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**New Studies Call Attention to Effects of Structural Inequities on Health in America**

(WASHINGTON, Dec. 4, 2020) – Four studies being presented during the 62nd American Society of Hematology (ASH) Annual Meeting and Exposition highlight the ways disparities and inequities affect the health threats faced by people in racial and ethnic minorities, as well as the quality of health care they receive.

"Examining racial inequities in our public health system is one area in which we can enhance outcomes and improve lives without a new drug or a new test," said press briefing moderator **Chancellor Donald, MD,** of Tulane University School of Medicine. "What is going to help correct these long-standing disparities is intention, more than science. We have science, we have treatments, but we see that these treatments are not equally applied to everyone. It's going to take intention and understanding from the medical community to approach this issue as a whole."

Two of the studies reveal connections between existing health disparities and the disproportionate effects of the COVID-19 pandemic on Black Americans and other racial minorities. The studies bolster evidence that people living with sickle cell disease (SCD), the majority of whom are Black, face heightened risks from COVID-19 infection, including a higher rate of severe COVID-19 complications at a younger age compared to the general population.

The other two studies examine racial disparities in outcomes among patients with acute myeloid leukemia, an aggressive type of blood cancer. Both studies found that racial minorities face a significantly worse prognosis than white patients; one examined how social factors such as socioeconomic disadvantage contribute to this difference and cause harm, while the other explored whether differences in care delivery or genetic factors may play a role.

"Race and ethnicity, among other factors, touch every facet of someone's life," said Dr. Donald. "If we are going to address health disparities, we have to identify where they exist. That takes calling out the different structures that may be propagating these problems. It may be an uncomfortable subject, but we must understand that discomfort is temporary, and that it is much less in terms of repercussions and severity than people suffering based solely on a social construct. It is important we facilitate this conversation at our annual meeting and beyond."

*This press briefing will take place on Friday, December 4, at 8 a.m. Pacific time on the ASH annual meeting virtual platform.*

**Sickle Cell Disease Associated with Increased Risk of COVID-19 Complications**
302: COVID-19 Outcomes in Individuals with Sickle Cell Disease and Sickle Cell Trait Compared to Blacks without Sickle Cell Disease or Trait

Individuals living with SCD experienced some COVID-19 complications more frequently than a similar group of Black individuals without SCD, according to a new study. The study did not find evidence that these individuals face an increased risk of death, however. Sickle cell trait was not associated with any increased risk from COVID-19.

"In our study, people with sickle cell disease had a higher risk of hospitalization, pain, and pneumonia within two weeks of COVID-19 diagnosis as compared to a general population of Black people matched with regard to age, gender, and other comorbidities," said lead study author **Ashima Singh, PhD,** of Medical College of Wisconsin in Milwaukee. "This speaks to a need for health equity for patients with sickle cell disease, as they are at risk of significantly more severe expression of COVID-19."

Black Americans have faced a disproportionate health burden from COVID-19. The researchers analyzed data from electronic health records to determine how COVID-19 infections in the general Black population compare to the impacts of the virus in people with SCD or sickle cell trait, the majority of whom are Black. They compared COVID-19 outcomes in 122 people with SCD and 172 people with sickle cell trait to a group of more than 15,000 Black individuals who did not have sickle cell disease or trait but otherwise had matching characteristics in terms of age, gender, and health conditions relevant to COVID-19 severity such as heart disease, diabetes, and lung disease.

The results revealed that among the COVID-19 patients with SCD, nearly half required hospitalization, 43% experienced pain, and 31% developed pneumonia. Among Black patients without sickle cell disease or trait, 23% required hospitalization, 13% experienced pain, and 20% developed pneumonia. Individuals living with SCD were also significantly younger and a higher proportion had asthma, type 1 diabetes, cerebral infarcts, or pre-existing liver conditions than Black patients in the comparison group. After matching the groups on age, gender, and comorbidities, patients with SCD continued to face more than twice the risk of hospitalization, pain, and pneumonia due to COVID-19 than Black patients without sickle cell disease or trait.

Individuals with SCD did not have a higher rate of death from COVID-19, after matching for age, gender, and other comorbidities. Although more research is needed to determine why, Dr. Singh noted that it is possible that the higher rate of hospitalizations among these patients helped ensure their COVID-19 infection was appropriately managed.

Sickle cell trait, a genetic status indicating a person has one copy of the sickle gene, is not considered a disease. The study found no difference in the effects of COVID-19 among those with sickle cell trait compared to the general Black population.

*Ashima Singh, PhD, Medical College of Wisconsin, will present this study in an oral presentation on Saturday, December 5, at 2:00 p.m. Pacific time on the ASH annual meeting virtual platform.*

**COVID-19 Poses High Risk for People Living with Sickle Cell Disease, Including Children**
16: Hospitalization and Case Fatality in Individuals with Sickle Cell Disease and COVID-19 Infection

A new study adds evidence to suggest SCD is an important risk factor for severe COVID-19 infection. Researchers analyzed 370 COVID-19 cases among people living with SCD and found that those with the disease were 6.2 times more likely to die from COVID-19 compared with the general Black population in the U.S. The majority of individuals living with SCD are Black, a group that has also suffered

disproportionate effects from COVID-19, although both diseases can affect people of any race or ethnicity.

"People with sickle cell disease are definitely a high-risk group," said study author **Lana Mucalo, MD,** of Medical College of Wisconsin in Milwaukee. "In particular, young adults and children with sickle cell disease are at higher risk for severe COVID-19 infection and hospitalization than the general population. That means they should be following recommended precautions such as mask-wearing, and their health care providers should be aware that they are at increased risk of severe illness."

The research draws data from SECURE-SCD, an international registry supported by Doris Duke Charitable Foundation that collects information about COVID-19 infections in individuals living with SCD, including details on hospitalization, severity, management strategies, and complications. The registry continues to collect data on individuals with sickle cell disease and COVID-19 infection.

Researchers compared hospitalization rates in the registry data to hospitalization rates among Black individuals in the Coronavirus Disease 2019 (COVID-19)-Associated Hospitalization Surveillance Network (COVID-NET), a national surveillance system that covers about 10% of the U.S. population. They compared case fatality rates (the proportion of patients with COVID-19 who died from it) in the registry to rates among Black individuals in publicly available data from the California Department of Public Health.

An analysis of the subset of 324 cases from the United States revealed people with SCD were more likely to be hospitalized with COVID-19 and to die from the disease than the general population, especially in younger age groups. People with SCD had a case fatality rate of 2.6% among those 18-34 years old and 11.9% among those 35-50 years old, far higher than the case fatality rate of less than 1% among the general Black population for both age categories. Almost two-thirds of those with SCD and COVID-19 required hospitalization, with nearly one in three of those hospitalizations occurring in children.

Among children with SCD who tested positive for COVID-19, those with a history of pulmonary hypertension, acute chest syndrome, or a previous hospitalization for pain were more likely to require hospitalization for COVID-19.

The researchers did not find any evidence that the SCD therapy hydroxyurea had any effect on COVID-19 severity or that people with different disease subtypes face different risks from COVID-19 infection. They plan to continue collecting data in the registry and examine how additional factors such as pregnancy may affect individuals' risk.

*Lana Mucalo, MD, Medical College of Wisconsin, will present this study in an oral presentation on Saturday, December 5, at 8:15 a.m. Pacific time on the ASH annual meeting virtual platform.*

**Neighborhood Disadvantage Associated with Increased Risk of Death from AML**
*217: The Role of Structural Violence in Acute Myeloid Leukemia Outcomes*

Black and Hispanic people with acute myeloid leukemia (AML) who live in socioeconomically disadvantaged neighborhoods in metropolitan Chicago were more likely to die from the disease than their non-Hispanic white counterparts, a 48% and 20% greater risk, respectively. While the existence of racial disparities in AML outcomes has been previously reported, this study examines how neighborhood disadvantage – perpetuated by social, economic, and political systems (termed "structural violence") – can set the stage for poorer outcomes in patients with AML.

"This is the first study to integrate individual clinical and disease specific data with census tract data on

the affluence, disadvantage, and segregation levels of the neighborhoods where patients live and analyze how these domains interact to influence outcomes for patients with AML," said senior study author **Irum Khan, MD,** of the University of Illinois at Chicago.

Such structural violence or sustained inequity is thought to expose particular groups of people to elevated risks that lead to higher rates of illness, reduced access to health care, and shorter lifespans; in this case, it is thought to contribute to racial/ethnic differences in leukemia-specific survival.

Dr. Khan and her team analyzed data from the medical records of 822 patients ages 18 to over 60 who were diagnosed with AML at one of six university-affiliated cancer centers in the Chicago area between 2012 and 2018. The researchers collected information on the patients' sex, race or ethnicity, age at diagnosis, co-existing health conditions, health insurance status, and genomic features of their cancer that suggested a better or worse outlook. They also collected U.S. Census data on the neighborhoods where patients lived and categorized those census tracts by their level of segregation, affluence, or disadvantage (collectively termed tract SES).

A total of 497 patients self-identified as non-Hispanic white; 126 as non-Hispanic Black; 117 as Hispanic; and 82 as other or unknown race. There were 445 males (53%) and 377 females in the cohort. Overall, patients who self-identified as Hispanic were younger and least likely to have concurrent health conditions. Black and Hispanic patients were more likely than non-Hispanic white patients to be morbidly obese (23% of non-Hispanic Black patients, 20% of Hispanic patients). About half (51%) of white patients had private health insurance compared with 25% of Black patients. Hispanic patients were most likely to lack health insurance.

The patient population distribution by census tract reflects Chicago's high levels of segregation. Black and Hispanic individuals were significantly more likely than white individuals to live in socially disadvantaged neighborhoods. Initial treatment for the patients' leukemia showed higher use of intensive chemotherapy in Hispanic patients possibly linked to their younger age and lower comorbidities, but comparable rates between Black and white patients. Interestingly, Hispanic and non-Hispanic Black patients had significantly higher rates of treatment complications, measured by intensive care unit admissions during initial chemotherapy (42% and 39%, respectively), compared to non-Hispanic white patients (25%). As previously reported, non-Hispanic black patients were less likely to undergo a stem cell transplant than whites and Hispanic patients.

After adjusting for patients' age, sex, and the institution where they were treated, the researchers found that census tract affluence, disadvantage, and segregation were all significant predictors of leukemia-related death. An analysis to tease out the relative effects of different biologic- and treatment-specific variables and neighborhood disadvantage showed that census tract SES variables could account for 81% of the Black-white disparity in AML-related death. "When we eliminate the SES tract disparity, the leukemia death difference between Black and white AML patients decreases from 58% to 11%," explained Dr. Khan.

Non-Hispanic Black patients were more likely than those of other races to have AML with high-risk genetic features. This suggests that further study is needed to explore whether living in disadvantaged neighborhoods is associated with environmental exposures that may heighten the risk of developing hard-to-treat forms of AML, Dr. Khan said.

Two limitations of the study are that it looked back at data from patients' medical records rather than following patients as they moved through diagnosis and treatment to determine obstacles to care, and it was unable to examine possible influences on individual socioeconomic position such as patients' education level, first language, or household income – data not readily available in patients' medical

records.

“These findings point to a need for more research on the social and economic barriers to successful treatment outcomes for patients with AML. Similar to molecular tailoring of therapy, evaluation of social determinants of health should be a key aspect of personalized leukemia therapy,” said Dr. Khan. “While the field is in its infancy, our analysis suggests that incorporating validated measures of social determinants of health into clinical care is likely to contribute significantly to narrowing disparities in leukemia survival.”

*Irum Khan, MD, University of Illinois at Chicago, will present this study during an oral presentation on Saturday, December 5, at 1:00 p.m. Pacific time on the ASH annual meeting virtual platform.*

**Study Suggests Young Black Patients with AML Have Poorer Survival than Whites Despite Receiving Same Standard of Care and Having Favorable Genetic Markers**
6: Poor Treatment Outcomes of Young (<60 Years) African American Patients Diagnosed with Acute Myeloid Leukemia (AML) (Alliance)

Despite advances in treating acute myeloid leukemia (AML), younger Black patients with this aggressive blood cancer have a 27% higher chance of dying compared with younger white patients. New research sought to explore factors that might be contributing to this disparity and found that even when Black patients received the same treatment and follow-up as their white counterparts, they still fared worse. This remained true in Black patients whose cancer carried certain genetic mutations (changes in the cell’s genes) that typically predict better prognosis and survival.

“Survival among young Black people with AML is strikingly and unacceptably worse than what we see in white patients with AML, particularly in younger patients,” said first author **Bhavana Bhatnagar, DO,** of The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James). “When we looked specifically at the mutations we see in AML, even when Black patients have specific good prognostic risk factors, they had poorer outcomes.”

For the multi-part study, Dr. Bhatnagar and her team first used the National Cancer Institute’s Surveillance Epidemiology End Results (SEER) database, which collects data on cancer cases, to identify 25,523 adults (18 years of age and older) diagnosed with AML between 1986 and 2015. They found that while survival for AML patients as a whole has improved across three decades, the survival disparities between Black and white patients with AML actually widened over time despite improved treatment and understanding of AML. They also identified a disparity in survival rates between young Black and white patients (under age 60), with three-year overall survival rates of 34% and 43%, respectively. Young Black patients with AML more often resided in metropolitan areas and came from households with an income below the poverty level. Yet, even after accounting for these and other factors, Black race was found to be a strong patient-related risk factor influencing survival.

Next, researchers wanted to see whether differences in survival persist in a clinical trial setting in which patients receive similar treatment protocols. They included 1,339 patients (7% Black and 93% white) treated on Cancer and Leukemia Group B/Alliance for Clinical Trials in Oncology protocols based on standard intensity therapy between 1986 and 2015. While there was no difference in complete remission rates, early death rates or relapse rates, median overall survival was seven months shorter among young Black patients (median of 1.2 years vs 1.8 years), suggesting that access to similar treatments might not alleviate racial gaps in survival, according to study authors.

“One of the biggest arguments for the poorer survival seen among Black patients with AML has been challenges with access to treatment, but what we found is that even if they have the same access to treatment and the same rates of remission, Black patients have significantly shorter survival time compared to white patients,” said Dr. Bhatnagar.

To delve deeper, the researchers conducted comprehensive genomic analyses to look at 81 genes commonly mutated in AML in the Alliance clinical trial cohort. Knowing what gene mutations are present in leukemia cells helps doctors diagnose specific types of AML and make treatment decisions. Notably, Black patients were found to have fewer *NPM1* mutations. AML patients with *NPM1* mutations very often go into remission with standard chemotherapy and, therefore, many do not need allogeneic stem cell transplant. So, Dr. Bhatnagar and her team were surprised to find that Black patients who had *NPM1*-mutated AML did not have the same favorable outcomes as white *NPM1*-mutated AML patients, including those *NPM1*-mutated patients who have no or low-level *FLT3*-ITD, which is considered to be a “favorable-risk” genetic profile.

“It was notable that several of the mutations that have known prognostic impact in AML patients as a whole – and that we typically use to classify patients’ disease – do not seem to carry the same prognostic relevance for younger Black patients.” said Dr. Bhatnagar. “Furthermore, when we looked at all younger AML patients, Black race was an independent predictor of poor outcome in both the SEER and Alliance data sets. This suggests that Black race by itself seems to be such a strong risk factor that it adds to the markers we usually rely on to risk-stratify patients.”

Larger studies are critically needed to corroborate these findings, and to investigate what social, environmental, and economic factors and potential differences in AML biology may contribute to poorer outcomes among Black Americans with AML.

*Bhavana Bhatnagar, DO, of The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, will present this study in a plenary presentation on Sunday, December 6, 2020 at 7:00 a.m. Pacific time on the ASH annual meeting virtual platform.*

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Additional press briefings will take place throughout the meeting on genome editing and cellular therapy, practice-changing clinical trials, COVID-19, and late-breaking abstracts. For the complete annual meeting program and abstracts, visit www.hematology.org/annual-meeting. Follow ASH and #ASH20 on Twitter, Instagram, LinkedIn, and Facebook for the most up-to-date information about the 2020 ASH Annual Meeting.

The American Society of Hematology (ASH) (www.hematology.org) is the world’s largest professional society of hematologists dedicated to furthering the understanding, diagnosis, treatment, and prevention of disorders affecting the blood. For more than 60 years, the Society has led the development of hematology as a discipline by promoting research, patient care, education, training, and advocacy in hematology. ASH publishes *Blood* (www.bloodjournal.org), the most cited peer-reviewed publication in the field, and *Blood Advances* (www.bloodadvances.org), an online, peer-reviewed open-access journal.