

Late conditions diagnosed 1–4 months following an initial COVID-19 encounter: a matched cohort study using inpatient and outpatient administrative data — United States, March 1–June 30, 2020

Jennifer R. Chevinsky, MD MPH; COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA; Epidemic Intelligence Service, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Guoyu Tao, PhD; COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Amy M. Lavery, PhD, MSPH; COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Esther A. Kukielka, DVM, PhD; COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA; Epidemic Intelligence Service, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Eleanor S. Click, MD PhD; COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Donald Malec, PhD; COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Lyudmyla Kompaniyets, PhD; COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Beau B. Bruce, MD PhD; COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Hussain Yusuf, MD; COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Alyson B. Goodman, MD; COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Meredith G. Dixon, MD; COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Jolene H. Nakao, MD; COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

S. Deblina Datta, MD; COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

William R. Mac Kenzie, MD; COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Sameer Kadri, MD, PhD; Clinical Epidemiology Section, Critical Care Medicine Department, National Institutes of Health Clinical Center, Bethesda, Maryland, USA

Sharon Saydah, PhD; COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Jennifer E. Giovanni, PhD; COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Adi V. Gundlapalli, MD, PhD; COVID-19 Response Team, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Corresponding author: Jennifer R. Chevinsky, kst3@cdc.gov. Phone: (404) 498-2890

Summary:

Our matched cohort analysis uses data from a large administrative all-payer database to explore the association of late conditions experienced 1–4 months following a COVID-19 encounter. Inpatient and outpatient adults were more likely to experience certain late health conditions than their respective inpatient and outpatient matched controls.

Accepted Manuscript

Abstract

Background

Late sequelae of COVID-19 have been reported; however, few studies have investigated the time-course or incidence of late new COVID-19-related health conditions (post-COVID conditions) after COVID-19 diagnosis. Studies distinguishing post-COVID conditions from late conditions caused by other etiologies are lacking. Using data from a large administrative all-payer database, we assessed the type, association, and timing of post-COVID conditions following COVID-19 diagnosis.

Methods

Using the Premier Healthcare Database Special COVID-19 Release (PHD-SR) (release date, October 20, 2020) data, during March–June 2020, 27,589 inpatients and 46,857 outpatients diagnosed with COVID-19 (case-patients) were 1:1 matched with patients without COVID-19 through the 4-month follow-up period (control-patients) by using propensity score matching. In this matched-cohort study, adjusted odds ratios were calculated to assess for late conditions that were more common in case-patients compared with control-patients. Incidence proportion was calculated for conditions that were more common in case-patients than control-patients during 31–120 days following a COVID-19 encounter.

Results

During 31–120 days after an initial COVID-19 inpatient hospitalization, 7.0% of adults experienced at least one of five post-COVID conditions. Among adult outpatients with COVID-19, 7.7% experienced at least one of ten post-COVID conditions. During 31–60 days after an initial outpatient encounter, adults with COVID-19 were 2.8 times as likely to experience acute pulmonary embolism as outpatient control-patients and were also more likely to experience a range of conditions affecting multiple body systems (e.g. nonspecific

chest pain, fatigue, headache, and respiratory, nervous, circulatory, and gastrointestinal system symptoms) than outpatient control-patients. Children with COVID-19 were not more likely to experience late conditions than children without COVID-19.

Conclusions

These findings add to the evidence of late health conditions possibly related to COVID-19 in adults following COVID-19 diagnosis and can inform health care practice and resource planning for follow-up COVID-19 care.

Keywords: COVID-19, Long COVID, SARS-CoV-2, COVID-19 Sequelae, Long Haulers

Accepted Manuscript

Late sequelae of coronavirus disease 2019 (COVID-19), the disease caused by SARS-CoV-2, have been reported (1). Several large COVID-19 survivor advocacy groups are raising awareness of symptoms persisting after initial illness including shortness of breath, chest tightness, and fatigue (2); however, few studies have investigated the time-course or incidence of late new COVID-19-related health conditions (post-COVID conditions) after SARS-CoV-2 infection (3–6). Studies distinguishing late conditions associated with COVID-19 from conditions caused by other etiologies are lacking (7).

There are multiple challenges with assessing post-COVID conditions. There is a need for following patients diagnosed with COVID-19 over time and an additional need to compare them with controls without COVID-19 to improve our understanding of conditions that may manifest after acute COVID-19 disease. Based on these needs, one challenge is that assessing post-COVID conditions requires longitudinal data. A second challenge is accessing a control population to be able to assess which conditions are associated with COVID-19 disease, rather than other factors such as age or care acuity. Initial prospective and observational studies have been uncontrolled (1–6). Large administrative databases with longitudinal data can be analyzed to identify a comparable control population using propensity score matching to provide information on late conditions possibly related to COVID-19. Using data from a large administrative all-payer database, we assessed the type, association, and timing of post-COVID conditions (1–4 months) following a COVID-19 diagnosis in inpatient and outpatient facility settings in a large group of patients.

Methods

Case-patients were identified from Premier Healthcare Database Special COVID-19 Release (PHD-SR) (release date, October 20, 2020) (8), an administrative all-payer database, which includes inpatient data from 922 hospitals and outpatient data from 934 hospitals, including 269 clinics with representation in all U.S. census regions, using standard *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM) discharge codes of U07.1 (COVID-19, virus identified) during April–June 2020 or B97.29 (Other coronavirus as the cause of disease classified elsewhere [recommended before the April 2020 release of U07.1]) during March–April 2020 (9). Index encounter was defined as the initial COVID-19 encounter (for case-patients) or a patient’s matched encounter (for control-patients) during March 1–June 30, 2020. Index encounter date was defined as the hospital discharge date for an inpatient encounter or encounter date for an outpatient encounter. The discharge date was used as a reference point for inpatient encounters for two primary reasons: (1) discharge date is commonly used as a reference point to assess for complications after a hospitalization and therefore could be a clinically useful point of reference and (2) this approach could limit the inclusion of acute symptoms and conditions in the findings by establishing a baseline for all inpatients after the hospitalization. Because the point of reference is different for inpatients and outpatients, the timeline for inpatient case-patients may be compared to the timeline for inpatient control-patients and the timeline for outpatient case-patients may be compared to the timeline for outpatient control-patients, however the timeline for inpatients and outpatients may not align and therefore should not be directly compared.

Clinical diagnoses established during January 2019 to the index encounter date in PHD-SR provided historical data on underlying conditions. Case-patients and control-patients were identified by using propensity score nearest-neighbor matching (10–12), a statistical technique for maximizing efficiency and for better isolating the effect of COVID-19 on the patient experiencing new conditions from the effect of other included variables. The match was based on propensity scores computed from patient demographics (age, sex, race, ethnicity, insurance status), clinical factors (number of previous inpatient encounters and conditions diagnosed before and at the index encounter), facility characteristics (urbanicity, region), and month of the index encounter. Inpatients and outpatients were matched separately. Outpatient encounters included the following facility settings: same day surgery, emergency, observation, diagnostic testing, recurring visits for services including dialysis, chemotherapy infusion and radiation, presurgical testing, and clinic. Inpatient encounters included exclusively a hospital facility setting. All other settings were excluded. Prior to matching, we excluded patients without at least one encounter preceding their index encounter in PHD-SR, who died during their index encounter, or who were pregnant at their index encounter. Potential control-patients who were diagnosed with COVID-19 during the four months after their index encounter were also excluded prior to matching.

ICD-10-CM codes recorded during encounters were classified to Clinical Classification Software Refined (CCSR) categories (13), which aggregates ICD-10-CM codes into clinically meaningful categories to form disease groupings. Diagnoses from encounters before (using the historical data from January 2019 to the index encounter date) and during the index encounter were classified as underlying or acute COVID-19 conditions. New persistent conditions (those newly starting during the index encounter and persisting after the index encounter) and exacerbations of underlying conditions (those starting prior to the index

encounter and worsening during or after the index encounter) were not assessed in this analysis because of challenges differentiating underlying conditions, acute conditions, and exacerbations in inpatient administrative data. Late conditions were defined as conditions not previously recorded as underlying or acute COVID-19 conditions during January 2019 through the index encounter date that occurred during 31–120 days (1 to 4 months) after the index encounter. Five CCSR categories were excluded from the late conditions analysis: pregnancy, perinatal, congenital malformations, external causes of morbidity, and factors influencing contact with health services (e.g. encounter for administrative purposes). Late conditions were identified using CCSR categories based on timing of occurrence after the index encounter date: 31–60 days, 61–90 days, and 91–120 days. The timeline was established using a variable that determined the days between each visit, allowing for a continuous timeline. Adjusted (for the matched variables with pairs as strata) odds ratios (aOR) and 95% confidence intervals (CI) were calculated using a conditional logit model for new conditions in case-patients compared with control-patients to identify post-COVID conditions that could be unique to patients with COVID-19, rather than searching for preestablished outcomes which could introduce additional bias. Among these statistically significant post-COVID conditions, the most common were selected for adult case-patients based on the highest incidence proportion to identify conditions that could be the most frequent new health conditions experienced 31–120 days after COVID-19 diagnosis.

A sensitivity analysis was conducted that restricted the control cohort to adult control-patients with a respiratory CCSR category during the index encounter to examine if results were consistent with the larger study's findings. The larger analysis was not restricted to control-patients with a respiratory CCSR category during the index encounter because many respiratory illnesses, like influenza, have been less common during the pandemic (14) and

healthcare seeking patterns during the pandemic have been dissimilar to healthcare seeking patterns in previous years (15), potentially introducing bias when matching to patients with respiratory viruses in previous years.

SAS (version 9.4; SAS Institute) was used for analyses. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy, and was determined to be exempt from review from the Institutional Review Board (See e.g., 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.).

Results

During March 1–June 30, 2020, from a total of 216,878 patients with a COVID-19 encounter, 27,589 inpatient case-patients and 46,857 outpatient case-patients were matched with their respective control-patients based on patient demographics, clinical factors, facility characteristics, and month of index encounter (Table 1). Among the 27,589 inpatient match pairs, 305 match-pairs were in children (aged <18 years) and 27,284 match-pairs were in adults (aged ≥18 years). Among the 46,857 outpatient match pairs, 2,368 match-pairs were in children and 44,489 match-pairs were in adults.

For adults, the incidence of post-COVID conditions was predominantly in the 31–60-day range rather than in the 61–90- or 91–120-day ranges. Adults with an initial inpatient COVID-19 encounter were significantly more likely to experience the following diagnoses in the 31-60 days after discharge compared to hospitalized adults without COVID-19: non-specific chest pain (aOR = 1.3; 95% CI = 1.0 – 1.7), respiratory system symptoms (aOR = 1.4; 95% CI = 1.1 – 1.8), circulatory system symptoms (aOR = 1.3; 95% CI = 1.1 – 1.7), and nervous system symptoms (aOR = 1.3; 95% CI = 1.1 – 1.6) (Table 2). Among 27,284 inpatient adult case-patients, 7.0%

newly experienced one or more of five identified most common post-COVID conditions during 31–120 days: respiratory symptoms (e.g. shortness of breath), nervous system symptoms (e.g. altered mental status), urinary tract infections, circulatory symptoms (e.g. tachycardia), and nonspecific chest pain (Table 3). Outpatient adult case-patients were more likely to experience a range of diagnoses corresponding to multiple body systems compared to outpatient adult control-patients (Table 2). During 31–60 days, adults with an outpatient index encounter for COVID-19 were more likely than outpatient control-patients to experience acute pulmonary embolism (aOR = 2.8; 95% CI = 1.3 – 6.0). During 31–120 days, 7.7% of 44,489 adults with an initial outpatient encounter for COVID-19 newly experienced one or more of ten identified post-COVID conditions: respiratory symptoms (e.g. shortness of breath), abdominal pain and other digestive/abdominal symptoms (e.g. diarrhea), nonspecific chest pain, nervous system symptoms (e.g. altered mental status), headache (including migraine), circulatory symptoms (e.g. tachycardia), fluid and electrolyte disorders (e.g. hypokalemia), malaise and fatigue, nausea and vomiting, and urinary tract infections (Table 3). Among 44,489 adult case-patients with an outpatient index encounter, 1,222 (2.8%) were later hospitalized during 31–120 days with the most common diagnoses including pneumonia and fluid and electrolyte disorders (Table 4).

Children with COVID-19 were not more likely to experience new diagnoses than children without COVID-19. The results of the sensitivity analysis that restricted the control cohort to adult control-patients with a respiratory CCSR category during the index encounter were consistent with the study findings with identification of new diagnoses in multiple body systems for adult case-patients.

Discussion

Among 27,284 inpatient adults and 44,489 outpatient adults who had a diagnosis of COVID-19, 7.0% and 7.7%, respectively, were newly diagnosed with one or more identified post-COVID conditions (31–120 days following their initial COVID-19 encounter as defined above) in a large administrative all-payer database. Children with COVID-19 were not more likely to experience post-COVID conditions than children without COVID-19. Because this study compared COVID-19 case-patients with control-patients who did not have COVID-19, it is probable that the identified post-COVID conditions in adults are related to COVID-19 rather than to other factors such as age or care setting. Furthermore, the findings of a sensitivity analysis suggest excess risk for adult patients with COVID-19 for experiencing conditions in multiple body systems, compared to adults with other respiratory diseases.

Other researchers have found evidence of continued COVID-19 illness or of a post-acute COVID-19 syndrome (2–5), with conditions that affect multiple body systems (16–18). A proposed population-based framework defined acute SARS-CoV-2 infection during days 0–14 after symptom onset, post-acute hyperinflammatory illness during days 14–30 after symptom onset, and late sequelae at >30 days from symptom onset (6). This study supports the existence of post-COVID conditions that might start after 30 days among some adults diagnosed with COVID-19.

Hypercoagulability and thromboembolic disorders have been reported following COVID-19 (1). In this study, inpatient adult case-patients with COVID-19 were not more likely to experience acute pulmonary embolism than control-patients after 31 days. During 31–60 days after the index encounter, non-pregnant adult patients with outpatient COVID-19 encounters were 2.8 times as likely as outpatient control-patients to experience acute

pulmonary embolism; acute pulmonary embolism continued to be more than two times as likely during 61–90 days. Most adults with outpatient COVID-19 encounters did not progress to moderate/severe acute disease (requiring subsequent inpatient care), although they were more likely than control-patients to experience a range of additional conditions involving multiple body systems (e.g. nonspecific chest pain, fatigue, headache, and respiratory, nervous, circulatory, and gastrointestinal system symptoms). Patients with an index inpatient encounter experienced a more limited list of new conditions compared to control-patients. This could be due to post-COVID conditions emerging during the initial hospitalization or due to similarities in new conditions that may have been experienced by both inpatient case-patients and inpatient control-patients following hospital discharge. Hospitalized adults might experience other persistent and new conditions (4) after hospital discharge that might last for months (3). Of note, both patients with an index inpatient or outpatient COVID-19 encounter were more likely to be diagnosed with nonspecific chest pain and neurological, circulatory, and respiratory symptoms in the post-acute period, though the timelines for experiencing these new symptoms may not align between inpatients and outpatients because of the different index encounter date reference points. Post-COVID conditions might arise through several mechanisms and might reflect effects of COVID-19 treatment and procedures, organ damage from the acute infection phase, manifestations of a persistent hyperinflammatory state, or an inadequate antibody response, or other unknown factors (19). Future analyses could assess possible predictors of post-COVID conditions and persistent symptoms, including underlying medical conditions (e.g. HIV, diabetes, or smoking), length of stay for initial hospitalization, additional markers of COVID-19 severity (e.g. ICU admission or mechanical ventilation), demographic factors,

and pregnancy and postpartum status. Future prospective studies could further describe symptoms recorded as post-COVID conditions.

The findings in this report are subject to at least six limitations. First, because the study relied on health care encounter information it might be subject to information bias and might not fully reflect hospitalization acuity or exact timing of condition onset. Patients with minor to moderate symptoms without COVID-19 might be less likely than patients with COVID-19 to seek care for multiple reasons, including fear of SARS-CoV-2 exposure in a medical facility, causing potential overestimation of odds ratios for post-COVID conditions. As COVID-19 is a novel disease, there may be additional reasons that health care providers would arrange for follow up encounters with their patients who experienced COVID-19 compared to patients without COVID-19. Second, potential misclassification among case-patients and control-patients could have occurred because of use of ICD-10-CM codes rather than laboratory data (20). Third, there could be changes in diagnostic or treatments patterns overtime that could have affected the incidence of new conditions. Fourth, these findings were not representative of all patients with SARS-CoV-2 infection or COVID-19 disease; recent surveys in the United Kingdom suggest that 14% of patients who tested positive for SARS-CoV-2 infection still had symptoms at 12 weeks, suggesting that additional persistent symptoms might exist that start at the time of acute infection (21). Persistent symptoms, starting at the time of acute disease were not assessed in this analysis. Individual patients might experience significant additional new conditions (22) as well as rare complications that were not represented within these findings (2,5), and some symptoms (e.g. cognitive impairment or post-exertional malaise) and conditions might not be well captured by ICD-10-CM codes. Fifth, this study included 2,673 children, nearly 90% of whom presented with an index outpatient encounter; studies with a larger pediatric population

might find associated post-COVID conditions in children that were not found in this study, such as multisystem inflammatory syndrome in children (22) or other post-COVID conditions. Finally, if patients did not seek healthcare services or if patients received care outside of hospitals submitting data to PHD-SR, information about their conditions were not captured, leading to potential missing data about prior or subsequent health conditions.

These findings suggest that at least 7.0% of adults after an initial inpatient COVID-19 encounter and 7.7% of adults after an initial outpatient COVID-19 encounter might newly experience certain late health conditions possibly related to COVID-19. Further studies for identifying, quantifying, and understanding post-COVID conditions are important for alerting and guiding clinicians on appropriate follow-up treatment plans for patients following a COVID-19 diagnosis. Clinicians might consider discussing signs and symptoms of thromboembolism and particularly acute pulmonary embolism, advising adult patients of what to be aware of and when to seek medical care (24). These findings add to the evidence of COVID-19 late sequelae for some adults and can inform clinical practice, research, and public health priorities, such as health care utilization and planning considerations beyond acute care. Increased awareness of the needed resources for follow-up care of patients with COVID-19, along with continued focus on SARS-CoV-2 infection prevention and vaccination strategies, is essential.

Acknowledgments/Conflicts:

John House, Premier Inc.; members of the CDC COVID-19 Response Data, Analytics, and

Visualization Task Force; members of the CDC COVID-19 Response Data Health Systems and

Worker Safety Task Force; members of the CDC Long COVID Community of Practice

Accepted Manuscript

References

1. Del Rio C, Collins LF, Malani P. Long-term Health Consequences of COVID-19. *JAMA*. 2020;324(17):1723–4.
2. Assaf G, Davis H, McCorkell L, et al. What does COVID-19 recovery actually look like? An analysis of the prolonged COVID-19 symptoms survey by Patient-Led Research Team. Patient Led Research for COVID-19. 2020.
<https://patientresearchcovid19.com/research/report-1/>.
3. Carfi A, Bernabei R, Landi F; Gemelli Against COVID-19 Post-Acute Care Study Group. Persistent symptoms in patients after acute COVID-19. *JAMA* 2020;324:603–5.
4. Halpin SJ, McIvor C, Whyatt G, et al. Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: A cross-sectional evaluation. *J Med Virol* 2021;93:1013–22.
5. Tenforde MW, Kim SS, Lindsell CJ, et al. Symptom duration and risk factors for delayed return to usual health among outpatients with COVID-19 in a multistate health care systems network—United States, March–June 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:993–8.
6. Datta SD, Talwar A, Lee JT. A proposed framework and timeline of the spectrum of disease due to SARS-CoV-2 infection: illness beyond acute infection and public health implications. *JAMA* 2020;324(22):2251–2.
7. Editorial. Facing up to Long COVID. *Lancet* 2020. 2020;396:1861.

8. Data in PHD-SR, formerly known as the PHD COVID-19 Database, are released every 2 weeks; release date October 20, 2020, access date October 21, 2020.
http://offers.premierinc.com/rs/381-NBB-525/images/PHD_COVID-19_White_Paper.pdf
9. Centers for Disease Control and Prevention. New ICD-10-CM code for the 2019 novel coronavirus (COVID-19), April 1, 2020.2020. Accessed online on October 6, 2020 at:
<https://www.cdc.gov/nchs/data/icd/Announcement-New-ICD-code-for-coronavirus-3-18-2020.pdf>
10. Baek S, Park SH, Won E, et al. Propensity score matching: a conceptual review for radiology researchers. Korean J Radiol. 2015 Mar-Apr;16(2):286-96.
11. SAS Institute Inc. 2016. SAS/STAT® 14.2 User's Guide. Cary, NC: SAS Institute Inc. Accessed online on January 20, 2020 at:
<https://support.sas.com/documentation/onlinedoc/stat/142/psmatch.pdf>
12. Ray WA, Murray KT, Hall K, et al. Azithromycin and the risk of cardiovascular death. N Engl J Med. 2012 May 17;366(20):1881-90.
13. AHRQ Clinical Classifications Software Refined (CCSR). Accessed online on December 14, 2020 at: https://www.hcup-us.ahrq.gov/toolssoftware/ccsr/ccs_refined.jsp
14. Olsen SJ, Azziz-Baumgartner E, Budd AP, et al. Decreased Influenza Activity During the COVID-19 Pandemic - United States, Australia, Chile, and South Africa, 2020. MMWR Morb Mortal Wkly Rep. 2020 Sep 18;69(37):1305-1309.
15. Czeisler MÉ, Marynak K, Clarke KEN, et al. Delay or Avoidance of Medical Care Because of COVID-19-Related Concerns - United States, June 2020. MMWR Morb Mortal Wkly Rep. 2020 Sep 11;69(36):1250-1257.

16. Zhao YM, Shang YM, Song WB, et al. Follow-up study of the pulmonary function and related physiological characteristics of COVID-19 survivors three months after recovery. *EClinicalMedicine* 2020;25:100463.
17. Puntmann VO, Carerj ML, Wieters I, et al. Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from coronavirus disease 2019 (COVID-19). *JAMA Cardiol* 2020;5(11):1265–73.
18. Lavery AM, Preston LE, Ko JY, et al. Characteristics of hospitalized COVID-19 patients discharged and experiencing same-hospital readmission—United States, March–August 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:1695–9.
19. Centers for Disease Control and Prevention. Post-COVID Conditions, Apr. 8, 2021. Accessed online on April 11, 2021 at: <https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects.html>
20. Kadri SS, Gundrum J, Warner S, et al. Uptake and Accuracy of the Diagnosis Code for COVID-19 among US Hospitalizations. *JAMA*. 2020 Dec 22;324(24):2553-2554.
21. Office for National Statistics. Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK: 1 April 2021. Accessed online on April 11, 2021 at: <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/1april2021>
22. COVID Symptom Study. How long does COVID-19 last? Kings College London, 2020. Accessed online on December 14, 2020 at: https://covid19.joinzoe.com/post/covid-long-term?fbclid=IwAR1RxlcmmdL-Efjh_al-

23. Centers for Disease Control and Prevention. Multisystem Inflammatory Syndrome in Children (MIS-C), Nov. 13, 2020. Accessed online on February 15, 2020 at: <https://www.cdc.gov/mis-c/index.html>

24. Centers for Disease Control and Prevention. Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19), Dec. 8, 2020. Accessed online on January 20, 2020 at: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>

Accepted Manuscript

TABLE 1: Characteristics of patients with COVID-19 (case-patients) compared with propensity-matched* patients without COVID-19 disease (control-patients), stratified by age group (<18 years, ≥18 years) and index encounter facility setting, from a large administrative all-payer database — United States, March 1–June 30, 2020

	No. (%)							
	27,589 inpatient match-pairs				46,857 outpatient match-pairs			
	Index inpatient encounter [†] in children <18 years		Index inpatient encounter [†] in adults ≥18 years		Index outpatient encounter [†] in children <18 years		Index outpatient encounter [†] in adults ≥18 years	
	Case-patients (N = 305)	Control-patients (N = 305)	Case-patients (N = 27,284)	Control-patients (N = 27,284)	Case-patients (N = 2,368)	Control-patients (N = 2,368)	Case-patients (N = 44,489)	Control-patients (N = 44,489)
Propensity score* (mean ± standard deviation)	0.92 ± 0.07	0.92 ± 0.07	0.78 ± 0.18	0.78 ± 0.18	0.96 ± 0.04	0.96 ± 0.04	0.95 ± 0.06	0.95 ± 0.06
Characteristics								
Demographic characteristics								
Age in years								
≤1	129 (42.3)	120 (39.3)	--	--	638 (26.9)	622 (26.3)	--	--
2–11	97 (31.8)	106 (34.8)	--	--	833 (35.2)	891 (37.6)	--	--
12–17	79 (25.9)	79 (25.9)	--	--	897 (37.9)	855 (36.1)	--	--
18–39	--	--	2,392 (8.8)	2,855 (10.5)	--	--	15,896 (35.7)	16,272 (36.6)
40–49	--	--	2,732 (10.0)	2,419 (8.9)	--	--	8,033 (18.1)	7,282 (16.4)
50–64	--	--	7,652 (28.1)	7,256 (26.6)	--	--	11,542 (25.9)	11,510 (25.9)
65–74	--	--	6,040 (22.1)	5,884 (21.6)	--	--	4,578 (10.3)	5,374 (12.1)
75–84	--	--	4,919 (18.0)	5,225 (19.2)	--	--	2,673 (6.0)	3,014 (6.8)
≥85	--	--	3,549 (13.0)	3,645 (13.4)	--	--	1,767 (4.0)	1,037 (2.3)
Race/Ethnicity								
White, non-Hispanic	82 (26.9)	96 (31.5)	13,140 (48.2)	12,890 (47.2)	488 (20.6)	491 (20.7)	17,021 (38.3)	16,665 (37.5)
Black, non-	73 (23.9)	65 (21.3)	7,049	7,207 (26.4)	522 (22.0)	495 (20.9)	10,867	11,187

Hispanic			(25.8)				(24.4)	(25.2)
Asian, non-Hispanic	92 (30.2)	92 (30.2)	614 (2.3)	580 (2.1)	41 (1.7)	31 (1.3)	1,046 (2.4)	1,064 (2.4)
Hispanic	43 (14.1)	41 (13.4)	3,621 (13.3)	3,756 (13.8)	1,022 (43.2)	1,050 (44.3)	10,868 (24.4)	10,843 (24.4)
Other, non-Hispanic	15 (4.9)	11 (3.6)	2,860 (10.5)	2,851 (10.5)	295 (12.5)	301 (12.7)	4,687 (10.5)	4,730 (10.6)
Sex								
Female	133 (43.6)	136 (44.6)	14,313 (52.5)	14,340 (52.6)	1,196 (50.5)	1,247 (52.7)	27,225 (61.2)	27,048 (60.8)
Male	172 (56.4)	169 (55.4)	12,958 (47.5)	12,939 (47.4)	1,171 (49.5)	1,120 (47.3)	17,220 (38.7)	17,413 (39.1)
Insurance status								
Medicare	1 (0.33)	3 (1.0)	16,150 (59.2)	16,088 (59.0)	17 (0.72)	21 (0.90)	10,483 (23.6)	10,390 (23.4)
Medicaid	223 (73.1)	212 (69.5)	4,725 (17.3)	4,779 (17.5)	1,783 (75.3)	1,821 (76.9)	10,632 (23.9)	10,769 (24.2)
Commercially insured	73 (23.9)	82 (26.9)	5,107 (18.7)	5,148 (18.9)	455 (19.2)	422 (17.8)	17,426 (39.2)	17,228 (38.7)
Other	6 (2.0)	10 (3.3)	1,302 (4.8)	1,269 (4.7)	113 (4.8)	104 (4.4)	5,948 (13.4)	6,102 (13.7)
Clinical characteristics^s								
≥1 hospitalization prior to index encounter	190 (62.3)	178 (58.4)	12,218 (44.8)	13,241 (48.5)	481 (20.3)	490 (20.7)	6,903 (15.5)	7,317 (16.5)
Encounters prior to index encounter; median (IQR)	2.0 (1–5)	2.0 (1–4)	2.0 (1–5)	2.0 (1–5)	2.0 (1–3)	2.0 (1–3)	2.0 (1–4)	2.0 (1–5)
Length of stay; median (IQR)	3 (2–6)	2 (1–5)	6 (3–11)	4 (2–6)	--	--	--	--
Intensive care unit (ICU) admissions	99 (32.5)	94 (30.8)	10,812 (39.6)	10,940 (40.1)	--	--	--	--
≥1 encounter 1–120 days after index encounter	129 (42.3)	103 (33.8)	12,376 (45.4)	12,365 (45.3)	711 (30.0)	629 (26.6)	21,084 (47.4)	18,883 (42.4)
≥1 encounter 31–120 days after index encounter	94 (30.8)	69 (22.6)	8,917 (32.7)	9,180 (33.7)	428 (18.1)	412 (17.4)	12,926 (29.1)	13,894 (31.2)
≥1 hospitalization 1–120 days after index encounter	38 (12.5)	36 (11.8)	5,144 (18.9)	5,541 (20.3)	24 (1.0)	30 (1.3)	3,968 (8.9)	1,710 (3.8)
≥1 hospitalization 31–120 days after index encounter	27 (8.9)	22 (7.2)	3,171 (11.6)	3,736 (13.7)	14 (0.6)	15 (0.6)	1,222 (2.8)	1,069 (2.4)
Deaths 1–120 days following index encounter	1 (0.3)	2 (0.7)	1224 (4.5)	641 (2.4)	0 (0)	1 (0.04)	311 (0.7)	65 (0.2)
Deaths 31–120 days following index encounter	0 (0)	1 (0.3)	257 (0.9)	282 (1.0)	0 (0)	0 (0)	74 (0.2)	33 (0.07)
Facility characteristics								

Region[†]								
Northeast	98 (32.1)	93 (30.5)	10,072 (36.9)	10,424 (38.2)	261 (11.0)	255 (10.8)	9,864 (22.2)	10,019 (22.5)
Midwest	49 (16.1)	43 (14.1)	6,693 (24.5)	6,421 (23.5)	384 (16.2)	361 (15.2)	10,028 (22.5)	9,889 (22.2)
South	143 (46.9)	149 (48.9)	8,487 (31.1)	8,384 (30.7)	1,550 (65.5)	1,564 (66.1)	20,569 (46.2)	20,495 (46.1)
West	15 (4.9)	20 (6.6)	2,032 (7.5)	2,055 (7.5)	173 (7.3)	188 (7.9)	4,028 (9.1)	4,086 (9.2)
Urban/Rural								
Urban	281 (92.1)	267 (87.5)	25,112 (92.0)	25,136 (92.1)	2,041 (86.2)	2,036 (86.0)	38,492 (86.5)	38,549 (86.7)
Rural	24 (7.9)	38 (12.5)	2,172 (8.0)	2,148 (7.9)	327 (13.8)	332 (14.0)	5,997 (13.5)	5,940 (13.4)
Index encounter[†] date (month)								
March	93 (30.5)	96 (31.5)	3,779 (10.2)	2,760 (10.1)	121 (5.1)	144 (6.1)	3,137 (7.1)	3,322 (7.5)
April	71 (23.3)	61 (20.0)	10,530 (38.6)	10,388 (38.1)	329 (13.9)	281 (11.9)	12,505 (28.1)	12,570 (28.3)
May	86 (28.2)	90 (29.5)	8,175 (30.0)	8,182 (30.0)	639 (27.0)	610 (25.8)	11,834 (26.6)	11,932 (26.8)
June	55 (18.0)	58 (19.0)	5,800 (21.3)	5,954 (21.8)	1,279 (54.0)	1,333 (56.3)	17,013 (38.2)	16,665 (37.5)

* Propensity score matching is a statistical technique used to achieve an even distribution of patient characteristics among case and control groups in order to compare two groups in an observed (non-randomized) population. In this analysis, propensity score matching was used to better isolate the effect of COVID-19 on the patient experiencing new conditions from the effect of other included variables. Case-patients and control-patients were matched on patient demographics (age, sex, race, ethnicity, insurance status), clinical factors (number of previous inpatient encounters and diagnoses before and at the index encounter), facility characteristics (urbanicity, region), and month of the index encounter. The presented propensity score is a measure of the mean \pm standard deviation for each of the individual propensity scores of the case-patients and control-patients. A similar propensity score between case-patients and control-patients indicates that the variables used to construct the propensity score have a similar distribution in case-patients and control-patients.

[†]For case-patients, an index encounter was defined as the initial encounter with a COVID-19 diagnosis during March–June 2020. For control-patients, an index encounter was defined as the patient’s propensity matched encounter that was used for comparison, during March–June 2020. For an inpatient encounter, the hospital discharge date was assigned as time 0. For an outpatient encounter, the encounter date was assigned as time 0. For case-patients and control-patients, historical data from January 2019 to the index encounter date was used for encounter information preceding the index encounter. All case-patients and control-patients included in this analysis had at least one encounter preceding their index encounter recorded in the large administrative all-payer database.

[§] Number of previous inpatient encounters and underlying and index encounter conditions are not presented in the table. Underlying and index encounter conditions were matched between case-patients and control-patients by disease category so that case-patients and control-patients had similar baseline and presenting conditions. The following variables were not included in the match, however they were included in the table to provide additional context on clinical characteristics of the case-patients and control-patients: number of patients with ≥ 1 hospitalization prior to an index encounter, number of encounters prior to the index encounter, number of patients with ≥ 1 encounter during 1–120 days after the index encounter, number of patients with ≥ 1 encounter during 31–120 days after the index encounter, length of stay (for index inpatient encounters), intensive care unit (ICU) admissions (for index inpatient encounter), deaths during 1–120 following index encounter, and deaths during 31–120 days after the index encounter. It is possible that birth hospitalization data may impact the measure of past hospitalizations for children.

[¶]*Northeast*: Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont; *Midwest*: Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, Wisconsin; *South*: Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, West Virginia; *West*: Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, Wyoming.

Table 2. Association between COVID-19 diagnosis and receiving a diagnosis of a new condition* in adult (aged ≥18 years) case-patients compared with matched control-patients, over time[†] (31–60, 61–90 and 91–120 days from index encounter[§]), stratified by index encounter care setting, from a large administrative all-payer database — United States, March 1–June 30, 2020

Patient category/body system/CCSR Categories	Adjusted Odds Ratio (95% CI) [¶]			
	1–30 days	31–60 days**	61–90 days**	91–120 days**
Inpatient index encounter (Hospital Discharge Date): Case-patients N = 27,284; Control-patients N = 27,284				
Blood				
Coagulation and hemorrhagic disorders	1.3 (1.0–1.6)	1.3 (0.95–1.7)	0.65 (0.46–0.90)	0.66 (0.45–0.97)
Circulatory				
Nonspecific chest pain	1.2 (0.97–1.5)	1.3 (1.0–1.7)	0.86 (0.65–1.1)	0.77 (0.58–1.0)
Circulatory signs and symptoms	1.1 (0.88–1.3)	1.3 (1.1–1.7)	0.78 (0.60–1.0)	0.72 (0.54–0.96)
Acute pulmonary embolism	1.5 (1.0–2.1)	1.4 (0.93–2.1)	1.2 (0.72–1.9)	1.2 (0.70–2.1)
Endocrine				
Malnutrition	1.4 (1.1–1.7)	1.2 (0.90–1.5)	1.2 (0.89–1.6)	1.1 (0.82–1.6)
Genitourinary				
Hematuria	0.87 (0.61–1.3)	1.5 (1.0–2.1)	1.4 (0.88–2.1)	1.1 (0.76–1.7)
Acute and unspecified renal failure	1.3 (1.0–1.6)	0.74 (0.56–0.99)	0.67 (0.48–0.92)	0.56 (0.39–0.80)
Infectious				
Fungal infections	1.2 (0.90–1.6)	1.5 (1.1–2.2)	1.0 (0.67–1.5)	1.1 (0.69–1.7)
Urinary tract infections	1.1 (0.88–1.4)	1.3 (1.0–1.7)	1.2 (0.93–1.6)	0.99 (0.76–1.3)
Other specified upper respiratory infections	1.1 (0.69–1.9)	1.8 (1.0–3.3)	--	--
Bacterial infections	1.7 (1.4–2.1)	1.1 (0.82–1.4)	0.97 (0.72–1.3)	1.1 (0.75–1.5)
Septicemia	1.8 (1.5–2.2)	1.2 (0.95–1.6)	0.81 (0.60–1.1)	0.94 (0.66–1.3)
Nervous system				
Nerve and nerve root disorders	--	2.2 (1.1–4.2)	1.4 (0.76–2.5)	--
Nervous system signs and symptoms	1.1 (0.89–1.3)	1.3 (1.1–1.6)	0.90 (0.70–1.1)	1.1 (0.86–1.5)
Myopathies	5.9 (2.8–12.4)	--	--	--
Neurocognitive disorders	1.6 (1.2–2.1)	1.2 (0.87–1.7)	1.1 (0.77–1.6)	1.1 (0.72–1.7)
Psychiatric				
Symptoms of mental and substance use conditions	2.0 (1.3–3.2)	1.3 (0.79–2.3)	0.65 (0.38–1.1)	1.0 (0.58–1.9)
Respiratory				
Respiratory signs and symptoms	1.4 (1.2–1.6)	1.4 (1.1–1.8)	1.2 (0.95–1.6)	1.3 (0.99–1.8)
Other specified and unspecified lower respiratory disease	1.7 (1.3–2.3)	1.8 (1.3–2.5)	1.6 (1.1–2.3)	1.5 (0.99–2.2)
Pneumonia (except that caused by tuberculosis)	5.5 (4.1–7.5)	1.3 (0.89–2.0)	0.88 (0.53–1.5)	1.0 (0.58–1.9)
Respiratory failure; insufficiency; arrest	3.3 (2.6–4.1)	1.0 (0.70–1.4)	0.93 (0.65–1.3)	0.73 (0.47–1.1)
Skin				
Pressure ulcer of skin	1.2 (0.92–1.6)	1.4 (1.1–1.9)	1.1 (0.82–1.5)	0.99 (0.72–1.4)
Other				
Diseases of mouth; excluding dental	1.4 (0.90–2.3)	2.5 (1.3–4.6)	1.5 (0.85–2.6)	--
Dysphagia	1.4 (1.1–1.8)	1.3 (1.0–1.8)	1.2 (0.83–1.6)	0.83 (0.56–1.2)

Fluid and electrolyte disorders	1.6 (1.3–2.1)	0.90 (0.63–1.3)	1.0 (0.68–1.5)	0.77 (0.52–1.2)
Shock	1.6 (1.3–2.0)	1.1 (0.84–1.5)	0.83 (0.58–1.2)	0.69 (0.47–1.0)
Outpatient index encounter (Encounter Date): Case-patients N = 44,489; Control-patients N = 44,489				
Blood				
Aplastic anemia	2.9 (2.4–3.5)	1.4 (1.1–1.8)	1.4 (1.1–1.8)	1.2 (0.90–1.6)
Acute posthemorrhagic anemia	1.9 (1.3–2.7)	1.9 (1.1–3.4)	1.0 (0.6–1.8)	--
Coagulation and hemorrhagic disorders	3.9 (3.0–5.0)	2.2 (1.4–3.5)	1.6 (1.0–2.6)	0.75 (0.46–1.2)
Nutritional anemia	1.4 (1.1–1.8)	1.3 (0.90–1.8)	1.4 (1.0–2.0)	0.95 (0.67–1.4)
Diseases of white blood cells	2.8 (2.3–3.5)	1.2 (0.8–1.7)	0.95 (0.65–1.4)	1.1 (0.80–1.6)
Circulatory				
Acute pulmonary embolism	5.2 (3.3–8.1)	2.8 (1.3–6.0)	2.3 (1.1–4.8)	--
Nonspecific chest pain	2.6 (2.2–3.0)	1.9 (1.5–2.3)	1.5 (1.2–1.9)	1.3 (1.0–1.6)
Heart failure	2.1 (1.6–2.8)	1.5 (1.1–2.1)	0.88 (0.61–1.3)	1.1 (0.70–1.6)
Circulatory signs and symptoms	2.3 (2.0–2.8)	1.5 (1.2–1.8)	1.0 (0.80–1.3)	0.98 (0.76–1.28)
Essential Hypertension	2.3 (2.0–2.8)	1.1 (0.90–1.4)	1.1 (0.90–1.5)	0.88 (0.67–1.16)
Hypertension with complications and secondary hypertension	2.1 (1.7–2.6)	1.3 (1.0–1.8)	1.2 (0.90–1.6)	0.97 (0.67–1.39)
Acute myocardial infarction	2.9 (1.9–4.6)	--	1.5 (0.8–3.1)	--
Conduction disorders	1.9 (1.4–2.6)	1.0 (0.70–1.6)	0.94 (0.57–1.5)	0.81 (0.5–1.3)
Cardiac dysrhythmias	2.4 (1.9–3.0)	1.0 (0.8–1.4)	1.2 (0.80–1.7)	1.2 (0.80–1.7)
Cardiac arrest and ventricular fibrillation	2.9 (1.7–4.7)	--	--	--
Hypotension	3.4 (2.5–4.4)	1.4 (0.90–2.0)	0.93 (0.60–1.4)	1.6 (0.90–2.8)
Acute phlebitis; thrombophlebitis and thromboembolism	3.7 (2.4–5.6)	1.7 (0.90–2.9)	1.1 (0.60–2.0)	1.3 (0.70–2.5)
Myocarditis and cardiomyopathy	1.5 (1.0–2.1)	0.7 (0.43–1.2)	0.76 (0.44–1.3)	0.82 (0.47–1.4)
Coronary atherosclerosis and other heart disease	1.4 (1.1–1.7)	0.83 (0.62–1.1)	0.88 (0.63–1.2)	1 (0.70–1.4)
Pulmonary heart disease	1.5 (1.0–2.2)	0.70 (0.41–1.2)	0.96 (0.57–1.6)	--
Sequela of cerebral infarction and other cerebrovascular disease	2.8 (1.5–5.1)	--	--	--
Other specified and unspecified circulatory disease	1.5 (1.1–2.3)	1.1 (0.70–1.9)	1.4 (0.80–2.3)	1.1 (0.60–2.0)
Gastrointestinal				
Nausea and vomiting	2.3 (2.0–2.8)	1.3 (1.0–1.7)	0.93 (0.74–1.2)	1.0 (0.80–1.4)
Intestinal obstruction and ileus	1.3 (0.80–1.9)	1.8 (1.1–3.2)	--	--
Abdominal pain and other digestive/abdomen signs and symptoms	2.1 (1.8–2.5)	1.3 (1.0–1.6)	0.92 (0.76–1.1)	0.93 (0.75–1.2)
Esophageal disorders	2.0 (1.7–2.3)	1.0 (0.80–1.3)	1.0 (0.80–1.2)	0.82 (0.64–1.1)
Diverticulosis and diverticulitis	1.5 (1.1–1.9)	0.74 (0.50–1.1)	1.1 (0.70–1.5)	1.1 (0.70–1.6)
Hemorrhoids	1.7 (1.3–2.2)	0.60 (0.39–0.91)	0.96 (0.64–1.4)	1.0 (0.60–1.6)
Hepatic failure	2.1 (1.1–3.8)	--	--	--
Gastrointestinal hemorrhage	1.5 (1.2–2.0)	1.4 (1.0–2.1)	0.7 (0.46–1.05)	1.1 (0.70–1.7)
Pancreatic disorders (excluding diabetes)	2.2 (1.3–3.7)	1.9 (1.0–3.5)	--	--
Other specified and unspecified gastrointestinal disorders	1.8 (1.5–2.2)	1.1 (0.8–1.4)	0.81 (0.60–1.1)	0.86 (0.62–1.2)
Ear				
Otitis media	2.4 (1.2–4.7)	--	--	--
Hearing loss	2.3 (1.5–3.7)	1.3 (0.70–2.4)	--	--
Endocrine				

Malnutrition	3.8 (2.7–5.4)	2.5 (1.5–4.2)	1.5 (0.90–2.5)	2.0 (1.1–3.5)
Diabetes mellitus with complication	2.9 (2.4–3.6)	1.6 (1.2–2.2)	1.3 (0.90–1.7)	1.1 (0.80–1.6)
Diabetes mellitus without complication	2.0 (1.6–2.5)	1.1 (0.80–1.5)	0.93 (0.67–1.3)	1.0 (0.70–1.5)
Thyroid disorders	1.6 (1.3–2.0)	1.1 (0.80–1.5)	1.3 (1.0–1.8)	1.1 (0.80–1.5)
Nutritional deficiencies	1.3 (1.0–1.7)	0.91 (0.65–1.3)	0.86 (0.62–1.2)	0.71 (0.49–1.0)
Obesity	2.8 (2.4–3.3)	1.2 (0.90–1.5)	1.0 (0.80–1.3)	0.90 (0.68–1.2)
Disorders of lipid metabolism	2.1 (1.8–2.5)	1.2 (0.90–1.5)	1.3 (1.0–1.6)	1.1 (0.90–1.5)
Pituitary disorders	2.1 (1.2–3.9)	--	--	--
Other specified and unspecified nutritional and metabolic disorders	2.8 (2.3–3.5)	1.2 (0.90–1.6)	0.78 (0.56–1.1)	1.1 (0.80–1.6)
Other specified and unspecified endocrine disorders	1.5 (1.0–2.1)	1.3 (0.80–2.0)	0.84 (0.51–1.4)	1.0 (0.60–1.6)
Eye				
Glaucoma	4.1 (2.1–8.2)	--	--	--
Genitourinary				
Inflammatory diseases of female pelvic organs	0.86 (0.55–1.3)	1.7 (1.0–2.6)	1.1 (0.70–1.8)	1.2 (0.70–2.1)
Acute and unspecified renal failure	4.1 (3.4–5.0)	1.2 (0.90–1.6)	1.3 (0.90–1.8)	1 (0.7–1.5)
Chronic kidney disease	2.5 (1.9–3.2)	1.3 (0.90–1.9)	1.1 (0.80–1.6)	0.96 (0.64–1.43)
Hematuria	1.4 (1.0–2.0)	1.3 (0.90–2.0)	0.67 (0.46–0.99)	1.4 (0.90–2.2)
Hyperplasia of prostate	2.1 (1.5–2.8)	0.97 (0.60–1.6)	1.4 (0.90–2.2)	1.5 (0.80–2.8)
Menopausal disorders	2.9 (2.1–4.1)	1.5 (0.90–2.5)	1.3 (0.80–2.0)	1.0 (0.60–1.8)
Urinary incontinence	1.9 (1.2–3.1)	1.3 (0.70–2.5)	--	--
Genitourinary signs and symptoms	1.6 (1.3–2.0)	1.2 (0.90–1.6)	0.92 (0.69–1.2)	0.99 (0.74–1.3)
Infectious				
Bacterial infections	5.5 (4.6–6.6)	1.7 (1.3–2.2)	1.5 (1.1–2.0)	1.6 (1.1–2.2)
Septicemia	9.2 (7.2–11.9)	2.0 (1.3–2.8)	1.7 (1.1–2.6)	1.9 (1.2–2.9)
Urinary tract infections	1.9 (1.6–2.3)	1.5 (1.2–1.9)	1.4 (1.1–1.9)	1.4 (1.0–1.8)
Other specified upper respiratory infections	3.1 (2.4–3.9)	1.6 (1.1–2.2)	1.2 (0.80–1.7)	1.1 (0.80–1.7)
Fungal infections	1.7 (1.1–2.4)	1.3 (0.80–2.0)	0.98 (0.63–1.5)	0.85 (0.51–1.4)
Intestinal infection	3.8 (2.3–6.1)	--	--	--
Parasitic, other specified and unspecified infections	2.0 (1.1–3.5)	1.1 (0.60–2.0)	--	--
Psychiatric				
Anxiety and fear-related disorders	2.2 (1.9–2.6)	1.3 (1.0–1.6)	0.93 (0.72–1.2)	0.81 (0.63–1.0)
Depressive disorders	2.1 (1.8–2.6)	1.0 (0.80–1.4)	0.97 (0.72–1.3)	0.76 (0.55–1.1)
Opioid-related disorders	2.3 (1.4–3.6)	--	--	--
Trauma and stressor-related disorders	2.3 (1.5–3.4)	0.94 (0.59–1.5)	1.1 (0.60–1.9)	--
Sedative-related disorders	3.7 (1.6–8.6)	--	--	--
Symptoms of mental and substance use conditions	1.9 (1.1–3.1)	--	--	--
Musculoskeletal				
Gout	1.6 (1.1–2.5)	1.3 (0.70–2.6)	1.3 (0.60–2.4)	2.2 (1.1–4.5)
Osteoarthritis	1.6 (1.3–2.0)	1.1 (0.80–1.4)	0.81 (0.61–1.1)	0.83 (0.59–1.2)
Paralysis (other than cerebral palsy)	2.3 (1.2–4.3)	--	--	--
Rheumatoid arthritis and related	2.6 (1.5–4.3)	--	--	--

disease				
Musculoskeletal pain, not low back pain	1.2 (1.1–1.4)	0.94 (0.79–1.1)	0.94 (0.79–1.1)	0.93 (0.76–1.1)
Muscle disorders	2.4 (1.6–3.4)	1.0 (0.70–1.6)	1.1 (0.70–1.6)	0.85 (0.53–1.4)
Nervous system				
Headache; including migraine	1.9 (1.6–2.3)	1.3 (1.1–1.7)	0.95 (0.75–1.2)	1.0 (0.80–1.3)
Neurocognitive disorders	6.8 (4.4–10.7)	3.2 (1.9–5.3)	1.7 (1.1–2.7)	2.5 (1.4–4.5)
Nervous system signs and symptoms	1.9 (1.6–2.2)	1.4 (1.1–1.7)	1.0 (0.8–1.2)	1.2 (1.0–1.5)
Other specified nervous system disorders	3.5 (2.8–4.5)	1.2 (0.90–1.7)	1.3 (0.90–1.9)	1.7 (1.1–2.6)
Polyneuropathies	1.9 (1.4–2.6)	1.3 (0.90–1.9)	0.91 (0.60–1.4)	1.1 (0.70–1.7)
Sleep wake disorders	2.2 (1.8–2.7)	1.2 (0.90–1.5)	0.86 (0.65–1.1)	0.92 (0.68–1.3)
Nervous system pain and pain syndromes	1.3 (1.1–1.6)	0.86 (0.65–1.1)	0.71 (0.53–0.96)	0.92 (0.68–1.2)
Epilepsy; convulsions	1.8 (1.2–2.8)	1.1 (0.60–2.0)	1 (0.60–1.8)	1.3 (0.60–2.4)
General sensation/perception signs and symptoms	1.7 (1.4–2.1)	1.2 (0.90–1.6)	0.86 (0.65–1.1)	0.67 (0.49–0.91)
Respiratory				
Pneumonia (except that caused by tuberculosis)	24.9 (20.1–31.0)	4.6 (3.3–6.6)	2.2 (1.5–3.3)	1.2 (0.80–1.8)
Respiratory failure; insufficiency; arrest	19.5 (15.5–24.7)	1.9 (1.3–2.6)	1.8 (1.2–2.7)	1.1 (0.70–1.8)
Respiratory signs and symptoms	4.2 (3.6–5.0)	1.6 (1.3–2.0)	1.1 (0.80–1.4)	1.4 (1.0–1.8)
Asthma	2.3 (1.9–2.9)	1.3 (0.90–1.8)	0.86 (0.60–1.2)	0.71 (0.47–1.1)
Pleurisy, pleural effusion and pulmonary collapse	2.4 (1.9–3.1)	1.3 (0.90–1.9)	0.84 (0.56–1.3)	1.3 (0.80–2.1)
Chronic obstructive pulmonary disease and bronchiectasis	1.7 (1.3–2.2)	0.87 (0.61–1.3)	0.67 (0.44–1.0)	0.68 (0.43–1.1)
Acute bronchitis	2.6 (1.9–3.6)	1.1 (0.60–2.1)	1.2 (0.60–2.1)	--
Pneumothorax	7.3 (3.3–16.1)	--	--	--
Other specified and unspecified lower respiratory disease	4.6 (3.6–6.0)	1.2 (0.81–1.9)	1.2 (0.74–2.0)	1.4 (0.90–2.2)
Skin				
Pressure ulcer of skin	2.9 (1.9–4.6)	1.9 (1.1–3.4)	2.8 (1.5–4.9)	3.0 (1.5–6.1)
Skin/subcutaneous signs and symptoms	1.4 (1.1–1.7)	1.0 (0.80–1.3)	0.93 (0.71–1.2)	0.95 (0.70–1.3)
Other				
Fluid and electrolyte disorders	4.3 (3.8–4.9)	1.6 (1.3–2.0)	1.1 (0.90–1.4)	1.2 (0.90–1.5)
Fever	4.3 (3.5–5.5)	2.3 (1.6–3.3)	1.3 (0.80–2)	1.5 (0.90–2.4)
Malaise and fatigue	2.6 (2.2–3.1)	1.5 (1.1–1.8)	0.84 (0.65–1.1)	1.1 (0.90–1.4)
Conditions due to neoplasm or the treatment of neoplasm	1.4 (0.80–2.6)	3.4 (1.5–7.4)	1.3 (0.60–2.4)	--
Shock	6.2 (4.2–9.1)	1.7 (0.90–3.4)	1.5 (0.80–3.1)	--
Syncope	1.5 (1.1–2.0)	0.89 (0.60–1.3)	0.78 (0.51–1.2)	1.1 (0.70–1.7)
Diseases of mouth; excluding dental	3.8 (2.3–6.1)	1.3 (0.80–2.3)	0.76 (0.44–1.3)	--
Dysphagia	1.7 (1.3–2.3)	1.3 (0.90–1.9)	1.4 (0.90–2.0)	1.0 (0.60–1.6)
Abnormal findings without diagnosis	1.7 (1.5–1.9)	1.2 (1.0–1.4)	1.0 (0.80–1.2)	0.93 (0.75–1.2)
Adverse effects of drugs and medicaments, initial encounter	3.7 (2.9–4.8)	1.2 (0.80–1.9)	1.1 (0.70–1.6)	0.79 (0.49–1.3)
Complication of other surgical or medical care, injury, initial	1.8 (1.1–2.8)	0.92 (0.51–1.6)	0.88 (0.50–1.6)	--

encounter				
Drug induced or toxic related condition	2.5 (1.7–3.5)	1.5 (0.80–2.6)	0.96 (0.53–1.7)	1.2 (0.70–2.2)
Other general signs and symptoms	1.8 (1.5–2.1)	1.1 (0.90–1.3)	0.88 (0.71–1.1)	0.85 (0.67–1.1)

Abbreviations: CCSR = Clinical Classification Software Refined Categories; COVID-19 = coronavirus disease

2019.

* New condition is defined as any CCSR category recorded 1 to 120 days after the index encounter that was not recorded in any preceding health care encounter during January 2019 through the index encounter. All case-patients and control-patients included in this analysis had at least one encounter preceding their index encounter recorded in the large administrative all-payer database. Adjusted odds ratios calculated from the presence of a new condition in 20 or fewer case-patients are not presented and instead are denoted by a symbol (--).

† Timeline was established using a variable that determined the days between each visit, allowing for a continuous timeline.

§ Among case-patients, an index encounter was defined as the initial encounter with a COVID-19 diagnosis during March–June 2020. Among control-patients, an index encounter was defined as the patient’s propensity matched encounter that was used for comparison, during March–June 2020. For an inpatient encounter, the hospital discharge date was assigned as time 0. For an outpatient encounter, the encounter date was assigned as time 0.

¶ Adjusted odds ratios and 95% confidence intervals were calculated using a conditional logit model for new conditions in case-patients compared with control-patients. The odds ratios were adjusted for patient demographics (age, sex, race, ethnicity, insurance status), clinical factors (number of previous inpatient encounters and diagnoses before and at the index encounter), facility characteristics (urbanicity, region), and month of the index encounter. Conditions that are statistically significantly more common in case-patients than control-patients are bolded.

** Post-COVID condition is defined as any CCSR category newly recorded 31–120 days after the index encounter that was not recorded in any preceding health care encounter from January 2019 through the index encounter.

Table 3: Most common post-COVID conditions* 31–120 days after an initial COVID-19 encounter by incidence proportion in adult (aged ≥18 years) case-patients, stratified by index encounter facility setting, from a large administrative all-payer database — United States, March 1–June 30, 2020

Condition (N [†])	Incidence proportion (31-120 days)
Inpatient Index Encounter	
≥1 of 5 post-COVID conditions (N = 27,284)	1900 (7.0)
Respiratory symptoms [§] (N = 14,602)	535 (3.7)
Nervous system symptoms [¶] (N = 19,503)	543 (2.8)
Urinary tract infections (N = 20,426)	410 (2.0)
Circulatory symptoms ^{**} (N = 22,810)	381 (1.7)
Nonspecific chest pain (N = 22,932)	359 (1.6)
Outpatient Index Encounter	
≥1 of 10 post-COVID conditions (N = 44,489)	3,418 (7.7)
Respiratory symptoms [§] (N = 23,571)	499 (2.1)
Abdominal pain and other digestive/abdominal symptoms ^{††} (N = 32,123)	667 (2.1)
Nonspecific chest pain (N = 35,940)	573 (1.6)
Nervous system symptoms [¶] (N = 34,903)	577 (1.7)
Headache including migraine (N = 36,882)	427 (1.2)
Circulatory symptoms ^{**} (N = 39,102)	440 (1.1)
Fluid and electrolyte disorders ^{§§} (N = 38,242)	429 (1.1)
Malaise and fatigue (N = 39,157)	417 (1.1)
Nausea and vomiting (N = 37,948)	401 (1.1)
Urinary tract infections (N = 39,476)	408 (1.0)

Abbreviations: COVID-19 = coronavirus disease 2019; CCSR = Clinical Classification Software Refined

Categories.

* Post-COVID condition is defined as any CCSR category newly recorded 31–120 days after the index encounter that was not recorded in any preceding health care encounter during January 2019 through the index encounter.

Among case-patients, an index encounter was defined as the initial encounter with a COVID-19 diagnosis during March–June 2020. For an inpatient encounter, the hospital discharge date was assigned as time 0. For an outpatient encounter, the encounter date was assigned as time 0. The incidence proportion was calculated for the conditions that were statistically significantly more common among case-patients than among matched control-patients without COVID-19 during 31-120 days. All case-patients and control-patients included in the analysis had at least one encounter preceding their index encounter recorded in the large administrative all-payer database.

[†] N, the denominator, represents the number of adult case-patients of the total 27,284 inpatient or 44,489 outpatient adult case-patients who were not previously diagnosed with the given condition in their index encounter or in a

preceding encounter. N, therefore, reflects the eligible adult population for a given post-COVID condition. Case-patients can be represented in more than one row if they experienced more than one of the post-COVID conditions.

[§] The top five respiratory symptoms ICD-10-CM codes, by frequency, include shortness of breath, cough, hypoxemia, dyspnea, and pleurodynia.

[¶] The top five nervous system symptoms ICD-10-CM codes, by frequency, include headache, altered mental status, disorientation, abnormalities of gait and mobility, and unspecified difficulty in walking.

^{**} The top five circulatory symptoms ICD-10-CM codes, by frequency, include tachycardia, palpitations, bradycardia, other symptoms and signs involving the circulatory and respiratory systems, and elevated blood-pressure reading.

^{††} The top five abdominal pain and other digestive/abdomen symptoms ICD-10-CM codes, by frequency, include unspecified diarrhea, unspecified abdominal pain, epigastric pain, generalized abdominal pain, and pelvic/perineal pain.

^{§§} The top five fluid and electrolyte disorders ICD-10-CM codes, by frequency, include hypokalemia, dehydration, hypo-osmolality hyponatremia, acidosis, and hyperkalemia.

Accepted Manuscript

TABLE 4: Most common new conditions* in adults (aged ≥18 years) following an inpatient or outpatient initial COVID-19 encounter, stratified by subsequent care setting (for outpatient index encounter), from a large administrative all-payer database — United States, March 1–June 30, 2020

Time since index encounter (days) [§]	Index encounter [†] care setting		
	Inpatient index encounter N = 27,284	Outpatient index encounter N = 44,489	
	Most common new conditions in adults (with subsequent inpatient/outpatient encounters) after an inpatient index encounter N = 27,284	Most common new conditions in adults with ≥1 subsequent hospitalization after an outpatient index encounter (1–120 days after index encounter) N = 3,968	Most common new conditions in adults without a subsequent hospitalization after an outpatient index encounter (1–120 days after index encounter) N = 40,521
1–30	<ol style="list-style-type: none"> 1. Respiratory symptoms[†] 2. Respiratory failure 3. Septicemia 4. Pneumonia 5. Bacterial infections^{**} 6. Shock 7. Malnutrition 8. Acute renal failure 9. Fluid and electrolyte disorders^{††} 10. Coagulation/hemorrhagic disorders^{§§} 	<ol style="list-style-type: none"> 1. Pneumonia 2. Respiratory failure 3. Fluid and electrolyte disorders 4. Bacterial infections 5. Septicemia 6. Obesity 7. Acute renal failure 8. Abnormal findings without diagnosis 9. Respiratory symptoms 10. Anxiety and fear-related disorders 	<ol style="list-style-type: none"> 1. Respiratory symptoms 2. Pneumonia 3. Abdominal pain and other digestive/abdominal symptoms^{¶¶} 4. Abnormal findings without diagnosis 5. Malaise and fatigue 6. Musculoskeletal pain 7. Nausea and vomiting 8. Nervous system symptoms^{***} 9. Circulatory symptoms^{†††} 10. Fluid and electrolyte disorders
31–60^{§§§}	<ol style="list-style-type: none"> 1. Respiratory symptoms 2. Nervous system symptoms 3. Circulatory symptoms 4. Urinary tract infections 5. Nonspecific chest pain 6. Pressure ulcer of skin 7. Lower respiratory disease^{¶¶¶} 8. Dysphagia 9. Fungal infections^{****} 10. Hematuria 	<ol style="list-style-type: none"> 1. Fluid and electrolyte disorders 2. Pneumonia 3. Bacterial infections 4. Anemia^{††††} 5. Respiratory failure 6. Septicemia 7. Respiratory symptoms 8. Nervous system symptoms 9. Anxiety and fear-related disorders 10. Nonspecific chest pain 	<ol style="list-style-type: none"> 1. Respiratory symptoms 2. Nonspecific chest pain 3. Abdominal pain and other digestive/abdominal symptoms 4. Nervous system symptoms 5. Headache including migraine 6. Malaise and fatigue 7. Circulatory symptoms 8. Nausea and vomiting 9. Urinary tract infections 10. Anxiety and fear-related disorders
61–90^{§§§§}	<ol style="list-style-type: none"> 1. Lower respiratory disease 	<ol style="list-style-type: none"> 1. Bacterial infections 2. Anemia 3. Respiratory failure 4. Septicemia 5. Urinary tract infections 6. Pneumonia 7. Pressure ulcer of skin 8. Neurocognitive disorders^{§§§§} 9. Coagulation/hemorrhagic disorders 10. Acute pulmonary embolism 	<ol style="list-style-type: none"> 1. Nonspecific chest pain 2. Urinary tract infections 3. Anemia 4. Pneumonia 5. Bacterial infections 6. Neurocognitive disorder 7. Coagulation/hemorrhagic disorders

91–120 ^{§§§}	No new conditions ^{¶¶¶¶¶}	1. Bacterial infections	1. Respiratory symptoms
		2. Septicemia	2. Urinary tract infections
		3. Other nervous system disorders ^{*****}	3. Other nervous system disorders
		4. Malnutrition	
		5. Neurocognitive disorders	
		6. Pressure ulcer of skin	

Abbreviation: COVID-19 = coronavirus disease 2019.

* Most common new conditions following an inpatient or outpatient index encounter with a COVID-19 diagnosis were determined by selecting up to 10 of the conditions with the highest incidence proportion with a statistically significant adjusted odds ratio (compared with control-patients) in each time-period.

† Among case-patients, an index encounter was defined as the initial encounter with a COVID-19 diagnosis during March–June 2020. Among control-patients, an index encounter was defined as the patient’s propensity matched encounter that was used for comparison, during March–June 2020. For an inpatient encounter, the hospital discharge date was assigned as time 0. For an outpatient encounter, the encounter date was assigned as time 0.

§ Timeline was established using a variable that determined the days between each visit, allowing for a continuous timeline.

¶ The top five respiratory symptoms ICD-10-CM codes, by frequency, include shortness of breath, cough, hypoxemia, dyspnea, and pleurodynia.

** The top five bacterial infections ICD-10-CM codes, by frequency, include other specified sepsis, sepsis with unspecified organism, unspecified bacterial pneumonia, unspecified *Escherichia coli* as the cause of diseases classified elsewhere, and other bacterial agents as the cause of diseases classified elsewhere.

†† The top five fluid and electrolyte disorders ICD-10-CM codes, by frequency, include hypokalemia, dehydration, hypo-osmolality hyponatremia, acidosis, and hyperkalemia.

§§ The top five coagulation and hemorrhagic disorders ICD-10-CM codes, by frequency, include unspecified thrombocytopenia, other primary thrombophilia, other secondary thrombocytopenia, unspecified coagulation defect, and other thrombophilia.

¶¶ The top five abdominal pain and other digestive/abdominal symptoms ICD-10-CM codes, by frequency, include diarrhea, unspecified abdominal pain, epigastric pain, generalized abdominal pain, and pelvic/perineal pain.

*** The top five nervous system symptoms ICD-10-CM codes, by frequency, include headache, altered mental status, disorientation, abnormalities of gait and mobility, and unspecified difficulty in walking.

††† The top five circulatory symptoms ICD-10-CM codes, by frequency, include tachycardia, palpitations, bradycardia, other symptoms and signs involving the circulatory and respiratory systems, and elevated blood-pressure reading.

§§§ Post-COVID condition is defined as any Clinical Classification Software Refined Categories (CCSR) category newly recorded 31–120 days after the index encounter that was not recorded in any preceding health care encounter during January 2019 through the index encounter. All case-patients and control-patients included in this analysis had at least one encounter preceding their index encounter recorded in the large administrative all-payer database.

¶¶¶ The top five lower respiratory disease ICD-10-CM codes, by frequency, include other specified respiratory disorders, other disorders of lung, unspecified pulmonary fibrosis, unspecified interstitial pulmonary disease, and chronic pulmonary edema.

**** The top five fungal infection ICD-10-CM codes, by frequency, include candida stomatitis, other urogenital candidiasis, unspecified candidiasis, candidiasis of vulva and vagina, and tinea unguium.

†††† The top five (aplastic) anemia ICD-10-CM codes, by frequency, include unspecified anemia, anemia in chronic kidney disease, anemia in other chronic diseases elsewhere classified, other pancytopenia, anemia in neoplastic disease.

§§§§ The top five other neurocognitive disorders ICD-10-CM codes, by frequency, include unspecified dementia without behavioral disturbance, delirium due to known physiological condition, dementia in other diseases classified elsewhere without behavioral disturbance, vascular dementia without behavioral disturbance, and unspecified Alzheimer's disease.

¶¶¶¶ No new statistically significant ($P < 0.05$) conditions in case-patients compared with matched control-patients.

***** The top five other nervous system disorders ICD-10-CM codes, by frequency, include metabolic encephalopathy, type 2 diabetes with diabetic neuropathy, toxic encephalopathy, unspecified encephalopathy, and other encephalopathy.