WHITE PAPER

A Detailed Study of Patients with Long-Haul COVID

An Analysis of Private Healthcare Claims

A FAIR Health White Paper, June 15, 2021



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Summary

Many patients recover from COVID-19 within a few weeks, but some exhibit persistent or new symptoms more than four weeks after first being diagnosed. Patients with such post-COVID conditions are variously referred to as having long-haul COVID, long COVID or post-acute sequelae of COVID-19 (PASC). Using longitudinal data from a database of over 34 billion private healthcare claim records, FAIR Health studied a total of 1,959,982 COVID-19 patients for the prevalence of post-COVID conditions 30 days or more after their initial diagnosis with COVID-19. To FAIR Health's knowledge, this is the largest population of COVID-19 patients so far studied for post-COVID conditions. The patients' post-COVID conditions were analyzed, with the most common conditions identified. Particular attention was given to age and gender, mental health conditions and death. Among the key findings:

- Of patients who had COVID-19, 23.2 percent had at least one post-COVID condition.
- Post-COVID conditions were found to a greater extent in patients who had more severe cases of COVID-19, but also in a substantial share of patients whose cases lacked symptoms. Of patients who were hospitalized with COVID-19, the percentage that had a post-COVID condition was 50 percent; of patients who were symptomatic but not hospitalized, 27.5 percent; and of patients who were asymptomatic, 19 percent.
- The five most common post-COVID conditions across all ages, in order from most to least common, were pain, breathing difficulties, hyperlipidemia, malaise and fatigue, and hypertension.
- The ranking of the most common post-COVID conditions varied by age group. For example, in the pediatric population (0-18), pain and breathing difficulties were the top two conditions, as in the all-ages cohort, but intestinal issues, rather than hyperlipidemia, were the third most common.
- Most of the post-COVID conditions that were evaluated were associated more with females than
 males. In the case of 12 conditions, however, males more commonly had the condition diagnosed
 than females. For example, of patients who had post-COVID cardiac inflammation, 52 percent
 were male and 48 percent female. By age, the largest share (25.4 percent) with this condition
 was found in a young cohort—individuals aged 19-29.
- Of the four mental health conditions evaluated as post-COVID conditions, anxiety was associated with the highest percentage of patients after COVID-19 in all age groups. Depression was second, adjustment disorders third and tic disorders fourth.
- The odds of death 30 days or more after initial diagnosis with COVID-19 were 46 times higher for patients who were hospitalized with COVID-19 and discharged than patients who had not been hospitalized (odds ratio [OR]=46.020, 95 percent confidence interval [CI], 34.778-60.897, *P*<0.001). Of COVID-19 patients who were hospitalized and discharged, 0.5 percent died 30 days or more after their initial diagnosis.
- Among COVID-19 patients with preexisting conditions, intellectual disabilities were associated with the highest odds of death 30 days or more after initial COVID-19 diagnosis (OR=3.082, 95 percent CI, 1.183-8.029, *P*=0.0212).

Background

Many patients recover from COVID-19 within a few weeks, but some exhibit persistent or new symptoms more than four weeks after first being diagnosed.¹ These post-COVID conditions can last for months— even nine months, according to one study²—and may be experienced by 10 to 30 percent of COVID-19

² Jennifer K. Logue et al., "Sequelae in Adults at 6 Months after COVID-19 Infection," *JAMA Network Open* 4, no. 2 (February 19, 2021): e210830, <u>https://doi.org/10.1001/jamanetworkopen.2021.0830</u>.



¹ Centers for Disease Control and Prevention (CDC), "Post-COVID Conditions," updated April 8, 2021, <u>https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects.html</u>.

patients.³ The conditions can include, among others, fatigue, cognitive difficulties (sometimes called "brain fog"), headache, numbness/tingling, loss of smell or taste, dizziness, heart palpitations, chest pain, shortness of breath, cough, sore throat, joint or muscle pain, excessive sweating, insomnia, depression, anxiety and fever.^{4,5,6} Patients with COVID-19, after the first 30 days of illness, are at higher risk of death than people who have not had COVID-19.⁷

Because this phenomenon is so new, much remains unknown about it. Even the name is unsettled: Patients with post-COVID conditions are variously referred to as having long-haul COVID, long COVID, post-COVID syndrome or post-acute sequelae of COVID-19 or of SARS-CoV-2 (PASC).^{8,9,10} The causes of long-haul COVID are still unknown. Theories include persistent immune activation after the acute phase; initial damage from the virus, such as damage to nerve pathways, that is slow to heal; and persistent presence of low-level virus.¹¹

Many studies of long-haul COVID have been relatively small. The study thought to be the largest to date, which made use of US Department of Veterans Affairs national healthcare databases, involved 73,435 non-hospitalized patients with COVID-19 and 13,654 hospitalized patients with COVID-19, as well as approximately 5 million controls.¹² Although the present study is a descriptive analysis without a control group, it includes more patients with COVID-19—a total of 1,959,982. To FAIR Health's knowledge, this is the largest population of COVID-19 patients so far studied for post-COVID conditions.

To perform this analysis, FAIR Health drew on longitudinal data from its database of over 34 billion private healthcare claim records from 2002 to the present. The nation's largest such repository, it is growing by over 2 billion claim records per year. All patients in the longitudinal dataset who had been diagnosed with COVID-19 from February to December 2020 were included, except for those with certain preexisting conditions (such as cancer and chronic kidney disease) that might have acted as confounders. The remaining 1,959,982 patients were studied for their case characteristics, such as age, gender and reaction to COVID-19 (i.e., asymptomatic, symptomatic, hospitalization, loss of taste or smell only). They were further studied for the prevalence of post-COVID conditions 30 days or more after their initial diagnosis with COVID-19. Their post-COVID conditions were analyzed, with the most common conditions identified. Particular attention was given to age and gender, mental health conditions and death.

¹² Al-Aly, "High-Dimensional Characterization of Post-Acute Sequelae of COVID-19."



³ Erica Carbajal, "Emerging Trends among COVID-19 Long-Haulers: 6 Physicians Weigh In," *Becker's Hospital Review*, April 16, 2021, <u>https://www.beckershospitalreview.com/public-health/emerging-trends-among-covid-19-long-haulers-6-physicians-weigh-</u>

in.html#:~:text=Early%20research%20estimates%20have%20shown,after%20the%20infection%20has%20cleared. ⁴ CDC, "Post-COVID Conditions."

⁵ Edith L. Graham et al., "Persistent Neurologic Symptoms and Cognitive Dysfunction in Non-hospitalized Covid-19 'Long Haulers,'" *Annals of Clinical and Translational Neurology* 8, no. 5 (May 2021): 1073-85, <u>https://doi.org/10.1002/acn3.51350</u>.

⁶ Yong Huang et al., "COVID Symptoms, Symptom Clusters, and Predictors for Becoming a Long-Hauler: Looking for Clarity in the Haze of the Pandemic," *medRxiv* (March 5, 2021), <u>https://doi.org/10.1101/2021.03.03.21252086</u>.

⁷ Ziyad Al-Aly, Yan Xie and Benjamin Bowe, "High-Dimensional Characterization of Post-Acute Sequelae of COVID-19," *Nature* (April 22, 2021), <u>https://doi.org/10.1038/s41586-021-03553-9</u>.

⁸ Felicity Callard and Elisa Perego, "How and Why Patients Made Long Covid," *Social Science & Medicine* 268 (January 2021): 113426, <u>https://doi.org/10.1016/j.socscimed.2020.113426</u>.

⁹ Berkeley Lovelace, Jr., "Dr. Fauci Says New Data Suggests 'Long' Covid Symptoms Can Last Up to 9 Months," CNBC, February 24, 2021, <u>https://www.cnbc.com/2021/02/24/fauci-says-new-data-suggest-long-covid-symptoms-can-last-up-to-9-months.html</u>.

¹⁰ Johns Hopkins Medicine, "COVID 'Long Haulers': Long-Term Effects of COVID-19," April 1, 2021,

https://www.hopkinsmedicine.org/health/conditions-and-diseases/coronavirus/covid-long-haulers-long-term-effects-of-covid19.

¹¹ Alvin Powell, "A Pandemic That Endures for COVID Long-Haulers," *Harvard Gazette*, April 13, 2021, https://news.harvard.edu/gazette/story/2021/04/harvard-medical-school-expert-explains-long-covid/.

This white paper is the eighth in FAIR Health's series of studies of the COVID-19 pandemic. Previous entries in the series have projected the costs of inpatient services for COVID-19 patients¹³; analyzed the impact of COVID-19 on hospitals and health systems,¹⁴ healthcare professionals,¹⁵ dental services¹⁶ and pediatric mental health¹⁷; profiled COVID-19 patients¹⁸; and reported on risk factors for COVID-19 mortality.¹⁹

FAIR Health is a national, independent nonprofit organization dedicated to bringing transparency to healthcare costs and health insurance information. The data in its repository of private healthcare claims are contributed by over 60 payors and third-party administrators who insure or process claims for private insurance plans. The dataset includes data on fully insured and employer self-funded plans and Medicare Advantage (Medicare Part C) enrollees, but not on uninsured individuals or those on Medicare Parts A, B and D.²⁰ Those insured under other government programs, such as Medicaid, CHIP, and state and local government programs, are also not included.

https://s3.amazonaws.com/media2.fairhealth.org/brief/asset/Healthcare%20Professionals%20and%20the%20Impact %20of%20COVID-19%20-%20A%20Comparative%20Study%20of%20Revenue%20and%20Utilization%20-%20A%20FAIR%20Health%20Brief.pdf.

https://s3.amazonaws.com/media2.fairhealth.org/brief/asset/Dental%20Services%20and%20the%20Impact%20of%2 0COVID-19%20-%20An%20Analysis%20of%20Private%20Claims%20-%20A%20FAIR%20Health%20Brief.pdf. ¹⁷ FAIR Health, *The Impact of COVID-19 on Pediatric Mental Health: A Study of Private Healthcare Claims*, A FAIR

Health White Paper, March 2, 2021, https://s3.amazonaws.com/media2.fairhealth.org/whitepaper/asset/The%20Impact%20of%20COVID-

<u>19%20on%20Pediatric%20Mental%20Health%20-%20A%20Study%20of%20Private%20Healthcare%20Claims%20-</u> %20A%20FAIR%20Health%20White%20Paper.pdf.

https://s3.amazonaws.com/media2.fairhealth.org/whitepaper/asset/Risk%20Factors%20for%20COVID-

<u>19%20Mortality%20among%20Privately%20Insured%20Patients%20-%20A%20Claims%20Data%20Analysis%20-%20A%20FAIR%20Health%20White%20Paper.pdf</u>.

²⁰ FAIR Health also receives the entire collection of claims for traditional Medicare Parts A, B and D under the Centers for Medicare & Medicaid Services (CMS) Qualified Entity Program, but those data are not a source for this report.



¹³ FAIR Health, COVID-19: The Projected Economic Impact of the COVID-19 Pandemic on the US Healthcare System, A FAIR Health Brief, March 25, 2020, <u>https://s3.amazonaws.com/media2.fairhealth.org/brief/asset/COVID-19%20-%20The%20Projected%20Economic%20Impact%20of%20the%20COVID-10%20Projected%20Economic%20Impact%20of%20the%20COVID-10%20Projected%20Economic%20Impact%20of%20the%20COVID-10%20Projected%20Economic%20Impact%20of%20the%20COVID-10%20Projected%20Economic%20Impact%20of%20the%20COVID-10%20Projected%20Economic%20Impact%20of%20the%20COVID-10%20Projected%20Economic%20Impact%20of%20the%20COVID-10%20Projected%20Economic%20Impact%20of%20the%20COVID-10%20Projected%20Economic%20Impact%20of%20the%20COVID-10%20Projected%20Economic%20Impact%20of%20the%20COVID-10%20Projected%20Economic%20Impact%20of%20the%20COVID-10%20Projected%20Economic%20Impact%20Projected%20Economic%20Impact%20Frojected%20Economic%20Impact%20Frojected%20Economic%20Impact%20Frojected%20Economic%20Impact%20Frojected%20Economic%20Impact%20Frojected%20Economic%20Impact%20Frojected%20Economic%20Economi</u>

^{19%20}Pandemic%20on%20the%20US%20Healthcare%20System.pdf.

¹⁴ FAIR Health, *Illuminating the Impact of COVID-19 on Hospitals and Health Systems: A Comparative Study of Revenue and Utilization*, A FAIR Health Brief, May 12, 2020,

https://s3.amazonaws.com/media2.fairhealth.org/brief/asset/Illuminating%20the%20Impact%20of%20COVID-19%20on%20Hospitals%20and%20Health%20Systems%20-

^{%20}A%20Comparative%20Study%20of%20Revenue%20and%20Utilization%20-

^{%20}A%20FAIR%20Health%20Brief.pdf.

¹⁵ FAIR Health, *Healthcare Professionals and the Impact of COVID-19: A Comparative Study of Revenue and Utilization*, A FAIR Health Brief, June 10, 2020,

¹⁶ FAIR Health, *Dental Services and the Impact of COVID-19: An Analysis of Private Claims*, A FAIR Health Brief, September 16, 2020,

¹⁸ FAIR Health, Key Characteristics of COVID-19 Patients: Profiles Based on Analysis of Private Healthcare Claims, A FAIR Health Brief, July 14, 2020,

https://s3.amazonaws.com/media2.fairhealth.org/brief/asset/Key%20Characteristics%20of%20COVID-19%20Patients%20-%20Profiles%20Based%20on%20Analysis%20of%20Private%20Healthcare%20Claims%20-%20A%20FAIR%20Health%20Brief.pdf.

¹⁹ FAIR Health, *Risk Factors for COVID-19 Mortality among Privately Insured Patients: A Claims Data Analysis*, A FAIR Health White Paper in Collaboration with the West Health Institute and Marty Makary, MD, MPH, from Johns Hopkins University School of Medicine, November 11, 2020,

Methodology

FAIR Health evaluated data in its longitudinal dataset based on the following criteria:

- February-March 2020: Identified all patients who had an ICD-10-CM diagnosis of B97.29 (other coronavirus as the cause of diseases classified elsewhere), which was a code used at that time for COVID-19 under guidance from the Centers for Disease Control and Prevention; and
- March-December 2020: Identified all patients who had a diagnosis of U07.1 (COVID-19).

An index date was created for each patient based on the first occurrence of one of these diagnoses. The initial total population of patients with COVID-19 was 2,290,442.

Comorbidities were established using the Centers for Medicare & Medicaid Services Chronic Conditions Data Warehouse (CCW)²¹ diagnosis categories, which include common chronic conditions (e.g., diabetes, hypertension) as well as other chronic, potentially disabling conditions. FAIR Health identified all patients who had at least two claims with different dates of service during a two-year period for any of the CCW conditions at least 30 days prior to their COVID-19 diagnosis.

All patients with the following CCW comorbidities were excluded from further analysis because these conditions could potentially skew the results of the analysis of post-COVID conditions:

- Cancers:
 - o Breast Cancer;
 - Colorectal Cancer;
 - Endometrial Cancer;
 - Leukemias and Lymphomas;
 - Lung Cancer;
 - Prostate Cancer;
 - Chronic Kidney Disease;
- Chronic Obstructive Pulmonary Disease (COPD);
- Cystic Fibrosis;
- Viral Hepatitis A, B, C, D or E;
- Human Immunodeficiency Virus (HIV) and/or Acquired Immunodeficiency Syndrome (HIV/AIDS);
- Liver Disease;
- Spina Bifida and Other Congenital Anomalies of the Nervous System; and
- Stroke.

•

This process removed 330,460 patients and resulted in a study population of 1,959,982 patients (COVID-19 patients less those with specified CCW comorbidities).

COVID-19 Reaction Type

Four separate indicators were established to determine how a patient reacted to COVID-19:

- Hospitalization
 - If a hospitalization was associated with the COVID-19 diagnosis.
- Symptomatic
 - If the patient was not hospitalized AND
 - If there were symptoms that were presumably related to COVID-19, such as J01* (acute sinusitis) or R05 (cough).
- Loss of Taste or Smell Only
 - o If the patient was not hospitalized AND

²¹ CMS Chronic Conditions Data Warehouse: <u>https://www2.ccwdata.org/web/guest/condition-categories</u>.



- If there were any diagnoses for the patient between R43.0 and R43.9 (disturbances of taste and smell) AND
- If the patient did not have other symptoms.
- Asymptomatic
 - o If the patient did not meet any of the above criteria.²²

Post-COVID Condition Identification

Using a set of 38 conditions seen in the FAIR Health data and reported on in the literature, FAIR Health identified the specific ICD-10-CM codes that were associated with these conditions. For example, malaise and fatigue used diagnoses such as R53.83 (other fatigue).

The post-COVID conditions evaluated were:

- Abnormal Heart Results;
- Abnormal Organ Tests;
- Adjustment Disorders;
- Anemia;
- Anxiety;
- Blood Clot;
- Breathing Difficulties;
- Cardiac Inflammation;
- Cognitive Impairment/Brain Fog;
- Depression;
- Diabetes;
- Eye Issues;
- General Signs and Symptoms;
- Gastroesophageal Reflux Disease (GERD);
- Hearing Loss;
- Heart Disease;
- High Levels (Glucose, Cholesterol, Blood Pressure [BP]);
- Hyperlipidemia;
- Hypertension;
- Intestinal Issues;
- Kidney Failure;
- Liver Disease;
- Loss of Taste or Smell²³;
- Malaise and Fatigue;
- Migraine and/or Headache;
- Overweight;
- Pain:
- Respiratory Disorder;
- Respiratory Distress;
- Skin Issues;
- Sleep Disorders;
- Stroke;
- Swallowing Difficulties;
- Thyroid Issues;
- Tic Disorders;

²³ Loss of taste or smell was evaluated but yielded no results. There were no complaints of this condition 30 days or more after the index date. Thus, a total of 37 conditions were evaluated and yielded results.



²²Patients listed as asymptomatic may have experienced symptoms but not have incurred a claim regarding those symptoms.

- Tinnitus;
- Vertigo; and
- White Blood Cell Disorders.

Once these conditions were determined, FAIR Health evaluated the study population and identified all the patients who had any one of these conditions 30 days or more after their index date of first diagnosis with COVID-19. Patients were tracked through February 2021.

FAIR Health then identified and excluded all patients who had any one of these conditions 30 days or more prior to their COVID-19 diagnosis. For example, patients who had the condition in 2017 would not be included in the analysis as they had complained of the issue previously. While their condition after COVID-19 could have been validly related to COVID-19, making this exclusion allowed for a clean patient population that had never previously had a claim for treatment of the condition, in case it resulted from a preexisting problem.

To ascertain odds ratios for patients reporting post-COVID conditions, statistical tests were run, using a binary logit model with Fischer's scoring optimization.

In addition to the post-COVID-19 conditions, FAIR Health evaluated death 30 days or more after the patient was diagnosed with COVID-19. Patients who had been hospitalized were included with this variable and data only if they had been discharged from the hospital prior to death. The discharge date and expiration date must have been on separate days, and the expiration date had to be after the discharge date.



Results

COVID-19 Cases

In the overall distribution of COVID-19 patients by age, the age group 19-29 was the largest cohort, representing 20.9 percent of all cases in the study population (figure 1). Large percentages were also associated with the age groups 30-39 (18.9 percent), 40-49 (18.3 percent) and 50-59 (18.7).

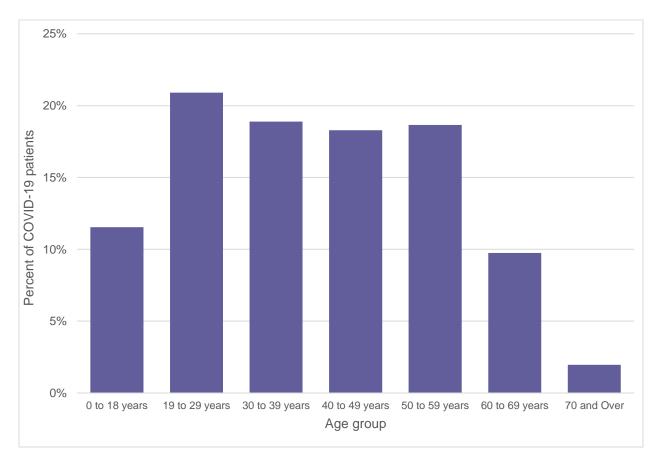


Figure 1. Distribution of COVID-19 patients by age group, February-December 2020



Month by month, the age distribution of COVID-19 cases changed (figure 2). For example, early in the pandemic, the age group 60 and over made up a large share (15.9 percent in February 2020 and 20.3 percent in March 2020), which diminished over time (11.5 percent in December 2020).

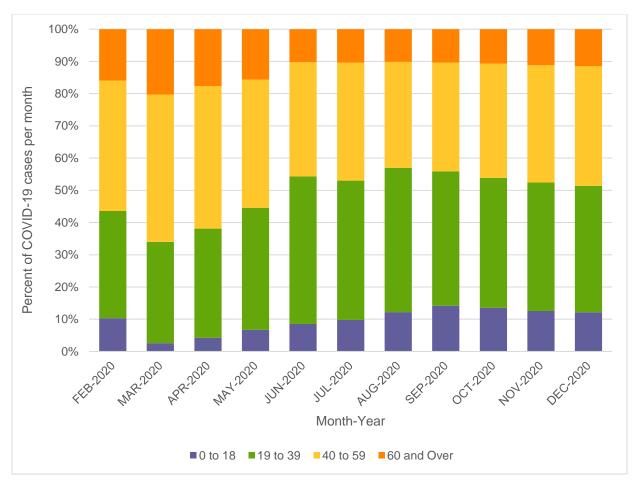


Figure 2. Distribution of COVID-19 cases by age group and month, February 2020-December 2020



COVID-19 cases were fairly evenly distributed by gender, with females making up 53 percent of the distribution and males 47 percent (figure 3).

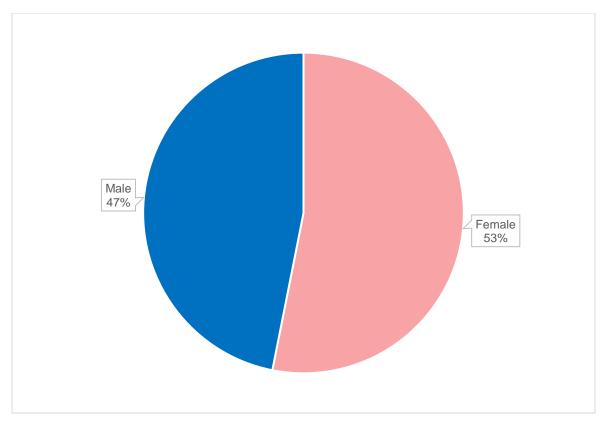


Figure 3. Distribution of COVID-19 cases by gender, February-December 2020



Of patients diagnosed with COVID-19, the largest share—55 percent—were asymptomatic (figure 4). A small percentage, one percent, had only one symptom, the loss of taste or smell. Thirty-nine percent had symptoms other than loss of taste or smell only, and were not hospitalized. Five percent were hospitalized.

It should be noted that these are reported symptoms. Patients listed as asymptomatic on the index date may have experienced symptoms afterward and not incurred a claim because they were not sick enough to seek medical care or did not choose to do so. Similarly, patients with loss of taste or smell as their only symptom may be underreported because they may not have consulted a provider for just that symptom.

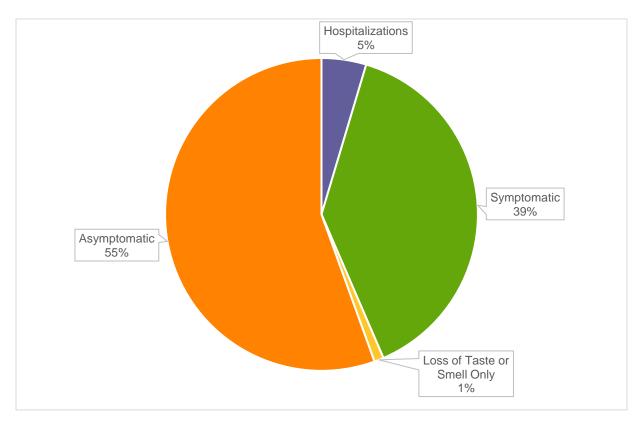


Figure 4. Distribution of COVID-19 cases by reaction type, February-December 2020



In almost all age groups, COVID-19 patients were more likely to be asymptomatic than symptomatic, except those who were 70 years and older (figure 5). The differential between the two categories of asymptomatic and symptomatic was most pronounced in the pediatric age group 0-18, in which 62.6 percent of patients were asymptomatic and 35.5 percent symptomatic. The differential was smaller in adult age groups.

The share of patients who were hospitalized increased progressively by age group from the youngest (1.0 percent) to the oldest (15.6 percent). The loss of taste and smell as the only symptom was more common in individuals 19 to 29 (1.5 percent) and 30 to 39 (1.3 percent) than any other age cohort.

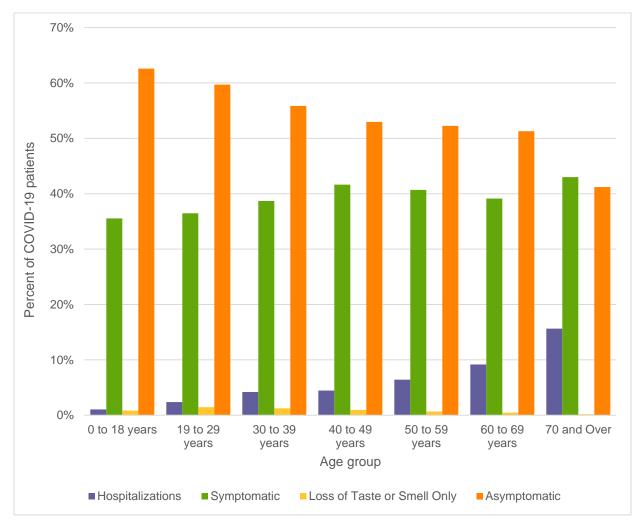


Figure 5. Distribution of COVID-19 reaction types by age group, February-December 2020



In February and March 2020, symptomatic patients outnumbered asymptomatic patients, because testing was not widely available (figure 6).²⁴ Most patients had to become sick or hospitalized to learn they had COVID-19. In April and May 2020, as availability of testing increased, the number of asymptomatic patients rose sharply and surpassed the number of symptomatic patients, reaching levels that were more or less maintained through December 2020. The percentage of hospitalizations, like the percentage of symptomatic patients, dropped greatly from February to May 2020.

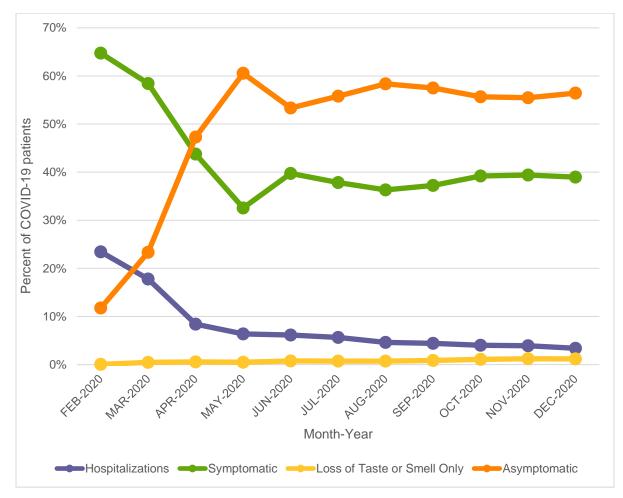


Figure 6. Distribution of COVID-19 reaction types by month, February 2020-December 2020

²⁴ Washington Post staff, "What We Know about Delays in Coronavirus Testing," Washington Post, April 18, 2020, <u>https://www.washingtonpost.com/investigations/2020/04/18/timeline-coronavirus-testing/</u>.



Post COVID Conditions: Overview

Of the 1,959,982 COVID-19 patients in the study population, 454,477 (23.19 percent) were identified as having a post-COVID condition 30 days or more after their index date of first diagnosis with COVID-19 (table 1). Almost half of the hospitalized patients (49.98 percent) experienced at least one post-COVID condition 30 days or more after their index date and after discharge. Of symptomatic patients, 27.48 percent had a post-COVID condition. Of asymptomatic patients, 18.95 percent had a post-COVID condition. No patients whose symptoms were restricted to loss of taste or smell were identified with a post-COVID condition (zero percent).

Table 1. Percent of patients with any post-COVID condition, by reaction type, March 2020-February2021

	Percent of Patients with Any Post-COVID Condition		
Total	23.19%		
Asymptomatic	18.95%		
Symptomatic	27.48%		
Hospitalized	49.98%		
Loss of Taste or Smell			
Only	0%		



Figure 7 shows the 15 conditions, across all ages, that patients most commonly experienced 30 days or more after their index date of first COVID-19 diagnosis (and never experienced before in their history in FAIR Health data).

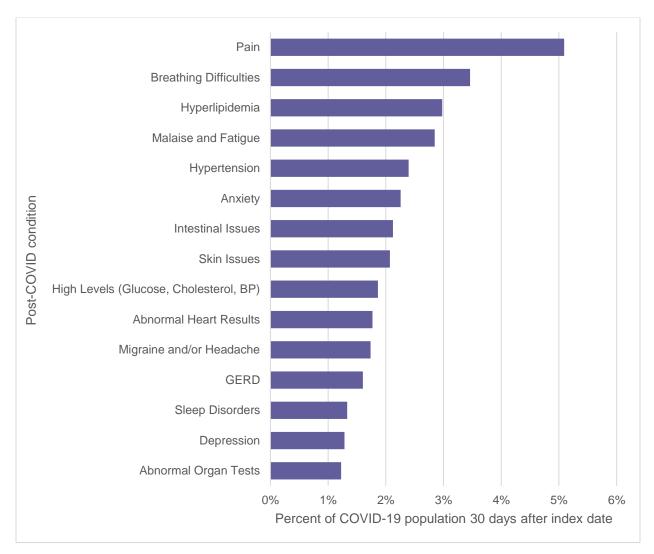


Figure 7. Top 15 post-COVID conditions by percent of COVID-19 population 30 days or more after index date, all ages, March 2020-February 2021

Pain. Pain was the top post-COVID condition, affecting 5.1 percent of COVID-19 patients 30 days or more after their initial diagnosis. Pain includes ICD-10-CM diagnoses such as M79.2, neuralgia and neuritis, unspecified, and M79.1, myalgia. Pain is frequently cited by other researchers as a common post-COVID condition,²⁵ though in some other studies fatigue is the most commonly reported symptom.²⁶

Patients who had been hospitalized had the highest odds of reporting post-COVID pain (odds ratio [OR]=2.941, 95 percent confidence interval [CI], 2.874-3.010, *P*<0.0001), and symptomatic individuals

²⁶ Logue, "Sequelae in Adults at 6 Months after COVID-19 Infection."



²⁵ CDC, "Post-COVID Conditions."

also had high odds of reporting the condition (OR=1.428, 95 percent CI, 1.409-1.447, *P*<0.0001). Patients who were asymptomatic were the reference group in both cases. Male patients were less likely than female patients to report this condition (OR=0.748, 95 percent CI, 0.738-0.758, *P*<0.0001).

Breathing difficulties. Breathing difficulties were the second most common post-COVID condition, affecting 3.5 percent of the total population after COVID-19. This includes diagnoses such as R06.00, dyspnea, unspecified, and R06.02, shortness of breath. Difficulty breathing, like pain, is often cited by other researchers as a common post-COVID condition.^{27,28}

As with pain, patients who were hospitalized had the highest odds of reporting post-COVID breathing difficulties (OR=5.775, 95 percent CI, 5.637-5.917, P<0.0001). Those with symptoms also had higher odds for breathing difficulties than asymptomatic patients (OR=2.062, 95 percent CI, 2.027-2.097, P<0.0001).

Hyperlipidemia and hypertension. Of particular interest were hyperlipidemia and hypertension, which appeared as, respectively, the third and fifth most common post-COVID diagnoses—even though, as noted above, these diagnoses had never been reported before in these patients' history. Hyperlipidemia occurred in 3 percent of COVID-19 patients, hypertension in 2.4 percent. Other researchers have observed these as post-COVID conditions,^{29,30} though it is possible that patients may have had the conditions before and not had them detected by providers.

Malaise and fatigue. Malaise and fatigue, which are commonly reported in the literature,^{31,32} were the fourth most common condition, affecting 2.9 percent of COVID-19 patients 30 days or more after their index date. As with pain and breathing difficulties, patients who had been hospitalized had higher odds of reporting this condition (OR=4.201, 95 percent Cl, 4.088-4.318, *P*<0.0001), and symptomatic patients also had higher odds (OR=1.736, 95 percent Cl, 1.705-1.768, *P*<0.0001).

³² Samir El Sayed, Doaa Shokry and Sarah Mohamed Gomaa, "Post-COVID-19 Fatigue and Anhedonia: A Cross-Sectional Study and Their Correlation to Post-Recovery Period," *Neuropsychopharmacology Reports* 41, no. 1 (March 2021): 50-55, https://doi.org/10.1002/npr2.12154.



²⁷ CDC, "Post-COVID Conditions."

²⁸ Angelo Carfi et al., "Persistent Symptoms in Patients after Acute COVID-19," *JAMA* 324, no. 6 (July 9, 2020): 603-605, <u>https://doi.org/10.1001/jama.2020.12603</u>.

²⁹ Vincenzo Roccaforte et al., "Altered Lipid Profile in Patients with COVID-19 Infection," *Journal of Laboratory and Precision Medicine* 6 (January 2021), <u>https://doi.org/10.21037/jlpm-20-98</u>.

 ³⁰ Vala, "COVID-19 Long-Haulers," August 15, 2020, <u>https://valahealth.com/posts/2020/08/15/covid-19-long-haulers/</u>.
 ³¹ Michael Marshall, "The Lasting Misery of Coronavirus Long-Haulers," *Nature* (September 14, 2020), https://www.nature.com/articles/d41586-020-02598-6.

The ranking of the top 15 post-COVID conditions varied by age group. Age groups from 0 to 59 are shown in table 2; ages 60 and over are not shown because their rankings were similar to the age group 50-59, with little variation. In the pediatric population (0-18), pain and breathing difficulties were the top two conditions, as in the all-ages cohort, but intestinal issues, rather than hyperlipidemia, were the third most common, accounting for 1.4 percent of all pediatric patients. Included in this category of diagnoses were R19.7, diarrhea unspecified; R11.10, vomiting, unspecified; and K59.09, other constipation. The fourth most common condition for this age group was anxiety, with 1.2 percent of these patients demonstrating this symptom.

	Age Group Ranking				
Post-COVID Condition	0 to 18	19 to 29	30 to 39	40 to 49	50 to 59
Pain	1	1	1	1	1
Breathing Difficulties	2	3	2	2	3
Intestinal Issues	3	5	7	11	8
Anxiety	4	2	4	6	12
Malaise and Fatigue	5	4	3	4	5
Migraine and/or Headache	6	6	6	10	15
Skin Issues	7	8	8	8	7
Depression	8	7	13	17	19
Adjustment Disorders	9	10	17	20	24
Abnormal Heart Results	10	9	10	9	9
GERD	11	11	12	12	10
Anemia	12	14	15	15	17
Hyperlipidemia	13	12	5	3	2
Sleep Disorders	14	15	14	13	13
General Signs and Symptoms	15	20	21	23	26
High Levels (Glucose, Cholesterol, BP)	16	13	9	7	6
Hypertension	25	17	11	5	4
Diabetes	28	22	20	14	11
Abnormal Organ Tests	20	19	19	16	14

Table 2. Top 15 Post-COVID conditions by age group ranking, March 2020-February 2021

In those 19-29 and 30-39 years of age, pain was also the top condition. Breathing difficulties were the second most common in those aged 30-39, accounting for 3.31 percent of patients in this age group, but ranking third in the 19-29 age cohort. Anxiety was the second most common post-COVID condition in the 19-29 age cohort, accounting for 2.64 percent of those patients.

There were several large discrepancies between the rankings in the age groups 19-29 and 30-39. Depression ranked 7th in the age group 19-29 and 13th in the age group 30-39. Adjustment disorders ranked 10th in the age group 19-29 and 17th in the age group 30-39. Hyperlipidemia ranked 12th in the age group 19-29 and 5th in the age group 30-39. Hypertension ranked 17th in the age group 19-29 and 11th in the age group 30-39.



There also were differences between the rankings in the age groups 40-49 and 50-59. Anxiety was the 6th most common condition in the age group 40-49 but the 12th most common in those aged 50-59. Migraines and headaches ranked 10th in the age group 40-49 and 15th in the age group 50-59. Intestinal issues ranked 11th in the age group 40-49 and 8th in the age group 50 to 59. GERD ranked 12th in those aged 40-49 and 10th in those aged 50-59.

Not all commonly reported post-COVID symptoms ranked in the top 15. For example, other researchers have found that tinnitus, or ringing or other noises in the ears, is a common post-COVID condition.³³ In FAIR Health's study, 0.21 percent of all COVID-19 patients reported this as a condition 30 days or more after their first diagnosis of COVID-19. It occurred in 0.4 percent of hospitalized patients, 0.3 percent of symptomatic patients and 0.2 percent of asymptomatic patients. As the odds ratios in table 3 show, unlike some of the other post-COVID conditions, tinnitus was only slightly more likely to occur in patients who were hospitalized or had symptoms.

Variable	Odds Ratio	95 Percent Confidence Interval		<i>P</i> Value
Patient Hospitalized	1.679	1.494	1.888	<0.0001
Symptomatic	1.364	1.28	1.453	<0.0001
Preexisting Condition: Asthma	1.301	1.156	1.466	<0.0001
Preexisting Condition: Fibromyalgia	1.323	1.212	1.443	<0.0001
Preexisting Condition: Hypothyroidism	1.202	1.085	1.332	0.0005
Preexisting Condition: Anxiety	1.269	1.159	1.39	<0.0001
Preexisting Condition: Migraine or Headache	1.410	1.241	1.602	<0.0001
Preexisting Condition: Hearing Impairment	1.873	1.602	2.191	<0.0001

Table 3. Odds ratios for tinnitus as a post-COVID condition, March 2020-February 2021

³³ Ibrahim Almufarrij and Kevin J. Munro, "One Year On: An Updated Systematic Review of SARS-CoV-2, COVID-19 and Audio-vestibular Symptoms," *International Journal of Audiology* (March 22, 2021), <u>https://doi.org/10.1080/14992027.2021.1896793</u>.



Gender

Of the post-COVID conditions that were evaluated and yielded results, most were associated more with females than males—by five percent or more. This is consistent with other research showing that women are more likely to report long-haul COVID than men.³⁴ However, in the case of 12 conditions in the FAIR Health data (including death after 30 days), males more commonly experienced the condition than females (figure 8). One of those conditions, stroke, showed some association with preexisting conditions, but not much. Patients who had any preexisting condition and COVID-19 were not much more likely to have a stroke 30 or more days after their diagnosis of COVID-19 than patients who had no preexisting condition (OR=1.137, 95 percent CI, 1.038-1.246, P=0.0056).

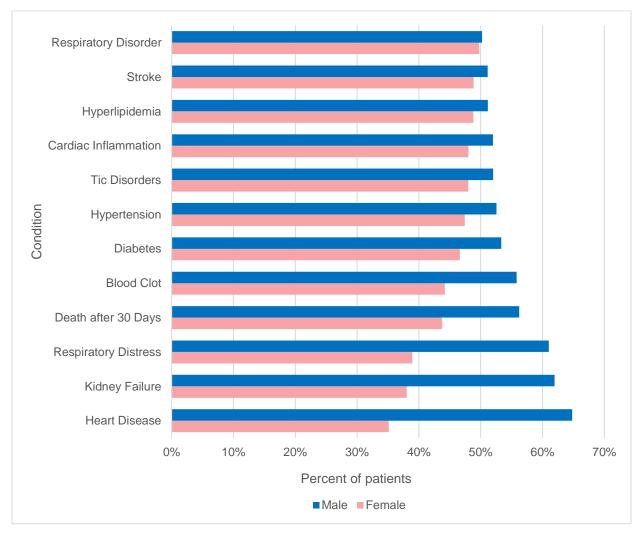


Figure 8. Post-COVID conditions more common in males than females, March 2020-February 2021

³⁴ Ingrid Torjesen, "Covid-19: Middle Aged Women Face Greater Risk of Debilitating Long Term Symptoms." *BMJ* 372 (March 25, 2021): n829, <u>https://doi.org/10.1136/bmj.n829</u>.



Cardiac inflammation is notable because the age distribution was skewed to a younger cohort (figure 9). Of patients who reported this condition, the largest share—25.4 percent—was in the age group 19-29. This was disproportionate to that age group's share of the population of COVID-19 patients overall, 20.9 percent (figure 1). Myocardial conditions such as cardiac inflammation are usually associated with older age.³⁵

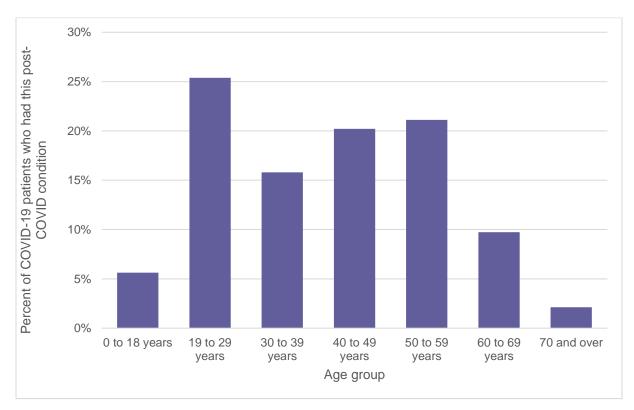


Figure 9. Distribution of patients with post-COVID cardiac inflammation by age, March 2020-February 2021

³⁵ Marc Appel, Stefan Frantz and Gustavo Campos Ramos, "Myocardial Inflammation Comes of Age," *Current Opinion in Physiology* 19 (February 2021): 47-54, <u>https://doi.org/10.1016/j.cophys.2020.09.006</u>.



The association between post-COVID cardiac inflammation and the age group 19-29 is supported by the odds ratios for this condition. All age groups shown in table 4 had a lower odds ratio for cardiac inflammation than the reference group of patients 19-29 years of age. (Odds ratios for three age groups— 30-39, 50-59 and 60-69—were not statistically significant.)

		95 Percent		
Age Group	Odds Ratio	Confidence Interval		<i>P</i> Value
0 to 18 years	0.420	0.291	0.606	0.0479
30 to 39 years	0.583	0.456	0.746	0.8601*
40 to 49 years	0.730	0.579	0.919	0.0088
50 to 59 years	0.653	0.518	0.825	0.1474*
60 to 69 years	0.490	0.363	0.661	0.1941*
70 and over	0.354	0.200	0.624	0.0446

Table 4. Odds ratios for cardiac inflammation as a post-COVID condition by age group, March2020-February 2021

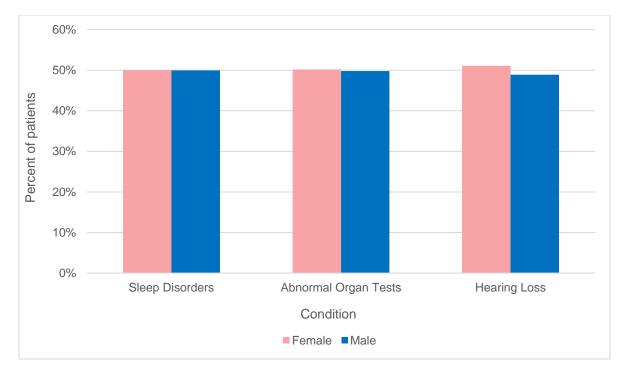
* not statistically significant

Also raising the odds for post-COVID cardiac inflammation were certain preexisting conditions, including hospitalization of a patient with COVID-19 and male gender (table 5). The reference group for male gender was female gender; for each other preexisting condition it was not having that condition.

Table 5. Preexisting conditions raising the odds for post-COVID cardiac inflammation, March
2020-February 2021

	Odds	95 Percent Confidence		
Preexisting Condition	Ratio	Interval		P Value
Patient Hospitalized with COVID-19	23.149	18.598	28.814	<0.0001
Muscular Dystrophy	12.637	3.031	52.685	0.0005
Symptomatic with COVID-19	3.160	2.574	3.88	<0.0001
Heart Failure	3.147	1.743	5.685	0.0001
Opioid Use Disorder	2.954	1.495	5.835	0.0018
Developmental Disorders	2.742	1.104	6.810	0.0298
Migraine and Chronic Headaches	1.632	1.167	2.281	0.0042
Asthma	1.580	1.189	2.101	0.0016
Fibromyalgia	1.577	1.240	2.006	0.0002
Male Gender	1.233	1.055	1.442	0.0087





Three conditions were distributed almost equally between males and females: sleep disorders, abnormal organ tests and hearing loss (figure 10).

Figure 10. Post-COVID-19 conditions with relatively even gender distribution, March 2020-February 2021



The remaining post-COVID conditions were more common in females than males, with the 10 highest disparities shown in figure 11. Thyroid issues, depression and migraines/headaches had the highest differential between females and males (a split of approximately 70 percent female/30 percent male in each case).

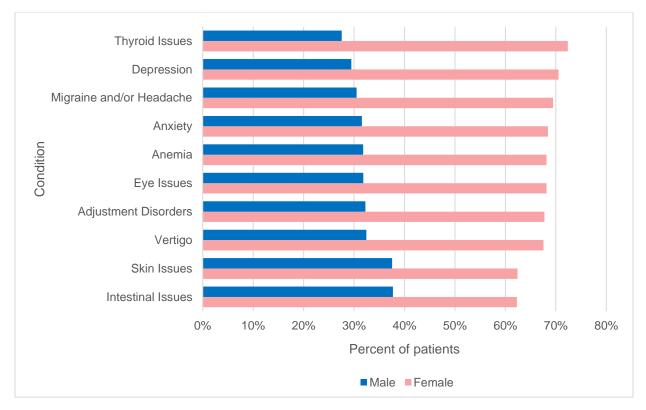


Figure 11. Ten post-COVID conditions more common in females than males with greatest disparity by gender, March 2020-February 2021



Mental Health

Of the four mental health conditions evaluated as post-COVID conditions, anxiety was associated with the highest percentage of patients in all age groups (figure 12). Depression was second for all age groups. Depression was also the only mental health condition that had a higher percentage of patients in the 60-and-older age group than the 19-39 age group. Both anxiety and depression are frequently cited in other research as post-COVID conditions.³⁶ In the FAIR Health data, adjustment disorders had the third highest percentage of patients after COVID-19 in all age groups and tic disorders the fourth.

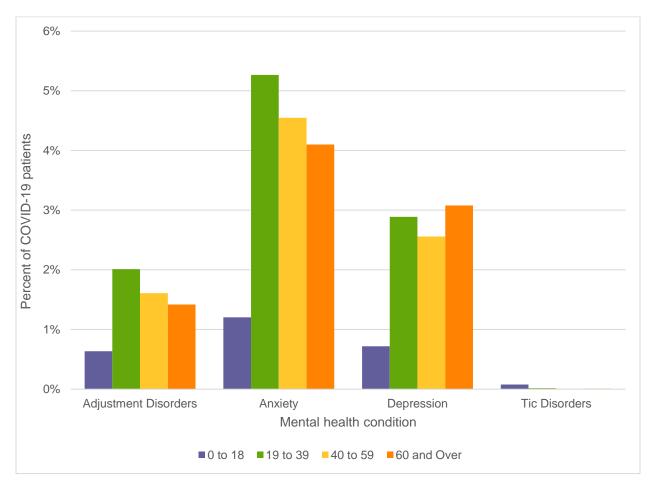


Figure 12. Post-COVID mental health conditions by age group, March 2020-February 2021

³⁶ CDC, "Post-COVID Conditions."



Notably, when the age group 19-29 was used as the reference group for adjustment disorders, all odds ratios were below 1 for the other age groups (table 6). (The age group 0-18 was not statistically significant.) This means that individuals who were 19-29 years of age had higher odds of developing post-COVID adjustment disorders than any other age group.

		95 Percent	
Age Group	Odds Ratio	Confidence Interval	<i>P</i> Value
0 to 18	0.690	0.650-0.733	0.0504*
30 to 39	0.970	0.928-1.015	<0.001
40 to 49	0.820	0.783-0.860	<0.001
50 to 59	0.646	0.615-0.679	<0.001
60 to 69	0.507	0.474-0.542	<0.001
70 to 79	0.550	0.524-0.662	<0.001

Table 6. Post-COVID adjustment disorders by age group and odds ratio, March 2020-February2021

* not statistically significant

Tic disorders were unusual in two respects (table 7). Using the age group 19-29 as the reference group, the age group 0-18 had the highest odds of reporting post-COVID tic disorders compared to other age cohorts. Also, patients with preexisting conditions had higher odds of developing this condition.

Table 7. Post-COVID tic disorders by variable and odds ratio, March 2020-February 2021

Variable	Odds Ratio	95 Percent Confidence Interval	<i>P</i> Value
0 to 18	7.158	5.80-9.892	<0.001
Preexisting Condition	1.969	1.544-2.510	<0.001



Females were more than twice as likely as males to seek care for post-COVID adjustment disorders, anxiety and depression (figure 13). The gender distribution for post-COVID tic disorders was more evenly distributed: 48 percent female, 52 percent male.

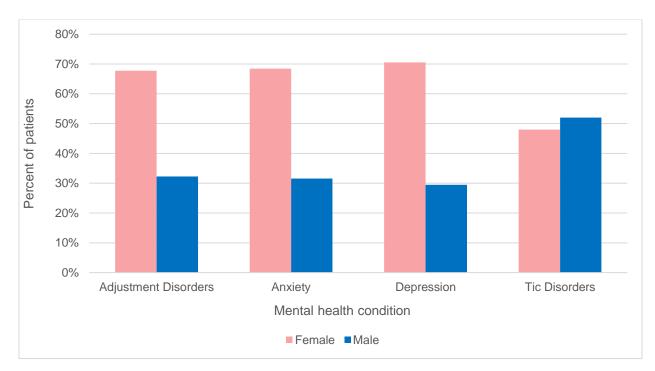


Figure 13. Post-COVID mental health conditions by gender, March 2020-February 2021



Death

Other researchers have found that patients with COVID-19 have a higher risk of death after the first 30 days of illness than individuals without COVID-19.³⁷

In the FAIR Health study, patients who were hospitalized and discharged had the highest percentage of deaths 30 days or more after their initial diagnosis with COVID-19 (figure 14). Of COVID-19 patients who were hospitalized and discharged, 0.45 percent died 30 days or more after their index date. Symptomatic patients who were not hospitalized had the second highest percentage of death (0.02 percent). Of asymptomatic patients, 0.01 percent died. Individuals who experienced only a loss of taste or smell had zero deaths 30 days or more after initial COVID-19 diagnosis.

Individuals who were hospitalized and discharged had higher odds of death than patients who had not been hospitalized (OR=46.020, 95 percent CI, 34.778-60.897, *P*<0.001) and symptomatic patients had higher odds of death than asymptomatic patients (OR=2.904, 95 percent CI, 2.130-3.961, *P*<0.001).

The top conditions associated with the death of a patient 30 or more days after their first COVID-19 diagnosis (including patients who had been hospitalized and discharged) were other sepsis, unspecified respiratory failure, cardiac arrest, aneurysms (brain, aortic, etc.) and pneumonia. Also in the list were acute kidney failure, endocarditis, pulmonary embolism and acute myocardial infarction.

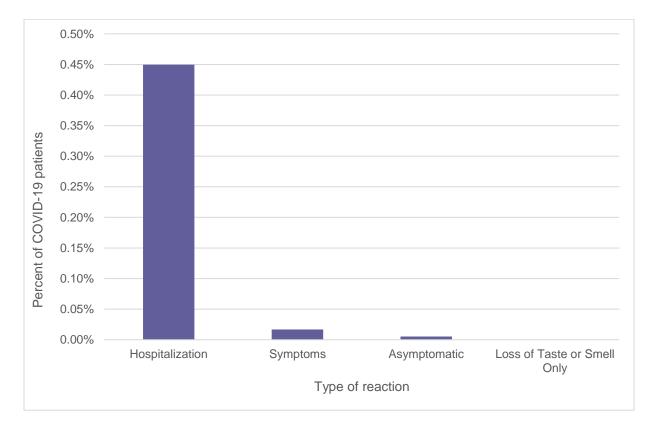


Figure 14. Percent of COVID-19 patients who died 30 days or more after index date by type of reaction, March 2020-February 2021

³⁷ Al-Aly, "High-Dimensional Characterization of Post-Acute Sequelae of COVID-19."



Regardless of age group, patients who were symptomatic (but not hospitalized) had a higher occurrence of death 30 days or more after their index date than asymptomatic patients (figure 15). The occurrence increased, however, with each successive age group. In patients 70 and over, 0.273 percent of symptomatic patients died compared to 0.139 percent of asymptomatic patients.

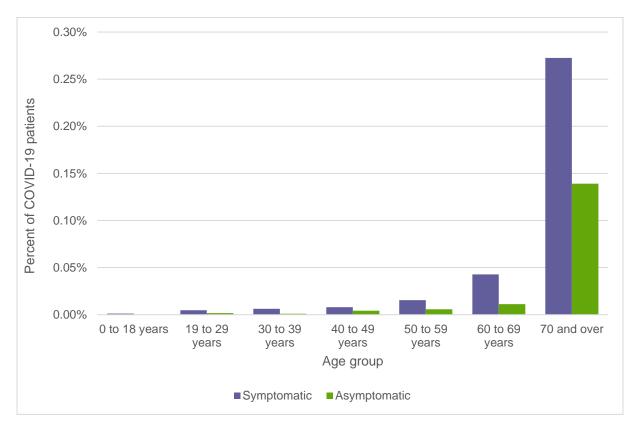


Figure 15. Percent of COVID-19 patients who died 30 days or more after index date by age group and type of reaction, March 2020-February 2021



Regardless of type of reaction (hospitalized, symptomatic, asymptomatic), males were more likely to die 30 days or more after their index date than females (figure 16). Of deaths in hospitalized patients, 57 percent occurred in males; of deaths in symptomatic patients, 53 percent occurred in males; and of deaths in asymptomatic patients, 55 percent occurred in males.

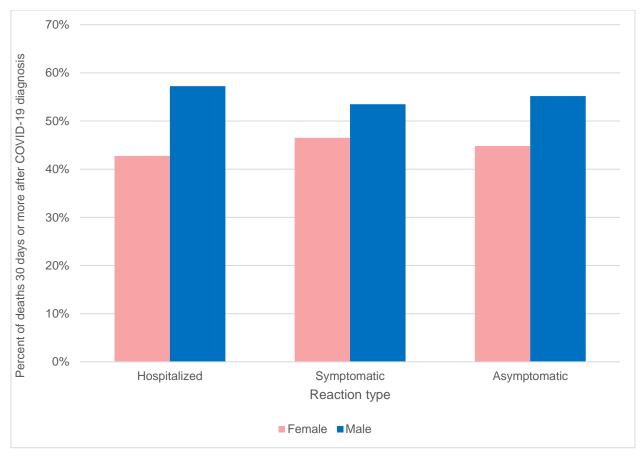


Figure 16. Percent of COVID-19 patients who died 30 days or more after index date by gender and type of reaction, March 2020-February 2021



Symptomatic and hospitalized patients who died 30 days or more after their index date differed little across all ages, and in the aggregate, in their average days to death (figure 17). In the age group 19-39, symptomatic patients had an average of 95.3 days from index date to death while the hospitalized cohort had an average number of days of 92.5. The age group 40-59 showed a similar pattern, with symptomatic patients dying an average of 93.6 days after their index date while, for the hospitalized cohort, the average was 93.74 days. In both cases, however, the asymptomatic cohort had a longer span, with those aged 19-39 having an average of 133.5 days and those aged 40-59 having 125.8 days.

In the cohort aged 60 years and older, asymptomatic patients were grouped much more closely with the symptomatic and hospitalized patients. In this age group, hospitalized patients lived an average of 85.6 days, symptomatic patients 75.5 days and asymptomatic patients 88.8 days.

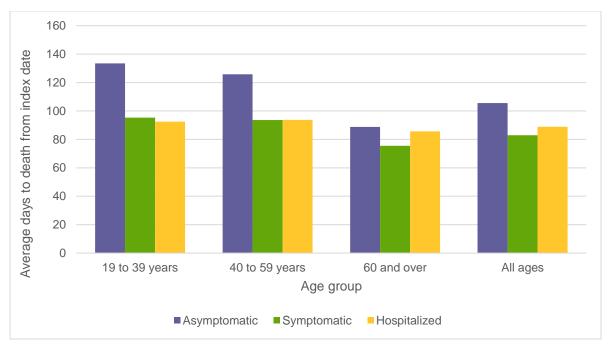


Figure 17. Average days from index date to death in COVID-19 patients who died 30 days or more after index date by age group and type of reaction, March 2020-February 2021



Among COVID-19 patients with preexisting conditions, as shown in figure 18, intellectual disabilities were associated with the highest odds of death 30 days or more after initial COVID-19 diagnosis (OR=3.082, 95 percent CI, 1.183-8.029, *P*=0.0212). This is consistent with a finding in a previous FAIR Health study that COVID-19 patients with intellectual disabilities and related conditions had the third highest risk of death from COVID-19 across all age groups.³⁸

Individuals with Alzheimer's disease and/or senile dementia also had higher odds of dying (OR=3.007, 95 percent CI, 2.136-4.232, *P*<0.001). The reference group for each preexisting condition was patients without that preexisting condition. Tobacco use and anemia are notable because they are not typically such strong predictors of death as in these findings. The odds ratio for tobacco use was 1.938 (95 percent CI, 1.368-2.746, *P*=0.002) and for anemia 1.426 (95 percent CI, 1.118-1.819, *P*=0.0043).

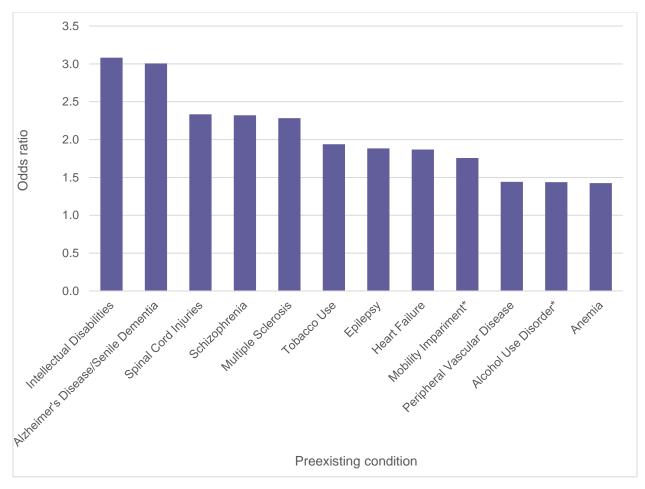


Figure 18. Top preexisting conditions associated with death of COVID-19 patients 30 days or more after index date, March 2020-February 2021

* not statistically significant

³⁸ FAIR Health, *Risk Factors for COVID-19 Mortality among Privately Insured Patients*.



Conclusion

This analysis of the largest population of COVID-19 patients so far studied for post-COVID conditions makes several notable findings. Of patients who had COVID-19, 23.2 percent had at least one post-COVID condition 30 days or more after their initial diagnosis with COVID-19. Post-COVID conditions were found to a greater extent in patients who had more severe cases of COVID-19, but also in a substantial share (19 percent) of patients whose cases were asymptomatic. The five most common post-COVID conditions, hyperlipidemia, malaise and fatigue, and hypertension. The ranking of the most common post-COVID conditions varied by age group.

Most of the post-COVID conditions that were evaluated were associated more with females than males. In the case of 12 conditions, however, males more commonly had the condition diagnosed than females. For example, of patients who had post-COVID cardiac inflammation, 52 percent were male and 48 percent female. By age, the largest share (25.4 percent) with this condition was found in individuals aged 19-29.

Of the four mental health conditions evaluated as post-COVID conditions, anxiety was associated with the highest percentage of patients after COVID-19 in all age groups. Depression was second, adjustment disorders third and tic disorders fourth.

The odds of death 30 days or more after initial diagnosis with COVID-19 were 46 times higher for patients who were hospitalized with COVID-19 and discharged than patients who had not been hospitalized. Of COVID-19 patients who were hospitalized and discharged, 0.5 percent died 30 days or more after their initial diagnosis.

The findings in this report are significant for all individuals who have long-haul COVID, as well as for providers, payors and policy makers. Additionally, FAIR Health hopes that these findings will be starting points for further research in this field.



About FAIR Health

FAIR Health is a national, independent nonprofit organization dedicated to bringing transparency to healthcare costs and health insurance information through data products, consumer resources and health systems research support. FAIR Health qualifies as a public charity under section 501(c)(3) of the federal tax code. FAIR Health possesses the nation's largest collection of private healthcare claims data, which includes over 34 billion claim records and is growing at a rate of over 2 billion claim records a year. FAIR Health licenses its privately billed data and data products—including benchmark modules, data visualizations, custom analytics and market indices—to commercial insurers and self-insurers, employers, providers, hospitals and healthcare systems, government agencies, researchers and others. Certified by the Centers for Medicare & Medicaid Services (CMS) as a national Qualified Entity, FAIR Health also receives data representing the experience of all individuals enrolled in traditional Medicare Parts A, B and D; FAIR Health includes among the private claims data in its database, data on Medicare Advantage enrollees. FAIR Health can produce insightful analytic reports and data products based on combined Medicare and commercial claims data for government, providers, payors and other authorized users. FAIR Health's free, award-winning, national consumer websites are <u>fairhealthconsumer.org</u> and <u>fairhealthconsumidor.org</u>. For more information on FAIR Health, visit <u>fairhealth.org</u>.

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