COVID 19: Immediate and Long-term Effects on Morbidity and Mortality

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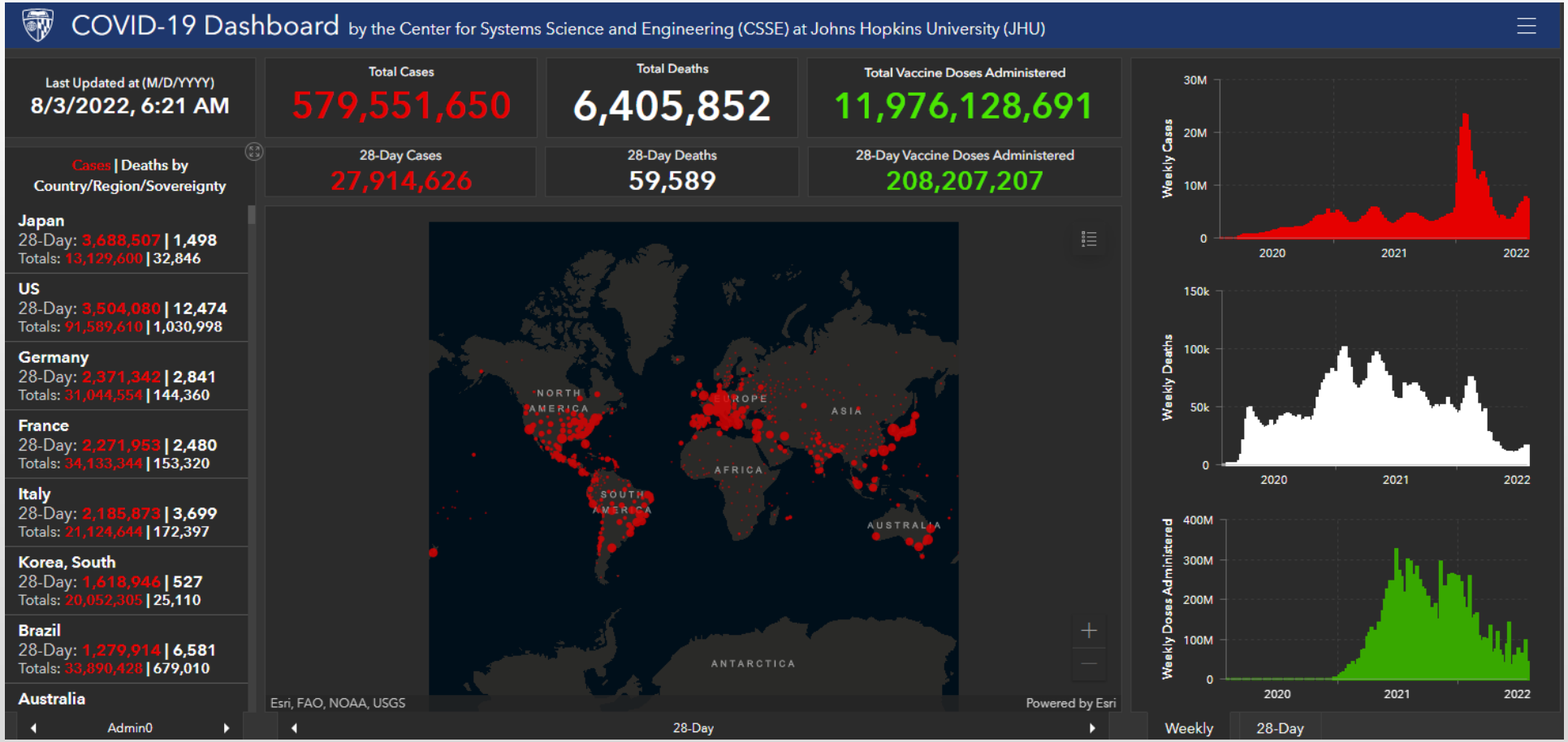
Case for consideration…

- 42 y/o M, $5MM ART
- App Dec ‘20: Accountant, Non-tobacco, No medical history
- Exam: clean, 6’0”, 260, no doctor
- Labs: A1c 5.8, Chol 235, HDL 33, otherwise normal
- Rx check: Prednisone, Hydroxychloroquine, and Ivermectin—10 days dispensed ~1 month prior to application
- Email from agent: prescribed for prevention of COVID-19
- Issue now? STD? Substandard? Preferred?
- If not, what?

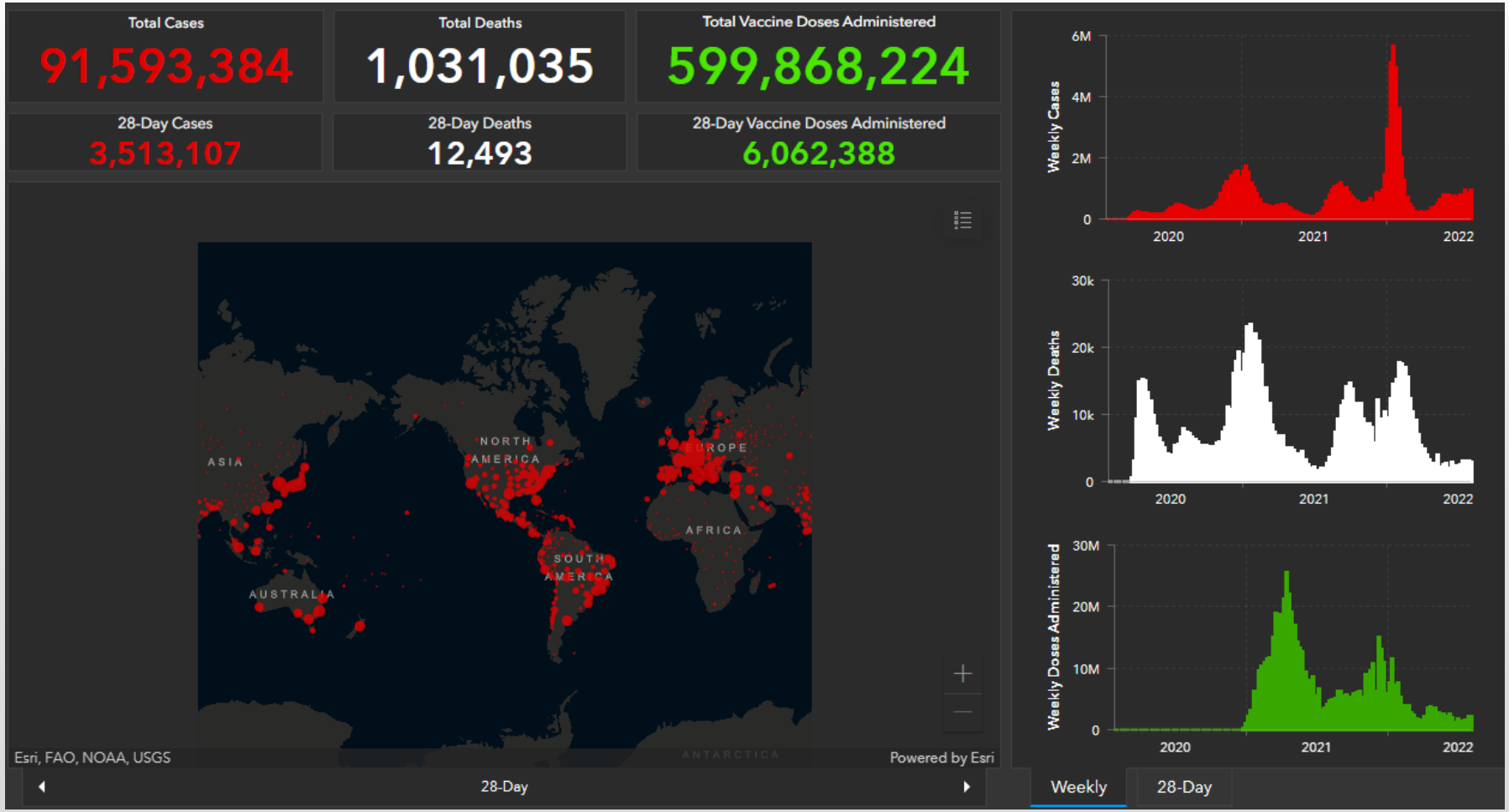
Agenda

- Acute COVID
  - Epidemiology
  - Disease manifestations
  - Morbidity
  - Mortality
- Long COVID
  - Epidemiology
  - Disease Manifestations
  - Morbidity
  - Mortality

Global view

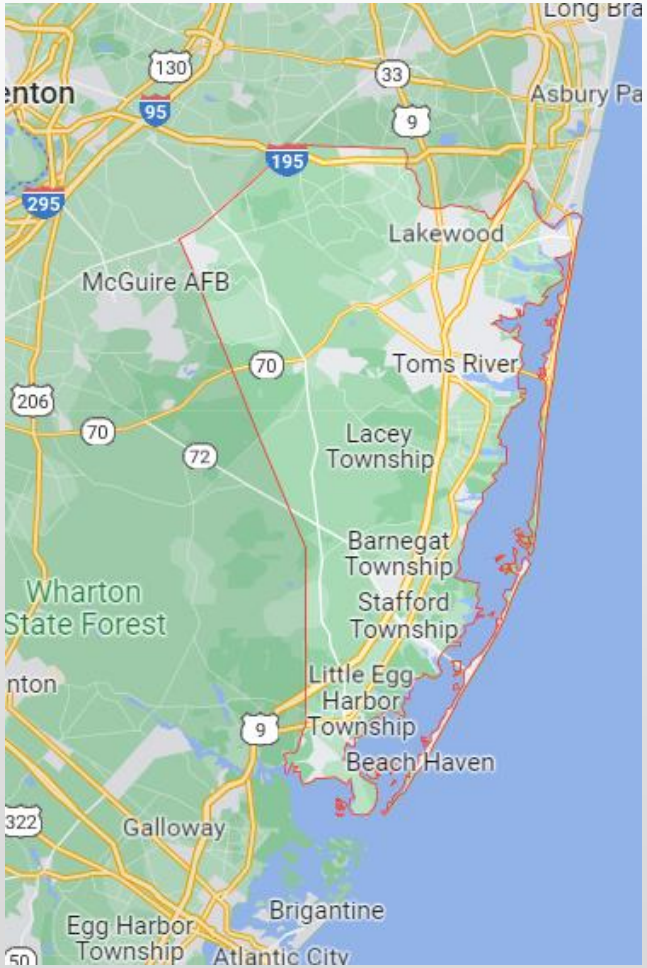

COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)
Last Updated at (M/D/YYYY)
8/3/2022, 6:21 AM
Total Cases
579,551,650
Total Deaths
6,405,852
Total Vaccine Doses Administered
11,976,128,691
28-Day Cases
27,914,626
28-Day Deaths
59,589
28-Day Vaccine Doses Administered
208,207,207
Cases | Deaths by Country/Region/Sovereignty
Japan
28-Day: 3,688,507 | 1,498
Totals: 13,129,600 | 32,846
US
28-Day: 3,504,080 | 12,474
Totals: 91,589,610 | 1,030,998
Germany
28-Day: 2,371,342 | 2,841
Totals: 31,044,554 | 144,360
France
28-Day: 2,271,953 | 2,480
Totals: 34,133,344 | 153,320
Italy
28-Day: 2,185,873 | 3,699
Totals: 21,124,644 | 172,397
Korea, South
28-Day: 1,618,946 | 527
Totals: 20,052,305 | 25,110
Brazil
28-Day: 1,279,914 | 6,581
Totals: 33,890,428 | 679,010
Australia
NORTH AMERICA
EUROPE
ASIA
AFRICA
SOUTH AMERICA
AUSTRALIA
ANTARCTICA
Esri, FAO, NOAA, USGS
Powered by Esri
Admin0
28-Day
Weekly Cases
30M
20M
10M
0
2020
2021
2022
Weekly Deaths
150k
100k
50k
0
Weekly Doses Administered
400M
300M
200M
100M
Weekly
28-Day

United States



Ocean County, NJ (NY Times 15 Feb 2022)

- 53% Vaccinated
- 26% Boosted
- 1:200 citizens DEAD from COVID!
- Worst place on Earth for COVID other than Peru.



Symptoms—Acute Infection

- Many are just like every other viral infection known to man
  - Asymptomatic (33%+)
  - Cough, fever, myalgias
  - Headache, sore throat, diarrhea, nausea/vomiting, fatigue
- But, there are some differences…
  - Dyspnea, sometimes profound
  - Loss of senses (smell=anosmia and taste=ageusia)
  - Chest pain (REALLY???)
  - Confusion

Severity and risk factors…

- What's the difference?
  - Most viruses seem to have "tropism" for single organ systems, especially respiratory or GI, and our bodies react in a predictable manner.
  - But: COVID-19 seems to have an affinity for ACE2 receptors that are in multiple organs, including the arterial tree, as evidenced by autopsy studies finding antigens and virus in Respiratory and GI tissue, as well as Heart, Brain, Liver, and Kidneys ☹. And sometimes our bodies react in untoward ways with this virus that results in an immune storm and occasionally significant alterations in the clotting cascade.
- Risk factors for severe illness: Age, Weight, HTN, Chronic disease of any major organ system, Smoking, Autoimmune diseases and use of DMARDS or Steroids, etcetera.
- What constitutes severe illness?
  - Hospitalization

Treatment (Mild-Moderate) UpToDate®

COVID-19 specific treatments for nonpregnant adults in the outpatient setting: Time windows for administration* and clinical considerations

Agent	Time window for administration after symptom onset (first day of symptoms is considered day 0)*	Clinical considerations
Nirmatrelvir-ritonavir	≤5 days	▪ Significant drug-drug interactions with many common medications; consult a reliable prescribing reference¶ to determine if nirmatrelvir-ritonavir use is appropriate or if risk can be safely mitigated with alteration of the patient's medication regimen. ▪ Reduce dose for eGFR 30 to 59 mL/min; avoid use in eGFR <30 mL/min and in severe hepatic impairment.
Remdesivir	≤7 days	▪ Requires parenteral administration over 3 days.
Bebtelovimab	≤7 days	▪ Requires parenteral administration.
High-titer convalescent plasma	≤8 days	▪ Transfusion requires parenteral administration. ▪ Blood typing and antibody screen required prior to administration.
Molnupiravir	≤5 days	▪ Avoid in pregnancy and in those at risk of pregnancy due to potential adverse effects on developing fetus.

Treatment (Severe)

Laboratory features associated with severe COVID-19[1-6]

Abnormality	Possible threshold
Elevations in:	
• D-dimer	>1000 ng/mL (normal range: <500 ng/mL)
• CRP	>100 mg/L (normal range: <8.0 mg/L)
• LDH	>245 units/L (normal range: 110 to 210 units/L)
• Troponin	>2× the upper limit of normal (normal range for troponin T high sensitivity: females 0 to 9 ng/L; males 0 to 14 ng/L)
• Ferritin	>500 mcg/L (normal range: females 10 to 200 mcg/L; males 30 to 300 mcg/L)
• CPK	>2× the upper limit of normal (normal range: 40 to 150 units/L)
Decrease in:	
• Absolute lymphocyte count	<800/microL (normal range for age ≥21 years: 1000 to 4800/microL)

Although these laboratory features are associated with severe disease in patients with COVID-19, they have not been clearly demonstrated to have prognostic value. We use the thresholds listed above to identify patients who may be at risk for severe disease; they are extrapolated from published cohort data and individualized to the reference values used at our laboratory. However, the specific thresholds are not well established and may not be applicable if laboratories use other reference values.

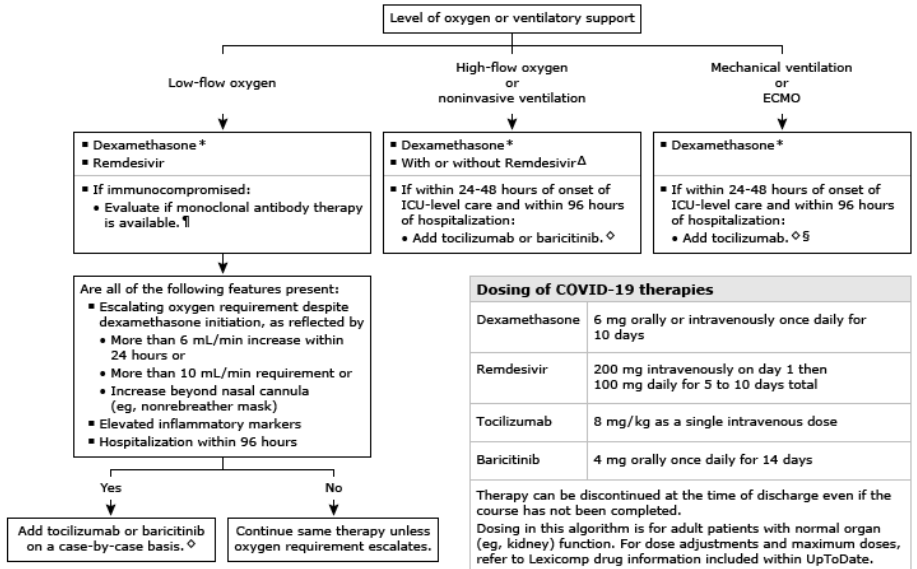
COVID-19: coronavirus disease 2019; CRP: C-reactive protein; LDH: lactate dehydrogenase; CPK: creatine phosphokinase.

References:

1. Guan WY, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020.
2. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395:497.
3. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020; 395:1054.
4. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020.
5. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72,314 cases from the Chinese Center for Disease Control and Prevention. JAMA 2020.
6. Ruan Q, Yang K, Wang W, et al. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med 2020.

UpToDate

Selection of COVID-19-specific therapy in adults who have severe disease requiring oxygen supplementation



Dosing of COVID-19 therapies

Dexamethasone	6 mg orally or intravenously once daily for 10 days
Remdesivir	200 mg intravenously on day 1 then 100 mg daily for 5 to 10 days total
Tocilizumab	8 mg/kg as a single intravenous dose
Baricitinib	4 mg orally once daily for 14 days

Therapy can be discontinued at the time of discharge even if the course has not been completed.
Dosing in this algorithm is for adult patients with normal organ (eg, kidney) function. For dose adjustments and maximum doses, refer to Lexicomp drug information included within UpToDate.

This algorithm covers our approach to selection of COVID-19-specific therapy only. Refer to other UpToDate content for discussion of other management issues, including management of hypoxia, prevention of thromboembolism, management of other complications, and care of pregnant and postpartum patients. The approach to COVID-19-specific therapy in individuals who have no oxygen requirement or who are seen in the outpatient setting is also covered elsewhere.

ECMO: extracorporeal membrane oxygenation; ICU: intensive care unit; CRP: C-reactive protein.

* If dexamethasone is unavailable, other glucocorticoids at equivalent doses are reasonable alternatives. For pregnant individuals, dexamethasone dosing is higher when fetal lung maturation is one of the goals; refer to other UpToDate content on COVID-19 in pregnancy.

¶ In the United States, monoclonal antibody therapy is not authorized or routinely available for hospitalized adults with severe COVID-19. However, it may be available for immunocompromised patients through an investigational new drug application (ie, through a request to the manufacturer).

Δ The clinical benefit of remdesivir is uncertain in patients who need support beyond low-flow oxygen, but it is reasonable to use it in those on high-flow or noninvasive ventilation.

◇ Tocilizumab and baricitinib should be used with caution in immunocompromised patients, among whom the safety of further immune modulation with such agents is uncertain.

§ We do not routinely use baricitinib in this population pending additional data, but it is a reasonable alternative if tocilizumab is not available.

CDC-Relative Mortality as of Aug ’22

Age group rate ratios compared to ages 18 to 29 years[1]

Rate compared to 18-29 years old[1]	0-4 years old	5-17 years old	18-29 years old	30-39 years old	40-49 years old	50-64 years old	65-74 years old	75-84 years old	85+ years old
Cases[2]	<1x	1x	Reference group	1x	1x	1x	1x	1x	1x
Hospitalization[3]	1x	<1x	Reference group	2x	2x	3x	5x	8x	10x
Death[4]	<1x	<1x	Reference group	4x	10x	25x	60x	140x	330x

All rates are relative to the 18 to 29 years age group. This group was selected as the reference group because it has accounted for the largest cumulative number of COVID-19 cases compared to other age groups. Sample interpretation: Compared with ages 18 to 29 years, the rate of death is four times higher in ages 30 to 39 years, and 330 times higher in those who are ages 85 years and older. (In the table, a rate of 1x indicates no difference compared to the 18 to 29 years age group.)

Underwriting pearls…

- Most COVID cases are asymptomatic or mild and truly require no additional steps to underwrite, but I sure like to know they are fully recovered prior to proceeding.
- Some COVID cases are NOT!
  - Keep in mind the risk factors for severe COVID
    - Age, weight, chronic disease of any sort
  - Keep in mind the organs that might be affected by COVID
    - Almost all of them, but especially lungs, liver, kidneys, brain, and heart
  - Those with severe COVID do worse than those with mild or asymptomatic infection with respect to both acute and chronic morbidity and mortality. UNDERWRITE ACCORDINGLY!
  - Keep your spidey senses about you for anything odd.

Case for consideration…

- 42 y/o M, $5MM ART
- App Dec ‘20: Accountant, Non-tobacco, No medical history
- Exam: clean, 6’0”, 260, no doctor
- Labs: A1c 5.8, Chol 235, HDL 33, otherwise normal
- Rx check: Prednisone, Hydroxychloroquine, and Ivermectin—10 days dispensed ~1 month prior to application
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Case for consideration…

- Records
  - Urgent Care with DOE, cough, fever, weakness
  - RR 22, Oxygen Saturation 93%, other vitals normal
  - Exam: dyspneic, rales in bilateral bases
  - CXR: bilateral infiltrates
  - Lab: WBC 12K with right shift (Lymphocytes predominant), COVID positive, ^ BUN and Creatinine (eGFR 55)
  - Rx given and to follow up with PCP 1 day
  - No other records available
- Issue now?
- If not, then what?

Case for consideration…

- Follow up with new PCP 2 months after application
- History of COVID for which he was treated with Ivermectin, Hydroxychloroquine, and Prednisone, now asymptomatic
- Exam:
  - VSS, Afebrile, Oxygen Sat 99%
  - Normal with respect to Lungs, Heart, Abdomen, Nodes, and Extremities
  - Neuro: A&O x 3, No gross deficits
  - Assessment/Plan: Well Adult, F/U 1 year

Long COVID

- Epidemiology
- Disease Manifestations
- Morbidity
- Mortality

Case for consideration—ABR Claim/Critical Illness

- 45 y/o F, $1MM
- Issued 1.5 years ago Preferred Plus
- Healthy until 6 months ago, then COVID resulted in critical illness…
- Hospitalized for 3 months in ICU acute care with renal and respiratory failure
- Kidneys resumed function but lungs were fibrosed
- LTAC 2 months on mechanical ventilation
- Discharged home on portable ventilator
- Claim filed—records show she could be listed for transplant, but she is not a candidate until she is better conditioned—starting PT for that purpose
- Payout: ~$939K

Synonyms and Definition

- Long COVID = Post-COVID Conditions = PASC (Post-Acute Sequelae of SARS-CoV-2 Infection) = Post-Acute COVID-19 = Chronic COVID-19 = U09.9 (unspecified post-COVID conditions) = Long Haul COVID
- CDC: Broad range of symptoms (physical and mental) that develop during or after COVID-19, continue for ≥2 months (i.e. three months from the onset), and are not explained by an alternative diagnosis.

AMERICAN NATIONAL

News > WebMD Health News

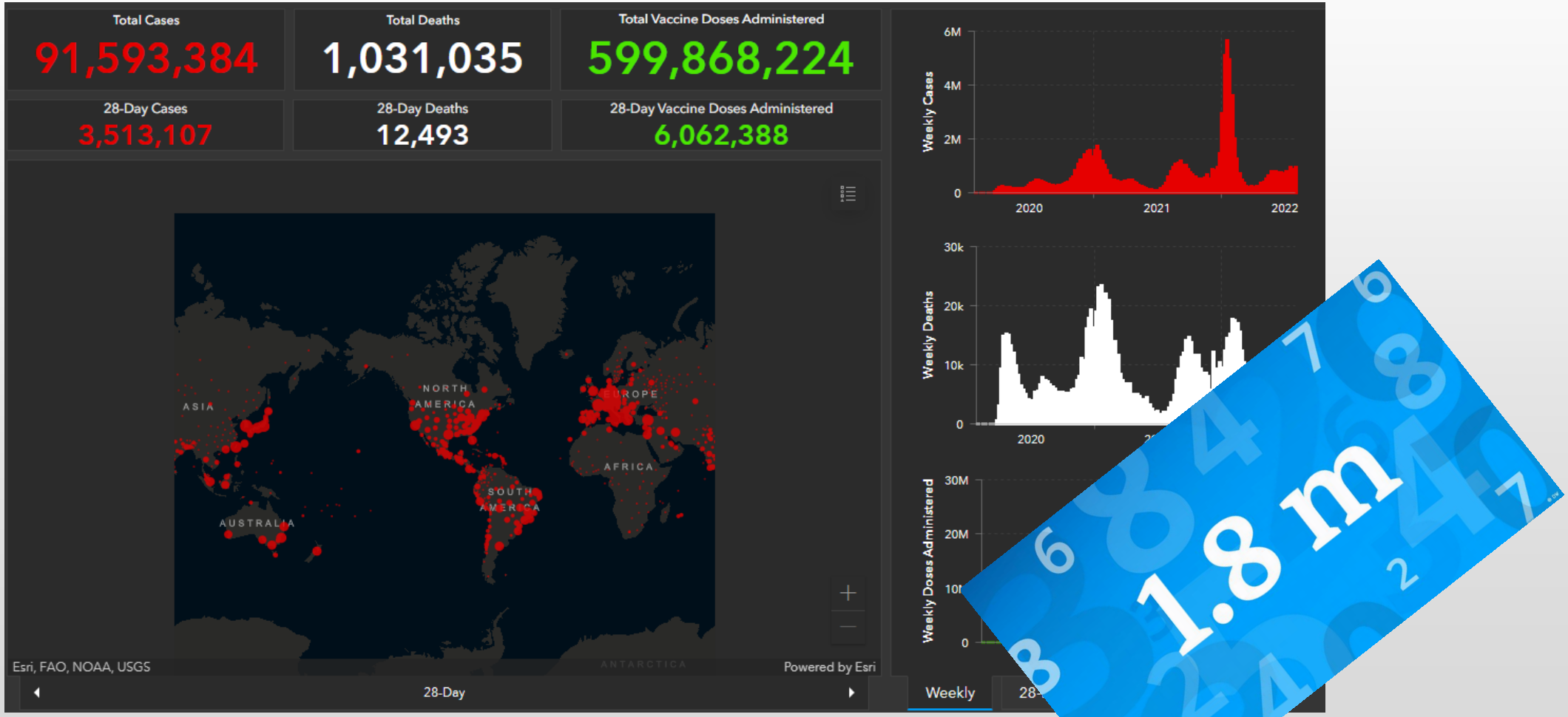
Sickness Lingers in 1 in 4 Kids Who Got COVID With Symptoms

Among more than 80,000 children and adolescents with COVID-19, 25% got symptoms that lasted for at least 4 to 12 weeks or new persistent symptoms that appeared within 12 weeks. Long COVID appeared in more than 29% of the hospitalized patients. Children who had severe COVID-19, obesity, allergy-related diseases, or other long-term health conditions were more likely to get long COVID.

Studies of Concern

- **SARS-CoV-2 is associated with changes in brain structure in UK Biobank:** *785 participants, ½ diagnosed with COVID*: (i) greater reduction in grey matter thickness and tissue-contrast in the orbitofrontal cortex and parahippocampal gyrus, (ii) greater changes in markers of tissue damage in regions functionally-connected to the primary olfactory cortex, and (iii) greater reduction in global brain size
- **Fulminant Myocarditis due to COVID-19**, a case study. **NIH**
- **COVID-19 Kidney Damage: A Known Complication**: Studies indicate **more than 30% of patients hospitalized with COVID-19 develop kidney injury**, and more than 50% of patients in the intensive care unit with kidney injury may require dialysis. **Hopkinsmedicine.org**
- **Covid-19: Long covid symptoms among hospital inpatients show little improvement after a year, data suggest: BMJ** 2230 patients: 30% severe, 20% very severe, and 11% moderate: problems with cognition.
- **Understanding and tracking the impact of long COVID in the United Kingdom. Nature Medicine:** about 1.1 million citizens of the UK are suffering from Long COVID

United States



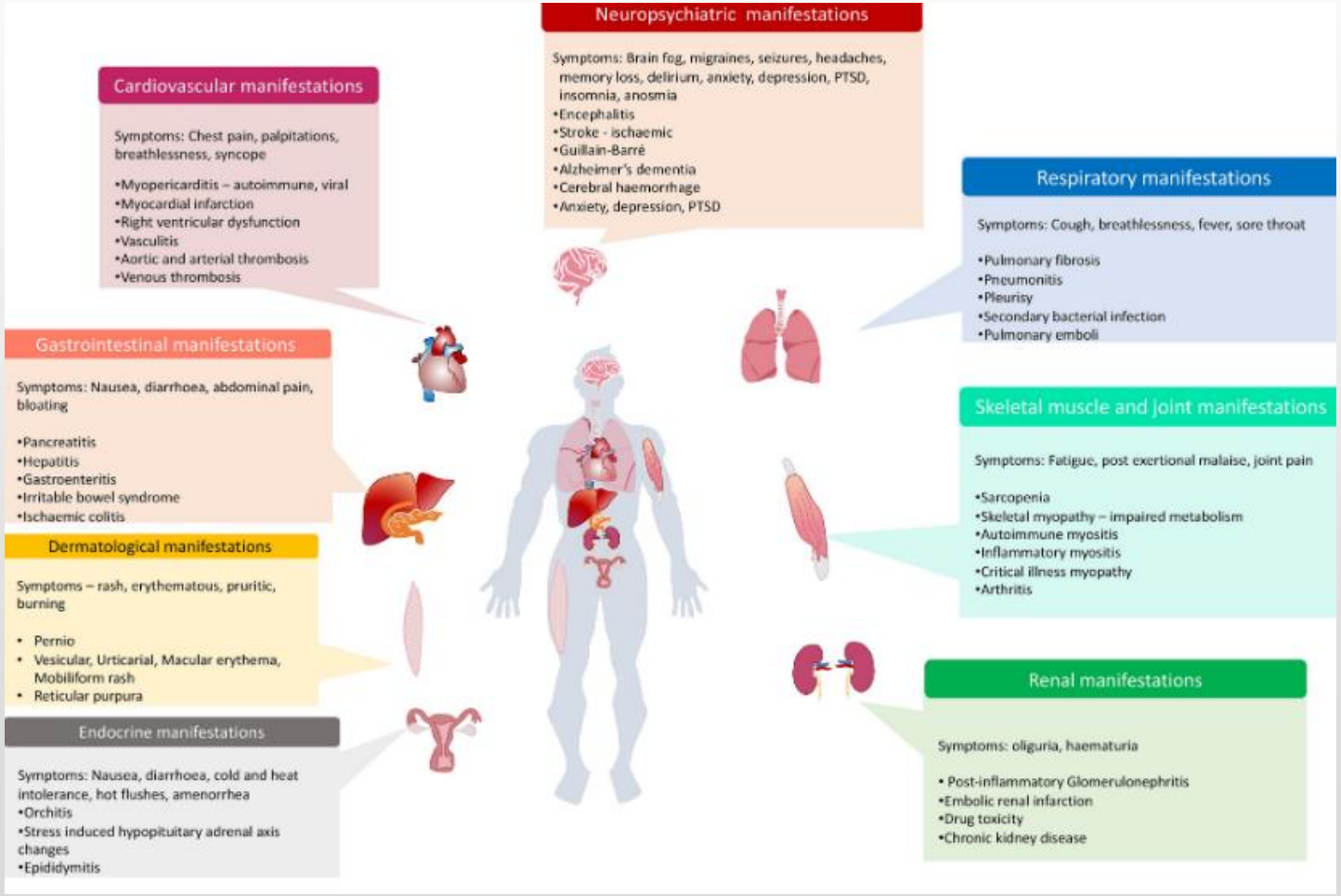
Report: 16 Million Working-Age Americans Have Long COVID, Keeping Up to 4 Million Out of Work

The annual cost of the lost wages alone is about $170 billion a year, according to the report from the Brookings Institution.

By Cecelia Smith-Schoenwalder

Aug. 25, 2022, at 3:09 p.m.

Manifestations of Long COVID–WHO



JAMA. 2022;328(7):676.

Risk factors…

- **In a new prospective observational cohort study of 2560 patients with mild COVID-19, COVID-19 vaccination was associated with a decreased prevalence of postacute sequelae of SARS-CoV-2 infection (PASC) in a dose-dependent fashion (three doses 16 percent, two doses 17.4 percent, and one dose 30 percent) compared with unvaccinated individuals (42.8 percent). Association Between BNT162b2 Vaccination and Long COVID After Infections Not Requiring Hospitalization in Health Care Workers**. Azzolini E, Levi R, Sarti R, Pozzi C, Mollura M, Mantovani A, Rescigno M JAMA. 2022;328(7):676.
- Between 52 and 87% of folks hospitalized with COVID have symptoms last 3-12 months after admission.
- In a variety of studies presented in UpToDate® rates for those with COVID-19 treated as an outpatient varied between 15-39%.
- Bottom lines:
  - Anyone with COVID is at risk for getting long COVID.
  - The best way to mitigate risk is to mitigate the risk of getting COVID in the first place.
  - Those at highest risk for LONG COVID are those with more severe initial infections.

Theories…

- Is Long COVID caused by hidden repositories of virus sneaking out and wreaking havoc?
- Is Long COVID caused by abnormal immune reactions started by the acute infection?
- Is Long COVID caused by abnormal cell signaling that is instigated by the virus?

Underwriting Implications

- Was or is the applicant infected?
- Did they require hospitalization? Mechanical ventilation?
- Have they fully recovered and gotten back to all normal activities?
- Are there indications of problems on labs, exam, APS?
  - Renal function, liver function, nutritional status, NT-proBNP
- If the applicant has ratable impairments that we know can result in severe infections, and therefore a higher risk for more complications and Long COVID, have they been immunized?
  - Obesity, HTN, HIV, Autoimmune Disease, Cancer

Treatment…

- Best served by seeking care at a center.
- Treatment depends on diagnosis and manifestations.
- Be aware of any treatments that appear out of keeping with admitted history…
  - New medications for kidneys, lungs, brain

Case for consideration

- 45 y/o M $5MM Term
- App: Hospitalized with COVID June 2021/no physician/otherwise nothing
- Exam: Admitted to same hospitalization/checkup 1 month ago/Preferred Plus
- Labs (including BNP): normal/Preferred Plus
- Rx Check: 1 month prior to application: Ventolin Nebulizer, Prednisone for 5 days.
- Proceed? Preferred Plus? Some other rating? Some other action?

Case for consideration…

- Medical Records from provider listed on Rx check–PCP.
- 1 month prior to application HPI: “was well until late last week when he developed coughing, sneezing, and a low-grade fever. Cough non-productive; temperature 100”
  - Exam: Oxygen Sat 98%, VSS, afebrile, wheezing, no rales or rhonchi, otherwise normal
  - Labs: CBC normal, CMP normal, COVID-19 negative
  - CXR: possible atelectasis in the right base, no other acute findings
  - Dx: Viral URI
  - Rx: Ventolin, Prednisone
  - F/U PRN

To summarize Long COVID

- Will likely occur in at least 2% of those who have acute infection, and my guess is that it will be 5% or more.
- Higher likelihood to occur in those with severe illness—keep in mind the risk factors for severe illness.
- Symptoms are all over the place with some being more indicative of mortality than others (severe disease of lung, liver, kidneys, CNS).
- The best treatment is prevention of initial infection.
- Treatment is primarily based on symptoms and manifestations at this point.
- Morbidity—for sure! Mortality from Long COVID is anybody's guess right now, but it will be higher than normal.

Sources not explicitly noted in the presentation:

- Johns Hopkins University CSSE data
- UpToDate®
- CDC
- NIH
- WHO
- Multiorgan and Renal Tropism of SARS-CoV-2. Puelles VG, Lütgehetmann M, Lindenmeyer MT, Sperhake JP, Wong MN, Allweiss L, Chilla S, Heinemann A, Wanner N, Liu S, Braun F, Lu S, Pfefferle S, Schröder AS, Edler C, Gross O, Glatzel M, Wichmann D, Wiech T, Kluge S, Pueschel K, Aepfelbacher M, Huber TB; N Engl J Med. 2020;383(6):590. Epub 2020 May 13.