JAIDS Journal of Acquired Immune Deficiency Syndromes Publish Ahead of Print
DOI: 10.1097/QAI.0000000000002795

Multi-Center Study of Outcomes Among Persons with HIV who Presented to US Emergency Departments with suspected SARS-CoV-2

Christopher L. Bennett, MD, MA;[1*] Emmanuel Ogele, MD;[2*] Nicholas R. Pettit, DO, PhD;[3] Jason J. Bischof, MD;[4] Tong Meng;[5] Prasanthi Govindarajan, MBBS, MAS;[1] Carlos A. Camargo Jr, MD, DrPH;[6] Kristen Nordenholz, MD, MSC;[7] Jeffrey A Kline, MD[3] on behalf of the RECOVER Investigators

[1]Department of Emergency Medicine, Stanford University School of Medicine, Palo Alto, CA

[2]Department of Emergency Medicine, Cook County Hospital, Chicago, IL

[3]Department of Emergency Medicine, Indiana University School of Medicine, Indianapolis, IN

[4]Department of Emergency Medicine, The Ohio State University Wexner Medical Center, Columbus, OH

[5]Department of Surgery, Stanford University School of Medicine, Palo Alto, CA

[6]Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA

[7]Department of Emergency Medicine, University of Colorado School of Medicine, Aurora, CO

[*]Both authors contributed equally to this work

Corresponding Author:

Jeffrey Kline MD

Department of Emergency Medicine

Indiana University School of Medicine

5th/3rd Bank Building, 3rd Floor

640 Eskenazi Avenue

Indianapolis, IN 46202

jefkline@iu.edu

Running Title: HIV patients with SARS-CoV-2 in US emergency departments

Word Count 2948

Funding: Funded by the Department of Emergency Medicine at Indiana University School of Medicine.

Conflicts of Interest: None

The RECOVER Investigators Group:

Thomas Aufderheide, MD - Medical College of Wisconsin, Milwaukee, WI

Joshua Baugh, MD - Massachusetts General Hospital, Boston, MA

David Beiser, MD - University of Chicago School of Medicine, Chicago, IL

Christopher Bennett, MD - Stanford University School of Medicine, Palo Alto, CA

Joseph Bledsoe, MD - Healthcare Delivery Institute, Intermountain Healthcare, Salt Lake City, UT

Carlos A. Camargo, MD, DrPH - Massachusetts General Hospital, Harvard Medical School, Boston, MA

Edward Castillo, PhD - University of California at San Diego, San Diego, CA

Makini Chisholm-Staker, MD - Mt. Sinai School of Medicine, New York, NY

D. Mark, Courtney, MD - University of Texas Southwestern, Dallas, TX

Elizabeth Goldberg, MD - Warren Alpert Medical School of Brown University, Providence, RI

Hans House, MD - University of Iowa School of Medicine, Iowa City, IA

Stacey House, MD - Washington University School of Medicine, St. Louise, MO

Timothy Jang, MD - David Geffen School of Medicine at UCLA, Los Angeles, CA

Christopher Kabrhel, MD - Massachusetts General Hospital, Boston, MA

Jeffrey A. Kline, MD- Indiana University School of Medicine, Indianapolis, IN

Stephen Lim, MD - Louisiana State University School of Medicine, New Orleans, New Orleans, LA

Troy Madsen, MD - University of Utah School of Medicine, Salt Lake City, UT

Danielle McCarthy, MD - Northwestern University, Feinberg School of Medicine, Chicago, IL

Andrew Meltzer, MD - George Washington University School of Medicine, Washington, DC, DC

Stephen Moore, MD - Penn State Milton S. Hershey Medical Center, Hershey, PA

Craig Newgard, MD - Oregon Health and Science University, Portland, OR

Kristen E. Nordenholz, MD - University of Colorado School of Medicine, Aurora, CO

Justine Pagenhardt, MD - West Virginia University School of Medicine, Morgantown, WV

Ithan Peltan, MD - Intermountain Healthcare, Salt Lake City, UT

Katherine L. Pettit, MD - Indiana University School of Medicine, Indianapolis, IN

Michael Pulia, MD - University of Wisconsin School of Medicine and Public Health, Madison, WI

Michael Puskarich, MD - Hennepin County Medical Center and the University of Minnesota, Minneapolis, MN

Lauren T. Southerland, MD - Ohio State University Medical Center, Columbus, OH

Scott Sparks, MD - Riverside Regional Medical Center, Newport News, VA

Danielle Turner-Lawrence, MD - Beaumont Health, Royal Oak, MI

Marie Vrablik, MD - University of Washington School of Medicine, Seattle, WA

Alfred Wang, MD - Indiana University School of Medicine, Indianapolis, IN

Anthony Weekes, MD - Atrium Health, Charlotte, NC

Lauren Westafer, MD - Baystate Health, Springfield, MA

John Wilburn, MD - Wayne State University School of Medicine, Detroit, MI

ABSTRACT

Background: There is a need to characterize patients with HIV with suspected severe acute respiratory syndrome coronavirus 2 (SARs-CoV-2).

Setting: Multicenter registry of patients from 116 emergency departments in 27 US states.

Methods: Planned secondary analysis of patients with suspected SARS-CoV-2, with (n=415) and without (n=25,306) HIV. Descriptive statistics were used to compare patient information and clinical characteristics by SARS-CoV-2 and HIV status. Unadjusted and multivariable models were used to explore factors associated with death, intubation, and hospital length of stay. Kaplan-Meier curves were used to estimate survival by SARS-CoV-2 and HIV infection status.

Results: Patients with both SARS-CoV-2 and HIV and patients with SARS-CoV-2 but without HIV had similar admission rates (62.7% versus 58.6%, p=0.24), hospitalization characteristics (e.g. rates of admission to the intensive care unit from the ED [5.0% versus 6.3%, p=0.45] and intubation [10% versus 13.3%, p=0.17]), and rates of death (13.9% versus 15.1%, p=0.65). They also had a similar cumulative risk of death (log-rank p=0.72). However, patients with both HIV and SARS-CoV-2 infections compared to patients with HIV but without SAR-CoV-2 had worsened outcomes, including increased mortality (13.9% versus 5.1%, p<0.01, log rank p<0.0001) and their deaths occurred sooner (median 11.5 days versus 34 days, p<0.01).

Conclusion: Among ED patients with HIV, clinical outcomes associated with SARS-CoV-2 infection are not worse when compared to patients without HIV, but SARS-CoV-2 infection increased risk of death in patients with HIV.

Keywords: HIV, emergency department, SARS-CoV-2, clinical outcomes

INTRODUCTION

SARS-CoV-2 is a leading cause of death in the US.[1] Despite extensive attempts to characterize SARS-CoV-2 infections and the concurrent pandemic in the broader medical literature,[2,3] less is known about SARS-CoV-2 in patients infected with HIV – either the characteristics of those who become infected with SARS-CoV-2 or the clinical outcomes that stem from concurrent HIV and SARS-CoV-2 infection.[4–10]

This is despite a population of over one million individuals in the US infected with HIV and a clear public health need for more information on the topic.[11,12] HIV can be treated with antiretroviral medication; the introduction of such therapies has increased life-expectancy for patients with HIV. However, patients with HIV suffer from excess morbidity (e.g. higher rates of diabetes, hypertension, chronic kidney disease, and cerebrovascular accidents compared to individuals without HIV infection).[13] This morbidity could portend that those with HIV and concurrent SARS-CoV-2 infection may have worse outcomes than individuals without HIV.[4,14] Depending upon treatment effectiveness, persons with HIV infection can have a wide range of immunocompetency, and therefore vulnerability to severity of viral infection.[4,13,14]

Thus, there is an urgent need to characterize the clinical features and outcomes of a large and heterogenous sample of patients with HIV and SARS-CoV-2 infections. This multi-center study helps address the current need for clinical information on SARS-CoV-2 in patients with HIV. We utilize a national registry of hospitals to assess a population of patients with and without HIV presenting to US emergency departments (ED) with suspected SARs-CoV-2

infections.[15,16] Our first objective was to present and compare clinical characteristics and outcomes of a population of patients (stratified by the presence or absence of HIV and presence or absence of SARS-CoV2 infection) presenting to US EDs with a suspected SARS-CoV-2 infection. Our second objective was to explore factors associated with both primary (death) and secondary (intubation and hospital length of stay) outcomes among the subpopulation with HIV. Our third objective was to compare survival estimates stratified by HIV and SARS-CoV-2 infection status.

METHODS

This study was a planned secondary analysis of a multicenter registry of patients from 45 medical centers, with 116 emergency departments in 27 US states, the RECOVER (REgistry of suspected COVID-19 in EmeRgency care) Network.[15,16] Our December 2020 data cut of the registry included 25,721 unique patients with a qualifying emergency department visit at participating medical centers for suspected SARS-CoV-2 infection and an accompanying polymerase chain reaction (PCR) based test for SARS-CoV-2. Patients with ED visits lacking a reasonable probability of being related to SARS-CoV-2 (e.g. trauma, alcohol or drug intoxication, or testing done purely for admission policy) were excluded from enrollment in the registry; all entries in the registry had a minimum of 30-day follow-up information.[15,16]

The registry utilized a REDCap platform (http://www.projectredcap.org) with 204 questions among seven domains (visit information, demographics, symptoms and risk factors, vital signs, past medical history, current medications, test results, and outcomes). As described previously, the platform utilized programming to force data entry for critical fields, perform error

checking, and ensure sensible alpha-numeric content and ranges for numeric data.[15,16] Data were obtained by abstractors using the local electronic health record at each study-site and supported by an administrative core and a steering committee. Training of data abstractors was done via teleconference with the principal investigator and supplemented by a program manager and extensive guidance documentation; this included guidance documented embedded in the REDCap.[15,16]

The protocol for the RECOVER Network was reviewed by the institutional review board at all participating sites. Detailed methodology (including study design, setting, registry development, patient selection, and other characteristics) for the RECOVER Network have been described elsewhere.[15,16] The population of interest for this study was patients in the registry with a documented HIV infection or AIDS. Patient data was stratified by SARS-CoV-2 and HIV test results - positive and negative.

Values were summarized and presented with descriptive statistics including medians with interquartile range (IQR) and proportions. We used chi-square tests and unpaired Student's t-tests to compare clinical characteristics and outcomes between the stratified groups and to compare patients with HIV stratified by SARS-CoV-2 status. To explore factors associated with our primary and secondary outcomes, which include death, intubation and hospital length of stay, we first calculated unadjusted odds ratios (ORs) and corresponding 95% confidence intervals (CIs) to determine whether the odds of experiencing the outcomes varied by factor; factors explored included age, sex, race, smoking status, obesity (defined by a body mass index greater

than 35 kg/m^2), insured status/type, and presence of a do not resuscitate order. Factors were selected based on prior studies and clinical judgment.[15-18] We then constructed multivariable logistic regression models to further identify associations between the aforementioned factors and outcomes. Given that death was our primary outcome of interest, we also constructed Kaplan-Meier curves comparing survival probabilities for patients with HIV (stratified by SARS-CoV-2 positive and negative status) and survival probabilities for patients with SARS-CoV-2 (stratified by HIV positive and negative status). Logrank tests were used to compare survival distributions. Per our *a priori* protocol, categorical data that were not charted were considered absent and not imputed.[15,16] Missing (>0.1%) continuous data (i.e. age, vital signs, and body mass index) were analyzed for monotonicity and replaced using multiple imputation.[15,16] Further, we tested for collinearity but did not identify any variables that were co-linear; we did not test for interaction. We were unable to include information about HIV treatment status and CD4 count in our analysis or modeling given a high degree of missingness (46% were missing); these data were not imputed. An α level of <0.01 was considered significant and all analyses were completed using SAS software (SAS Institute Inc., Cary, NC, USA).[19]

RESULTS

Patient Characteristics

We identified 415 patients from the RECOVER registry with HIV (1.6% of our data cut of the registry); 201 (48%) patients with HIV were found to have a PCR confirmed SARS-CoV-2 infection. Characteristics of these patients stratified by SARS-CoV-2 and HIV infection status are presented in **Table 1**. Patients with both SARS-CoV-2 and HIV (compared to those with

SARS-CoV-2 but without HIV) were more often male (76.1% versus 52.4%), more often identified as Black or African American (59.7% versus 34.8%), were more often insured through either Medicaid or Medicare (70.1% versus 57.0%), and were more often undomiciled (4.0% versus 1.1%). With some exceptions, such as cancer (13.4% versus 6.8%) and some types of substance use (e.g. tobacco [20.9% versus 7.1%], marijuana [5.5% versus 1.6%], or methamphetamine [3.0% versus 0.3%]) the past medical and substance use histories of the two populations were similar.

Patients who were SARS-CoV-2 negative but HIV positive (compared to patients with neither SARS-CoV-2 nor HIV infections) were more often male (74.3% versus 45.5%), more often identified as Black or African American (44.9% versus 22.3%), more often insured through either Medicaid or Medicare (59.3% versus 48.7%), and more often undomiciled (15.0% versus 4.2%). Again, with some exceptions, such as some types of substance use (e.g. tobacco [43.0% versus 23.3%], cocaine use [7.5% versus 2.3%], and marijuana (18.2% versus 7.2%), the medical and substance use histories of the two populations were similar (**Table 1**).

Risk Factors and Presenting Symptoms

Patient's self-reported risk factors for infection, presenting symptoms, and days since symptom onset (stratified by SARS-CoV-2 and HIV infection status) are presented in **Table 2**. With a few exceptions (e.g. patients with both SARS-CoV-2 and HIV infections, compared to patients with SARS-CoV-2 but without HIV infection, less often had exposure to SARS-CoV-2 from nursing homes [1.5% vs 8%] but were more likely to report abdominal pain [44.8% versus 35.1%] or chest pain [53.2% versus 42.4%]), self-reported risk factors and presenting symptoms

were similar across the strata. Further, days since symptom onset were similar across the strata (median of 4 days of symptoms for both HIV positive and negative patients with SARS-CoV-2 infections and a median of 3 days of symptoms for both HIV positive and negative patients without SARS-CoV-2 infections), **Table 2**.

Clinical Outcomes

Clinical characteristics of patients upon arrival to the ED along with hospitalization characteristics (if admitted) are presented in **Table 3** stratified by SARS-CoV-2 and HIV status. Patients with both SARS-CoV-2 and HIV (compared to patients with SARS-CoV-2 but without HIV) had similar ED triage vitals (e.g. median oxygen saturations upon arrival of 96% and 93%, p=0.48) and admission rates (62.7% versus 58.6%, p=0.24); those that were admitted also had similar hospitalization characteristics (e.g. 5.0% versus 6.3% [p=0.45]were admitted to the intensive care unit from the ED and 10% versus 13.3% [p=0.17]required respiratory support with intubation), and rates of death (13.9% versus 15.1%, p=0.65). Further, among the subgroups of patients with SARS-CoV-2 who died, those who died did so at similar times (death occurred a median number of 11.5 days [HIV positive] versus 8 days [HIV negative] from the initial ED visit, p=0.57). Patients without SARS-CoV-2 but with HIV (compared to patients without either SARS-CoV-2 or HIV) had similar ED triage vitals and, for the subpopulation admitted, similar hospitalization characteristics and outcomes (**Table 3**).

Comparison of Patients with HIV Stratified by SARS-CoV-2 Infection Status

Information specific to the subpopulation of patients with HIV (both with and without SARS-CoV-2 infections) is presented in the **Supplemental Table, http://links.lww.com/QAI/B720**. Patients with both HIV and SARS-CoV-2 infections (compared to patients with HIV but without SAR-CoV-2) were older (median ages of 57 years versus 50 years, $p<0.001$), more often identified as Black or African American (59.7% versus 44.9%, $p<0.01$), but were less often undomiciled (4% versus 15%, $p<0.001$). Further these patients were more often admitted to the hospital (62.7% versus 49.1%, $p<0.01$), required respiratory support with intubation (10% versus 3.3%, $p<0.01$), had longer hospital length of stays (median of 7 days versus 4 days, $p<0.01$), more frequently died (13.9% versus 5.1%, $p<0.01$) and among the subpopulation that died – they died more quickly (death occurred a median number of 11.5 days versus 34 days from the initial ED visit, $p<0.01$).

Factors associated with Death, Intubation, and Hospital Length of Stay among patients with HIV

In unadjusted analyses of factors associated with the outcomes of death, intubation, and hospital length of stay, among the subpopulation of patients with HIV and SARS-CoV2, we found that identifying as White was associated with an increased odds of death (OR 3.06 [95% CI 1.19-7.86]) and intubation (OR 4.10 [1.47-11.44]); identifying as Black was associated with a decreased odds of respiratory support through intubation (OR 0.25 [0.09-0.69]). In multivariable analyses of the subpopulation of patients with HIV and SARS-CoV-2, we found that identifying

as Black was associated with a decreased odds of death (OR 0.24 [95% CI: 0.08-0.70]) and respiratory support through intubation (OR 0.17 [95% CI: 0.05-0.60]).

Survival Analysis

Kaplan-Meier Survival estimates for the population of patients with SARS-CoV-2 (stratified by HIV positive and negative status) are presented in **Figure 1**; patients with HIV and SARS-CoV-2 infections had a similar probability of death at any given point compared to patients without HIV but with SARS-CoV-2 infection (log-rank p=0.72). Survival estimates for the population of patients with HIV (stratified by SARS-CoV-2 positive and negative status) are presented in **Figure 2**; patients with both HIV and SARS-CoV-2 infections had a higher probability of death compared to patients with HIV but without SARS-CoV-2 at any point (log rank p<0.0001).

DISCUSSION

We found a population of 415 patients with HIV within the RECOVER Network. Nearly half of those with HIV were SARS-CoV-2 positive. With some exceptions, the groups had similar characteristics and similar (median) duration of symptoms prior to presenting to US EDs for care. Expectedly, patients with SARS-CoV-2 (both HIV positive and negative) died at higher rates, were more often intubated, and had longer hospital length of stays – compared to those without SARS-CoV-2. However, patients with HIV and SARS-CoV-2 did not appear to have markedly worse outcomes (death, intubation, hospital length of stay) compared to patients without HIV but with SARS-CoV-2.

Our study is not the first to demonstrate that outcomes associated with SARS-CoV-2 are not worse among patients with an HIV infection (compared to those without an HIV infection).[20-24] A US multi-center study that included 404 patients with HIV found no differences in outcomes through propensity-matched analysis.[20] Of note, most (70%) patients in this study had a history of antiretroviral therapy (ART).[20] These findings are congruent with a Zambian study of 443 hospitalized patients with HIV;[21] HIV was not found to be independently associated with poor outcomes (caveat being that those with severe HIV disease were more likely to develop severe SARS-CoV-2 or to die of SARS-CoV-2).[21] A third study that did not identify worse outcomes also represented a population of patients with controlled HIV infections (e.g. 94% had viral load <20 copies/mL).[22]

However, reports have differed.[4,25] One recent US study (2,988 persons living with HIV concurrently infected with SARS-CoV-2) demonstrated that hospitalization rates were higher among those without viral suppression and among those with lower CD4 counts.[4] This is in the context of recent work from the World Health Organization (WHO) that reported HIV infection (among individuals with concurrent SARS-CoV-2 infections) was independently associated with a higher risk of death.[25] Of note, much like our current work, this WHO study was limited given that ART information was absent for a majority (60%) of patients.

Although the overall impressions of these works appear conflicting, one potential underlying explanation is that SARS-CoV-2 associated clinical outcomes may be more related to the severity of an HIV infection (e.g. high viral low, low CD4 count, and absence of ART) and not necessarily just the presence (or absence) of an HIV infection. Given this, it is possible that our similar outcomes among patients with SARS-CoV-2 and an HIV infection (compared to those without an HIV infection) may stem from a population of patients with controlled or less

severe HIV infections. Unfortunately, given the high degree of missingness on HIV treatment status and CD4 count in our secondary analysis, we are unable to confirm this or offer a more thorough explanation. Future work remains necessary.

We further found that the population with both HIV and SARS-CoV-2 disproportionately identified as Black or African American. HIV disproportionately impacts those who identify as Black or African American;[12] these findings likely stem from the disproportionate burden of SARS-CoV-2 (both population prevalence and overall mortality) seen within Black and African American communities across the US.[26,27] These are the same Black communities that suffer from clearly demonstrated, longstanding, inequities in both health risks and outcomes that existed well before the start of the current pandemic.[26,27]

Interestingly, and counter to our *a priori* thoughts, patients with SARS-CoV-2 infections were less often smokers. Recent work suggests that smoking is an independent risk factor for both hospital admission and death from SARS-CoV-2.[28,29] However, there is limited evidence to support this phenomenon and contradictory thoughts on the association of tobacco use and SARS-CoV-2 infection do exist.[28-30] We are uncertain as to the implications of this current finding in our HIV positive population (a finding that was also noted among the larger, primary, analysis). Unfortunately, an explanation is beyond the limited scope of this current work. Further study is required and is currently being completed in the larger RECOVER Network.

Limitations

There are several limitations to this work, the first and most notable of which is missing information on both HIV treatment status and CD4 count and our inability to account for these in

our study. This is a limitation shared by other work on the topic.[25] Our work was a planned secondary analysis of a larger, national, registry. The primary study was focused on characterizing patients who presented to US emergency departments with suspected SARS-CoV-2 infections. Despite each site and investigator attempting to obtain this information, in many situations the information was not present in the electronic health record. Given the possibility that SARS-CoV-2 related outcomes may be dependent on severity of HIV infection, it would have been of interest to explore whether patients not on ART or with deranged CD4 cell count and HIV viral load had similar outcomes.[4,21]

However, independent of either treatment status or CD4 count, there is still a clear need for our work (and works like our current study) that explores outcomes (including mortality) associated with SARS-CoV-2 infections in patients with HIV – and how these findings compare to individuals without HIV. Our findings add to the literature base and will be useful given the ongoing global pandemic and conversation around risk stratification and vaccine prioritization for patients with HIV.[4,11]

A second limitation of this work stems from the site-to-site variability and potential concerns for generalizability inherent to any national, multi-center registry (e.g. hospital-specific ICU admission practices or policies on invasive oxygen techniques); a limitation likely more compounded given that SARS-CoV-2 prevalence and hospital resources were likely not equal across sites (e.g. hospitals in regions with higher SARS-CoV-2 prevalence may have had limited ability to offer invasive respiratory support).[15,16] We are unable to account for the possible contributions of site-specific differences given the sample size presented here, the period of study for this population, and the changing epicenters of SARS-CoV-2 infections across the US.

Despite these limitations, to our knowledge, our work is the first such report that focuses on patients with HIV who presented to US emergency departments with suspected SARs-CoV-2 infections and also includes information on both hospitalization characteristics and patient mortality. Our work is also one of the few studies not limited to a single center or region,[5–7,9] but instead reflects a national, multi-center registry.[4,8,10]

Conclusion

We present findings from a national registry of hospital EDs on patients with (and without) HIV who presented to US emergency departments with a suspected SARs-CoV-2 infection. We expectedly find that patients with SARS-CoV-2 fare worse than those without SARS-CoV-2. However, we do not find worse outcomes for patients with both SARS-CoV-2 and HIV compared to those with SARS-CoV-2 but without HIV.

REFERENCES

1. Woolf SH, Chapman DA, Lee JH. COVID-19 as the Leading Cause of Death in the United States. *JAMA*. 2021;325(2):123-124. doi:10.1001/jama.2020.24865

2. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497-506. doi:10.1016/S0140-6736(20)30183-5

3. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med*. 2020;382(8):727-733. doi:10.1056/NEJMoa2001017

4. Tesoriero JM, Swain CE, Pierce JL, et al. COVID-19 Outcomes Among Persons Living With or Without Diagnosed HIV Infection in New York State. *JAMA Netw Open*. 2021;4(2):e2037069. doi:10.1001/jamanetworkopen.2020.37069

5. Vizcarra P, Pérez-Elías MJ, Quereda C, et al. Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort. *Lancet HIV*. 2020;7(8):e554-e564. doi:10.1016/S2352-3018(20)30164-8

6. Blanco JL, Ambrosioni J, Garcia F, et al. COVID-19 in patients with HIV: clinical case series. *Lancet HIV*. 2020;7(5):e314-e316. doi:10.1016/S2352-3018(20)30111-9

7. Calza L, Bon I, Borderi M, et al. COVID-19 Outcomes in Patients With Uncontrolled HIV-1 Infection. *J Acquir Immune Defic Syndr*. 2021;86(1):e15-e17. doi:10.1097/QAI.0000000000002537

8. Del Amo J, Polo R, Moreno S, et al. Incidence and Severity of COVID-19 in HIV-Positive Persons Receiving Antiretroviral Therapy : A Cohort Study. *Ann Intern Med*. 2020;173(7):536-541. doi:10.7326/M20-3689

9. Sachdev D, Mara E, Hsu L, et al. COVID-19 Susceptibility and Outcomes Among People Living With HIV in San Francisco. *J Acquir Immune Defic Syndr*. 2021;86(1):19-21. doi:10.1097/QAI.0000000000002531

10. Sigel K, Swartz T, Golden E, et al. Coronavirus 2019 and people living with human immunodeficiency virus: outcomes for hospitalized patients in new york city. *Clin Infect Dis*. 2020;71(11):2933-2938. doi:10.1093/cid/ciaa880

11. Certain Medical Conditions and Risk for Severe COVID-19 Illness | CDC. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html. Accessed May 6, 2021.

12. Basic Statistics | HIV Basics | HIV/AIDS | CDC. https://www.cdc.gov/hiv/basics/statistics.html#:~:text=An%20estimated%201.2%20million%20people,not%20know%20they%20had%20HIV.&text=In%20the%2050%20states%20and%20the%20District%20of%20Columbia. Accessed August 6, 2021.

13. Mayer KH, Loo S, Crawford PM, et al. Excess Clinical Comorbidity Among HIV-Infected Patients Accessing Primary Care in US Community Health Centers. *Public Health Rep*. 2018;133(1):109-118. doi:10.1177/0033354917748670

14. Dauby N. Potential impact of COVID-19 in people living with HIV: experience from previous 21st century coronaviruses epidemics. *AIDS*. 2020;34(8):1255-1256. doi:10.1097/QAD.0000000000002555

15. Kline JA, Pettit KL, Kabrhel C, Courtney DM, Nordenholz KE, Camargo CA. Multicenter registry of United States emergency department patients tested for SARS-CoV-2. *Journal of the American College of Emergency Physicians Open*. 2020;1(6):1341-1348.

doi:10.1002/emp2.12313

16. Kline JA, Camargo CA Jr, Courtney DM, et al. Clinical prediction rule for SARS-CoV-2 infection from 116 U.S. emergency departments 2-22-2021. PLoS One. 2021 Mar 10;16(3):e0248438. doi: 10.1371/journal.pone.0248438.

17. Dietz W, Santos-Burgoa C. Obesity and its Implications for COVID-19 Mortality. *Obesity (Silver Spring)*. 2020 Jun;28(6):1005. doi: 10.1002/oby.22818.

18. Himmelstein DU, Woolhandler S. Health Insurance Status and Risk Factors for Poor Outcomes With COVID-19 Among U.S. Health Care Workers: A Cross-Sectional Study. *Ann Intern Med*. 2020 Sep 1;173(5):410-412. doi: 10.7326/M20-1874.

19. Chen SY, Feng Z, Yi X. A general introduction to adjustment for multiple comparisons. J Thorac Dis. 2017;9(6):1725-1729. doi:10.21037/jtd.2017.05.34

20. Hadi YB, Naqvi SFZ, Kupec JT, Sarwari AR. Characteristics and outcomes of COVID-19 in patients with HIV: a multicentre research network study. AIDS. 2020 Nov 1;34(13):F3-F8. doi: 10.1097/QAD.0000000000002666.

21. Chanda D, Minchella PA, Kampamba D, et al. COVID-19 Severity and COVID-19-Associated Deaths Among Hospitalized Patients with HIV Infection - Zambia, March-December 2020. MMWR Morb Mortal Wkly Rep. 2021 Jun 4;70(22):807-810. doi: 10.15585/mmwr.mm7022a2. PMID: 34081684; PMCID: PMC8174678.

22. Gervasoni C, Meraviglia P, Riva A, et al. Clinical Features and Outcomes of Patients With Human Immunodeficiency Virus With COVID-19. Clin Infect Dis. 2020 Nov 19;71(16):2276-2278. doi: 10.1093/cid/ciaa579.

23. Nagarakanti SR, Okoh AK, Grinberg S, Bishburg E. Clinical outcomes of patients with

COVID-19 and HIV coinfection. J Med Virol. 2021 Mar;93(3):1687-1693. doi: 10.1002/jmv.26533.

24. Inciarte A, Gonzalez-Cordon A, Rojas J, et al. Clinical characteristics, risk factors, and incidence of symptomatic coronavirus disease 2019 in a large cohort of adults living with HIV: a single-center, prospective observational study. AIDS. 2020 Oct 1;34(12):1775-1780. doi: 10.1097/QAD.0000000000002643.

25. WHO Global Clinical Platform for COVID-19: Clinical features and prognostic factors of COVID-19 in people living with HIV hospitalized with suspected or confirmed SARS-CoV-2 https://apps.who.int/iris/bitstream/handle/10665/342697/WHO-2019-nCoV-Clinical-HIV-2021.1-eng.pdf. Accessed August 6, 2021.

26. Weiser JK, Tie Y, Beer L, Neblett Fanfair R, Shouse RL. Racial/Ethnic and Income Disparities in the Prevalence of Comorbidities that Are Associated With Risk for Severe COVID-19 Among Adults Receiving HIV Care, United States, 2014-2019. *J Acquir Immune Defic Syndr*. 2021;86(3):297-304. doi:10.1097/QAI.0000000000002592

27. Blake H, Brown N, Follette C, Morgan J, Yu H. Black, Indigenous, People of Color, and International Students: Experiences and Resolutions Beyond COVID-19. *Am J Public Health*. 111(3):384-386. doi:10.2105/AJPH.2020.306118

28. Lowe KE, Zein J, Hatipoglu U, Attaway A. Association of Smoking and Cumulative Pack-Year Exposure With COVID-19 Outcomes in the Cleveland Clinic COVID-19 Registry. *JAMA Intern Med*. January 2021. doi:10.1001/jamainternmed.2020.8360

29. Patanavanich R, Glantz SA. Smoking Is Associated With COVID-19 Progression: A Meta-analysis. *Nicotine Tob Res*. 2020;22(9):1653-1656. doi:10.1093/ntr/ntaa082

30. Berlin I, Thomas D, Le Faou A-L, Cornuz J. COVID-19 and Smoking. *Nicotine Tob Res*. 2020;22(9):1650-1652. doi:10.1093/ntr/ntaa059

Figure 1: Kaplan Meier Survival Estimates for patients with SARS-CoV-2 infections stratified by HIV positive (red) and HIV negative (blue) status

Figure 2: Kaplan Meier Survival Estimates for patients with HIV stratified by SARS-CoV-2 positive (red) and SARs-CoV-2 negative (blue) status

Table 1: Characteristics of patients in RECOVER Network stratified by SARS-CoV-2 and HIV status

	SARS-CoV-2 Positive					SARS-CoV-2 Negative				
	HIV Positive n=201		HIV Negative n=13,236			HIV Positive n=214		HIV negative n=12,070		
	n	(%)	n	(%)		n	(%)	n	(%)	
Demographics										
Age in years, median (IQR)	57 (48-63)		59 (43 - 71)			50 (39-58)		53 (36 - 66)		
Female Sex	48	23.9	6,294	47.6		55	25.7	6,579	54.5	
Race										
American Indian or Alaska Native	0	0	59	0.4		1	0.5	82	0.7	
Asian	0	0	410	3.1		4	1.9	361	3.0	
Black or African American	120	59.7	4,610	34.8		96	44.9	2,695	22.3	
Native Hawaiian or Other Pacific Islander	1	0.5	35	0.3		2	0.9	59	0.5	
White	28	13.9	3,826	28.9		83	38.8	7,399	61.3	
Other	52	25.9	4,298	32.5		28	13.1	1,495	12.4	
Ethnicity										
Hispanic or Latino	45	22.4	3,689	27.9		33	15.4	1,343	11.1	
Insurance										
Private	54	26.9	4,129	31.2		69	32.2	4,885	40.5	
Medicaid or Medicare	141	70.1	7,541	57.0		127	59.3	5,879	48.7	
Uninsured	3	1.5	1,091	8.2		14	6.5	879	7.3	
Undomiciled	8	4.0	146	1.1		32	15.0	503	4.2	
Past Medical History										
Atrial Fibrillation	12	6.0	835	6.3		10	4.7	1,123	9.3	
Cancer (either active or inactive)	27	13.4	896	6.8		31	14.5	1,840	15.2	
Chronic Obstructive Pulmonary Disease	18	9.0	672	5.1		25	11.7	1,591	13.2	
Current Tobacco Smoker	42	20.9	944	7.1		92	43.0	2,807	23.3	
Diabetes Mellitus	55	27.4	3,219	24.3		44	20.6	2,718	22.5	
Heart Failure	13	6.5	897	6.8		21	9.8	1,458	12.1	
Hyperlipidemia	39	19.4	3,062	23.1		65	30.4	3,527	29.2	
Hypertension	86	42.8	5,254	39.7		74	34.6	5,246	43.5	
Prior Ischemic Heart Disease	9	4.5	647	4.9		17	7.9	1,377	11.4	
BMI, median (IQR)	27.3 (23.7-31.6)		30 (25.7 - 35.4)			25.6 (21.5-31.2)		28.1 (23.6 - 33.8)		
Prior organ transplant	8	4.0	162	1.22		1	0.5	264	2.19	
Other Substance Use										
Cocaine Use	3	1.5	64	0.5		16	7.5	281	2.3	
Daily Alcohol	4	2.0	350	2.6		25	11.7	1,054	8.7	
Injection drug use	1	0.5	17	0.1		6	2.8	152	1.3	
Marijuana	11	5.5	214	1.6		39	18.2	873	7.2	
Methamphetamine use	6	3.0	38	0.3		28	13.1	267	2.2	
Opioid dependency	2	1.0	27	0.2		14	6.5	254	2.1	

Abbreviations: BMI (body mass index), HIV (human immunodeficiency virus), IQR (interquartile range), RECOVER (REgistry of suspected COVID-19 in EmeRgency care), SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2)

Table 2: Self-reported risk factors for infection and presenting symptoms stratified by SARS-CoV-2 and HIV infection status

	SARS-CoV-2 positive					SARS-CoV-2 Negative				
	HIV Positive n=201		HIV Negative n=13,236			HIV Positive n=214		HIV negative n=12,070		
	n	(%)	n	(%)		n	(%)	n	(%)	
Self-Reported Risk Factors										
None	24	11.9	1,562	11.8		77	36.0	4,130	34.2	
Travel to US from country with known endemic disease	0	0	99	0.7		4	1.9	205	1.7	
Sick contacts without confirmed SARS-CoV-2	9	4.5	957	7.2		12	5.6	934	7.7	
Unemployed or retired, social contact with friends, family and/or general public	52	25.9	3,460	26.1		54	25.2	2,422	20.1	
Employment										
Non-health care worker, contact with family, and/or friends and/or general public	94	46.8	4,662	35.2		22	10.3	2,193	18.2	
Healthcare worker with patient contact	2	1.0	418	3.2		4	1.9	763	6.3	
Close contact with a person with known/suspected SARS-CoV-2	10	5.0	1,147	8.7		7	3.3	370	3.1	
Institutional Exposure										
Hospital	2	1.0	251	1.9		7	3.3	588	4.9	
Nursing Home	3	1.5	1,064	8.0		3	1.4	476	3.9	
Assisted Living facility	0	0	172	1.3		1	0.5	216	1.8	
Prison, Jail, or Correctional Facility	0	0	39	0.3		1	0.5	71	0.6	
Other	16	8.0	881	6.7		16	7.5	836	6.9	
Presenting Symptoms										
Abdominal Pain	90	44.8	4,650	35.1		26	12.1	1,527	12.7	
Chest Pain	107	53.2	5,606	42.4		45	21.0	2,628	21.8	
Cough										
Dry	129	64.2	8,614	65.1		96	44.9	5,235	43.4	
Wet	12	6.0	893	6.7		35	16.4	1,566	13.0	
Diarrhea	82	40.8	4,834	36.5		36	16.8	1,615	13.4	
Fatigue / Malaise	56	27.9	3,736	28.2		36	16.8	2,667	22.1	
Fever	131	65.2	9,034	68.3		102	47.7	4,718	39.1	
Headache	82	40.8	4,990	37.7		28	13.1	1,759	14.6	
Joint Pain	14	7.0	1,364	10.3		9	4.2	308	2.6	
Muscle Aches	59	29.4	4,213	31.8		49	22.9	2,188	18.1	
Nausea/Vomiting	96	47.8	5,606	42.4		40	18.7	2,565	21.3	
Olfactory/taste disturbance	4	2.0	694	5.2		3	1.4	149	1.2	
Rash	46	22.9	2,785	21.0		3	1.4	126	1.0	
Rhinorrhea	48	23.9	2,897	21.9		21	9.8	1,240	10.3	
Shortness of Breath	137	68.2	291	2.2		112	52.3	313	2.6	
Sore throat	63	31.3	3,625	27.4		26	12.1	1,927	16.0	
Wheezing	22	10.9	1,490	11.3		8	3.7	606	5.0	
Days Since Symptom Onset, Median (IQR)	4 (2-7)		4 (2-7)			3 (1.5-7)		3 (1-7)		

Abbreviations: HIV (human immunodeficiency virus), IQR (interquartile range), SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), US (United States)

Table 3: Patient clinical characteristics and outcomes stratified by SARS-CoV-2 and HIV status

	SARS-CoV-2 Positive					SARS-CoV-2 Negative				
	HIV Positive n=201		HIV Negative n=13,236			HIV Positive n=214		HIV negative n=12,070		
	n	(%)	n	(%)		n	(%)	n	(%)	
ED Triage Vitals										
Oxygen saturation, median (IQR)	96 (94-98)		93 (83-96)			98 (96-99)		95 (92-97)		
Temperature (°C), median (IQR)	37 (36.7-37.7)		37.1 (36.7-37.8)			36.9 (36.6-37.2)		36.8 (36.6-37.2)		
Systolic blood pressure, median (IQR)	128 (115-147)		131 (118-146)			129 (117-145)		135 (120-151)		
Diastolic blood pressure, median (IQR)	77 (69-86)		77 (68-86)			80 (69-90.8)		81 (70-90)		
Heart Rate, median (IQR)	98 (84-111)		95 (82-108)			97 (82-110)		91 (79-105)		
Respiratory Rate, median (IQR)	19 (17-22)		19 (18-21)			18 (17-20)		18 (17-20)		
Hypotension in ED	23	11.4	1,233	9.3		30	14.0	1,546	12.8	
Lowest oxygen saturation (%) in ED, median (IQR)	94 (90-97)		93 (83-96)			96 (94-97.8)		95 (92-97)		
Arrived in Cardiac Arrest	2	1.0	90	0.7		0	0	64	0.5	
Admitted to hospital	126	62.7	7,758	58.6		105	49.1	5,671	47.0	
Hospitalization Characteristics										
Admitted to intensive care unit from ED	10	5.0	832	6.3		14	6.5	804	6.7	
Transferred to ICU during admission	19	9.5	1,248	9.4		9	4.2	314	2.6	
Circulatory Support										
Vasopressors	19	9.5	1,651	12.5		14	6.5	601	5.0	
Extracorporeal Membrane Oxygenation	3	1.5	110	0.8		6	2.8	161	1.3	
Ventilatory Support										
Supplemental Oxygen	78	38.8	5,025	38.0		58	27.1	2,851	23.6	
High Flow Oxygen	6	3.0	907	6.9		4	1.9	420	3.5	
Noninvasive Positive Pressure Ventilation	12	6.0	836	6.3		5	2.3	346	2.9	
Intubation	20	10.0	1,756	13.3		7	3.3	550	4.6	
Hospital length of stay in days, median (IQR)	7 (4-14)		7 (4-13)			4 (2-6.8)		4 (2-7)		
Died	28	13.9	1,995	15.1		11	5.1	670	5.6	
If patient died, number of days from ED visit, median (IQR)	11.5 (5-15.5)		8 (4-15)			34 (7-55)		12 (4-34)		

Abbreviations: ED (Emergency Department), HIV (human immunodeficiency virus), ICU (Intensive Care Unit), IQR (interquartile range), SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), US (United States)

Figure 1: Kaplan Meier Survival Estimates for patients with SARS-CoV-2 infections stratified by HIV positive (red) and HIV negative (blue) status

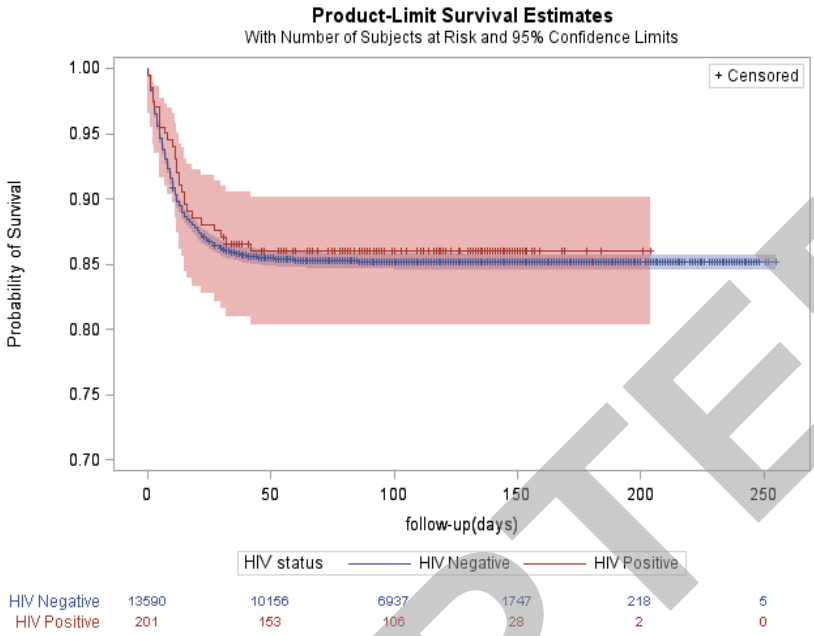

Figure 2: Kaplan Meier Survival Estimates for patients with HIV stratified by SARS-CoV-2 positive (red) and SARs-CoV-2 negative (blue) status