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Understanding the social determinants of health and genetic factors contributing to the differences observed in COVID-19 incidence and mortality between underrepresented and other communities

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Abstract: COVID-19 has been a devastating disease, especially in underrepresented communities. Data has shown that Indigenous peoples, Latinx communities, and Black Americans have a 3.3, 2.4, and 2 times higher mortality rate than White communities, respectively, due to COVID-19. Therefore, in this paper, we sought to understand how Social Determinants of Health and genetic factors influence COVID-19 incidence, mortality rates, and complications by assessing existing literature. Studies showed that identifying with a racial/ethnic minority, being homeless, housing insecurity, lower household median income, and living in an area with decreased air quality were associated with higher incidence and mortality from COVID-19. Analyses of these studies also showed a lack of resources to collect patients' social determinants of health, revealing an urgent need to create databases with information on local support programs and operationalize the referral and tracking outcomes to address the health inequities for Black, Indigenous, and Latinx communities.

Keywords: Social determinants of health ■ COVID-19 ■ Coronavirus ■ Incidence ■ Mortality ■ Inequality

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INTRODUCTION

Coronavirus Disease 2019 (COVID-19) has been devastating, especially in underserved communities that experience a mortality rate up to three times higher than white communities.1 Without further research to understand the higher mortality rate in Black, Indigenous, and Latinx communities, these communities will continue to experience higher infection rates, mortality, and lower quality of life (QOL) after COVID-19 infections.

Social determinants of health (SDoH) refer to factors outside of a person's genes that can affect their health and outcomes, such as economic stability, educational level, and food and housing security. Additionally, racism and discrimination have been shown to affect an individual's health and well-being. Therefore, race, ethnicity, gender identity, sexual orientation, and other aspects of a person's identity are also considered SDoH.2,3 SDoH has been shown to contribute up to 40% towards an individual's health outcomes.4-6 In previous health outcomes studies, inequities in the distribution of SDoH have been shown to disproportionately impact Black, Indigenous, and Latinx communities, and COVID-19 was no exception. Data from the APM Research lab demonstrated that age-adjusted mortality rates for Indigenous peoples, Latinx communities, and Black Americans have a mortality rate that is 3.3, 2.4, and 2 times higher than White communities, respectively.1

It is unclear to what extent the observed differences in mortality from COVID-19 are due to a patient's SDoH or genetic makeup. To understand how SDoH or genetic factors may be impacting COVID-19 patients, reliable data needs to be collected and analyzed. Inconsistent collection of race and ethnicity at COVID-19 testing sites and hospitals caring for patients hinder a clear understanding of how COVID-19 affects these groups.7 Inconsistencies in reporting deaths may also obscure the correct number of deaths associated with COVID-19. Elucidating the mechanisms underlying these higher mortality rates would allow the development of targeted solutions and enhanced treatments, all serving to improve health equity across communities.

This paper seeks to understand how SDoH and genetic factors influence COVID-19 incidence rates, mortality rates, and complications. Data sources were reviewed from national, state, and hospital registries to examine their reliability and attempt to understand the effects of genetics and SDoH on the incidence and mortality rate differences observed between underrepresented and White communities.
METHODS
To understand the association of race, ethnicity, and social determinants of health with COVID-19 incidence and death rates, we reviewed data for COVID-19 testing and mortality and the accuracy and completeness of data collected. To understand the relation of SDoH and COVID-19, a literature search was conducted with search terms “COVID-19”, “social determinants of health”, “race”, “ethnicity”, “homelessness”, “incidence”, “mortality”, and “financial.” The collected SDoH papers were read to determine the factors examined, the results observed, and how SDoH was collected.

To understand the incidence and mortality of COVID-19 and possible associations it may hold with the genetic makeup of an individual, the terms “COVID-19”, “genetic basis”, and “genes” were searched.

The articles focusing on genetic makeup were read to determine how data was collected, genetic factors observed, and the results observed. All the papers were analyzed for how demographic data and COVID incidence and mortality data were obtained for each study’s population.

RESULTS
We found ten pertinent research papers focused on SDoH and COVID-19 incidence and mortality. Six articles were found that studied the genetic profiles of COVID-19 patients and the relation to the incidence, level of symptoms, and mortality.

Data from site-specific studies were collected from the health center’s electronic health records (EHR), allowing for the demographic and COVID-19 incidence/mortality data to be directly correlated to the patient. For larger city-, state-, or nationwide studies, population demographic data was derived from general demographics stats, such as the American Community Survey, United States Census Bureau, and publicly available state data. The COVID-19 data reported for the larger city-, state-, or nationwide studies consisted of COVID-19 incidence, hospitalization, and mortality. The COVID-19 data for the more extensive studies were collected from publicly available COVID-19 databases, such as the John Hopkins University dataset, New York Times GitHub repository, state department of health data. The study by Nash et al. was an exception, as they recorded all their data from surveys completed by their participants. Therefore, for most large-scale and nationwide studies, population demographics were correlated with publicly available COVID-19 data for a specified region or the nation. Detailed information on data collection sources for SDoH and genetic basis papers are available in Tables 1 and 2, respectively, with additional details on Table 3.

The studies reported on potential associations between SDoH and COVID-19 incidence and mortality. A higher incidence and mortality from COVID-19 were associated with identifying with as Black, Latinx, and Indigenous communities. Other associated factors included homelessness, housing insecurity, lower household median income, and living in an area with decreased air quality. Additionally, increased COVID-19 incidence was also found to be associated with a non-English language as their primary language, a higher number of people within a household, lower level of education, lack of health insurance, being a person with disabilities, less computer internet access, and living in a densely populated city. There was a negative correlation between COVID-19 incidence and having Asian or non-Hispanic White ancestry. Between Organization for Security and Co-operation in Europe (OSCE) countries, COVID-19 mortality was positively correlated with inequality and predicted relative poverty and negatively correlated with a higher national income.

Analysis of papers examining genetic and biological factors associated with COVID-19 incidence and severity showed a correlation between HLA-C*07:29 and B*15:27 allele frequencies, ACE2 DNA polymorphisms, and COVID-19 incidence and neurological complications. A recent paper also found a possible association between soluble lectin CD209, single-nucleotide polymorphism rs505922-C, and the severity of COVID-19 symptoms or complications. Due to the novelty of COVID-19, several commentary papers have also been published discussing potential genetic factors that could contribute to the observed differences in COVID-19 incidence and mortality. One such commentary study hypothesized a potential association with TMPRSS2 DNA polymorphisms and genetic susceptibility with COVID-19 due to collected data from African American populations. A possible association between lipoprotein(a) and COVID-19 cardiovascular complications has also been hypothesized. Additionally, glutathione deficiency has been hypothesized as a potential risk factor for a more severe COVID-19 presentation due to glutathione’s role in handling oxidative stress and inflammation in the body and decreased reduced glutathione levels present in aging populations, people with chronic diseases, people assigned male at birth, and smokers.

DISCUSSION
Our results show that SDoH factors positively correlate with increased incidence, hospitalization, and mortality
| Paper Authors          | Sample Size       | SDOH Factors Examined                  | Data Collection Location          | Method of Data Collection                | % of Cases Where Race Could Not Be Determined | % or Correlation of COVID Incidence or Hospitalizations Related to SDOH | % or Correlation of COVID Deaths Related to SDOH |
|-----------------------|-------------------|----------------------------------------|-----------------------------------|----------------------------------------|-----------------------------------------------|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| Price-Haywood, et al. | 3481 patients     | Race, ethnicity                        | Ochsner Health                    | Extracted from health systems EHR      | N/A                                           | 76.9% Black                                                                         | 70.6% Black                                                                       |
| HSU, et al.           | 2729 patients     | Race, ethnicity, and homelessness      | Boston Medical Center             | Extracted from BMC’s EHR                | 8.70%                                         | 44.6% Black, 30.1% Latinx                                                          | 49% Black, 18.4% Latinx                                                        |
| Joseph, et al.        | 326 patients      | Race/ethnicity                         | Massachusetts General Hospital     | Extracted from EMR                      | N/A                                           | 8.3% Black, 43.6% Latinx                                                          | N/A                                                                              |
| Ogunyemi, et al.      | 7104 COVID tested patients | Gender, race, age, sexual orientation, incarceration, homelessness, primary language, current address, air pollution, high school graduation, college graduate, violent crimes, access to exercise, physical inactivity, and water violations | Arrowhead Regional Medical Center (ARMC) in Colton, California | N/A                                      | Increased risk of testing positive for COVID-19 was associated with Hispanic ancestry, a non-English language as their primary language, higher number of people within a household, lower level of education, lack of health insurance, being a person with disabilities, lower median household income, less computer/internet access, living in a densely populated city, and more air pollution. Decreased risk of testing positive for COVID-19 was associated with identifying as African American, Asian, or as non-Hispanic White ancestry | N/A                                                                            |

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| PAPER AUTHORS | SAMPLE SIZE | SDOH FACTORS EXAMINED | DATA COLLECTION LOCATION | METHOD OF DATA COLLECTION | % OF CASES WHERE RACE COULD NOT BE DETERMINED | % OR CORRELATION OF COVID INCIDENCE OR HOSPITALIZATIONS RELATED TO SDOH | % OR CORRELATION OF COVID DEATHS RELATED TO SDOH |
|---------------|-------------|-----------------------|--------------------------|---------------------------|-----------------------------------------------|---------------------------------------------------------------------|------------------------------------------------|
| CORREA-AGUDELO, ET AL. | 2439 counties, 1,300,169 patients | Race/ethnicity, poverty level, air quality | 49 states | Demographic: Derived from American Community Survey COVID data: Johns Hopkins University dataset | N/A | Racial minorities, Latinx populations, polluted and regional air hub areas, and highly populated neighborhoods were correlated with increased risk of death related to COVID-19 | N/A |
| ABEDI, ET AL. | 369 counties | Total population, mobility, race, poverty level, median income, education, disability, rate of insured population | Nationwide | Mobility data: Google Demographic: Derived from State-level data COVID data: Laboratory testing samples and state department of health | N/A | 1981/million Black, 947/million Latinx (658/million White) | 211/million Black, 82/million Latinx |
| WADHERA, ET AL. | 5 New York boroughs | Race, ethnicity, and household median income | New York | Population data: Derived from American Community Survey COVID data: NYC Department of Health and Mental Hygiene | N/A | Higher rate of COVID-19 hospitalization in the Bronx compared to other New York boroughs | Higher rate of mortality in the Bronx compared to other New York boroughs |
| MAHAJAN, ET AL. | 2886 counties | Race | Nationwide | Racial and population totals: Derived from CDC website COVID data: New York Times GitHub repository | N/A | Positive correlation between identifying as Black and COVID-19 cases in county | Positive correlation between identifying as Black and COVID-19 deaths in county |

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Table 1 depicts the papers that studied social determinants of health (SDoH) and their relationship to COVID incidence and/or mortality. The table outlines the size of each study, location where data was collected, methodology of data collection, and the COVID-19 outcomes as they related to SDoH. All of the papers studied showed a positive correlation between SDoH and increased incidence, hospitalizations, or mortality from COVID-19.
from COVID-19. One of the SDoH factors associated with a higher incidence of COVID-19 is experiencing homelessness. Living in cramped shared areas, lack of access to hygienic supplies and showers, and lack of access to care are environments that ease the spread of viral infections. Similar reasoning could explain why living in crowded households and neighborhoods is positively correlated with COVID-19 incidence and mortality.

Other SDoH factors such as lower household income, air pollution, race, and ethnicity were also positively correlated with COVID-19 incidence and mortality. Increased asthma morbidity is correlated with the SDoH factors of economic disadvantage, smoke exposure, race, and ethnicity. Asthma is also a risk factor for COVID-19 mortality and is correlated with increased hospitalizations due to COVID-19 in adolescents. Therefore, the relationship between asthma and SDoH could be responsible for the association observed between SDoH and increased COVID-19 incidence and mortality. Since an individual’s level of education is directly correlated with household income, the correlation between income and COVID-19 incidence may also explain the correlation between a lower level of education and increased COVID-19 incidence.

Health literacy is defined as the skills needed to successfully communicate and function in the healthcare environment, with factors such as English as a second language leading to decreased health literacy. Previous research has shown that reduced health literacy is correlated with increased hospitalization and emergency room use and poorer health outcomes. Research has also shown that people with disabilities have an increased likelihood of delaying or foregoing care, leading to healthcare disparities. The poorer health outcomes and healthcare disparities observed in people who speak English as a second language and people with disabilities, respectively, could be used to understand the increased COVID-19 incidence observed in these groups.

Site-specific studies consistently reported certain factors of SDoH, such as race/ethnicity and homelessness for individual patients. This can be attributed to the fact that data could be directly gathered from each patient’s record. Conversely, the more extensive studies collected SDoH factors from publicly available datasets, which were then correlated with the corresponding region or state’s COVID-19 incidence, complication, and mortality rates. While this is a helpful method to collect preliminary data regarding a novel disease, previous studies show that aggregate census data is not a reliable indica-

**Table 2.** Elements of studies that examined genetic components of subjects and their COVID-19 outcomes.

| AUTHORS         | FACTORS EXAMINED                                                                 | SAMPLE SIZE | LOCATION OF DATA COLLECTION |
|-----------------|----------------------------------------------------------------------------------|-------------|-----------------------------|
| STRAFELLA, ET AL. | ACE2 genetic variability and COVID-19 related neurological complications          | 268 patients | Italy                       |
| WANG, ET AL.    | HLA allele frequencies and COVID-19 occurrence                                    | Samples from 82 COVID patients | China                       |
| KATZ, ET AL.    | Soluble lectin CD209, single-nucleotide polymorphism rs80922-C and COVID-19 severity | 4856 patients | Jackson, Mississippi; Framingham, Massachusetts; Sweden |
| HOU, ET AL.     | ACE2 and TMPRSS2 DNA Polymorphisms and susceptibility to COVID-19                | Commentary paper | N/A                         |
| MORIARTY, ET AL.| Lp(a) levels and thrombosis during or after COVID-19 infection                   | Commentary paper | N/A                         |
| POLONIKOV       | Glutathione deficiency and COVID-19 severity                                     | Commentary paper | N/A                         |

Table 2 depicts the papers that studied or hypothesized potential genetic factors that could contribute to COVID-19 incidence or morality. The table outlines the author of the paper, the genetic factors studied, the sample size or commentary nature of the study, and the location of data collection.
Table 3. Outline of the 10 SDoH and COVID-19 studies and their major findings.

| PAPER AUTHORS            | SAMPLE SIZE            | SDOH FACTORS EXAMINED                                           | STUDY FINDINGS                                                                                                                                                                                                 |
|--------------------------|------------------------|-----------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PRICE-HAYWOOD, ET AL.    | 3481 patients          | Race, ethnicity                                                 | - Increased odds of hospital admission associated with black race, public insurance, obesity, residing in a low-income neighborhood, and an increased score on the Charlson Comorbidity Index.                                        |
|                          |                        |                                                                 | - Association between deaths within hospital due to COVID-19 and age, clinical factors, and biomarkers were found.                                                                                           |
| HSU, ET AL.              | 2729 patients          | Race, ethnicity, and homelessness                               | - Hispanic patients had a higher rate of hospitalization than Black or White patients                                                                                                                       |
|                          |                        |                                                                 | - Prevalence of older age, underlying conditions, and sex was higher amongst patients who were hospitalized                                                                                                  |
|                          |                        |                                                                 | - White patients had a higher case-fatality rate than Black or Hispanic patients, as they made up the oldest age group.                                                                                     |
| JOSEPH, ET AL.           | 326 patients           | Race/ethnicity                                                  | - Chest radiographs upon admission showed racial and ethnic minority patients were more likely to have increased COVID-19 disease severity.                                                              |
|                          |                        |                                                                 | - Higher modified radiographic assessment of Lung Edema severity scores were associated with an increased chance of adverse clinical outcomes in non-white patients.                                |
| OUNYEMI, ET AL.          | 7104 COVID tested      | Gender, race, sexual orientation, incarceration, homelessness,   | - Spanish speaking and Hispanic people have a significantly higher risk of testing positive for COVID-19                                                                                                |
|                          | patients               | primary language, current address, air pollution, high school   | - Geographical areas with lower COVID-19 positive results were correlated with being less crowded, wealthier, higher educations, and increased health rankings.                                               |
|                          |                        | graduation, college graduate, violent crimes, access to        |                                                                                                                                                                                                             |
|                          |                        | exercise, physical inactivity, and water violations             |                                                                                                                                                                                                             |
| CORREA-AGUDELO, ET AL.   | 2439 counties, 1,300,169 | Race/ethnicity, poverty level, air quality                      | Racial minorities, Latinx populations, polluted and regional air hub areas, and highly populated neighborhoods were correlated with increased risk of death related to COVID-19                                            |
|                          | patients               |                                                                 | - Counties with diverse demographics, higher education, income level, and total population were at a higher risk of COVID-19 infection                                                                    |
|                          |                        |                                                                 | - Counties with smaller population, higher disability rates and poverty levels had a higher rate of COVID-19 mortality                                                                                |
| ABEDI, ET AL.            | 369 counties           | Total population, mobility, race, poverty level, median income, |                                                                                                                                                                                                             |
|                          |                        | education, disability, rate of insured population              | The Bronx (highest proportion of racial and ethnic diversity, lowest education levels, and increased levels of people living in poverty when compared with the 4 other boroughs) had the highest rate of COVID-19 related hospitalizations and deaths. |
| WADHERA, ET AL.          | 5 New York boroughs    | Race, ethnicity, and household median income                    |                                                                                                                                                                                                             |

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tor for individual-level SDoH assessment for minority groups. Therefore, more reliable methods of collecting the individual SDoH directly from patients must be implemented.

Establishing a hospital-based database to collect SDoH from all patients consistently is a challenging endeavor. Not only would it require the development and upkeep of such a database, but it might also entail healthcare professionals collecting and inputting SDoH data. Health professionals already face an overwhelming amount of work, especially during a pandemic. Introducing additional responsibilities to their workload could increase the risk of anxiety, depression, and other mental health disorders. Additionally, to collect SDoH accurately, it would require a process to be developed to ascertain SDoH information from patients, represent SDoH data in medical records, refer patients to the appropriate support services, and analyze follow-up interventions’ outcomes. Developing these initiatives would require time and implementation, two things that are limited and difficult to execute during COVID-19 surges.

Healthcare workers are often not equipped with the necessary resources and programs to collect SDoH from patients, help address the patient’s needs, and refer them to appropriate support programs related to their SDoH. Data collection from patients via electronic means has been proposed and implemented as early as 1966. However, New approaches need to be developed for how SDoH data can be efficiently collected and processed. Collecting data directly from patients using the web or mobile apps without intermediate may be efficient and scalable. In addition to creating databases to collect SDoH, there is a need to create databases with information on local support programs and operationalize the referral and tracking outcomes. It has been shown that certain SDoH is related to lower telemedicine use. Thus, it is also essential to understand how to overcome health and technology literacy and ensure that patients have adequate access to the developed databases and online resources and transportation to said locations.

The collection of SDoH from individual patients will allow for more accurate observations and conclusions about patient outcomes to be drawn. Additionally, a standardized compilation of SDoH data would allow for the appropriate support services to be offered to patients for maximum treatment efficacy, such as the necessary resources for a patient without insurance to obtain medication. The systematic collection of SDoH may also allow for adequate follow-up of patients to ensure that they were provided with resources to observe the effectiveness and impact of treatments.

However, various hurdles exist in collecting SDoH data. Methods to collect SDoH must be reliable and feasible in workflow and consistently recorded in medical records. Understanding which SDoH factors, such as race/ethnicity, housing, food insecurity, income level, education level, occupation, and zip code, would be most relevant to collect must also be determined. Additionally, identifying local support services offered to patients and maintaining a database of these services and contacts is something most institutions currently do not have and would have difficulty maintaining. Once such databases exist, an algorithm could be developed to match patients to the appropriate support service and measure the outcomes.

| PAPER AUTHORS   | SAMPLE SIZE | SDOH FACTORS EXAMINED                                                                 | STUDY FINDINGS                                                                                                                                 |
|-----------------|-------------|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| MAHAJAN, ET AL. | 2886 counties | Race                                                                                 | Percentage of African Americans residing in a county and COVID-19 cases and deaths in that county had a significant positive relationship          |
| NASH, ET AL.    | 6738 Participants | Gender, race, ethnicity, educational level, employment, household income, neighborhood setting, household crowding | Incidence of COVID-19 was higher in males, Black and Hispanic identities, essential workers, and people living in rural vs. urban settings.     |
| SEPULVEDA & BROOKER | 22 OECD countries  | National median income and relative poverty                                            | Higher COVID-19 mortality is significantly associated with income inequality.                                                                        |

Table 3 outlines the 10 studies that sought to understand how SDoH affected COVID-19 incidence, hospitalizations, and/or mortality. The table depicts the studies authors, size, factors examined, and major findings.
The conclusions drawn in this paper are subject to multiple limitations. First, the availability of data on SDoH for COVID-19 patients is limited. Additionally, data on the relation between an individual’s genetic makeup and incidence and mortality of COVID-19 is preliminary. Therefore, generalizable conclusions cannot yet be made. Additionally, the external generalizability for site-specific study results might be limited to their specific patient populations, as their data and findings are solely based on their patient populations and catchment area. Multiple studies cited in this paper used aggregated population-level data and not individual patient data and outcomes, leading to a potentially less accurate reflection of the COVID-19 patient population. Due to the novelty of COVID-19 and the limited data still available, the studies cited in this paper may not represent the complete relationship between SDoH and COVID-19 incidence and mortality. Lastly, COVID-19 cases may have been underreported, as many patients with mild symptoms could not have confirmatory testing for COVID-19.

IMPLICATIONS
The effects that SDoH has on an individual’s health and QOL have become exacerbated by the COVID-19 pandemic and have had a tangible impact on patient outcomes. In this paper, we analyzed studies that showed that SDoH, such as identifying as Black or Latinx, experiencing homelessness, and having a lower median household income, correlates with higher COVID-19 incidence and mortality rates. The observed disparity in COVID-19 outcomes could be bridged by public health agencies increasing their communication of SDoH risk factors to health providers, as the CDC has begun doing. Professional organizations can also communicate strategies for screening their patient’s SDoH and improving community outreach to vulnerable populations for testing, vaccinations, and education on when patients need medical assistance. Academic researchers should continue to analyze data to provide the best evidence for public health strategies. Civic leaders should develop evidence-based public health strategies that incorporate SDoH considerations.

This papers’ analyses also demonstrated that there is currently a lack of resources to collect patients’ SDoH, which should be addressed. There is an urgent need to create databases with information on local support programs and operationalize the referral and tracking outcomes. Implementing such databases could be the first step to address the health inequities that have existed for Black, Indigenous, and Latinx communities in the USA, especially regarding conditions and diseases that have a widespread impact on our society.

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No ethics approval was required since this paper is a literature review.

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