



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.

COVID-19 infection in hypereosinophilic syndrome: A survey-based analysis



David F. Espinoza, BA^a, Lauren Wetzler, PA-C^a, Nicole Holland, MSN^a, Neshen Moodley^b, Jeananne Ware, CRNP^a, Amy Klion, MD^a, and Paneez Khoury, MD, MHSc^a

Clinical Implications

This survey-based study of participants with hypereosinophilic syndrome suggests that neither eosinophilia nor depletion of eosinophils impact the severity of coronavirus disease infection and that there is no increased risk of vaccination against coronavirus disease 2019 in this patient population.

The role of eosinophils in coronavirus disease 2019 (COVID-19) infection remains controversial. As in other febrile illnesses, including sepsis and influenza, decreased blood eosinophil levels are frequent in COVID-19 infection and have been associated with increased disease severity.¹ Moreover, retrospective studies of patients with asthma and eosinophilic gastrointestinal disorders suggest that eosinophilia and/or type 2 inflammatory responses may be protective against severe manifestations of COVID-19 infection.^{2,3} Although these data led some to suggest early in the pandemic that eosinophil-depleting biologics may be detrimental in COVID-19 infection, published studies examining the association between biologic therapy and the incidence and severity of COVID-19 infections in patients with asthma do not support this hypothesis.⁴ Moreover, increased eosinophilic pulmonary inflammation has been reported in patients with fatal COVID-19 infection,⁵ consistent with a possible pathogenic role of eosinophils in the most severe cases.

Hypereosinophilic syndromes (HESs) are a heterogeneous group of rare disorders defined by hypereosinophilia and eosinophil-related disease manifestations.⁶ Although any organ system can be involved in HESs, the skin, respiratory, and gastrointestinal tracts are most commonly affected. HESs can be divided into clinical subtypes, including myeloid, lymphoid, and idiopathic variants, which have implications with respect to etiology, clinical manifestations, response to therapy, and prognosis. To explore the effects of HES treatment and COVID-19 in patients with HESs, 238 participants with HESs actively enrolled on a natural history study of eosinophilic disorders (NCT00001406), who had previously consented to email correspondence, were invited to participate in serial REDCap⁷ surveys (see Figure E1 in this article's Online Repository at www.jaci-inpractice.org). The first surveys were distributed in November 2020 and included questions about demographic characteristics, HES status, and COVID testing. Follow-up surveys, which included vaccination and Centers for Disease Control and Prevention (CDC) guideline adherence questions, were emailed in July 2021 to all 238 participants. Because of the study time frame (November 1, 2020, to October 1, 2021), none of the COVID-19 cases were likely due to the Omicron

variant, first reported in the United States by the CDC on November 22, 2021.⁸

A total of 160 unique participants responded to at least 1 survey between November 18, 2020, and October 1, 2021, of which 98 responded to follow-up surveys between July 1, 2021, and October 1, 2021. Of the 160 unique responders, 51.3% were males; 82.5% identified as White, 6.3% as Black, and 4.4% as Asian (Table I). A total of 105 (65.6%) participants had been tested for COVID-19 at least once, of which 23 (21.9%) tested positive between March 2020 and September 2021 (HESCOVID+). There were no demographic differences between the HESCOVID+ participants and those who reported no history of COVID-19 (HESWELL). The geographic distribution of the reported cases of COVID-19 infection closely mirrors that of the total participants (see Figure E2 in this article's Online Repository at www.jaci-inpractice.org).

The distribution of HES subtypes was significantly different between the HESWELL and HESCOVID+ groups ($P < .005$, Freeman-Halton test), with a significantly decreased proportion of idiopathic HES and nearly significantly increased proportion of lymphoid variant HES in the HESCOVID+ group compared with the entire cohort (0% vs 18.5%, $P = .017$, and 34.8% vs 10.9%, $P = .052$, respectively, central Fisher exact test corrected for multiple comparisons) (Table I). The prevalence rates of asthma and diabetes were similar in the HESCOVID+ and HESWELL groups (47.8% vs 40.9% and 0% vs 10.2%, respectively; $P =$ nonsignificant), as was the proportion of participants taking medication for HES (82.6% vs 83.9%; $P =$ nonsignificant). Most participants (83.8%) were taking HES medications, including 62 who were receiving an eosinophil-lowering biologic (mepolizumab or benralizumab) (Table II). Although the numbers are small, no significant differences in prevalence were detected for any of the medications or medication categories between the HESWELL and HESCOVID+ groups.

Four (17.4%) of the HESCOVID+ participants were hospitalized, all of whom had significant risk factors for severe COVID (body mass index > 35 [$n = 3$], severe asthma [$n = 3$] and cardiovascular disease [$n = 3$] in 3 patients, and a history of vaping tobacco in the fourth). One patient died of bacterial sepsis after COVID-19 infection. All 4 hospitalized patients had lymphoid variant HES and were receiving 1 or more treatment for HES (prednisone [$n = 3$], ruxolitinib [$n = 1$], mepolizumab [$n = 1$]) at the time of COVID-19 infection, although eosinophilia was uncontrolled in 2 of the 4 ($>1500/\text{mm}^3$ at the visit before infection). The hospitalization rate in the HESCOVID+ group (17.4%) was similar to that reported by the CDC for all individuals who tested positive for SARS-CoV-2 between February 12, 2020, and March 28, 2020 (21%; $P =$ nonsignificant), but higher than the 9% hospitalization rate reported for individuals with no underlying health condition.⁹ Although there was a trend toward a lower rate in the HESCOVID+ group compared with that in patients with chronic lung disease in the same CDC report (37.5%; $P = .051$),⁹ rates of COVID-19 infection in a large cohort of patients with asthma that included a significant proportion of patients on biologic therapy reported hospitalization rates (26.1%) similar to those in the current study.⁴

TABLE I. Demographic and clinical characteristics of the study participants

Characteristic	HESWELL cohort* (n = 137)	HES COVID+ cohort (n = 23)
Sex: female, n (%)	65 (47.4)	12 (52.2)
US resident, n (%)	130 (94.9)	21 (91.3)
White, n (%)	110 (80.3)	22 (95.7)
Age (y), median (range)	53 (6-88)	50 (21-73)
Additional risk factors		
Current smoker, n (%)†	9 (6.6)	3 (13.0)
Asthma, n (%)	56 (40.9)	11 (47.8)
Diabetes, n (%)	14 (10.2)	0 (0)
Cardiovascular disease, n (%)	28 (20.4)	4 (17.4)
Geo mean BMI (range)	25.4 (14.1-38.5)	27.8 (16.6-56.3)
HES subtype, n (%)‡		
MHES	19 (13.9)	1 (4.3)
LHES	15 (10.9)	8 (34.8)
Overlap	63 (46.0)	14 (60.9)
IHES	36 (26.3)	0
HEUS	4 (2.9)	0
Symptoms in month before filling out survey (patient report), n (%)	55 (40.1)	9 (39.1)
Change in therapy in 3 mo before filling out survey (patient report), n (%)	19 (13.9)	5 (21.7)
Vaccinated, n (%)§		
Moderna (mRNA-1273) vaccine	86 of 95 (90.5)	15 of 21 (71.4)
Pfizer (BNT162b2) vaccine	37 of 86 (43.0)	1 of 15 (6.7)
J&J (JNJ-78436735) or AstraZeneca (ChAdOx1-S)	48 of 86 (55.8)	12 of 15 (80.0)
Vaccinated before infection, n (%)	1 of 86 (1.2)	2 of 15 (13.3)
Vaccinated before infection, n (%)	NA	3 of 15 (20.0)
Hospitalized for treatment of COVID, n	NA	4
Died from COVID-related complications, n	NA	1

NA, Not available/applicable.

*Cohort that had no history of COVID or positive COVID test result (does not include the COVID+ cohort).

†Includes tobacco or other inhaled substances.

‡HES subtypes: MHES, myeloid HES defined by clinical or molecular evidence of an eosinophilic myeloid neoplasm; LHES, lymphoid variant HES defined by the presence of an aberrant and/or clonal T-cell population; overlap HES, single-organ HES or defined eosinophilic syndrome that overlaps in clinical presentation with idiopathic HES (eg, eosinophilic gastrointestinal disorders or eosinophilic granulomatosis with polyangiitis); HEUS, hyper-eosinophilia of undetermined significance defined as hyper-eosinophilia without symptoms or clinical manifestations; and IHES, idiopathic HES defined as HES that does not fit in any of the other categories.

§ $P < .03$, Fisher exact test; data provided are restricted to the 116 participants who answered vaccination questions (added after July 1, 2021, after vaccines became available in the United States).

A total of 116 (72.5%) participants responded to the vaccination questions. The vaccination rate in the HESCOVID+ group was lower than that in the HESWELL group (71.4% vs 90.5%; $P = .029$). Three of the 15 HESCOVID+ vaccinated participants were immunized before their reported COVID-19 infection. Five of the 101 vaccinated participants reported an increase in eosinophil count or eosinophil-related symptoms after immunization. In only 1 case did this lead to a change in HES

TABLE II. HES medications

Medication	HESWELL cohort* (n = 137)	HES COVID+ cohort (n = 23)
Any HES medication	115 (83.9)	19 (82.6)
Glucocorticoids	58 (42.3)	9 (39.1)
Oral	45 (32.8)	8 (34.8)
Swallowed	13 (9.5)	1 (4.3)
Inhaled therapy†	53 (38.7)	9 (39.1)
Biologic therapy	55 (40.1)	11 (47.8)
Mepolizumab	37 (27.0)	8 (34.8)
Benralizumab	16 (11.7)	1 (4.3)
Other‡	2 (1.5)	2 (8.7)
Tyrosine kinase inhibitors	19 (13.9)	2 (8.7)
Imatinib or nilotinib (PDGFR)	11 (8.0)	1 (4.3)
Ruxolitinib or tofacitinib (JAK)	8 (5.8)	1 (4.3)
Cytotoxic therapy	11 (8.0)	1 (4.3)
Hydroxyurea	6 (4.4)	0
Methotrexate	5 (3.6)	1 (4.3)
Immunomodulatory therapy	13 (9.5)	0
IFN- α	4 (2.9)	0
Mycophenolate mofetil	4 (2.9)	0
Cyclosporine	3 (2.2)	0
Other immunomodulatory§	2 (1.5)	0
Other	3 (2.2)	0

JAK, Janus kinase; PDGFR, platelet derived growth factor receptor.

Values are n (%).

*Cohort that had no history of COVID or positive COVID test (does not include the COVID+ cohort).

†Inhaled steroids and/or β -agonists.

‡Dupilumab (n = 2), omalizumab (n = 1), and lilecetumab (n = 1).

§Intravenous immunoglobulin (n = 1) and lenalidomide (n = 1).

||Dexpramipexole (n = 1), montelukast (n = 1), romidepsin (n = 1).

therapy (a transient increase in prednisone dose 2 weeks after the second dose of the Pfizer vaccine).

Consistent with published data in patients with other eosinophil-associated disorders,¹ the data from this survey suggest that patients with HESs are no more likely to have severe COVID-19 infection than the general population and that treatment does not represent a major risk factor for severe disease. Equally important, despite isolated reports of the development of eosinophilic disorders temporally related to COVID-19 vaccination, clinically significant exacerbation of HESs (ie, requiring alteration of therapy) was reported in less than 1% of vaccinated participants.

Although encouraging, this study has limitations. As in any survey-based study, the reliability of the data is limited by the accuracy of patient reporting and bias can be introduced if one of the study outcomes (eg, COVID-19 infection) results in reduced response rates. Although the number of participants was small due to the rarity of HESs, the response rate was high (67.2%), and the demographic and clinical characteristics of the participants are comparable to those in the 604 participants currently or previously enrolled on the same natural history protocol. Moreover, chart review of the 78 survey nonresponders revealed 44 participants for whom data were available regarding COVID-19 infection over the entire study period identified only 2 additional cases of COVID-19 infection in 44 participants, neither of whom had a severe presentation. Finally, the variability in COVID-19 infection rates and the introduction of immunization during the study time

frame complicated selection of an appropriate database for comparison of infection and hospitalization rates, and, perhaps more important, the application of the findings to Omicron (and future variants) is uncertain. Despite these limitations, the findings from this study suggest that patients with HESs are at no greater risk of COVID-19 infection, complications from COVID, or adverse events following immunization with currently available COVID-19 vaccines.

^aNational Institute of Allergy and Infectious Disease, National Institutes of Health, Bethesda, Md

^bInternational Biomedical Research Support Program, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Md
This work was funded by the Intramural Research Program, National Institute of Allergy and Infectious Diseases, National Institutes of Health.

Conflicts of interest: None of the authors declare a conflict of interest.

Received for publication January 17, 2022; revised February 16, 2022; accepted for publication February 22, 2022.

Available online March 3, 2022.

Corresponding author: Paneez Khoury, MD, MHSc, Human Eosinophil Section, National Institutes of Allergic and Infectious Diseases, National Institutes of Health, 10 Center Dr, Bethesda, MD 20892. E-mail: khouryp@niaid.nih.gov.
2213-2198

Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology

<https://doi.org/10.1016/j.jaip.2022.02.019>

REFERENCES

1. Rosenberg HF, Foster PS. Eosinophils and COVID-19: diagnosis, prognosis, and vaccination strategies. *Semin Immunopathol* 2021;43:383-92.
2. Qeadan F, Chehade M, Tingey B, Egbert J, Dellon ES, Peterson KA. Patients with eosinophilic gastrointestinal disorders have lower in-hospital mortality rates related to COVID-19. *J Allergy Clin Immunol Pract* 2021;9:4473-6.
3. Ferastraoraru D, Hudes G, Jerschow E, Jariwala S, Karagic M, de Vos G, et al. Eosinophilia in asthma patients is protective against severe COVID-19 illness. *J Allergy Clin Immunol Pract* 2021;9:1152-62.
4. Izquierdo JL, Almonacid C, González Y, Del Rio-Bermudez C, Ancochea J, Cardenas R, et al. The impact of COVID-19 on patients with asthma. *Eur Resp J* 2021;57:2003142.
5. Kim D-M, Kim Y, Seo J-W, Lee J, Park U, Ha N, et al. Enhanced eosinophil-mediated inflammation associated with antibody and complement-dependent pneumonic insults in critical COVID-19. *Cell Rep* 2021;37:109798.
6. Valent P, Klion AD, Horny H-P, Roufosse F, Gotlib J, Weller PF, et al. Contemporary consensus proposal on criteria and classification of eosinophilic disorders and related syndromes. *J Allergy Clin Immunol* 2012;130:607-612.e9.
7. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, et al. The REDCap consortium: building an international community of software platform partners. *J Biomed Inform* 2019;95:103208.
8. Jansen L, Tegomoh B, Lange K, Showalter K, Figliomeni J, Abdalhamid B, et al. Investigation of a SARS-CoV-2 B.1.1.529 (Omicron) variant cluster—Nebraska, November-December 2021. *MMWR Morb Mortal Wkly Rep* 2021; 70:1782-4.
9. CDC COVID-19 Response Team. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019—United States, February 12-March 28, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:382-6.

ONLINE REPOSITORY

COVID-19 Assessment in HES

Page 1

Dear research participant,

We are collecting information regarding experience with COVID-19 testing, symptoms and treatment in patients with hypereosinophilia. In the following survey we will use “you” or “patient” to refer to the participant with hypereosinophilia. Whether or not you have been diagnosed with confirmed COVID-19, we invite you to fill out this survey.

Filling out this survey should take no more than 5-10 minutes of your time. We may contact you again over the next year to gather additional information and/or send you additional surveys.

Note that this survey is best taken on a laptop or desktop computer in one sitting, as you will not be able to return to a partially completed survey.

Thank you for your participation!

Assigned EOS number

(EOS: #### (0001 - 1500))

If the patient is being assisted in completing this assessment, or if this assessment is being completed by another party, please specify relationship of this person to the patient

- Not applicable
- Spouse or partner
- Parent
- Child
- Sibling
- Friend
- Other

Specify other relationship

FIGURE E1. RedCap survey questionnaires.

Confidential

Page 2

Patient information	
If you are filling out this form for a family member or friend with HES, please try your best to fill the form out as accurately as possible. Hereafter "you" will refer to the patient in question. If you do not know the answer to a question please select "don't know" or "unknown."	
1. Patient's current age	_____
2. Country of residence	<input type="radio"/> USA <input type="radio"/> Other
2a. Specify other country	_____
2b. State of residence in the USA	_____ (e.g.: AL, CA, MN, WA)
3. Gender	<input type="radio"/> Male <input type="radio"/> Female <input type="radio"/> Non-binary/third gender <input type="radio"/> Other <input type="radio"/> Prefer not to say
3.1 Specify other gender	_____
4. Race	<input type="radio"/> White <input type="radio"/> Black <input type="radio"/> American Indian/Native Alaskan <input type="radio"/> Asian <input type="radio"/> Native Hawaiian/Pacific Islander <input type="radio"/> Unknown/NA <input type="radio"/> Other <input type="radio"/> Prefer not to say
4a. Specify other race	_____
5. Ethnicity	<input type="radio"/> Latino/Latina/Latinx <input type="radio"/> Not-Latino/Latina/Latinx <input type="radio"/> Unknown <input type="radio"/> Other <input type="radio"/> Prefer not to say
5a. Specify other ethnicity	_____
6. Patient's weight	_____ (##)
6. Or weight	<input type="radio"/> Unknown/Prefer not to say
6a. Weight units	<input type="radio"/> kg <input type="radio"/> lb

16/01/2022 03:40

projectredcap.org



FIGURE E1. Continued

Confidential

Page 3

7. Patient's height	<hr/> (###)
7. Or height	<input type="radio"/> Unknown/Prefer not to say
7a. Height units	<input type="radio"/> cm <input type="radio"/> inches

Confidential

Page 4

Patient's HES information

1. Date of HES diagnosis (year)
- 2000
 - 2001
 - 2002
 - 2003
 - 2004
 - 2005
 - 2006
 - 2007
 - 2008
 - 2009
 - 2010
 - 2011
 - 2012
 - 2013
 - 2014
 - 2015
 - 2016
 - 2017
 - 2018
 - 2019
 - 2020
 - 2021
 - Other
 - Not applicable
 - Unknown

1a. Specify other year

2. List HES symptoms and health problems associated with HES experienced at the time of diagnosis

3. Currently taking medication for HES?
(please include medications within the past month even if recently stopped)
- Yes
 - No
 - Don't know

- 3a. Currently taking oral HES medications?
- Yes
 - No

- 3a1. Please select all that apply
- Hydroxyurea
 - Tyrosine kinase (e.g. imatinib, nilotinib, dasatinib)
 - JAK inhibitors (e.g., tofacitinib, ruxolitinib)
 - Methotrexate
 - Cellcept (mycophenolate mofetil)
 - Cyclosporine
 - Azathioprine
 - Oral Corticosteroids (e.g. prednisone, medrol)
 - Swallowed budesonide
 - Swallowed fluticasone
 - Other

3a1. Specify other oral HES medication(s)

- 3b. Currently receiving biologic or injectable medications?
- Yes
 - No

16/01/2022 03:40

projectredcap.org



FIGURE E1. Continued

Confidential

Page 5

3b1. Please select all that apply

- Benralizumab
- Dupilumab
- Omalizumab
- Reslizumab
- Mepolizumab
- Methotrexate inj
- Interferon alpha inj
- Other

3b1. Specify other biologic or injectable medication(s) _____

3c. Currently using inhaled medications?

Yes
 No

3c1. Please specify all that apply

- Advair
- Albuterol
- Symbicort
- Dulera
- Flovent
- Qvar
- Other

3c1. Specify other inhaled medication(s) _____

3c2. If having used inhalers in the past month, have they been used regularly as prescribed?

Yes
 No

4. Have you ever been diagnosed with any of these conditions?
(Indicate all that apply)

- Coronary artery disease
- Heart failure
- Heart rhythm abnormality
- High blood pressure
- History of stroke or heart attack
- Other heart problems
- Diabetes
- Asthma
- COPD (emphysema)
- Other lung disease
- Chronic kidney disease
- Chronic liver disease
- Other
- None of the above

4a. Please specify other _____

4b. Please specify if:
Other heart problems, other lung disease or chronic liver disease _____

4c. Currently taking any medications for the conditions indicated above?

Yes
 No

4c1. Please list the medications being taken _____

5. Currently smoke cigarettes?

Yes
 No

FIGURE E1. Continued

Confidential

Page 6

5a. How many cigarettes smoked?

 (1-50)

5b. [hes5a] cigarettes smoked per
 Day
 Week
 Month

5c. Number of years smoking?

 (1-70)

6. Ever smoked cigarettes in the past?
 Yes
 No

6a. How many cigarettes smoked?

 (1-50)

6b. [hes6a] cigarettes smoked per
 Day
 Week
 Month

6c. Number of years smoked?

 (1-70)

7. Currently vaporize other tobacco products?
 Yes
 No

7a. How many times?

 (1-50)

7b. [hes7a] times per
 Day
 Week
 Month

8. Currently smoke anything else?
 Yes
 No

8a. Please specify what else

8b. How many times smoked?

 (1-50)

8c. [hes8b] times per
 Day
 Week
 Month

8d. For how long been smoking [hes8a]?
 (months or years) _____
 (1-70)

FIGURE E1. Continued

Confidential

Page 7

8e. Specify time unit

- Months
- Years

16/01/2022 03:40

projectredcap.org



FIGURE E1. Continued

Confidential

Page 8

Patient's current HES status (prior to COVID-19)	
1. Had any HES symptoms in the past month?	<input type="radio"/> Yes <input type="radio"/> No
1a. Specify what symptoms were experienced	_____
1b. How often have the symptoms occurred?	<input type="radio"/> Daily <input type="radio"/> Often <input type="radio"/> Sometimes <input type="radio"/> Rarely
1c. How severe are the symptoms?	<input type="radio"/> Mild <input type="radio"/> Moderate <input type="radio"/> Severe
2. Had to change medications to control HES symptoms or eosinophil counts in the past 3 months?	<input type="radio"/> Yes <input type="radio"/> No
2a. Please specify	_____

FIGURE E1. Continued

Confidential

Page 9

Patient COVID-19 Screening Questions	
1. Did patient or doctor suspect any COVID-19 infection?	<input type="radio"/> Yes <input type="radio"/> No
1.1 Did you report this episode in the previous survey?	<input type="radio"/> Yes <input type="radio"/> No
1a. What was the approximate date when this suspicion arose?	_____
2. Did the patient have any known exposure to coronavirus?	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Don't know
2a. Exposed how? (select all that apply)	<input type="checkbox"/> Occupational exposure <input type="checkbox"/> Travel <input type="checkbox"/> Household contact <input type="checkbox"/> Other
2a. Please specify other	_____
2b. What was the approximate date of the exposure?	_____
3. Was the patient tested for COVID-19?	<input type="radio"/> Yes <input type="radio"/> No
3a. Reason for testing?	<input type="checkbox"/> Known exposure <input type="checkbox"/> Symptomatic <input type="checkbox"/> Occupational screening program <input type="checkbox"/> Other
3a. Specify other	_____
3a1. If patient was symptomatic, how many days were symptoms experienced before being tested?	_____ (0 - 45 days)
3b. What type of test was used? (select all that apply)	<input type="checkbox"/> Nasal swab (PCR) <input type="checkbox"/> Antibody test (blood test) <input type="checkbox"/> Other
3b. Specify other	_____
3c. What was the date of the first test?	_____
3d. Were any of the tests positive for COVID-19?	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Don't know

FIGURE E1. Continued

Confidential

Page 10

3d1. Which test(s) was/were positive for COVID-19?

(select all that apply)

- Nasal swab (PCR)
- Antibody test (blood test)
- Other
- Don't know

3d1. Specify other

Thank you for participating. We may make contact in the future for a similar survey.

Confidential

Page 11

COVID-19 Questions

1. If suspected or confirmed to have COVID-19, which of the following symptoms were experienced?

	Mild	Moderate	Severe	No	Don't know
a. Fatigue	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
b. Fever	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
c. Chills	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
d. Headache	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
e. Sore throat	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
f. Difficulty breathing	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
g. Malaise/Weakness	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
h. Muscle aches	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
i. Nausea	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
j. Vomiting	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
k. Abdominal Pain	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
l. Loss of appetite	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
m. Diarrhea	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
n. Runny nose or congestion	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
o. Loss of smell	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
p. Loss of taste	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
q. Confusion	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
r. Other	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

1b. What was the highest temperature experienced?

(#. #)

1b. Temperature units

- Celcius
 Fahrenheit

1r. Specify other

2. Did the patient visit an emergency room for suspected COVID-19 infection?

- Yes
 No

2a. Was the patient hospitalized?

- Yes
 No

2a1. How many days was the patient hospitalized for?

(1 - 99)

2a2. Placed on nasal or high flow oxygen?

- Yes
 No

2a3. Placed on non-invasive ventilation (BiPAP)?

- Yes
 No

16/01/2022 03:40

projectredcap.org



FIGURE E1. Continued

Confidential

Page 12

2a4. Treated in the intensive care unit (ICU)? Yes
 No

2a5. Intubated/placed on a respirator? Yes
 No

3. Were any regular HES medications changed because of a suspected or proven COVID19 diagnosis? Yes
 No
 Unknown

3a. Please specify what was stopped or changed _____

4. Did the patient develop any complications of COVID19 infection? (such as kidney problems, heart problems, blood clots, or bacterial infections) Yes
 No

4a. Select all that apply Kidney problems (e.g. kidney failure or need for dialysis)
 Heart problems (e.g. myocarditis (inflammation of the heart) or heart failure)
 Blood clots
 Bacterial infection
 Other

4a. Specify other _____

5. Did the patient receive any experimental treatment? Yes
 No

5a. Please select all that apply Azithromycin
 Chloroquine
 Hydroxychloroquine
 Favipiravir
 Intravenous immunoglobulin (IVIG)
 Lopinavir/ritonavir
 Oseltamivir
 Remdesivir
 Ruxolitinib (JAK inhibitor)
 Steroids (such as prednisone or solumedrol or dexamethasone)
 Tocilizumab (IL-6 inhibitor)
 Plasma from recovered patients
 Other

5a. Specify other _____

5b. Was this treatment received as part of a clinical trial? Yes
 No
 Unknown

6. Did COVID-19 symptoms resolve? Yes
 No

FIGURE E1. Continued

Confidential

Page 13

6a. What symptoms are still being experienced?

6b. How many days in total did the patient experience symptoms?

_____ (0 - 99)

Confidential

Page 14

Vaccination Status

Please complete the Vaccination Status survey.

Thank you!

16/01/2022 03:40

projectredcap.org 

FIGURE E1. Continued

Confidential

Page 15

Vaccination Status				
Have you been vaccinated against SARS-CoV-2?	<input type="radio"/> Yes <input type="radio"/> No			
a. Which vaccine did you receive?	<input type="radio"/> Moderna <input type="radio"/> Pfizer-BioNTech <input type="radio"/> J&J / Janssen <input type="radio"/> AstraZeneca <input type="radio"/> Other <input type="radio"/> Don't know			
a. Specify other	_____			
b. When did you receive your first vaccine?	_____			
OR	<input type="radio"/> Don't know			
b. Don't know				
c. Have you or will you receive a second dose?	<input type="radio"/> Yes <input type="radio"/> No			
c1. Date of 2nd dose	_____			
OR	<input type="radio"/> Don't know			
c1. Don't know				
d. Did you have any adverse reactions to one or both doses?	<input type="radio"/> Yes <input type="radio"/> No (If 'Yes', indicate severity of reactions experienced.)			
	No	Mild	Moderate	Severe
i. Redness at the injection site	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ii. Pain at the injection site	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
iii. Swelling at the injection site	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
iv. Fever	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
v. Chills	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
vi. Muscle/joint/body aches	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
vii. Headache	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
viii. Fatigue	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
ix. Nausea	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
x. Other	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
x. Specify other	_____			

FIGURE E1. Continued

Confidential

Page 16

e. Did you experience worsening of your eosinophil count or eosinophil-related symptoms after receiving either dose of the vaccine? Yes
 No

e1. After which dose? First
 Second
 Both

e2. What got worse? _____

e3. Did you have an eosinophil count checked? Yes
 No

e3a. Please provide the absolute eosinophil count OR WBC count and % eosinophils
(We may contact you to obtain these results.)

OR Not available

e3a. Not available

f. Did you stop, start or change the dose of any of your eosinophil therapies in the 2 weeks BEFORE you got either dose of the vaccine? Yes
 No

f1. After which dose? First
 Second
 Both

f2. Which medication? _____

f3. Please describe the change

g. Did you stop, start or change the dose of any of your eosinophil therapies in the 2 weeks AFTER you got either dose of the vaccine? Yes
 No

g1. After which dose? First
 Second
 Both

g2. Which medication? _____

g3. Please describe the change

Do you plan to be vaccinated? Yes
 No
 Undecided

16/01/2022 03:40

projectredcap.org



FIGURE E1. Continued

Confidential

Page 17

a. Why?

Are you currently working?

- Yes
 No

a. Are you currently working outside of your home?

- Yes
 No

a1. When did you start working outside of your home after the start of the COVID-19 pandemic?

OR

a1. Not applicable

- Not applicable
(Have been working outside of my home throughout the pandemic)

FIGURE E1. Continued

Confidential

Page 18

During 2020, what precautions did you follow in an indoor setting (e.g. grocery store, restaurant)?				
	All of the time	Most of the time	Some of the time	Never
a. Wear a mask	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
b. Stay 6 feet away from people not part of your household	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
c. Wash/sanitize hands frequently	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
d. Avoid crowds/large gatherings	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

FIGURE E1. Continued

Confidential

Page 19

What precautions do you CURRENTLY follow in an indoor setting (e.g. grocery store, restaurant)?				
	All of the time	Most of the time	Some of the time	Never
a. Wear a mask	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
b. Stay 6 feet away from people not part of your household	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
c. Wash/sanitize hands frequently	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
d. Avoid crowds/large gatherings	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

FIGURE E1. Continued

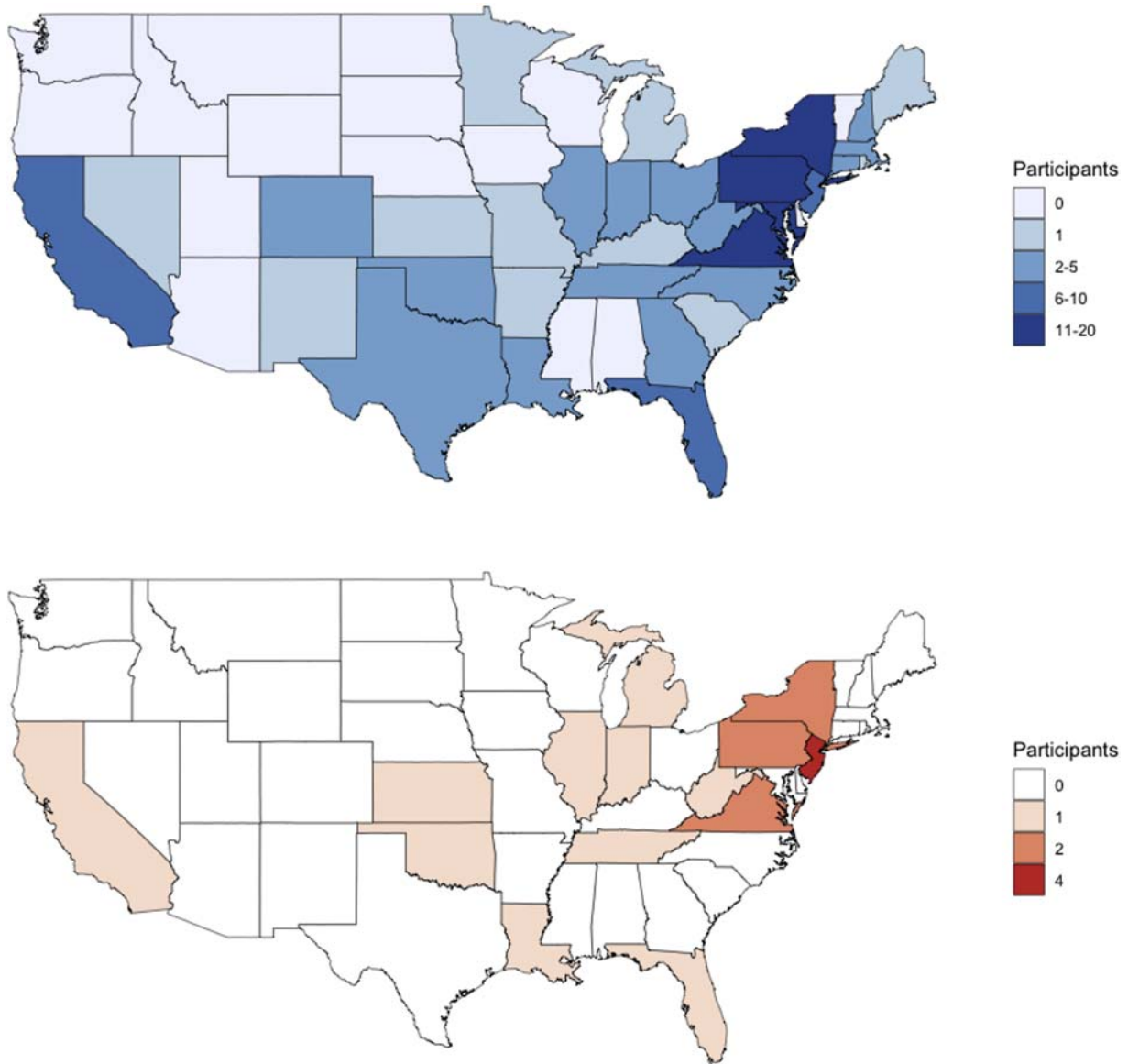


FIGURE E2. Geographic distribution of survey responders living in the United States. The number of participants by state is shown for all US survey responders (n = 151) in blue and for only the HESCOVID+ participants (n = 21) in red. Nine additional participants resided outside of the continental United States.