Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Introduction

COVID-19, caused by the SARS-CoV-2 virus, quickly overwhelmed the world affecting all people. Data emerged identifying older age and certain comorbidities as risk factors for hospitalization, intensive care unit (ICU) admission, severe disease, and death [1]. However, additional reports noted uneven distribution with greater impact among certain communities, particularly among persons older than 50 years, women, and minority groups [2]. Indeed, Pacific Islander, Hispanic or Latino, Indigenous, as well as Black or African American persons are disproportionately affected by COVID-19 [3–5].

During the early stages of the pandemic, limited data were available for optimal management of patients with COVID-19. In May 2020, the U. S. Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for remdesivir establishing it as the standard of care for hospitalized patients with COVID-19 [6]. Although, data supporting efficacy and safety of remdesivir in minority groups under “compassionate use” program were scant, thereby limiting
generalizability [7]. In order to combat the higher rates of SARS-CoV-2 infection, hospitalization, and death among these groups, it is crucial to identify therapies for COVID-19 that are not only safe and efficacious but are also generalizable. To avoid exacerbating health inequities, COVID-19 clinical trials must satisfy the requirements established by the National Institutes of Health (NIH) to ensure equitable enrollment allowing for equal representation from underrepresented communities while reporting data on racial and ethnic groups in a transparent manner.

In a previously published ‘Perspective’ in the New England Journal of Medicine [8], we identified underrepresentation of minority groups in the initial remdesivir clinical trials, the Adaptive Covid-19 Treatment Trial (ACTT-1) funded by the National Institute of Allergy and Infectious Diseases (NIAID) [9] and the Gilead-funded study (GS-U.S.-540-5773) [10]. Therefore, the purpose of this literature review was to assess the demographic characteristics of COVID-19 clinical trial participants from clinical trials early in the pandemic to determine whether enrollment was equitable across the U.S. In addition, we sought to compare demographic characteristics of COVID-19 clinical trial participants to national COVID-19 data to ensure clinical trials reflect the actual population with COVID-19.

2. Methods

2.1. Search strategy

A literature search was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist [11] using the PubMed database from December 1, 2019, to November 24, 2020, with the following search terms: 2019-ncov, COVID-19, SARS-CoV-2, clinical trial, randomized controlled trial, observational study, and veterinary. To capture additional results, keyword searches were performed using various versions and plural endings of the keyword with the title/abstract field tag. Full details of the search strategy are provided in the supplementary appendix (supplementary table 1).

2.2. Inclusion criteria

Articles were eligible for inclusion if the study was 1) a randomized controlled trial evaluating a pharmacotherapy treatment, not including convalescent plasma, for patients in the inpatient or outpatient setting with COVID-19, defined by laboratory-detected SARS-CoV-2; 2) published between December 1, 2019 to November 24, 2020; 3) written in the English language; and 4) included at least one or more sites in the U.S. Preprints from NIH-funded research available on PubMed, as a result of the NIH Preprint Pilot [12], identified from the search strategy were also screened for inclusion. Though convalescent plasma was used widely throughout the U.S. based on an expanded-access program and emergency use authorization issued by the FDA [13], randomized controlled trials employing convalescent plasma were excluded from our review due to certain minority groups being more hesitant to receive blood products as a result of fear, cultural, ethical and religious beliefs, as well as medical mistrust [14].

2.3. Study identification

Articles were screened by title and abstract for inclusion by three reviewers (DBC, VSP, AMJ), who then examined the full text to ensure each article met inclusion criteria. Disagreements were resolved by discussion between co-authors, when necessary.

2.4. Data extraction

Three reviewers (DBC, VSP, AMJ) independently extracted the following data from each article: study title, study sites, pharmacotherapy treatment interventions, number and demographic data of patients screened and included in each group, as well as whether demographic data was readily provided in the main text or supplementary appendix, and funding information. Study data were collected and managed using REDCap electronic data capture tools hosted at the University of Georgia [15,16].

2.5. National COVID-19 data

We used COVID-19 case surveillance data provided by the Centers for Disease Control and Prevention (CDC) Case Surveillance Task Force [17] to retrieve national COVID-19 data from March 2020 to November 2020 to ensure consistency between the enrollment dates for each study and the COVID-19 national data while accounting for delays in reporting. National COVID-19 data included demographic characteristics and outcomes for each COVID-19 case. Age was grouped into the following categories: 18 to 49 years, 50 to 64 years, and 65 years and older. Sex was reported as male, female, or unknown to describe a person whose sex was unknown, missing, or not available. Race and ethnicity were collected separately. Race categories included American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, or White or Caucasian, as well as a combined category of multiracial or some other race. Additionally, unknown race was used to describe a person whose race was unknown, missing, or not available. Ethnicity categories included Hispanic or Latino and non-Hispanic or Latino, as well as an unknown category to describe a person whose ethnicity was unknown, missing, or not available.

2.6. Data analysis

Descriptive statistics were calculated to characterize age, sex, race, and ethnicity of patients enrolled in the included COVID-19 clinical trials and for comparisons with national COVID-19 data.

3. Results

A total of 4472 articles were identified. After removing duplicates, 4469 articles were screened by title and abstract for eligibility, of which 4301 were excluded (supplementary fig. 1) [11]. Of the remaining 168 full-text randomized controlled trials assessed, 152 were excluded, resulting in a total of 16 studies [9,10,18–31], which evaluated 10 different pharmacotherapy treatments and represented 8169 patients, included in this review.

3.1. Study characteristics

The majority were placebo-controlled (n = 11, 69%) [9,18,21,26,28,30,31] and included hospitalized patients with COVID-19 (n = 11, 69%) [9,10,19,25,27,29] (supplementary table 2). Though all studies included at least one or more sites in the U.S., 8 studies had sites in Massachusetts [9,10,19,21,23,24,26,30] and Pennsylvania [9,10,19,21,23,26,27,30], while no sites were present in Alaska, North Dakota, West Virginia, and Wyoming. Additionally, two studies [9,10] included international sites. Notably, individual study site locations were not applicable for 2 studies [18,28], which were conducting using an internet-based model. Enrollment periods were listed for most studies, of which participant enrollment began earlier in the calendar year for clinical trials of hospitalized patients. Median enrollment was shorter in clinical trials of hospitalized patients compared to non-hospitalized patients (46.5 days [range 20 to 100 days] vs 67.5 days [range 45 to 117 days], respectively). Demographic data were reported for each study arm in 81% (n = 13) of studies [9,10,19,21,23,24,26–31]. Median number of participants was higher in studies of nonhospitalized patients (n = 452 [range 20 to 1062] vs n = 243 [range 152 to 2795]). All but one [20] of the included studies received funding, which was most often acquired from pharmaceutical companies [10,19,22–24,30], the U.S. Federal Government
In order to determine external validity of the 16 included COVID-19 clinical trials, we compared demographic data from enrolled participants to national demographic and outcome data from March 2020 to November 2020 using COVID-19 case surveillance [17]. The COVID-19 case surveillance database provides patient-level data from U.S. states, territories, and affiliates. Data were abstracted to characterize national COVID-19 cases, hospitalizations, and deaths by age group, sex, race, and ethnicity.

3.2. Age

Mean or median age ranged from 36 to 67 years across all studies (Fig. 1). Thirteen (81%) studies [9,10,18,20,21,23–25,27–31] reported mean or median age of 40 years or more among all study arms, whereas ten (63%) studies [9,10,20–25,27,29] reported mean or median age of 50 years or more. However, only three (19%) studies [10,22,25] enrolled patients with a median or mean age of 60 years or more among all study arms. Mean or median age was 36 to 67 years among studies of hospitalized patients compared to 39 to 46 years among studies enrolling nonhospitalized patients. However, only one study [19] of hospitalized patients reported a mean or median age less than 40 years among any study arms.

Based on national COVID-19 data, the monthly number of confirmed COVID-19 cases increased over the 9-month period for adult patients of any age group (supplementary fig. 2). At least 50% of COVID-19 cases occurred in patients 18 to 49 years, except during April (median 61% [range 48% to 67%]) (Fig. 1, supplementary fig. 3). Median percentage of cases among patients 50 to 64 years was 23% (range 20% to 29%), while cases among those 65 years or older peaked in April and then remained below 20% (median 16% [range 13% to 25%]). Hospitalizations were lowest among patients 18 to 49 years (median 26% [range 21% to 34%]) and highest among those 65 years or older (median 47% [range 39% to 53%]). Additionally, patients 65 years or older comprised

![Fig. 1. Distribution of participants enrolled in COVID-19 clinical trials according to mean or median age compared to national COVID-19 data. The figure displays the mean or median age of participants enrolled in COVID-19 clinical trials [9,10,18–31]. Studies who presented mean or median age for the entire study population are represented by one circle, whereas studies who presented mean or median age for each study arm are represented by more than one circle. Age was grouped into 18 to 49 years, 50 to 64 years, and 65 years and older in the data provided by the Centers for Disease Control and Prevention (CDC) Case Surveillance Task Force [17]. Based on these data, 61% of COVID-19 cases occurred in patients 18 to 49 years (gray box with diagonal stripes). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)](image-url)
more than 75% of COVID-19-related deaths throughout the 9-month period (median 93% [range 79% to 96%]).

3.3. Sex

Male participants ranged from 26% to 100% of patients randomized to any study arm across all 16 studies (Fig. 2). In 63% (n = 10) of studies [9,10,20–25,27,29], males comprised more than half of the study population. Four studies [9,10,23,29] included at least 60% male participants and two studies [22,27] included at least 70% male participants. However, male participants were the minority sex among all studies of nonhospitalized patients.

Median percentage of COVID-19 cases nationally was higher among females (median 51% [range 48% to 52%]) compared to males (median 46% [range 46% to 49%]) (Fig. 2, supplementary fig. 4). However, higher median percentage of male patients required hospitalization (median 50% [range 48% to 55%] vs median 47% [range 42% to 48%]). In addition, more male patients died throughout the 9-month period (median 52% [range 45% to 63%] vs median 48% [range 37% to 55%]).

3.4. Race and ethnicity

Both race and ethnicity were reported separately in four (25%) studies [9,23,24,31] but were combined when reported in five (31%) studies [21,25–27,30], while two (13%) [10,29] and four (25%) [18–20,28] studies reported only race or ethnicity, respectively. Among those reporting race and ethnicity separately, two studies [9,24] included five racial categories (White or Caucasian, Black or African American, Asian American, American Indian/Alaska Native, and Native Hawaiian/Pacific Islander), while the other two studies included three (White or Caucasian, Black or African American, Asian American, American Indian/Alaska Native, and Native Hawaiian/Pacific Islander) and four (White or Caucasian, Black or African American, and Asian American) categories. Additionally, all four studies [9,23,24,31] included ethnicity categories of ‘Hispanic or Latino’ or ‘Not Hispanic or Latino’. However, three (19%) studies [10,22,27] did not

Fig. 2. Distribution of participants enrolled in COVID-19 clinical trials according to sex compared to national COVID-19 data. The figure displays the percentage of female (gray solid bar, horizontal) and male (blue bar, horizontal) participants enrolled in COVID-19 clinical trials [9,10,18–31] in comparison to the percentage of female (gray bar, vertical) and male patients (blue bar, vertical) from the data provided by the Centers for Disease Control and Prevention (CDC) Case Surveillance Task Force [17]. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)
include ‘Hispanic or Latino’ within race or ethnicity categories. Most studies included at least one or more additional race or ethnicity category listed as ‘multi-race’ [9,21], ‘mixed’ [27], or ‘other’ [18,19,23,24,26–29,31]. ‘Unknown’ and ‘not reported’ were also included in five (31%) studies [9,18,24–26,31].

While race and ethnicity categories varied, enrolled participants were more likely to be more likely to be White or Caucasian (median 55% [range 15% to 88%]) than Hispanic or Latino (median 24% [range 4% to 82%]) or Black or African American (median 16% [range 1% to 45%]) (Fig. 3). White or Caucasian patients made up 50% (range 15% to 71%) of participants enrolled in hospitalized studies and 70% (range 47% to 88%) of participants enrolled in nonhospitalized studies. Black or African American patients accounted for a higher percentage of the enrolled population in studies of hospitalized patients compared to nonhospitalized patients (median 19% [range 1% to 45%] vs median 5% [range 3% to 25%], respectively). Similarly, Hispanic or Latino patients comprised a higher percentage of the study population in hospitalized trials (median 39% [range 10% to 82%] vs median 5% [range 4% to 44%]).

Across all study arms, White or Caucasian patients made up the majority of participants in 75% (n = 12) of studies [9,10,18,22–24,26–31], while Hispanic or Latino patients, when race and ethnicity were reported as combined categories, represented the majority of enrolled participants in 19% (n = 3) studies [20,21,25]. Among any study arm, median percentage of White or Caucasian patients was 57% (range 0% to 88%) compared to 13% (range 0% to 100%) for Black or African American patients. Among the four studies that reported race and ethnicity separately, median percentage of Hispanic or Latino patients was 21% (range 4% to 45%). Only three of those studies [9,24,31] reported non-Hispanic or Latino ethnicity, which

![Fig. 3. Distribution of participants enrolled in COVID-19 clinical trials according to race and ethnicity compared to national COVID-19 data. The figure displays percentage of Black or African American (gray bar, horizontal), Hispanic or Latino (light blue bar, horizontal), and White or Caucasian (blue bar, horizontal) participants enrolled in COVID-19 clinical trials [9,10,18–31] in comparison to the percentage of Black or African American (gray bar, vertical), Hispanic or Latino (light blue bar, vertical), and White or Caucasian (blue bar, vertical) patients from the data provided by the Centers for Disease Control and Prevention (CDC) Case Surveillance Task Force [17]. Race and ethnicity data are were inconsistently reported by all clinical trials. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)](image-url)
accounted for a median of 71% (range 49% to 93%) of all enrolled participants. Percentage of American Indian/Alaska Native patients randomized to any study arm ranged from 0% to 9%, while Native Hawaiian/Pacific Islanders comprised between 0.5% and 12% of participants among any study arm. Race and ethnicity were reported as ‘unknown’ for 0.78% to 16% and 3% to 6% of patients, respectively, while ‘other’ as either race or ethnicity was reported in up to 16% of participants.

Findings from national COVID-19 data suggested White or Caucasian patients experienced a higher percentage of COVID-19 cases throughout the 9-month period (median 39% [range 30% to 53%]) compared to Black or African American patients (median 10% [range 6% to 14%]) (Fig. 3, supplementary fig. 5). Similarly, median percentage of hospitalizations was 50% (range 36% to 61%) in White or Caucasian patients and 15% (range 9% to 23%) in Black or African American patients. Mortality was higher in White or Caucasian patients than in Black or African American patients (median 76% [range 45% to 89%] vs median 9% [range 3% to 25%], respectively). Percentage of COVID-19 cases, hospitalizations, and deaths trended upward among White or Caucasian patients but trended downward among Black or African American patients from March to November. American Indian or Alaska Native, Asian, Native Hawaiian or Other Pacific Islander, as well as individuals who report more than one race or as some other race comprised less than 5% of COVID-19 cases, hospitalizations, and deaths across the 9-month period. Race was unknown for a median of 44% (range 34% to 51%) of COVID-19 cases, 29% (range 21% to 35%) of hospitalizations, and 10% (range 7% to 26%) of deaths. Unknown race was highest in March and gradually decreased through November across COVID-19 cases, hospitalizations, and deaths.

COVID-19 cases were higher among non-Hispanic or Latino patients (median 39% [range 33% to 50%]) compared to Hispanic or Latino patients (median 11% [range 8% to 17%]) (supplementary fig. 6). Additionally, non-Hispanic or Latino patients were hospitalized more frequently than Hispanic or Latino patients (median 59% [range 47% to 67%] vs median 12% [range 8% to 21%], respectively). Non-Hispanic or Latino patients accounted for at least 60% of deaths throughout the 9-month period (median 69% [range 60% to 84%]). Ethnicity was unknown for a median of 48% (range 42% to 53%) of COVID-19 cases, 37% (range 31% to 46%) of hospitalizations, and 11% (range 8% to 27%) of deaths. Unknown race was highest in March and gradually decreased through November across COVID-19 cases, hospitalizations, and deaths.

4. Discussion

This review sought to assess whether enrollment in COVID-19 clinical trials was equitable across the U.S. by comparing the demographic characteristics of enrolled participants in COVID-19 clinical trials [9,10,18–31] to national COVID-19 data. While 90% (n = 47/52) of all U.S. states and territories included at least one clinical trial site, 46% (n = 24) and 23% (n = 12) had at least four and six clinical trial sites, respectively. Of the U.S. regions, 79% (n = 11/14) of western states, 89% (n = 8/9) of northeastern states, 94% (n = 15/16) of southern states, and 100% (n = 11/11) of midwestern states had at least one clinical trial site. Though clinical trial sites were widely distributed throughout most of the U.S., geographic proximity varied significantly with the majority of sites located near metropolitan areas based on a geographic analysis of 310 COVID-19 clinical trials from January 20, 2020, to September 20, 2020 [32]. Drive times greater than one hour were identified for 31% of the U.S. population, but affected 76% of those living in rural areas. Two studies [18,28] were conducted using an internet-based model, which could improve access to clinical trials for some patients, though many do not have the necessary resources or proficiency [34].

Though most cases of COVID-19 were observed in patients 18 to 49 years, this group accounted for few hospitalizations and even fewer deaths over the 9-month period. On the contrary, persons at least 65 years accounted for the smallest percentage of COVID-19 cases, but highest percentage of hospitalizations and more than 75% of deaths. However, only two studies reported mean or median age of 65 years or more among any study arm [22,25].

Females accounted for a slightly higher percentage of COVID-19 cases compared to males, but male patients comprised a greater percentage of COVID-19-related hospitalizations and deaths. However, sex was unknown approximately 3% of cases of hospitalizations each month. Similarly, median percentage of female participants was 55% (range 51% to 72%) among trials of nonhospitalized patients whereas median percentage of male participants was 60% (range 47% to 75%) among trials of hospitalized patients.

Race and ethnicity were inconsistently reported throughout the included studies. Only two studies [9,24] satisfied criteria established by the NOT-OD-15-089 [35], which requires race and ethnic categories be presented separately and include two categories for ethnicity (Hispanic or Latino and Not Hispanic or Latino) and at least five categories for race (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, and White). In some cases, limited data regarding race and ethnicity were provided in the manuscript but additional details were included in supplementary appendices. However, in at least two studies [26,28], race and ethnicity were not reported in the manuscript and were buried in the supplementary data. Supplementary materials are frequently not subjected to the same rigorous peer review as the manuscript [36].

White or Caucasian patients represented the highest percentage of enrolled participants in most of the included clinical trials. Additionally, White or Caucasian patients accounted for the highest percentage of all COVID-19 cases and COVID-19-related hospitalizations compared to persons of any other racial group for all 9 months, nationally. Indeed, the median percentage of White or Caucasian participants was 3.4 times greater than Black or African American participants enrolled in any of the studies, but 3.3 times greater based on national data. Across all clinical trials, the median percentage of White or Caucasian participants was 2.6 times and 14 times higher compared to Black or African American participants enrolled in clinical trials evaluating hospitalized and nonhospitalized patients, respectively. Nationally, the median percentage of COVID-19 cases and COVID-19-related hospitalizations among White or Caucasian patients was 3.9 times and 3.3 times higher compared to Black or African American patients, respectively. Non-Hispanic or Latino patients accounted for a median percentage of 3.4 times more clinical trial participants, as well as 3.5 times more COVID-19 cases and 4.9 times more COVID-19-related hospitalizations, based on national data, compared to Hispanic or Latino patients.

Additionally, differences were noted in the use of and definitions for ‘unknown’ or ‘other’ race and ethnicity categories throughout the studies included in this review. Unfortunately, this is not limited to clinical trials as race and ethnicity were unknown for a median of 44% and 48% of all COVID-19 cases, as well as 29% and 37% of COVID-19-related hospitalizations, respectively, based on COVID-19 case surveillance nationally [17]. Though race and ethnicity are social constructs that have no biological or scientific meaning, reporting demographic characteristics allows for consideration and identification of potential disparities among the study population while minimizing unintentional bias. Recently, recommendations for reporting race and ethnicity to ensure inclusivity, consistency, and clarity in scientific literature were published in The Journal of the American Medical Association (JAMA) [37].

Overall, demographic characteristics of participants enrolled in COVID-19 clinical trials and national data may seem similar, but comparisons within individual studies suggests otherwise. Proportional representation based on age, sex, race, and ethnicity was evident in some trials, but not in others. While almost 75% of hospitalized patients with COVID-19 were at least 50 years of age across the U.S., multiple clinical trials [18,26,28,30,31] reported median or mean age less than 50 years. COVID-19 cases and hospitalizations were relatively evenly
split between males and females, but males comprised the majority of enrolled participants in most clinical trials. Median percentage of White or Caucasian patients versus Black or African American patients ranged from 1.1 [22] to 64 [29] times and 2.8 [31] to 23.7 [18] times higher for individual clinical trials enrolling hospitalized and nonhospitalized patients, respectively. Direct comparisons of demographic data reported in clinical trials to publicly available national data are limited by the lack of standard of categories and definitions used in each. In addition, widespread underreporting of patients’ race or ethnicity cripple precise comparisons.

4.1. Limitations

While we systematically abstracted data from 16 COVID-19 clinical trials to compare demographic characteristics, data were not consistently reported and were inadequate in some cases. National COVID-19 case data are welcome resources to improve the understanding of and response to the COVID-19 pandemic but are fraught with large proportions of unknown data. Additionally, granularity in manuscripts detailing the study design and findings, as well as publicly available databases on the pandemic are limited.

5. Conclusion

Overall, participants often did not reflect the actual population with COVID-19 and demographic characteristics were inconsistently reported. Lack of homogeneously reporting demographic reporting characteristics of COVID-19 clinical trial participants limits the generalizability of study findings. To improve the response to COVID-19, and future pandemics, demographic characteristics will need to be reported in a transparent manner, while ensuring equitable selection and enrollment of participants coupled with detailed presentations of demographic and outcomes data.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article. The use of REDCap™ was supported by the National for Center Advancing Translational Sciences of the National Institutes of Health under Award Number UL1TR002378. The content is solely the responsibility of the authors and does not represent the official views of the National Institutes of Health.

Declaration of Competing Interest

None.

Data availability

Data are available on reasonable request.

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jct.2022.106997.

References

[1] CDC, Underlying Medical Conditions Associated with High Risk for Severe COVID-19, Information for Healthcare Providers, 2021. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlying-conditions.html (Accessed October 12 2021).

[2] CDC, COVID Data Tracker. https://covid.cdc.gov/covid-data-tracker/#datastream-home, 2022 (Accessed January 17 2022).

[3] The Atlantic, The COVID Racial Data Tracker. https://covidtracking.com/race, 2021 (Accessed June 2 2021).

[4] APM Research Lab, The Color of Coronavirus: COVID-19 Deaths by Race and Ethnicity in the U.S. https://www.apmresearchlab.org/covid-deaths-by-race, 2021 (Accessed June 2 2021).

[5] Centers for Disease Control and Prevention (CDC), COVID-19 Racial and Ethnic Health Disparities. https://www.cdc.gov/coronavirus/2019-ncov/community/h health-equity/racial-ethnic-disparities/index.html, 2020 (Accessed June 2 2021).

[6] FDA, Coronavirus (COVID-19) Update: FDA Issues Emergency Use Authorization for Potential COVID-19 Treatment. https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-emergency-use-authorization-potential-covid-19-treatment, 2020 (Accessed June 2 2021).

[7] J. Green, N. Ohmagari, D. Shih, G. Diaz, E. Asperges, A. Castagna, T. Feldt, G. Green, M.L. Green, F.X. Lesure, E. Nicastri, R. Oda, K. Yeo, E. Quiros-Roldan, A. Studemirje, J. Redinski, S. Ahmed, J. Bertnet, D. Chelliah, D. Chen, S. Chihara, S.H. Cohen, J. Cunningham, A. Armimino Montfore, S. Ismaili, H. Kato, G. Lapadula, E. L’Her, T. Maeno, S. Majumder, M. Massari, M. Mora-Rillo, Y. Mutoh, D. Nguyen, E. Verweij, A. Zoulafy, A.O. Osinun, A. DeZure, Y. Zhao, L. Zhong, A. Chokkalingam, E. Elbouwari, T. Lelep, L. Timb, I. Henne, S. Sellers, H. Cao, S.K. Tan, L. Winterbourne, F. Desai, R. Merz, A. Gaggar, R.P. Myers, D. M. Brainard, R. Childs, T. Flanigan, Compassionate use of remdesivir for patients with severe Covid-19, N. Engl. J. Med. 382 (24) (2020) 2327-2336.

[8] D.B. Chastain, S.P. Onofe, A.F. Henao-Martinez, C. Franco-Paredes, J.S. Chastain, H. N. Young, Racial disproportionality in Covid clinical trials, N. Engl. J. Med. 383 (9) (2020), e59.

[9] J.H. Beigel, K.M. Tomashke, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hobbman, H.Y. Chu, A. Luertemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Pareek, S.D. Paredes, A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M.D. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Faktenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Fett, J.D. Netton, H.T. Buggens, T. Bonnert, M. Green, M.G. Menzies, H. Akini, O. Nkay, H.C. Lane, A.S. Gorse, Renmin Hospital for the treatment of Covid-19 final report, N. Engl. J. Med. 383 (19) (2020) 1813-1826.

[10] J.D. Goldman, D.C.B. Lye, D.S. Hui, K.M. Marks, R. Bruno, R. Montejoano, C. D. Spinner, M. Galli, M.Y. Ahn, R.G. Nabhay, Y.S. Chen, D. SenGupta, R.H. Hyland, A. Dechert, H. Cao, X. Wei, A. Gaggar, C. Brann, W. J. Towner, J. Muñoz, K.M. Mullane, F.M. Marty, K.T. Tashima, G. Diaz, A. Subramanian, Remdesivir for 5 or 10 days in patients with severe Covid-19, N. Engl. J. Med. 383 (19) (2020) 1827-1837.

[11] M.J. Page, J.E. McKenzie, P.M. Bossuyt, I. Boutron, T.C. Hoffmann, C.D. Mulrow, L. Shanmee, J.M. Tetelaff, E.A. Ald, S.B. Brennan, R. Chou, J. Glanville, J. M. Grimshw, A. Hrobjartsson, M.M. Lalu, T. Li, E.W. Loder, E. Mayo-Wilson, S. McDonald, L.A. McGuinness, L.A. Stewart, J. Thomas, A.C. Tri, J.R. Welch, P. Whiting, D. Moher, The PRISMA 2020 statement: an updated guideline for reporting systematic reviews, BMJ 372 (2021), n71.

[12] NIH, NIH Preprint Pilot. https://www.ncbi.nlm.nih.gov/pmc/about/nihpreprints/, 2020 (Accessed June 2 2021).

[13] M.J. Joyner, K.A. Bruno, S.A. Klassen, K.L. Kunze, P.W. Johnson, E.R. Lesser, C.D. Mulrow, M.J. Page, J.E. McKenzie, P.M. Bossuyt, I. Boutron, T.C. Hoffmann, C.D. Mulrow, L. Shanmee, J.M. Tetelaff, E.A. Ald, S.B. Brennan, R. Chou, J. Glanville, J. M. Grimshw, A. Hrobjartsson, M.M. Lalu, T. Li, E.W. Loder, E. Mayo-Wilson, S. McDonald, L.A. McGuinness, L.A. Stewart, J. Thomas, A.C. Tri, J.R. Welch, P. Whiting, D. Moher, The PRISMA 2020 statement: an updated guideline for reporting systematic reviews, BMJ 372 (2021), n71.

[14] A.M.N. Renzaho, M.J. Polonsky, The influence of acculturation, medical mistrust, and perceived discrimination on knowledge about blood donation and blood donation status, Transfusion 53 (55) (2013) 1625-1715.

[15] P.A. Harris, R. Taylor, B.L. Minor, V. Elliott, M. Fernandez, L. O’Neal, M. McLeod, G. Delacqua, F. Delacqua, J. Kirby, S.N. Duda, R.E. Consortium, The REDCap consortium: building an international community of software platform partners, J. Biomed. Inform. 95 (2019), 103208.

[16] P.A. Harris, R. Taylor, R. Thielke, J. Payne, N. Gonzalez, J.G. Conde, Research electronic data capture (REDCap) – a metadata-driven methodology and workflow process for providing translational research informatics support, J. Biomed. Inform. 42 (2009) 377-381.

[17] CDC, COVID-19 Case Surveillance Public Use Data with Geography. https://data.cdc.gov/Covid-Surveillance/Covid-19-Case-Surveillance-Public-Use-Data-with-Ge- nhmnc-b4w4, 2021 (Accessed October 27 2021).

[18] D.R. Bouwes, R. Rajasingham, Safety of hydroxychloroquine among outpatient clinical trial participants for COVID-19, Open Forum Infect. Dis. 7 (11) (2020) ofaa500.

[19] J. Miller, C. Bruen, M. Schnau, J. Zhang, S. Ali, A. Lind, Z. Stoecker, K. Stauderman, S. Hebbar, Auxora versus standard of care for the treatment of severe or critical COVID-19 pneumonia: results from a randomized controlled trial, Crit. Care 24 (1) (2020) 502.

[20] G. Sakoulas, M. Gerailis, S. Kilar, K.L. Greenwood, M. Habib, A. Vyas, M. Ghafoorian, V.N.K. Dintyala, F. Hadad, Intravenous immunoglobulin plus
