

## **COVID-19 Pandemic** -- The Virus & Infection



Kevin T. Kavanagh, MD, MS Health Watch USA <sup>sm</sup>



### **COVID-19: What Is A Coronavirus ?**



# Coronavirus Disease 2019 (COVID-19) is caused by the SARS-CoV-2 Virus



The Corona Virus is composed of a strand of RNA surrounded by a lipoprotein capsule. The capsule is surrounded by spike proteins which are key to cellular entry.

RNA viruses have a high mutation rate. Those mutations involving the spike protein are of importance.

There are two types of antibodies:

- Binding, which binds to the not critical parts of the virus.
- Neutralizing, binds to the spike proteins and inhibits cell entry.

There are four other coronavirus which cause about 20% of colds <u>https://www.cdc.gov/coronavirus/general-information.html</u>

However, this one is different. It is related to the MERS and SARS corona virus which are very serious and rare viruses. Unlike the "cold" coronaviruses, SARS-CoV-2 attached to the ACE-2 receptor which is found though out the body. And a runny nose which is often caused by common coronaviruses, is a rare symptom with COVID-19.

### **COVID-19: Immunity**



## EPIDEMIOLOGY & INFECTION

<u>Epidemiol Infect</u>. 1990 Oct; 105(2): 435–446. doi: <u>10.1017/s0950268800048019</u> PMCID: PMC2271881 PMID: <u>2170159</u>

The time course of the immune response to experimental coronavirus infection of man.

K. A. Callow, H. F. Parry, M. Sergeant, and D. A. Tyrrell



The coronavirus studied in the paper provided immunity which last about 1 year. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2271881/

#### Coronavirus protective immunity is short-lasting

 Arthur WD Edridge, Joanna M Kaczorowska, Alexis CR Hoste, Margreet Bakker, Michelle Klein, Maarten F Jebbink, Amy Matser, Cormac Kinsella, Paloma Rueda, Maria Prins, Patricia Sastre, Martin Deijs, 
 Lia van der Hoek
 doi: https://doi.org/10.1101/2020.05.11.20086439

An alarmingly short duration of protective immunity to coronaviruses was found. Reinfections occurred frequently at 12 months post-infection and there was for each virus a substantial reduction in antibody levels as soon as 6 months post-infection.



Prolonged Natural Immunity Has Not Been Supported by Recent Studies, Especially In Those Who Are Asymptomatic or Have Mild Symptoms.

- A recent study in Nature found that at 39 days post infection 33% had a low neutralizing antibody level. <u>https://www.nature.com/articles/s41586-020-2456-9</u>
- Another study out of China found that 2 to 3 months after symptom onset "Forty percent of asymptomatic individuals became seronegative and 12.9% of the symptomatic group became negative for IgG in the early convalescent phase." <u>https://www.nature.com/articles/s41591-020-0965-6</u>

### **COVID-19: Mutates & Different Strains**



# The virus has already mutated and at least two strains exist, but the clinical importance is still being studied.

#### Spike mutation pipeline reveals the emergence of a more transmissible form of SARS-CoV-2

B Korber, WM Fischer, S Gnanakaran, H Yoon, J Theiler, W Abfalterer,
B Foley, EE Giorgi, T Bhattacharya, MD Parker, DG Partridge, CM Evans, TM Freeman, TI de Silva,
TI de Silva,
De behalf of the Sheffield COVID-19 Genomics Group, CC LaBranche,
DC Montefiori
doi: https://doi.org/10.1101/2020.04.29.069054

"The mutation Spike D614G is of urgent concern; it began spreading in Europe in early February, and when introduced to new regions it rapidly becomes the dominant form. .... These finding have important implications for SARS-CoV-2 transmission, pathogenesis and immune interventions."

Los Alamos National Laboratory & University of Sheffield, UK

nttps://www.biorxiv.org/content/10.1101/2020.04.29.069054v2

Daily Mail: "TWO strains of the killer coronavirus are spreading around the world – and 70% of infected patients have caught the more aggressive and contagious type, study claims" (China) https://www.dailymail.co.uk/health/article-8073543/TWO-strains-killer-coronavirus-spreading-study-claims.html

#### Good news there may be some cross immunity provided by exposure to other

coronaviruses https://medicalxpress.com/news/2020-07-scientists-uncover-sars-cov-specific-cell-immunity.html

### COVID-19: Antibody Levels in Communities



Sweden: Swedish antibody study shows long road to immunity as COVID-19 toll mounts: "A Swedish study found that just 7.3 percent of Stockholmers developed COVID-19 antibodies by late April." <a href="https://www.reuters.com/article/us-health-coronavirus-sweden-strategy/swedish-antibody-study-shows-long-road-to-immunity-as-covid-19-toll-mounts-idUSKBN22W2YC">https://www.reuters.com/article/us-health-coronavirus-sweden-strategy/swedish-antibody-study-shows-long-road-to-immunity-as-covid-19-toll-mounts-idUSKBN22W2YC</a>

**Spain:** "Antibody levels in Spain were also lower than expected. "Seroprevalence was **5.0%** (95% CI 4.7–5.4) by the point-of-care test and 4.6% (4.3–5.0) by immunoassay"" <u>https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31483-5/fulltext</u>

USA: Los Angeles: "Only 2.1% tested positive for antibodies... 1,014 adults were tested in the county between May 8 and 12. The results suggest that only about 165,000 L.A. County adults have antibodies to the coronavirus — an estimate nearly 50% lower than the first study's results." https://www.latimes.com/california/story/2020-06-05/how-many-people-in l-e-actually have-coronavirus-why-health-officials-still-dont-know-for-sure

USA: Los Angeles: "...the SARS-CoV-2 spike protein antibodies ranged from 1.0% in the San Francisco Bay area (collected April 23-27)" https://lamanetwork.com/journals/jamainternalmedicine/fullarticle/2768834

USA: New York: "...6.9% of persons in New York City (collected March 23-April 1)." https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2768834

### **COVID-19: Antibody Levels in Patients**



#### South Korean Study:

The Korean Herald: "According to the Korea Centers for Disease Control and Prevention (KCDC), 111 people have tested positive for the new coronavirus again, after they were released from quarantine."

"They also said earlier the COVID-19 virus may remain latent in certain cells in the body and attack the respiratory organs again once reactivated"

http://www.koreaherald.com/view.php?ud=20200412000213&np=3&mp=1

https://www.reuters.com/article/us-health-coronavirus-southkorea/south-korea-reports-

recovered-coronavirus-patients-testing-positive-again-idUSKCN21S15X

285 re-positive cases were investigated, 44% of these cases had symptoms, but none were infectious (no live viruses were isolated).

https://www.cdc.go.kr/board/board.es?mid=a3040200000&bid=0030

### COVID-19: Infectivity – R0





#### **EMERGING INFECTIOUS DISEASES**°

Volume 26, Number 7—July 2020

High Contagiousness and Rapid Spread of Severe Acute Respiratory Syndrome Coronavirus 2

Steven Sanche<sup>1</sup>, Yen Ting Lin<sup>1</sup>, Chonggang Xu, Ethan Romero-Severson, Nick Hengartner, and Ruian Ke⊠ Author affiliations: Los Alamos National Laboratory, Los Alamos, New Mexico, USA

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#### Abstract

Severe acute respiratory syndrome coronavirus 2 is the causative agent of the ongoing coronavirus disease pandemic. Initial estimates of the early dynamics of the outbreak in Wuhan, China, suggested a doubling time of the number of infected persons of 6–7 days and a basic reproductive number (R<sub>0</sub>) of 2.2–2.7. We collected extensive individual case reports across China and estimated key epidemiologic parameters, including the incubation period (4.2 days). We then designed 2 mathematical modeling approaches to infer the outbreak dynamics in Wuhan by using high-resolution domestic travel and infection data. Results show that the doubling time early in the epidemic in Wuhan was 2.3–3.3 days. Assuming a serial interval of 6–9 days, we calculated a median R<sub>0</sub> value of 5.7 (95% CI 3.8–8.9). We further show that active surveillance, contact tracing, quarantine, and early strong social distancing efforts are needed to stop transmission of the virus.

https://wwwnc.cdc.gov/eid/article/26/7/20-0282 article

R0 (pronounced "R naught") is a measurement of the infectivity of a pathogen. A R0 of three means that on average one infected individual will spread it to three other people.

It is estimated that SARS-CoV-2 has an R0 of 5.7 placing it in the same category of Smallpox, Polio and Mumps. The season flu has an R0 of 1.3.

### **COVID-19: Herd Immunity**





# My patient caught Covid-19 twice. So long to herd immunity hopes?

Emerging cases of Covid-19 reinfection suggest herd immunity could be wishful thinking.

By D. Clay Ackerly | Jul 12, 2020, 9:40am EDT

https://www.vox.com/2020/7/12/21321653/getting-covid-19-twice-reinfection-antibody-herd-immunity

- With an R0 of 5.7 It would take over 80% of the population to become immune.
- Even if this happened with the observation of fading immunity in individuals and low rates of immunity in communities, it is unlikely Herd Immunity will naturally take place.
  https://www.pbs.org/wgbh/nova/article/herd-immunity/

Our Best Strategy is either the use of Masks/Social Distancing/Hand Hygiene OR a Vaccine OR Both.

### **COVID-19: Tests**



#### There Are Three Types of Tests

https://www.npr.org/sections/health-shots/2020/05/01/847368012 how-reliable-are-covid-19-tests-depends-which-one-you-mean

#### **Molecular Tests: RT-PCR (Reverse Transcription-Polymerase Chain Reaction )**, Rapid

**Tests.** These tests identifies the RNA of the Virus.

-- Very low false positive rates and acceptable false negative rates when performed in a laboratory setting. Usually takes less than 48 hrs. to get back results.

-- The rapid tests may have a high false negative rate of between 10% to 15%. However, can give a result in as early as 15 to 45 mins. Thus, much better screening than temperature checks. Two examples are the Abbott and Cepheid Tests.

-- https://www.cdc.gov/flu/professionals/diagnosis/molecular-assays.htm

- Antibody Test This test is used to diagnosis if you had the infection and may be immune. However, there has been a problem with many of manufacturers producing tests which may have a very high false positive rate – They do not distinguish between other coronavirus. This has confounded some of the previous research on prevalence of immunity in communities. https://www.nprorg/sections/health-shots/2020/05/04/850195471/fda-cracks-down-on-antibody-tests-forcoronavirus
- Antigen Test. This tests for viral proteins, similar to the strep and flu test. Is very quick, but has had questionable reliability. If reliable this test could be a game changer. https://www.npr.org/2020/07/08/888846302/

**Pool Testing:** This involves collecting samples from a number of individuals (between 3 to 50) and testing all at once. If all are negative then all are cleared, if positive, then you need to test each one individually. https://www.nbcnews.com/health/health.news/fda-authorizes-first-covid-19-test-people-without-symptoms-n1235119





Illustration: Anna & Elena Balbusso

## We Thought It Was Just a Respiratory Virus

We were wrong.

By Ariel Bleicher and Katherine Conrad • UCSF Magazine

• Summer 2020

"However, infection with SARS-CoV-2 usually doesn't feel like a cold. Fewer than 20% of infected people who eventually show up at a hospital report having had a sore throat or runny nose. During the first few days of being infected, you're more likely to have a fever, dry cough or, peculiarly, lose your sense of smell or taste."

#### Watch for symptoms

People with COVID-19 have had a wide range of symptoms reported – ranging from mild symptoms to severe illness. Symptoms may appear **2-14 days after exposure to the virus.** People with these symptoms may have COVID-19:

- Fever or chills
- Cough
- Shortness of breath or difficulty breathing
- Fatigue
- Muscle or body aches
- Headache
- New loss of taste or smell
- Sore throat
- Congestion or runny nose
- Nausea or vomiting
- Diarrhea

#### **Very long Incubation Period**

-- Symptoms appear 2 to 14 days after exposure Death occurs 2 to 4 weeks after symptoms appear -- Diagnosed cases also lag behind the onset of symptoms. Exceptions are in patients identified with case tracking & asymptomatic carriers.

This list does not include all possible symptoms. CDC will continue to update this list as we learn more about COVID-19.

https://www.cdc.gov/coronavirus/2019-ncov/community/schools-childcare/index.html





Altered mental status/Confusion

Centers for Disease Control and Prevention CDC 24/7: Saving Lives, Protecting People™

Hospitalization Rates and Characteristics of Patients Hospitalized with Laboratory-Confirmed Coronavirus Disease 2019 — COVID-NET, 14 States, March 1-30, 2020

	Age group (yrs), no./total no. (%)			
Symptom <sup>§§</sup>	Overall	18–49	50-64	≥65 years
Cough	155/180 (86.1)	43/47 (91.5)	54/60 (90.0)	58/73 (79.5)
Fever/Chills	153/180 (85.0)	38/47 (80.9)	53/60 (88.3)	62/73 (84.9)
Shortness of breath	144/180 (80.0)	40/47 (85.1)	50/60 (83.3)	54/73 (74.0)
Myalgia	62/180 (34.4)	20/47 (42.6)	23/60 (38.3)	19/73 (26.0)
Diarrhea	48/180 (26.7)	10/47 (21.3)	17/60 (28.3)	21/73 (28.8)
Nausea/Vomiting	44/180 (24.4)	12/47 (25.5)	17/60 (28.3)	15/73 (20.5)
Sore throat	32/180 (17.8)	8/47 (17.0)	13/60 (21.7)	11/73 (15.1)
Headache	29/180 (16.1)	10/47 (21.3)	12/60 (20.0)	7/73 (9.6)
Nasal congestion/Rhinorrhea	29/180 (16.1)	8/47 (17.0)	13/60 (21.7)	8/73 (11.0)
Chest pain	27/180 (15.0)	9/47 (19.1)	13/60 (21.7)	5/73 (6.8)
Abdominal pain	15/180 (8.3)	6/47 (12.8)	6/60 (10.0)	3/73 (4.1)
Wheezing	12/180 (6.7)	3/47 (6.4)	2/60 (3.3)	7/73 (9.6)

11/180 (6.1)

3/47 (6.4)

2/60 (3.3)

6/73 (8.2)

https://www.cdc.gov/mmwr/volumes/ 69/wr/mm6915e3.htm

### **COVID-19: Asymptomatic Carriers**



 Review
 > Otolaryngol Head Neck Surg. 2020 Jul;163(1):3-11. doi: 10.1177/0194599820926473.

 Epub 2020 May 5.

#### The Prevalence of Olfactory and Gustatory Dysfunction in COVID-19 Patients: A Systematic Review and Meta-analysis

Jane Y Tong <sup>1</sup>, Amanda Wong <sup>2</sup>, Daniel Zhu <sup>2</sup>, Judd H Fastenberg <sup>2</sup> <sup>3</sup>, Tristan Tham <sup>2</sup> <sup>3</sup>

- Ten studies were analyzed for olfactory dysfunction (n = 1627), demonstrating 52.73% (95% CI, 29.64%-75.23%) prevalence among patients with COVID-19.
- Nine studies were analyzed for gustatory dysfunction (n = 1390), demonstrating 43.93% (95% CI, 20.46%-68.95%) prevalence.



Health

#### Coronavirus: Sense of smell and taste 'improve for most'

By Smitha Mundasad Health reporter, BBC News

#### **Coronavirus: Key symptoms**

BBC



July 3, 2020

"Almost 90% of people who lost their sense of smell or taste while infected with Covid-19 improved or recovered within a month, a study has found."

https://www.bbc.com/news/health-53265280

### **COVID-19: Asymptomatic Spread**



#### nature medicine

Brief Communication | Published: 15 April 2020

# Temporal dynamics in viral shedding and transmissibility of COVID-19

Xi He, Eric H. Y. Lau <sup>I</sup>, Peng Wu, Xilong Deng, Jian Wang, Xinxin Hao, Yiu Chung Lau, Jessica Y. Wong, Yujuan Guan, Xinghua Tan, Xiaoneng Mo, Yanqing Chen, Baolin Liao, Weilie Chen, Fengyu Hu, Qing Zhang, Mingqiu Zhong, Yanrong Wu, Lingzhai Zhao, Fuchun Zhang, Benjamin J. Cowling, Fang Li & Gabriel M. Leung



Nature Medicine 26, 672–675(2020) Cite this article

"We estimated that 44% (95% confidence interval, 25–69%) of secondary cases were infected during the index cases' presymptomatic stage, in settings with substantial household clustering, active case finding and quarantine outside the home."

## **COVID-19: Asymptomatic Spread**



# **Eurosurveillance** Europe's journal on infectious disease surveillance, epidemiology

## Estimating the generation interval for coronavirus disease (COVID-19) based on symptom onset data, March 2020

Tapiwa Ganyani<sup>1</sup> (b), Cécile Kremer<sup>1</sup> , Dongxuan Chen<sup>2,3</sup> , Andrea Torneri<sup>1,4</sup> , Christel Faes<sup>1</sup> , Jacco Wallinga<sup>2,3</sup> , Niel Hens<sup>1,4</sup>

#### The proportion of pre-symptomatic transmission was:

- 48% (95% Crl: 32–67) for Singapore and
- 62% (95% CrI: 50–76) for Tianjin.

https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.17.2000257



CDC Director On Models For The Months To Come: 'This Virus Is Going To Be With Us'

March 31, 2020 · 5:16 AM ET

Robert Redfield: ".... a significant number of individuals that are infected actually remain asymptomatic. That may be as many as 25%. That's important, because now you have individuals that may not have any symptoms that can contribute to transmission, and we have learned that in fact they do contribute to transmission."

https://www.npr.org/sections/health-shots/2020/03/31/824155179/cdc-director-on-models-for-the-months-tocome-this-virus-is-going-to-be-with-us



### **COVID-19: Asymptomatic Carriers**



#### **Annals of Internal Medicine**<sup>®</sup>

Reviews | 3 Jun 2020

Prevalence of Asymptomatic SARS-CoV-2 Infection

A Narrative Review

Daniel P. Oran, AM, Eric J. Topol, MD 🛛 🝺 View fewer authors 🗙

The Authors Reviewed 16 Studies Which Reported Rates of Asymptomatic Infection in Different Groups of Patients.

- The likelihood that approximately 40% to 45% of those infected with SARS-CoV-2 will remain asymptomatic suggests that the virus might have greater potential than previously estimated to spread silently and deeply through human populations.
- Asymptomatic persons can transmit SARS-CoV-2 to others for an extended period, perhaps longer than 14 days.

#### **COVID-19: Severe Outcome**



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#### Morbidity and Mortality Weekly Report (<u>MMWR</u>)

#### Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) — United States, February 12–March 16, 2020

Weekly / March 27, 2020 / 69(12);343-346

https://www.cdc.gov/mmwr/volumes/69/wr/mm6912e2.htm

TABLE. Hospitalization, intensive care unit (ICU) admission, and case– fatality percentages for reported COVID–19 cases, by age group — United States, February 12–March 16, 2020

Age group (vrs)	%*				
(no. of cases)	Hospitalization	ICU admission	Case-fatality		
0–19 (123)	1.6–2.5	0	0		
20–44 (705)	14.3-20.8	2.0-4.2	0.1-0.2		
45–54 (429)	21.2-28.3	5.4-10.4	0.5-0.8		
55–64 (429)	20.5-30.1	4.7-11.2	1.4–2.6		
65–74 (409)	28.6-43.5	8.1–18.8	2.7-4.9		
75–84 (210)	30.5-58.7	10.5-31.0	4.3-10.5		
≥85 (144)	31.3–70.3	6.3–29.0	10.4–27.3		
Total (2,449)	20.7-31.4	4.9–11.5	1.8–3.4		

\* Lower bound of range = number of persons hospitalized, admitted to ICU, or who died among total in age group; upper bound of range = number of persons hospitalized, admitted to ICU, or who died among total in age group with known hospitalization status, ICU admission status, or death. The cases described in this report include both COVID-19 cases confirmed by state or local public health laboratories, as well as those with a positive test at the state or local public health laboratories and confirmation at CDC.

CDC COVID-19 Response Team

### **COVID-19: Co-Morbidities**



	Age group (yrs), no./total no. (%)			
Underlying condition	Overall	18–49	50-64	≥65 years
Any underlying condition	159/178 (89.3)	41/48 (85.4)	51/59 (86.4)	67/71 (94.4)
Hypertension	79/159 (49.7)	7/40 (17.5)	27/57 (47.4)	45/62 (72.6)
Obesity⁵	73/151 (48.3)	23/39 (59.0)	25/51 (49.0)	25/61 (41.0)
Chronic metabolic disease <sup>¶</sup>	60/166 (36.1)	10/46 (21.7)	21/56 (37.5)	29/64 (45.3)
Diabetes mellitus	47/166 (28.3)	9/46 (19.6)	18/56 (32.1)	20/64 (31.3)
Chronic lung disease	55/159 (34.6)	16/44 (36.4)	15/53 (28.3)	24/62 (38.7)
Asthma	27/159 (17.0)	12/44 (27.3)	7/53 (13.2)	8/62 (12.9)
Chronic obstructive pulmonary disease	17/159 (10.7)	0/44 (0.0)	3/53 (5.7)	14/62 (22.6)
Cardiovascular disease**	45/162 (27.8)	2/43 (4.7)	11/56 (19.6)	32/63 (50.8)
Coronary artery disease	23/162 (14.2)	0/43 (0.0)	7/56 (12.5)	16/63 (25.4)
Congestive heart failure	11/162 (6.8)	2/43 (4.7)	3/56 (5.4)	6/63 (9.5)
Neurologic disease	22/157 (14.0)	4/42 (9.5)	4/55 (7.3)	14/60 (23.3)
Renal disease	20/153 (13.1)	3/41 (7.3)	2/53 (3.8)	15/59 (25.4)
Immunosuppressive condition	15/156 (9.6)	5/43 (11.6)	4/54 (7.4)	6/59 (10.2)
Gastrointestinal/Liver disease	10/152 (6.6)	4/42 (9.5)	0/54 (0.0)	6/56 (10.7)
Blood disorder	9/156 (5.8)	1/43 (2.3)	1/55 (1.8)	7/58 (12.1)
Rheumatologic/Autoimmune disease	3/154 (1.9)	1/42 (2.4)	0/54 (0.0)	2/58 (3.4)
Pregnancy <sup>++</sup>	3/33 (9.1)	3/33 (9.1)	N/A	N/A



Centers for Disease Control and Prevention CDC 24/7: Saving Lives, Protecting People™

Hospitalization Rates and Characteristics of Patients Hospitalized with Laboratory-Confirmed Coronavirus Disease 2019 — COVID-NET, 14 States, March 1–30, 2020

https://www.cdc.gov/mmwr/volumes/69/wr/ mm6915e3.htm

#### As obesity's link to COVID-19 grows, one family that lost 24-year-old daughter diets together

 Jayne O'Donnell
 USA TODAY

 Published 12:40 p.m. ET May 23, 2020 | Updated 2:10 p.m. ET Jun. 3, 2020

https://www.usatoday.com/story/news/2020 /05/23/obesity-makes-covid-19-risk-largerhospitals-challenges-muchharder/5221600002/





Prolonged symptom duration and disability are common in adults hospitalized with severe coronavirus disease 2019 (COVID-19) -- CDC COVID-19 Response Team

https://www.cdc.gov/mmwr/volumes/69/wr/mm6930e1.htm

### **COVID-19: Persistent Symptoms**



# JAMA Network

#### Persistent Symptoms in Patients After Acute COVID-19

Angelo Carfì, MD<sup>1</sup>; Roberto Bernabei, MD<sup>1</sup>; Francesco Landi, MD, PhD<sup>1</sup>; et al JAMA. Published online July 9, 2020. doi:10.1001/jama.2020.12603



patients: mean of **2** months post COVID-19 first symptoms: -- 87.4% reported persistence of

- at least 1 symptom,
- -- Shortness of Breath (dyspnea) (43%),
- -- Tiredness (53%),
- -- Worsened quality of life was observed among 44.1% of patients

#### **COVID-19: Persistent Symptoms**



Centers for Disease Control and Prevention CDC 24/7: Saving Lives, Protecting People™ Morbidity and Mortality Weekly Report (MMWR)

Weekly / July 31, 2020 / 69(30);993-998

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



\* 294 patients responded to 14–21-day interview, did not report a previous positive SARS-CoV-2 test before the reference test, and answered questions about symptoms; 276 (94%) of these reported one or more symptoms at the time of SARS-CoV-2 RT-PCR testing; those who were interviewed at 7 days were excluded, with 274 included here.

Characterizing return to baseline health among outpatients with milder COVID-19 illness

## 35% had not returned to their usual state of health when interviewed

#### 2–3 weeks after testing. Including:

- 26% among those aged 18–34 years,
- 32% among those aged 35–49 years;
- 47% among those aged  $\geq$ 50 years

https://www.cdc.gov/mmwr/volumes/69/wr/ mm6930e1.htm

### **COVID-19: Persistent Symptoms**



#### Forbes

Jun 13, 2020, 07:09am

Report Suggests Some 'Mildly Symptomatic' Covid-19 Patients Endure Serious Long-Term Effects



#### Joshua Cohen Contributor 🛈

#### Healthcare

I write about prescription drug value, market access, healthcare systems, and ethics of distribution of healthcare resources

https://www.forbes.com/sites/joshuacohen/2 020/06/13/report-suggests-some-mildlysymptomatic-covid-19-patients-endureserious-long-term-effects/

#### Long Haulers

A study from the Lung Foundation in the Netherlands surveyed 1,622 patients who had reported long-term effects of COVID-19. 91% of the patients were not hospitalized.

- 88% reported intense fatigue
- 74% shortness of breath
- 45% reported chest pressure
- 40% headaches
- 35% muscle aches
- 29% dizziness

# AND 90% stated they had problems with simple daily activities.

https://nos.nl/artikel/2337012-longfonds-ernstigeklachten-onder-coronapatienten-die-thuisherstelden.html

### COVID-19: Persistent Symptoms Tiredness & Brain Fog



# The Atlantic

## COVID-19 Can Last for Several Months

The disease's "long-haulers" have endured relentless waves of debilitating symptoms and disbelief from doctors and friends.

Ashley Shew: "... as the pandemic progresses, the number of people with medium-to-long-term disabilities will increase. "Some science fiction and more than a few tech bros—have led us to believe in a nondisabled future," "But whether through environmental catastrophe, or new viruses, we can expect more, exacerbated, and new disabilities." "

https://www.theatlantic.com/health/archive/2020/06/covid-19-coronavirus-longtermsymptoms-months/612679/

### COVID-19: Persistent Symptoms Neurological Syndromes





The emerging spectrum of COVID-19 neurology: clinical, radiological and laboratory findings 👌

Ross W Paterson, Rachel L Brown, Laura Benjamin, Ross Nortley, Sarah Wiethoff, Tehmina Bharucha, Dipa L Jayaseelan, Guru Kumar, Rhian E Raftopoulos, Laura Zambreanu ... Show more

#### Neurological Diagnoses in 43 SARS-CoV-2 patients. 5 major categories:

- Encephalopathies (*n* = 10) with delirium/psychosis
- Inflammatory CNS syndromes (n = 12) which included encephalitis (n = 2), acute disseminated encephalomyelitis (n = 9).
- Ischemic strokes (n = 8) associated with hypercoagulability of the blood (4 with pulmonary thromboembolism)
- Peripheral neurological disorders (n = 8): Guillain-Barré syndrome (n = 7), brachial plexopathy (n = 1).
- 5 patients with miscellaneous central nervous system disorders.

Longitudinal follow-up studies will be necessary to ascertain the long-term neurological and neuropsychological consequences of this pandemic.

### COVID-19: Persistent Symptoms Hypercoagulation – Stroke and MI



Hematological findings and complications of COVID-19 Terpos E, Ioannis Ntanasis-Stathopoulos I, Ismail Elalamy I, et. al

Am J Hematol. 2020 May 23 : 10.1002/ajh.25829. doi: 10.1002/ajh.25829

#### "COVID-19 infected patients, whether hospitalized or ambulatory, are at high risk for venous thromboembolism, and an early and prolonged pharmacological thromboprophylaxis with low molecular weight heparin is highly recommended."

"Furthermore, blood hypercoagulability is common among hospitalized COVID-19 patients. Elevated D-Dimer levels are consistently reported, whereas their gradual increase during disease course is particularly associated with disease worsening. Other coagulation abnormalities such as PT and a PTT prolongation, fibrin degradation products increase, with severe thrombocytopenia lead to life-threatening disseminated intravascular coagulation (DIC), which necessitates continuous vigilance and prompt intervention."

### COVID-19: Persistent Symptoms Hypercoagulation – Stroke and MI



#### Pulmonary Embolism in Patients With COVID-19

-- Over a 20% incidence of Pulmonary Embolisms in ICU Patients https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.120.047430

#### Incidence of thrombotic complications in critically ill ICU patients with COVID-19

-- 31% incidence of thrombotic complications in ICU patients with COVID-19. Klok FA, Kruip MKHA, van der Meer MJN, et al. "Our findings reinforce the recommendation to strictly apply pharmacological thrombosis prophylaxis in all COVID-19 patients admitted to the ICU, and are strongly suggestive of increasing the prophylaxis towards high-prophylactic doses, even in the absence of randomized evidence."

https://pubmed.ncbi.nlm.nih.gov/32291094/

### COVID-19: Persistent Symptoms Heart



JAMA Network - China: "In this cohort study of 416 consecutive patients with confirmed COVID-19, cardiac injury occurred in 19.7% of patients during hospitalization, and it was one independent risk factor for in-hospital mortality." *51% of those with heart damage died compared to 4.5% without damage. -- March 25, 2020.* https://jamanetwork.com/journals/jamacardiology/fullarticle/2763524

JAMA Network - Germany: In the autopsies of 39 patients (78 to 89 years) who died of the virus, the virus was found in 24 (61.5%) patients, with high cardiac viral loads in 16 patients. July 27, 2020.

https://jamanetwork.com/journals/jamacardiology/fullarticle/2768914

JAMA Network - Germany: "In this cohort study including 100 patients recently recovered from COVID-19 identified from a COVID-19 test center, cardiac magnetic resonance imaging revealed cardiac involvement in 78 patients (78%) and ongoing myocardial inflammation in 60 patients (60%)" *Hospitalized patients who recovered and were a minimum of 2 weeks from original diagnosis. – July, 27, 2020.* 

https://jamanetwork.com/journals/jamacardiology/fullarticle/2768916

### COVID-19: Persistent Symptoms Kidney



#### Kidney disease is associated with in-hospital death of patients with COVID-19

Of 701 patients admitted to Wuhan Hospital, at the time of admission 50% had proteinuria and 27% had hematuria. 5% developed acute kidney injury and this was associated with an increased risk of mortality. https://pubmed.ncbi.nlm.nih.gov/32247631/

#### Kidney injury seen in more than a third of hospitalized COVID-19 patients

Over a third of 5,449 patients admitted to Northwell Health developed acute kidney injury (AKI) and 14% of AKI patients required dialysis. 90% of patients who required ventilator support developed acute kidney failure. <u>https://www.reuters.com/article/us-health-coronavirus-kidney/kidney-injury-seen-in-more-than-a-third-of-hospitalized-covid-19-patients-u-s-study-idUSKBN22Q0U7</u>

### COVID-19: Persistent Symptoms Lung



#### THE LANCET Respiratory Medicine

#### Pulmonary fibrosis secondary to COVID-19: a call to arms?

Paolo Spagnolo ⊠ • Elisabetta Balestro • Stefano Aliberti • Elisabetta Cocconcelli • Davide Biondini • Giovanni Della Casa • et al. Show all authors

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30222-8/fulltext

The sicker a patient is the more likely they will develop pulmonary fibrosis. Most patients who require ventilator support or ECMO with COVID-19 may develop pulmonary fibrosis. Many requiring oxygen administration are expected to have permanent lung injury but the extent of which requires further research.

There is even concern that lung damage can occur in about half of the asymptomatic patients:

https://www.msn.com/en-us/health/medical/scientists-see-lung-damage-in-asymptomatic-covid-19patients/ar-BB16aukf

https://www.msn.com/en-us/health/medical/new-arizona-concern-study-shows-asymptomatic-covidpatients-could-have-long-term-lung-damage/ar-BB16bOgX

### **COVID-19: Persistent Disability**



We need to start to view COVID-19 as a long-term disease in many individuals and treat the virus with the respect it deserves.

We should stop referring to patients as "recovered" when in fact all too many just "survived". You recover when you return to normal health and activities.