these disorders while undergoing these treatments.

Using patients' genetic profile to inform AML treatment could help reduce racial disparities

[Abstract 368](#): Intensification of Therapy and Pharmacogenetic Personalization Mitigate Racial Disparities in Pediatric Acute Myeloid Leukemia Outcomes

In a new study, a multi-gene metric known as ACS10, which accounts for variability in multiple genes simultaneously, revealed a close link between genetic factors and racial disparities in pediatric AML outcomes. Researchers say using the metric to optimize treatment approaches for each patient could potentially lead to better outcomes, particularly among Black children.

Because the chemotherapy drugs used to treat AML are activated inside the body, a person's genes can influence drug activation and the response to treatment. The new study bolsters evidence that the ACS10 score, which combines 10 genetic factors into a single metric, can be used to help elucidate genetic drivers of racial disparities and inform treatment decisions. Researchers say it provides new evidence that some induction regimens result in better outcomes than other regimens for people with lower ACS10 scores, a status that is more common among Black patients.

"Incorporating the ACS10 score into diagnostic processes can help us use our chemotherapy options more strategically," said Jatinder K. Lamba, PhD, associate dean for research and graduate education, professor in the College of Pharmacy at the University of Florida, a member of the UF Health Cancer Center, and the study's lead author. "We are always running after new drugs, but we see that there are smarter ways to use existing drugs. I'm hoping this [metric] will go into standard guidelines, so that we can use the genetics to inform the regimen."

Since routine diagnostic tests already include the genetic features that are combined for the ACS10 score, Dr. Lamba said that incorporating ACS10 scores into diagnostic processes would be an easy addition to the existing testing and should be feasible to do at low cost.

For the study, the researchers analyzed data from two previous AML clinical trials that together included 86 Black patients and 359 white patients. The trials included comprehensive genetic information for each patient and involved three different treatment regimens as initial therapy: low-dose cytarabine, daunorubicin, and etoposide (LDAC), higher doses of these same drugs (HDAC), or clofarabine and cytarabine (Clo/AraC).

The results showed no significant differences between Black and white patients overall in terms of various measures of response to treatment, survival, and relapse. However, significant differences

emerged when researchers took both race and ACS10 scores into account. Black patients with low ACS10 scores had significantly better outcomes when they received the HDAC or Clo-AraC regimen than when they received LDAC.

“If you give patients with a lower ACS10 score an augmented therapy, you can really significantly improve their outcome,” said Dr. Lamba. The researchers also found a substantial racial gap in the distribution of ACS10 scores. While just 30% of white patients had a low ACS10 score, 73% of Black patients did. This difference, combined with the relationship between low ACS10 scores and poor response to LDAC treatment, likely explains some of the racial disparities in AML survival that have been reported previously.

Other studies suggest that low ACS10 scores are especially prevalent among Black children in Africa, where AML mortality rates are persistently high. Dr. Lamba suggested that further studies should be conducted in Africa to see if tailoring treatments based on this metric could help to improve outcomes.

Although the panel testing protocol for ACS10 scores is not readily available in most clinics today, researchers said it should be feasible to deploy relatively quickly since the individual components of the test are available.

Jatinder Lamba, University of Florida, presented this study in an oral presentation on Saturday, December 9, 2023.

Analysis finds males lead two out of three active R01 NIH grants involving classical hematology research

[Abstract 5113](#): A 10 Year Analysis of Gender Distribution in National Institutes of Health Funding for Non-Malignant Hematology

A new analysis finds that in the last decade, two thirds of active R01 grants – among the most prestigious and competitive types of medical research funding awarded by the National Institutes of Health (NIH) – that related to classical, or non-malignant hematology subjects are led by male investigators and only one third by female investigators. However, while the proportion of grants awarded to men remained fairly constant, the proportion of active grants led by women increased about 36% over the study period.

“This study extends previous work showing that, as in other medical research fields such as cardiology, oncology, and gastroenterology, male investigators continue to receive a preponderance of these top-level grants,” said Sara Khan, DO, a resident physician at HCA Healthcare and the University of South Florida Morsani College of Medicine, and the study’s principal investigator.

R01 grants are awarded to individual investigators for discrete research projects and provide up to five years of support.

“Historically, women have been underrepresented in hematology and, consequently, are less likely to receive research grants,” she said. “While it’s encouraging that there was an upward trend in the number of grants to female investigators over the 10-year period we looked at, a significant gender gap remains.”

Dr. Khan and her colleagues accessed the NIH RePORTER database to pull data on all active and recently awarded R01 grants. They then wrote a series of codes (R script) to analyze the datasets each year between 2012 and 2022, applying 45 classical, non-malignant hematology terms and conditions (for example, hemophilia, Factor V Leiden, sickle cell disease, anemia, thrombosis, embolism). After running analyses to identify grants that included mention of these terms, they used a validated tool to predict gender, which Dr. Khan and colleagues said is 85% accurate. Over this 10-year period, there were 250,031 active R01 grants involving classical-hematology-related research, of which 67.1% were led by male researchers and 32.9% by female researchers.

The researchers also looked to see whether gender breakdown in R01 grants varied by institute or research focus area and how that changed over time. They found that in 2012, just two NIH institutes – the National Institute of Nursing Research and the National Institute of Minority Health and Health Disparities – awarded more than 50% of their active R01 grants to female researchers. In 2022, these two institutes continued to award more than half of their R01 grants to female researchers, and two additional institutes – the National Institute of Child Health and Human Development and National Center for Complementary and Integrative Health – also made more than 50% of their R01 grant awards to women.

Two NIH institutes, the National Heart, Lung, and Blood Institute (NHLBI) and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) award the largest number of R01 grants in **classical hematology**. In 2012, both of these institutes awarded 27% of these grants to female researchers. In 2022, the proportion of R01s awarded to female researchers had increased to 33% at NHLBI and to 36% at NIDDK.

Three institutes – the National Institute of General Medical Sciences (NIGMS), National Institute of Neurological Disorders and Stroke (NINDS), and National Institute of Biomedical Imaging and Bioengineering (NIBIB) – awarded less than 25% of their R01 grants to female researchers in 2012. In 2022, only the NIBIB still made less than 25% of its R01 grant awards to female investigators.

“NIGMS and NINDS have made steps toward promoting diversity and inclusivity in research funding,” Dr. Khan said. “While some NIH agencies are making progress toward gender parity, the continuing large disparity in R01 awards by the NIBIB calls for further attention and action.”

Most R01 grants are awarded to physicians and scientists who work in university-affiliated medical centers and medical schools. Published data on the proportion of female physicians and scientists working in hematology in these centers are scant, but one study, published in JCO Oncology Practice in 2020, found that slightly over a third (35.7%) of physicians in clinical faculty positions in university departments of hematology and oncology in the United States were women. Among faculty who held at least one NIH research grant of any kind, 24.5% were women. Female

physicians tended to have fewer years of experience than their male counterparts and hold more junior academic positions (e.g., 44.9% were assistant professors).

A limitation of the current study is that the research team was able to analyze only data for R01 grant recipients and not for all applicants for these awards, Dr. Khan said. Thus, they could not determine whether male and female applicants for R01 grants were funded at similar rates. According to NIH data, the success rate – that is, the proportion of applicants who were awarded a grant – for “R01-equivalent” awards was 20.1% in 2021 and 21.6% in 2022.

Because many of the classical hematology terms applied often coexist with research pertaining to other conditions, including many blood cancers, solid tumors, heart conditions, and gastrointestinal diseases, the research does not isolate non-malignant hematology grants. Rather, it included any R01 research grant that included these terms in the research abstract or title. Still, the research team said their findings call attention to the need to address gender disparities in NIH funding.

“We need more research aimed at understanding the reasons for persistent gender disparities in R01 grant funding in non-malignant hematology and other fields,” Dr. Khan said. “This should help to identify the policy changes that may be needed to promote gender equity and bridge the gap that we’re currently seeing.”

Sara Khan, HCA Florida Bayonet Point, presented this study in the poster hall on Monday, December 11, 2023.

Outcomes for patients with multiple myeloma fall short in the real world compared with clinical trials

[Abstract 541](#): Comparison of the Efficacy in Clinical Trials Versus Effectiveness in the Real-World of Treatments for Multiple Myeloma: A Population-Based Cohort Study

People treated for multiple myeloma in real-world hospital settings experienced a 75% higher rate of death than was reported in clinical trials for common myeloma treatments, according to a new study.

While the findings are disappointing, researchers say they can enhance informed decision making by giving clinicians, regulators, and patients a more accurate picture of the expected risks and benefits of cancer treatments. The analysis also underscores the limitations of clinical trials in predicting outcomes among patient populations that are typically different from those in clinical trials in terms of demographics, health status, and care settings, such as community practices versus academic medical centers.

“The criteria for clinical trial eligibility are often quite stringent, so the results are not always generalizable,” said Alissa Visram, MD, of Ottawa Hospital Research Institute, and the study’s lead author. “It’s not a surprise that real-world patients don’t do as well as those in clinical trials, but our study is the first to quantify the difference. It suggests we need to change our frame of

reference and better contextualize what outcomes we would expect our patients to have.”

Multiple myeloma is an incurable blood cancer that leads plasma cells to proliferate out of control. It is difficult to diagnose early because it is rare, and symptoms often go unrecognized. Many patients face a poor prognosis even with available treatments.

Researchers compared rates of death, progression-free survival, and adverse events reported in phase III clinical trials for seven multiple myeloma treatment regimens with outcomes among 3,951 patients who received these same treatments in the provincial health system of Ontario, Canada’s largest province, between 2007-2020. The treatments that were included were lenalidomide/dex [Rd] and bortezomib/Rd for newly diagnosed patients who were ineligible for a stem cell transplant, and carfilzomib/Rd, carfilzomib/dex, daratumumab/Rd, daratumumab/bortezomib/dex, and pomalidomide/dex for patients with relapsed multiple myeloma.

Overall, real-world patients saw a 44% higher rate of disease progression or death and a 75% higher rate of death, on average, compared with clinical trial participants. Using hospitalization as a proxy for assessing rates of serious adverse events among real-world study participants, researchers found comparable rates of serious adverse events among clinical trial participants and real-world patients.

Pomalidomide/dex was the only regimen that performed as well as or slightly better in the real world than in clinical trials, which researchers believe may be due to the use of this regimen in a real-world patient population with comparable or slightly fewer exposures to prior therapies.

The study was not designed to determine what led to the differences that were observed. However, researchers noted that several factors are likely at play. Real-world patients were on average older and had more comorbidities than those in clinical trials. It has been previously shown that real-world patients often have more comorbidities than patients in clinical trials and, therefore, may not have tolerated treatments, as well as those tested in a clinical trial setting, Dr. Visram added.

In addition, clinical trials are typically carried out in medical centers that see a high volume of patients with rare diseases, where clinicians are likely to be more experienced in administering complex treatment regimens and handling toxicities compared with clinicians in community medical centers where many patients receive care in the real world. Finally, researchers noted that people in historically marginalized populations are often disproportionately excluded from clinical trials and may lack resources for keeping up with clinic visits, which can lead to poorer outcomes.

Such factors can lead to significant gaps between clinical trials and real-world settings in terms of patients’ health status and the care they receive. “As clinicians, we need to acknowledge that outcomes might not be as good in the real world,” said Dr. Visram. “We often use clinical trial results to explain to patients what to expect with treatment, but it’s important to understand that you may be doing more harm if you don’t know whether this [clinical trial result] is actually

applicable to your patient.”

Researchers said that further study is needed to better understand the factors that account for the poorer outcomes observed in real-world settings. In addition, Dr. Visram noted that including more diverse participants in clinical trials and conducting trials in community health centers may lead to results that better reflect what can be expected in the real world.

Alissa Visram, Ottawa Hospital Research Institute, presented this study in an oral presentation on Sunday, December 10, 2023.

Mental health disorders tied to poorer outcomes following venetoclax therapies for AML

[Abstract 388](#): Psychiatric and Substance Use Disorders Are Independent Predictors of Treatment Response and Outcomes in United States Veterans with Newly Diagnosed Acute Myeloid Leukemia Treated with Venetoclax Combinations

A new study conducted in U.S. veterans suggests that people with psychiatric or substance use disorders face a markedly higher risk of poor outcomes, including early death, after being treated with venetoclax combination therapies for AML compared with patients who do not have a recent history of these disorders. Researchers say the findings could help explain why venetoclax combinations have had worse outcomes in real-world populations than in clinical trials.

“Psychiatric diagnoses and a history of substance dependence are prevalent problems, not only among veterans but also in the general public,” said Michelle Hyunju Lee, MD, instructor of medicine at Harvard Medical School and hematologist at Massachusetts General Hospital, and the study’s lead author. “We have to pay closer attention to these potentially intervenable comorbidities, and we need to get to the root of why people with these disorders are not doing as well. Perhaps early intervention with proper support and resources may improve outcomes.”

AML is a cancer of the blood and bone marrow that accounts for about 1% of new cancer cases each year. It is associated with a relatively poor survival rate but can be cured with a hematopoietic stem cell transplant for patients who are healthy enough to undergo this intensive treatment. First-line treatments include induction chemotherapy or combination therapies that include the oral cancer drug venetoclax.

Venetoclax combinations offer a less intensive treatment option for patients who are ineligible for chemotherapy, but these therapies show less favorable outcomes in real-world populations than in clinical trials. To find out whether psychiatric and substance use disorders may play a role, researchers analyzed health records of 452 U.S. veterans who received frontline venetoclax combination therapies for AML, primarily through the Veterans Affairs health care system.

They found that patients who experienced a psychiatric disorder within the three years preceding their AML treatment were nearly twice as likely to die within 60 days of starting AML treatment and 28% more likely to die overall compared with those who did not have a mental health disorder. Having a substance use disorder was associated with lower odds of achieving complete

remission, a measure of the degree to which cancer responds to treatment.

The study population had a high rate of psychiatric and substance use disorders, which are more common among veterans than the general population. Forty-six percent had at least one psychiatric diagnosis, 19% had a substance use disorder, and 11% had both. Study participants also had a relatively high rate of early death; 20% of participants died within 60 days of starting their AML treatment and the median overall survival was just over seven months.

The association between early death and mental health disorders was independent of age, socio-demographics, markers of disease risk, and the particular venetoclax combination therapy used. Although the study was not designed to determine the mechanisms involved, Dr. Lee said that mental health disorders could potentially contribute to biological differences in the response to treatment or pose barriers for medication adherence. A new cancer diagnosis could also potentially trigger a resurgence or worsening of mental health issues.

“While venetoclax combinations have increased the number of patients who can be treated, we still have much to learn in the real world about who can tolerate these regimens well, especially in patients with mental health and other medical comorbid conditions,” said Dr. Lee, formerly of Boston Medical Center and Boston University School of Medicine.

Dr. Lee added that the association of psychiatric and substance use disorders with negative AML outcomes may partially explain the disparity in outcomes between trials and real-world practice, given that many patients are excluded from trial participation on the basis of their mental health conditions. With rising numbers of Americans being diagnosed with such comorbidities, she stressed the importance of finding ways to expand clinical trial access for patients with AML.

Only 3% of study participants underwent a stem cell transplant, which Dr. Lee characterized as a strikingly low proportion given that nearly half of participants were young enough to be eligible for this curative treatment, and other real-world studies in adults treated with venetoclax combinations have shown transplant rates of 8% to 18%. Mental health disorders were significantly more common among younger veterans in the study and no patients with a substance use disorder received a transplant, although it is unclear whether the presence of these disorders had a direct role in determining why so few patients underwent a stem cell transplant.

The researchers plan to further analyze the data to determine whether the timing or delivery of treatment, the number of doctor visits or rate of appointment no-shows, or the timing of active psychiatric or substance use disorders could play a role in the associations that were observed. Insights into these factors could help to pinpoint the optimal strategies to intervene and better support patients affected by psychiatric and substance use disorders during AML treatment.

Michelle Lee, Massachusetts General Hospital, presented this study in an oral presentation on Saturday, December 9, 2023.

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