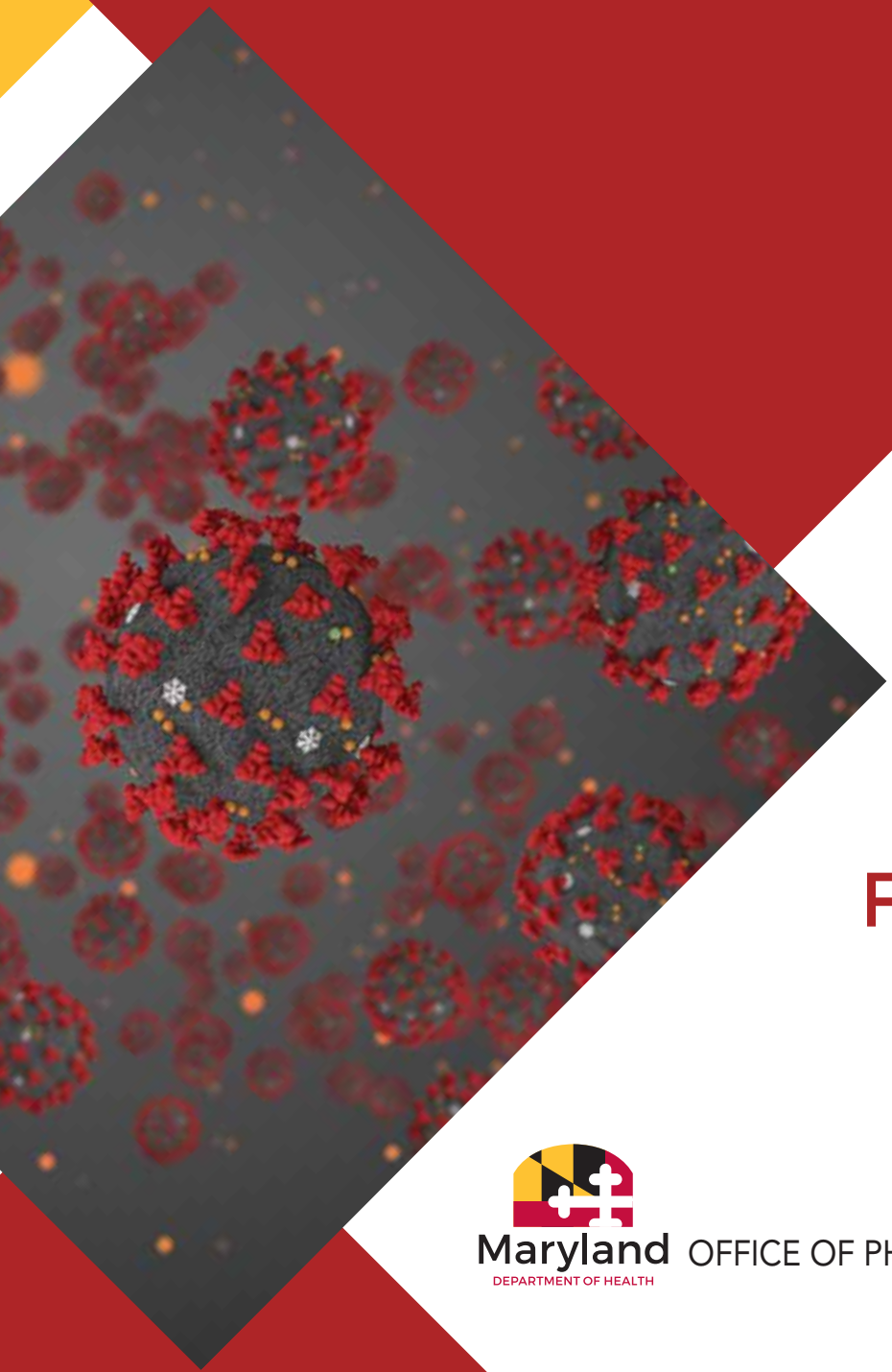
COVID-19: Prevention to Protection



Continuing Education Seminar

Saturday, February 27, 2021

Maryland DEPARTMENT OF HEALTH
OFFICE OF PHARMACY SERVICES

Notes:

Continuing Medical Education (CME) &
Pharmacy Continuing Education (ACPE) Seminar

COVID-19: Prevention to Protection

Virtual Live Program
on
Saturday, February 27, 2021

8:30 am – Registration	
8:45 am – Introductions	Maryland Department of Health Office of Pharmacy Services
9:00 am – COVID-19 – Disease Risk Factors, Treatments and Therapeutics	Eleanor Wilson, MD Meagan Deming, MD Institute for Human Virology University of Maryland School of Medicine
11:50 am - Break	
12:00 pm – Maryland Department of Health COVID-19 Update	David Blythe, MD Director Infectious Disease Epidemiology and Outbreak Response Bureau Maryland Department of Health
1:00 pm – Closing Remarks	Maryland Department of Health Office of Pharmacy Services
1:15 pm - Adjourn	

The views and opinions expressed by the speakers are not necessarily the views and opinions of the State of Maryland Department of Health.

****This event will be recorded for future use. By attending, you agree to participate in audio and/or visual recording****

CE Program Sponsorship:
This program is co-sponsored by The Maryland Department of Health (MDH) Office of Pharmacy Services (OPS) in collaboration with Health Information Designs, a KEPRO company.

CE Accreditation Statement:
The Alabama Pharmacy Association Research and Education Foundation (APAREF) is accredited by the Accreditation Council for Pharmacy Education (ACPE), as a provider of continuing pharmacy education.

Statement of Credit (ACPE):
The Alabama Pharmacy Association (APA) will upload your continuing education credit information to CPE Monitor. You will be able to view and print your continuing education credits from CPE Monitor. The statement of credit should be retained as proof of attendance in the event of an audit by the State Board of Pharmacy. **In order to receive ACPE credits you must sign your name on all sign-in sheets and turn in an evaluation form for each presentation at the end of the program. You also must provide your NABP e-Profile ID # as well as the month and day of your date of birth to receive credit.**

CME Accreditation Statement:
This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through joint providership of MedChi, The Maryland State Medical Society, The Maryland Department of Health Office of Pharmacy Services, and Health Information Designs/KEPRO. MedChi is accredited by the ACCME to provide continuing medical education for physicians.

CME Designation:
MedChi designates this live activity for a maximum of (4) *AMA PRA Category 1 Credit(s)™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

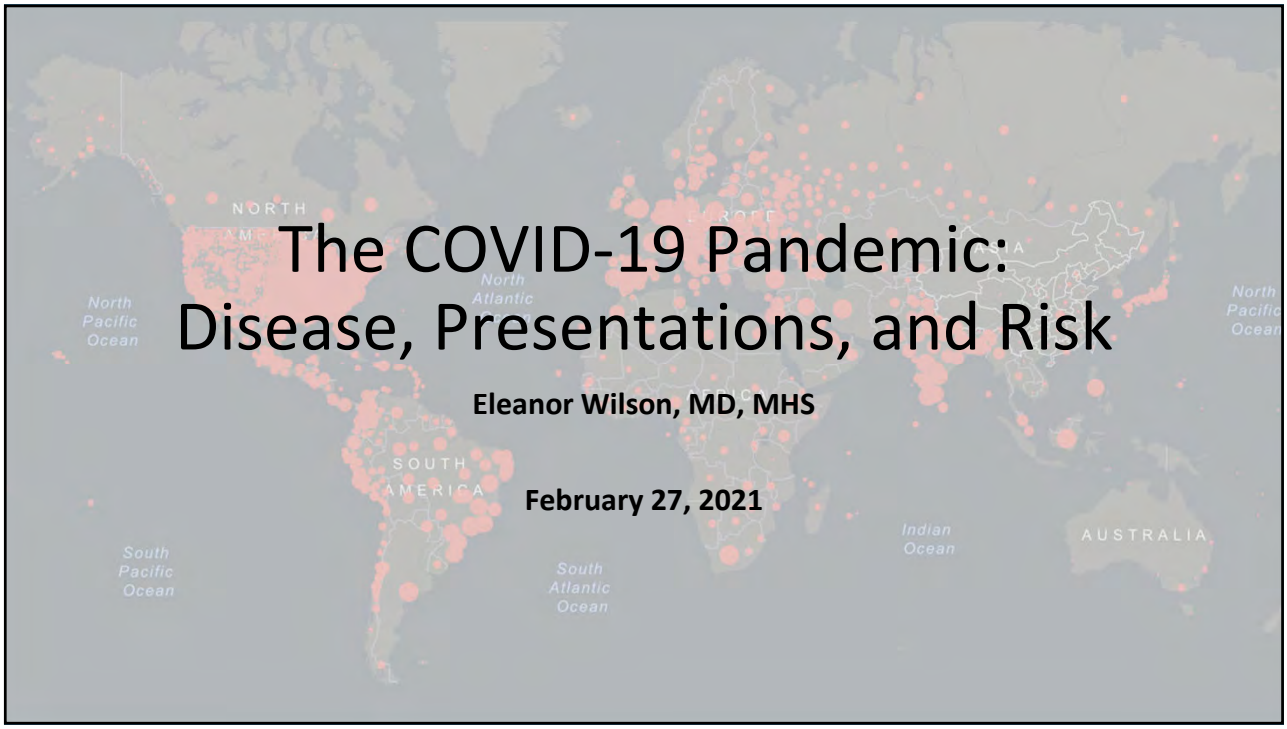
Presenter Disclosure:

- Dr. Blythe states that he does not have relevant financial relationship with commercial interests and will not be discussing "Off-Label" uses of products or devices. This information is on file with Health Information Designs/KEPRO.
- Dr. Deming states that she does not have relevant financial relationship with commercial interests and will be discussing "Off-Label" uses of products or devices. This information is on file with Health Information Designs/KEPRO.
- Dr. Wilson states that she does not have relevant financial relationship with commercial interests and will not be discussing "Off-Label" uses of products or devices. This information is on file with Health Information Designs/KEPRO.

Planner Disclosure:
Dr. Boyer states that she does not have relevant financial relationships with commercial interests and will not be discussing "Off-Label" uses of products or devices. This information is on file with Health Information Designs/KEPRO.

Program Disclosure:
Support provided by Health Information Designs, LLC.

Activity Type: Knowledge-Based



The COVID-19 Pandemic: Disease, Presentations, and Risk

Eleanor Wilson, MD, MHS

February 27, 2021

1

Objectives

At the end of this talk, you should

- Be able to state the common and uncommon clinical presentations of COVID-19 with an emphasis on the impact of age and comorbidities on outcomes
- Review available and upcoming COVID-19 therapeutic strategies

Conflicts of Interest

I am a PI of an NINDS R21 evaluating long term neurologic effects following COVID-19.

I am a sub-investigator on Janssen's COVID-19 vaccine trial (NCT04509947) and other treatment trials that I will not be discussing.

2

CC: 49yoM with shortness of breath

49yo Hispanic man presents with 7 days of progressive shortness of breath, 4 days of productive cough, pleuritic chest pain, and dyspnea on exertion. He bought a home oximeter, which showed SaO2 of 68%; feeling this couldn't be correct, he came to the ED for a recheck.

Review of systems: + chills, diaphoresis, sore throat, cough, shortness of breath, chest pain, myalgias
denies fever, abdominal pain, diarrhea, rash

Past Medical History: NIDDM, HgbA1c 7.2 (May 2020)

Medications: Glipizide 2.5mg daily, Metformin 1000mg BID, Atorvastatin 10mg daily

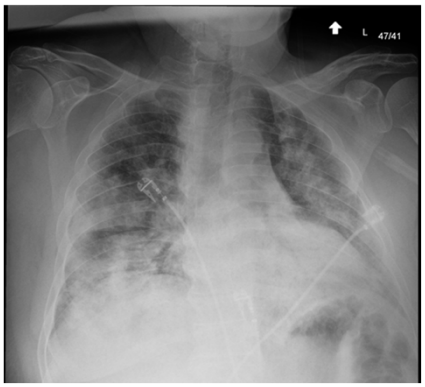
Social History: Married but separated, sexually active with women, lives with his adult daughter, no tobacco or alcohol use, works as a truck driver

3

CC: 49yoM with shortness of breath

Physical Exam: **T** 37.3 °C (99.1 °F) **WT** 94.2kg (BMI 31 kg/m^2) **HR** 112 **BP** 126/89 **RR** 24 **SpO2** 72%

Gen: in acute distress, tachypneic, speaking in 3-4 word sentences
HEENT: normal, op clear
CV: Tachycardic, regular, no murmurs
Pulm: Normal breath sounds, good air movement bilaterally throughout
Abd: nontender, nondistended, no rebound, no guarding
MSK: no swelling, tenderness, or deformity, delayed cap refill
Neuro: alert and oriented, grossly intact, no focal deficits



Labs:

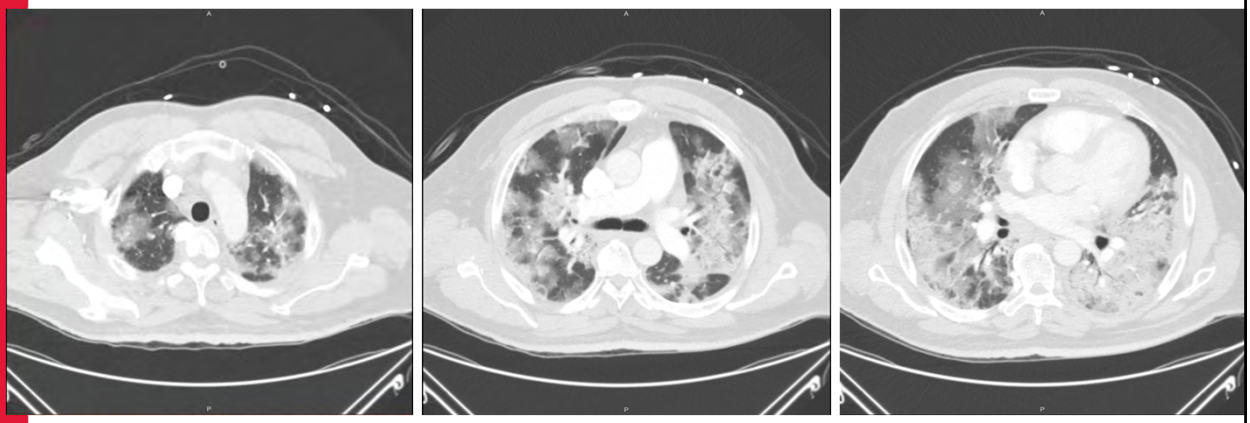
WBC 7.5	Hgb 11.6
84.7% pmns 9.1% lymphs	
Plt 344	

139	103	0.47
4.1	25	12

281

4

CC: 49yoM with shortness of breath



5

CC: 49yoM with shortness of breath

What is the most likely diagnosis in February 2019?

A. Influenza A
B. Parainfluenza
C. Respiratory Syncytial Virus
D. Rhinovirus
E. Human Coronavirus

6

CC: 49yoM with shortness of breath

What is the most likely diagnosis in February 2019?

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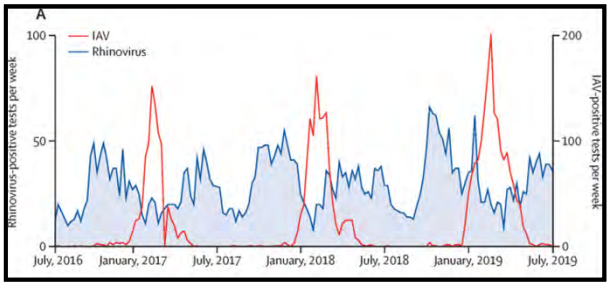

Anchi et al, Lancet Microbe Oct 1 2020;1(6):E254-62

7

CC: 49yoM with shortness of breath

What is the most likely diagnosis in February 2021?

A. Influenza A
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8

CC: 49yoM with shortness of breath

What is the most likely diagnosis in February 2021?

A. Influenza A
B. Parainfluenza
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D. Rhinovirus
E. Human Coronavirus

9

CC: 49yoM with shortness of breath

What is the most likely diagnosis in February 2021?

A. Influenza A
B. Parainfluenza
C. Respiratory Syncytial Virus
D. Rhinovirus
~~**E. Human Coronavirus**~~ **SARS-CoV-2 (COVID-19)**

10

CC: 49yoM with shortness of breath

What is the most likely diagnosis in February 2021?

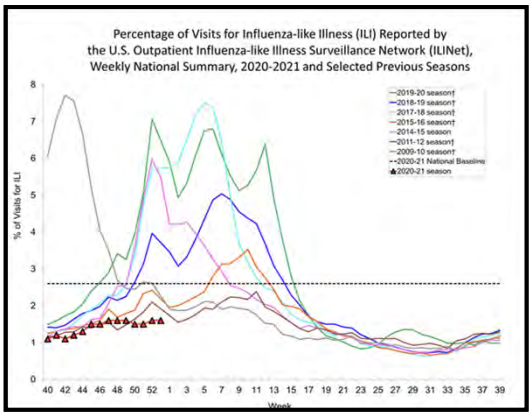
~~A. Influenza A~~

~~B. Parainfluenza~~

~~C. Respiratory Syncytial Virus~~

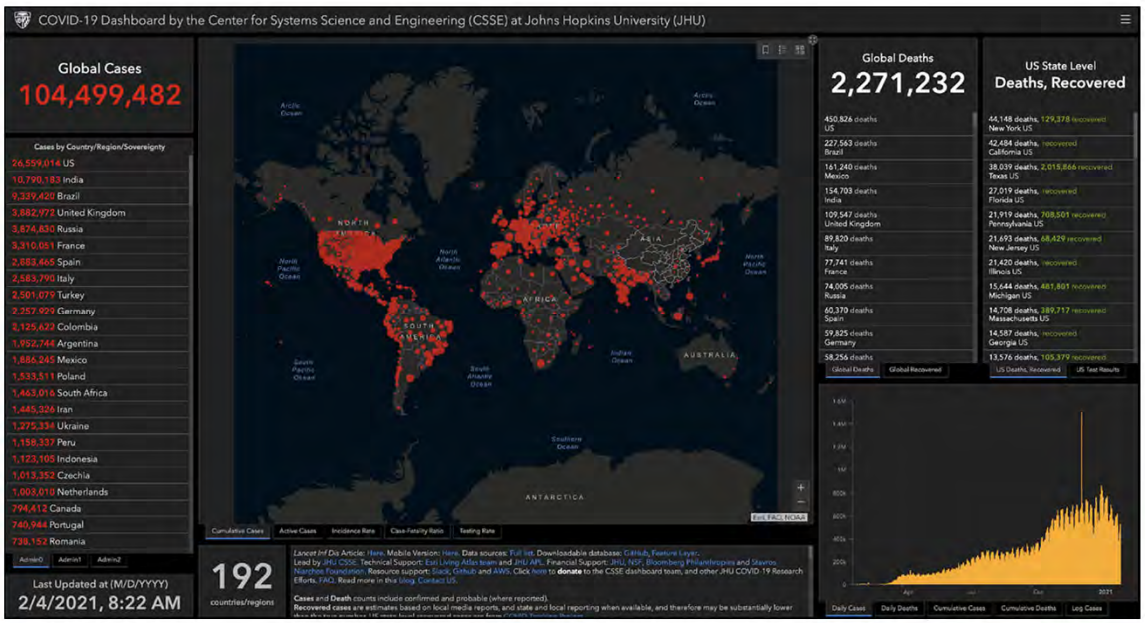
~~D. Rhinovirus~~

E. SARS-CoV-2 (COVID-19)



https://www.cdc.gov/flu/weekly/weeklyarchives2020-2021/week53.htm

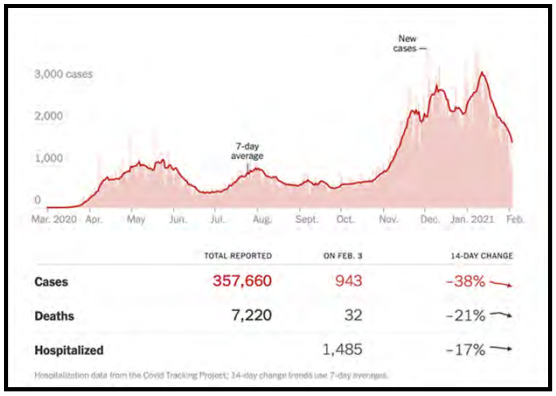
11

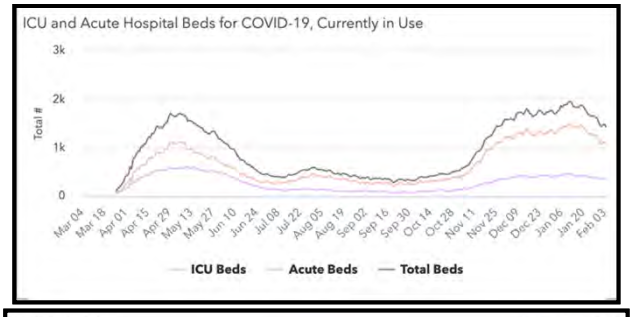


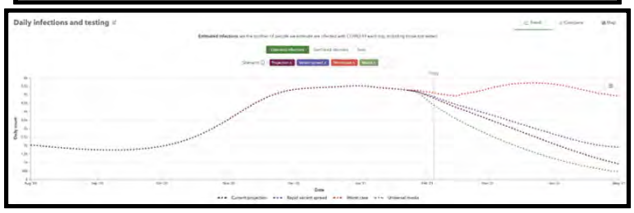
COVID-19 Dashboard by the Center for Systems Science and Engineering at Johns Hopkins University, accessed 2/4/2021

12

Maryland Coronavirus Cases







NYTimes https://www.nytimes.com/interactive/2020/us/maryland-coronavirus-cases.html, accessed 2/4/2021
Maryland COVID-19 Data Dashboard, https://coronavirus.maryland.gov, accessed 2/4/2021
IMHE Health Data https://covid19.healthdata.org/united-states-of-america/maryland?view=total-deaths&tab=trend, accessed 2/4/2021

13

Respiratory Viruses

- Influenza
- Parainfluenza
- RSV
- Rhinovirus
- Adenovirus
- Human Coronavirus

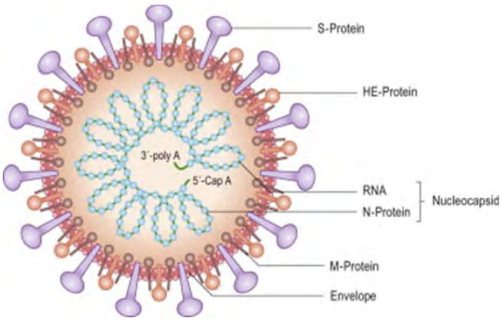
Responsible for 15-40% of all common cold-like infections

- Enteroviruses (Coxsackie, Echo)
- Human Parechovirus (1999)
- Human Metapneumovirus (2001)
- Bocavirus (2005)
- Zoonotic agents:
  Hendra virus (1994), Nipah virus (1998), SARS (2003), MERS (2013)

14

Coronaviruses

- Single-stranded positive-sense RNA viruses
- 4 seasonal human coronaviruses (HCoV): 229E, NL63, OC43, HKU1
- Endemic in bats – risk of zoonotic infection to humans



15

3 Novel Coronaviruses emerged in the last 18 years

SARS-CoV (2002)

Severe Acute Respiratory Syndrome-associated coronavirus

- 8,098 cases w/774 deaths, ~10% CFR
- 30 countries affected
- Economic loss ~$80-100 billion
- Nov 2002 – July 2003

MERS-CoV (2012)

Middle East Respiratory Syndrome-associated coronavirus

- 2,499 cases w/861 deaths, ~35% CFR
- 27 countries affected
- Economic loss?
- April 2012 – present

COVID-19

SARS-CoV-2

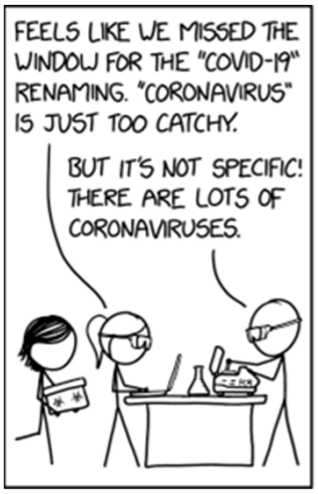
- **105 million** cases w/ **2.3 million** deaths, ~1-2% CFR
- 192 countries affected
- Economic loss?
- Dec 2019 – present

16

What's in a name?

Coronavirus or COVID-19 or SARS-CoV-2 or Wuhan or novel coronavirus or…

The disease:
Corona**V**irus **I**nfectious **D**isease 2019
(COVID-19)



https://xkcd.com/2275/

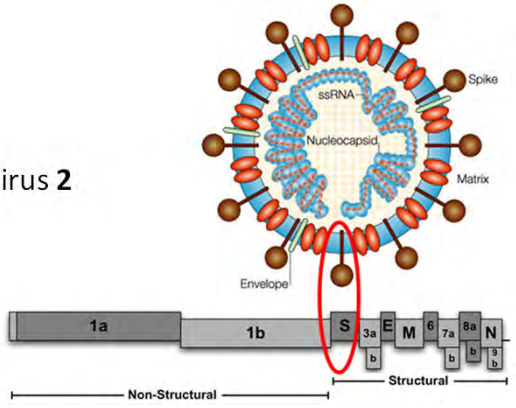
17

What's in a name?

Coronavirus or COVID-19 or SARS-CoV-2 or Wuhan or novel coronavirus or…

The disease:
Corona**V**irus **I**nfectious **D**isease 2019
(COVID-19)

The virus:
Severe **A**cute **R**espiratory **S**yndrome **C**oronavirus **2**
(SARS-CoV-2)



18

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The disease:
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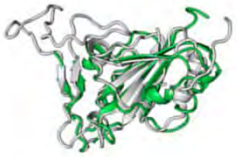
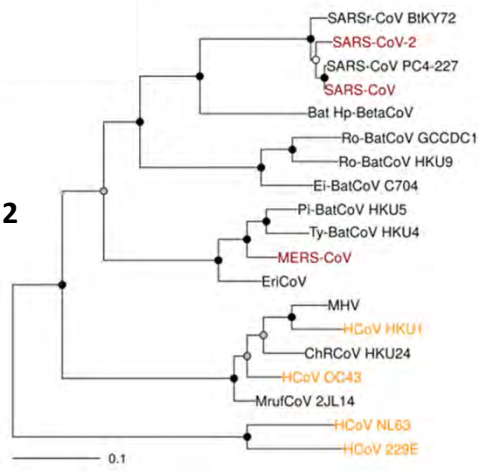
(COVID-19)

The virus:
Severe **A**cute **R**espiratory **S**yndrome **C**oronavirus **2**
(SARS-CoV-2)

80% sequence identity to SARS-CoV





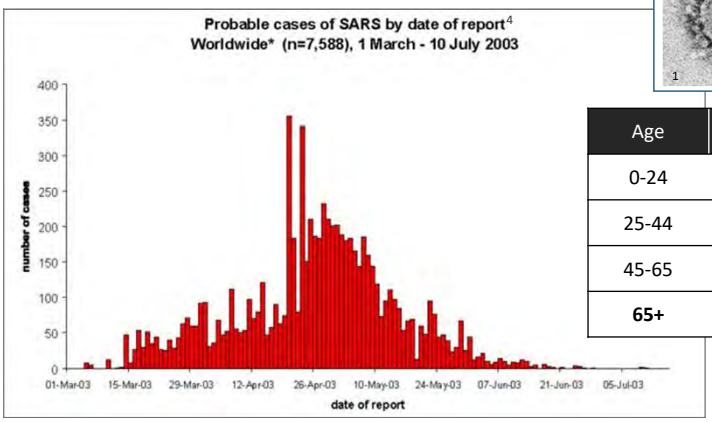
Gorbalenya AE, Baker SC, Baric RS, Groot RJ De, Gulyaeva AA, Haagmans BL, et al. Severe acute respiratory syndrome-related coronavirus: The species and its viruses – a statement of the Coronavirus Study Group. BioRxiv 2020. https://doi.org/10.1101/2020.02.07.937862.
Wrapp D, Wang N, Corbett K, Goldsmith J, Hsieh C-L, Abiona O, et al. Cryo-EM Structure of the 2019-nCoV Spike in the Prefusion Conformation. Science (80-) 2020:1–9.

19

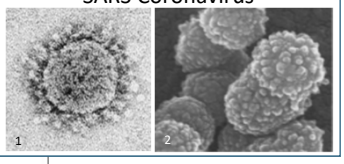
CoV outbreaks: Severe Acute Respiratory Syndrome

2002, China: ~8437 infected worldwide, 774 deaths.(**10% CFR**)

- Severe atypical pneumonia
- **Single spillover - controlled by public health measures alone**
- **Progressive age-dependent mortality**



SARS Coronavirus



Age	Mortality[3]
0-24	0%
25-44	6%
45-65	15%
65+	**52%**

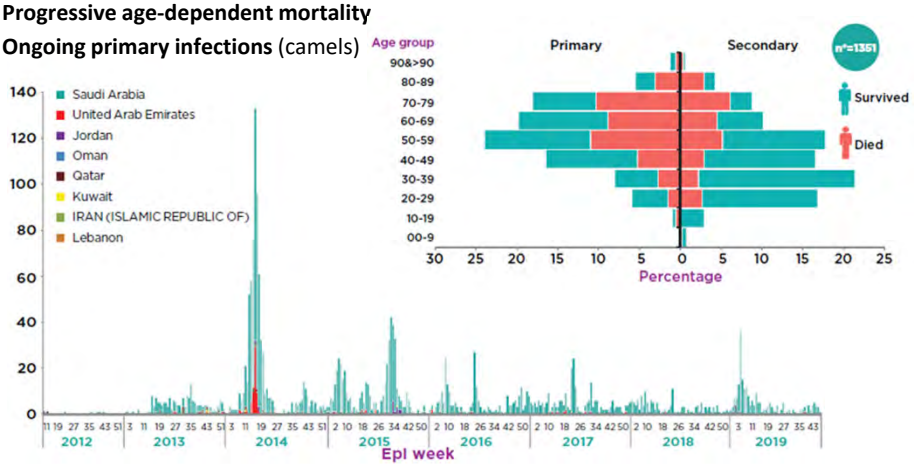
1. Lin Y, et al. (2004) Antivir Ther (Lond) 9: 287–289.
2. Ksiazek TG et al. (2003) N Engl J Med 348: 1953–1966.

20

CoV outbreaks: Middle East Respiratory Syndrome

2012, Saudi Arabia: 2494 cases (lab-confirmed), 858 deaths. (**35% CFR**)

- Severe atypical pneumonia
- **Progressive age-dependent mortality**
- **Ongoing primary infections** (camels)

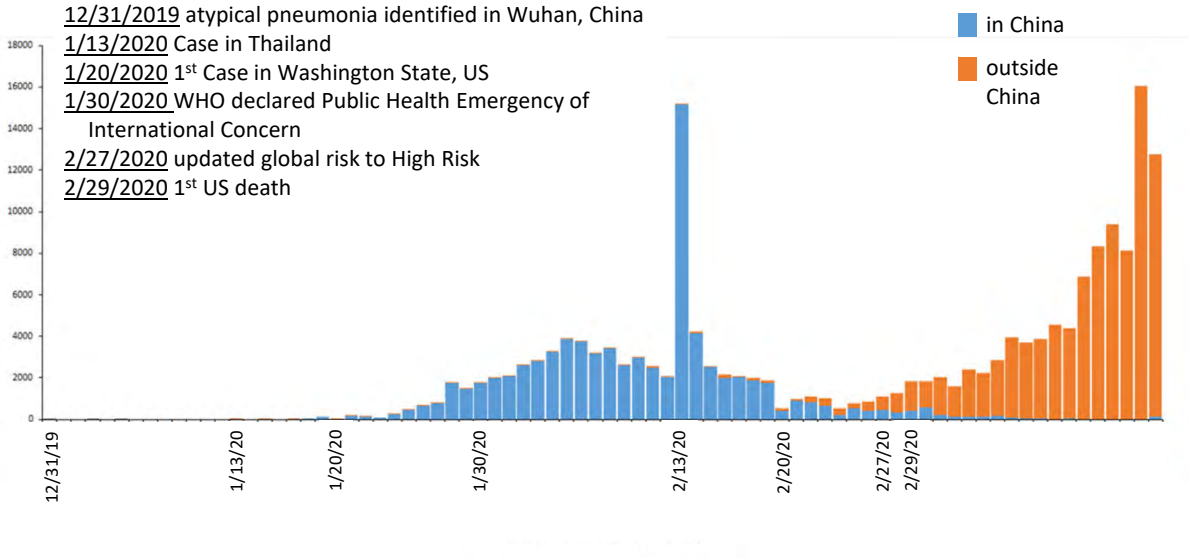


MERS situation update, November 2019. WHO. http://www.emro.who.int/health-topics/mers-cov/mers-outbreaks.html (Accessed 3/2/20)

21

Coronavirus Infectious Disease 2019 (COVID-19)

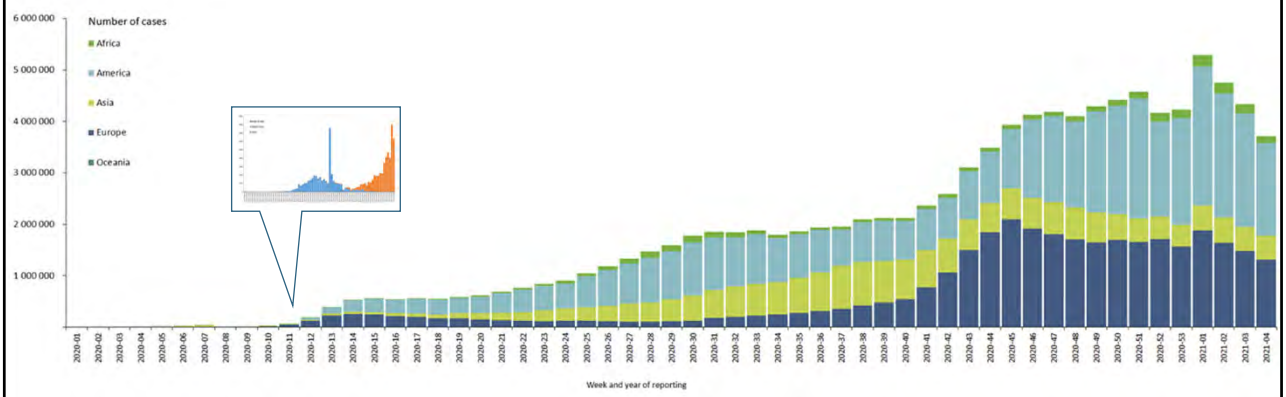
12/31/2019 atypical pneumonia identified in Wuhan, China
1/13/2020 Case in Thailand
1/20/2020 1st Case in Washington State, US
1/30/2020 WHO declared Public Health Emergency of International Concern
2/27/2020 updated global risk to High Risk
2/29/2020 1st US death



https://www.ecdc.europa.eu/en/geographical-distribution-2019-ncov-cases

22

COVID-19 Cases



https://www.ecdc.europa.eu/en/geographical-distribution-2019-ncov-cases

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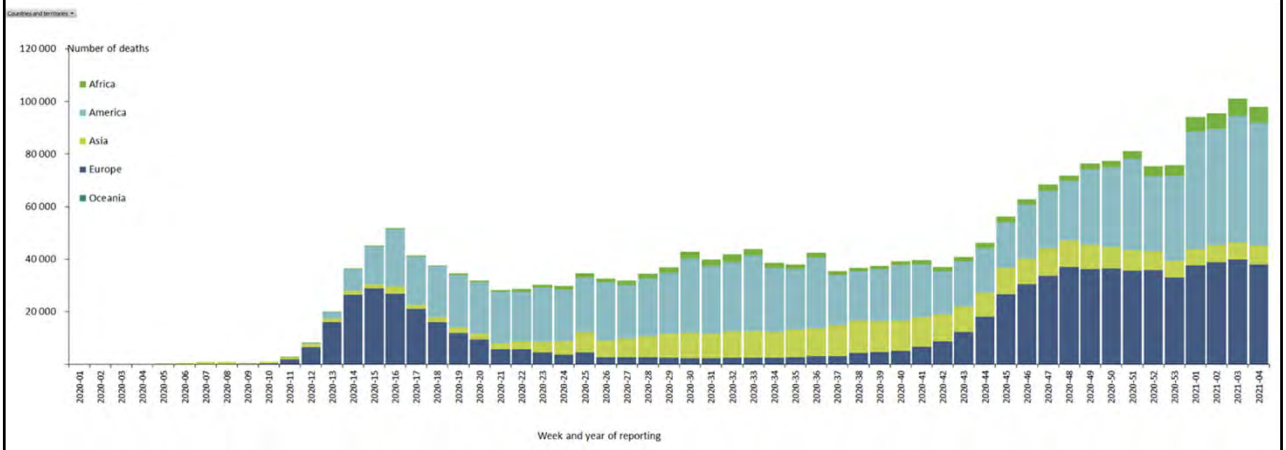
COVID-19 Deaths

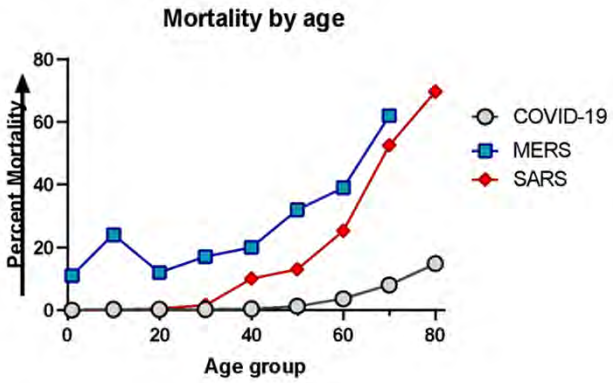


https://www.ecdc.europa.eu/en/geographical-distribution-2019-ncov-cases

24

COVID-19 Spectrum of Illness

- ~80% **mild-moderate**
- 13.8% **severe**
  - dyspnea, RR ≥30/minute, O2 sat ≤93%, PaO2/FiO2 ratio <300, and/or lung infiltrates >50% of the lung field within 24-48 hours
- 6.1% are **critical**
  - respiratory failure, septic shock, and/or multiple organ dysfunction/failure
  - **Crude CFR 1.4-4%**

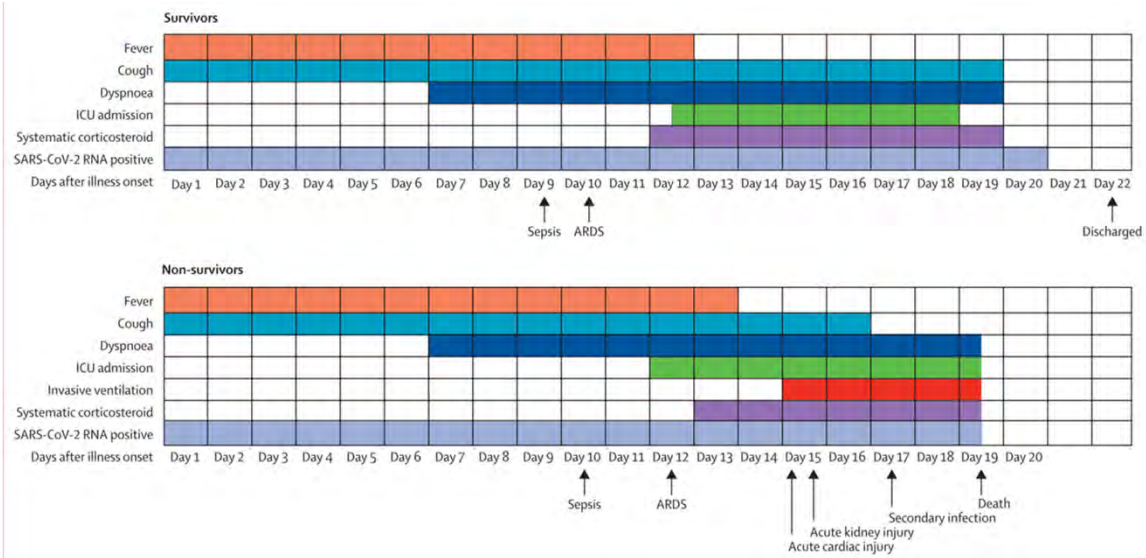


Wu, Z. et al. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China; Summary of a Report of 72,314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. Feb 24, 2020.
Chan-yeung M, Xu R. SARS: epidemiology. Respirology 2003;8:S9–S14.

25

Clinical Course

191 patients in 2 hospitals in Wuhan, China
- 137 discharged, 54 died **(28%)**

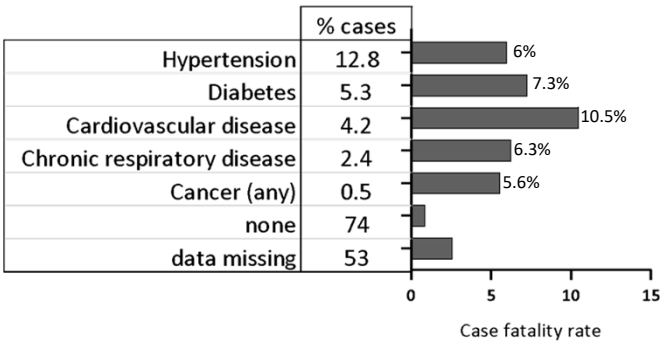


Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;6736:1–9.

26

Clinical Course

- 191 patients in 2 hospitals in Wuhan, China
  - 137 discharged, 54 died **(28%)**
  - 48% had comorbidity:
    - 58 (30%) hypertension, 36 (19%) diabetes, 15 (8%) coronary artery disease



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Wu, Z. et al. 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. Feb 24, 2020

27

CC: 49yoM with shortness of breath

Which of these is a risk factor for death **in this patient** due to COVID-19?

A. Age
B. Sex
C. Race/ethnicity
D. Diabetes mellitus
E. Obesity

28

CC: 49yoM with shortness of breath

Which of these is a risk factor for death **in this patient** due to COVID-19?

A. Age
B. Sex
C. Race/ethnicity
D. Diabetes mellitus
E. Obesity

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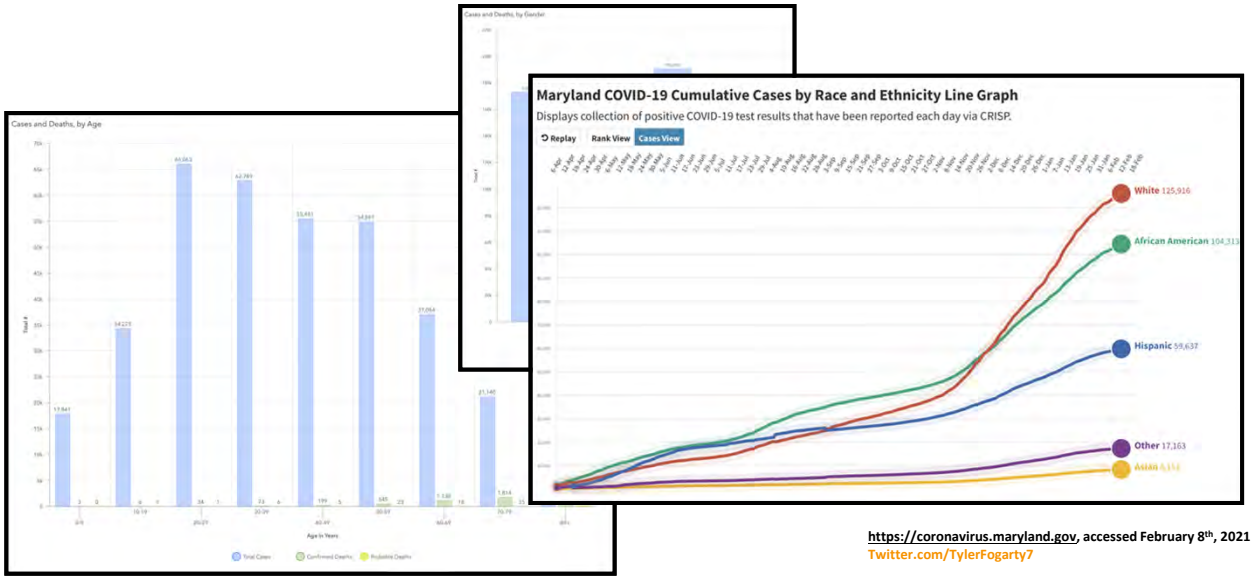
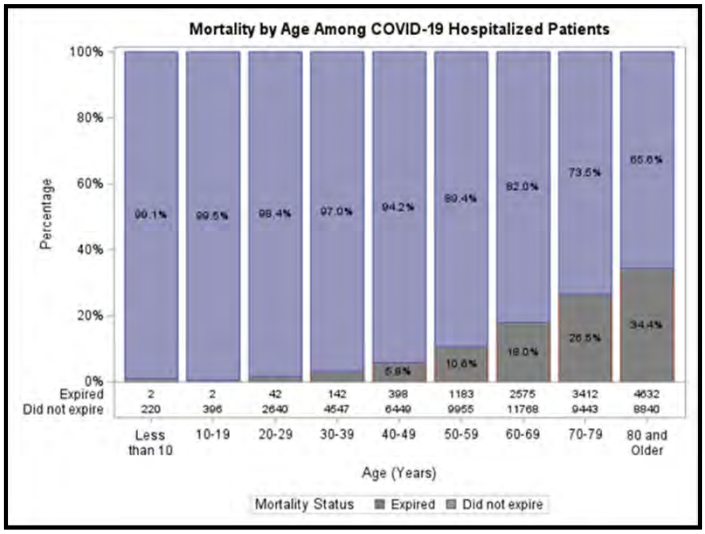
COVID-19 Cases and Deaths Stratified



https://coronavirus.maryland.gov, accessed February 8th, 2021
Twitter.com/TylerFogarty7

30

COVID-19 Cases and Deaths Stratified



Goodman KE, Impact of Sex and Metabolic Comorbidities on COVID-19 Mortality Risk Across Age Groups: 66,646 Inpatients Across 613 U.S. Hospitals. *Clin Infect Dis*. 2020 Dec 18:ciaa1787. doi: 10.1093/cid/ciaa1787.

31

CC: 49yoM with shortness of breath

Which of these is a risk factor for death due to COVID-19?

A. Age
B. Sex
C. Race/ethnicity
D. Diabetes mellitus
E. Obesity

Age (Years)	Relative Risk of Death
20-39	**0.21**
40-49	**0.47**
50-59	REF
60-69	**1.72**
70-79	**2.70**
80+	**4.26**

Goodman KE, Impact of Sex and Metabolic Comorbidities on COVID-19 Mortality Risk Across Age Groups: 66,646 Inpatients Across 613 U.S. Hospitals. Clin Infect Dis. 2020 Dec 18:ciaa1787. doi: 10.1093/cid/ciaa1787.

32

CC: 49yoM with shortness of breath

Which of these is a risk factor for death due to COVID-19?

A. Age
B. Sex
C. Race/ethnicity
D. Diabetes mellitus
E. Obesity

Sex	Relative Risk of Death
Female	REF
Male	**1.30**

Goodman KE, Impact of Sex and Metabolic Comorbidities on COVID-19 Mortality Risk Across Age Groups: 66,646 Inpatients Across 613 U.S. Hospitals. Clin Infect Dis. 2020 Dec 18:ciaa1787. doi: 10.1093/cid/ciaa1787.

33

CC: 49yoM with shortness of breath

Which of these is a risk factor for death due to COVID-19?

A. Age
B. Sex
C. Race/ethnicity
D. Diabetes mellitus
E. Obesity

Race	Relative Risk of Death
White	REF
Black	**0.90**

Ethnicity	Relative Risk of Death
Non Hispanic	REF
Hispanic	**0.95**

Goodman KE, Impact of Sex and Metabolic Comorbidities on COVID-19 Mortality Risk Across Age Groups: 66,646 Inpatients Across 613 U.S. Hospitals. Clin Infect Dis. 2020 Dec 18:ciaa1787. doi: 10.1093/cid/ciaa1787.

34

CC: 49yoM with shortness of breath

Which of these is a risk factor for death due to COVID-19?

A. Age
B. Sex
C. Race/ethnicity
D. Diabetes mellitus
E. Obesity

Comorbidity	Relative Risk of Death
Congestive Heart Failure	**1.16**
Chronic lung disease	1.02
Liver disease	**1.09**
Renal Failure	**1.12**
Malignancy	**1.30**
Uncomplicated diabetes	1.01

Goodman KE, Impact of Sex and Metabolic Comorbidities on COVID-19 Mortality Risk Across Age Groups: 66,646 Inpatients Across 613 U.S. Hospitals. Clin Infect Dis. 2020 Dec 18:ciaa1787. doi: 10.1093/cid/ciaa1787.

35

CC: 49yoM with shortness of breath

Which of these is a risk factor for death due to COVID-19?

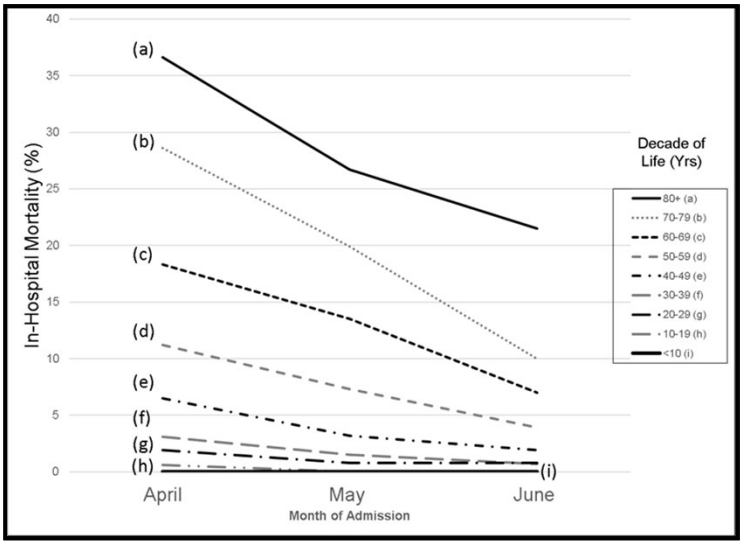
A. Age
B. Sex
C. Race/ethnicity
D. Diabetes mellitus
E. Obesity

Obesity by Age	Relative Risk of Death
20-39	**1.92**
40-49	**1.57**
50-59	**1.33**
60-69	**1.26**
70-79	**1.16**
80+	**1.11**

Goodman KE, Impact of Sex and Metabolic Comorbidities on COVID-19 Mortality Risk Across Age Groups: 66,646 Inpatients Across 613 U.S. Hospitals. Clin Infect Dis. 2020 Dec 18:ciaa1787. doi: 10.1093/cid/ciaa1787.

36

COVID-19 Cases and Deaths Over Time



Goodman KE, Impact of Sex and Metabolic Comorbidities on COVID-19 Mortality Risk Across Age Groups: 66,646 Inpatients Across 613 U.S. Hospitals. Clin Infect Dis. 2020 Dec 18:ciaa1787. doi: 10.1093/cid/ciaa1787.

37

CC: 49yoM with shortness of breath

Clinical Course:

1/18 Presented to the ED with hypoxia, placed on 6L NCO2, tested COVID-19 +, started steroids

1/19 Admitted to ICU, ↑ work of breathing with SpO2 60-70%, required HFNC at 40L/100%, started remdesivir

1/21 Required intubation, mechanical ventilation

1/24 Developed fevers to 39.7 °C (103.5 °F), sputum cultured

1/25 Sputum grew Klebsiella pneumonia, imaging suggestive of superimposed ventilator-associated bacterial pneumonia

2/11 Trach placed to facilitate slow wean from ventilator

2/15 Weaned to trach collar

2/21 Decannulated

2/22 Discharged to rehab facility

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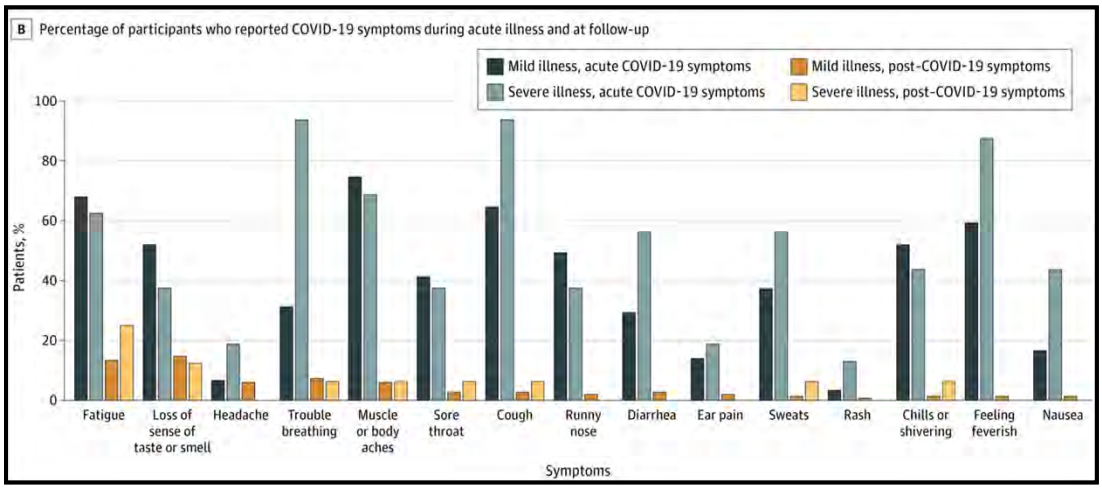
Long Term Sequelae following COVID-19



JAMA Network

From: **Sequelae in Adults at 6 Months After COVID-19 Infection**
JAMA Netw Open. Feb 19, 2021;4(2):e210830. doi:10.1001/jamanetworkopen.2021.0830

39

COVID-19 Diagnosis

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CC: 49yoM with shortness of breath

How would you test for COVID-19?

A. History and clinical course are diagnostic
B. PCR Testing
C. Antibody Testing
D. Sputum Culture
E. Antigen Testing

41

CC: 49yoM with shortness of breath

How would you test for COVID-19?

A. History and clinical course are diagnostic
B. PCR Testing - NP Swab for Respiratory Viral Panel
C. Antibody Testing
D. Sputum Culture
E. Antigen Testing

	1 1/18/2021 2023
Adenovirus DNAAmp...	Not Detected
Bordetella paraper...	Not Detected
Bordetella pertuss...	Not Detected
Chlamydia pneumoni...	Not Detected
Coronavirus 229E R...	Not Detected
Coronavirus HKU1 R...	Not Detected
Coronavirus NL63 R...	Not Detected
Coronavirus OC43 R...	Not Detected
SARS-CoV-2 (COVID-...	Detected * c !
Human Metapneumovi...	Not Detected
Influenza A RNAAm...	Not Detected
Influenza B RNAAm...	Not Detected
Mycoplasma pneumon...	Not Detected
Parainflu 1 Virus ...	Not Detected
Parainflu 2 Virus ...	Not Detected
Parainflu 3 Virus ...	Not Detected
Parainflu 4 Virus ...	Not Detected
Rhinovirus/Enterov...	Not Detected
RSV RNAAmplification	Not Detected
Resp Virus PCR Int...	See Note *

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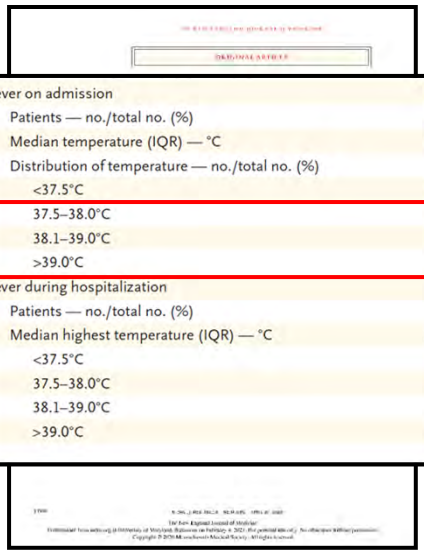
COVID-19 Diagnosis



Fever on admission					
Patients — no./total no. (%)	473/1081 (43.8)	391/910 (43.0)	82/171 (48.0)	24/66 (36.4)	449/1015 (44.2)
Median temperature (IQR) — °C	37.3 (36.7–38.0)	37.3 (36.7–38.0)	37.4 (36.7–38.1)	36.8 (36.3–37.8)	37.3 (36.7–38.0)
Distribution of temperature — no./total no. (%)					
<37.5°C	608/1081 (56.2)	519/910 (57.0)	89/171 (52.0)	42/66 (63.6)	566/1015 (55.8)
37.5–38.0°C	238/1081 (22.0)	201/910 (22.1)	37/171 (21.6)	10/66 (15.2)	228/1015 (22.5)
38.1–39.0°C	197/1081 (18.2)	160/910 (17.6)	37/171 (21.6)	11/66 (16.7)	186/1015 (18.3)
>39.0°C	38/1081 (3.5)	30/910 (3.3)	8/171 (4.7)	3/66 (4.5)	35/1015 (3.4)
Fever during hospitalization					
Patients — no./total no. (%)	975/1099 (88.7)	816/926 (88.1)	159/173 (91.9)	59/67 (88.1)	916/1032 (88.8)
Median highest temperature (IQR) — °C	38.3 (37.8–38.9)	38.3 (37.8–38.9)	38.5 (38.0–39.0)	38.5 (38.0–39.0)	38.3 (37.8–38.9)
<37.5°C	92/926 (9.9)	79/774 (10.2)	13/152 (8.6)	3/54 (5.6)	89/872 (10.2)
37.5–38.0°C	286/926 (30.9)	251/774 (32.4)	35/152 (23.0)	20/54 (37.0)	266/872 (30.5)
38.1–39.0°C	434/926 (46.9)	356/774 (46.0)	78/152 (51.3)	21/54 (38.9)	413/872 (47.4)
>39.0°C	114/926 (12.3)	88/774 (11.4)	26/152 (17.1)	10/54 (18.5)	104/872 (11.9)

Guan, et al NEJM 382;18 April 30, 2020

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COVID-19 Diagnosis

Symptoms — no. (%)					
Conjunctival congestion	9 (0.8)	5 (0.5)	4 (2.3)	0	9 (0.9)
Nasal congestion	53 (4.8)	47 (5.1)	6 (3.5)	2 (3.0)	51 (4.9)
Headache	150 (13.6)	124 (13.4)	26 (15.0)	8 (11.9)	142 (13.8)
Cough	745 (67.8)	623 (67.3)	122 (70.5)	46 (68.7)	699 (67.7)
Sore throat	153 (13.9)	130 (14.0)	23 (13.3)	6 (9.0)	147 (14.2)
Sputum production	370 (33.7)	309 (33.4)	61 (35.3)	20 (29.9)	350 (33.9)
Fatigue	419 (38.1)	350 (37.8)	69 (39.9)	22 (32.8)	397 (38.5)
Hemoptysis	10 (0.9)	6 (0.6)	4 (2.3)	2 (3.0)	8 (0.8)
Shortness of breath	205 (18.7)	140 (15.1)	65 (37.6)	36 (53.7)	169 (16.4)
Nausea or vomiting	55 (5.0)	43 (4.6)	12 (6.9)	3 (4.5)	52 (5.0)
Diarrhea	42 (3.8)	32 (3.5)	10 (5.8)	4 (6.0)	38 (3.7)
Myalgia or arthralgia	164 (14.9)	134 (14.5)	30 (17.3)	6 (9.0)	158 (15.3)
Chills	126 (11.5)	100 (10.8)	26 (15.0)	8 (11.9)	118 (11.4)
Signs of infection — no. (%)					
Throat congestion	19 (1.7)	17 (1.8)	2 (1.2)	0	19 (1.8)
Tonsil swelling	23 (2.1)	17 (1.8)	6 (3.5)	1 (1.5)	22 (2.1)
Enlargement of lymph nodes	2 (0.2)	1 (0.1)	1 (0.6)	1 (1.5)	1 (0.1)
Rash	2 (0.2)	0	2 (1.2)	0	2 (0.2)
Coexisting disorder — no. (%)					
Any	261 (23.7)	194 (21.0)	67 (38.7)	39 (58.2)	222 (21.5)
Chronic obstructive pulmonary disease	12 (1.1)	6 (0.6)	6 (3.5)	7 (10.4)	5 (0.5)
Diabetes	81 (7.4)	53 (5.7)	28 (16.2)	18 (26.9)	63 (6.1)
Hypertension	165 (15.0)	124 (13.4)	41 (23.7)	24 (35.8)	141 (13.7)
Coronary heart disease	27 (2.5)	17 (1.8)	10 (5.8)	6 (9.0)	21 (2.0)
Cerebrovascular disease	15 (1.4)	11 (1.2)	4 (2.3)	4 (6.0)	11 (1.1)
Hepatitis B infection¶	23 (2.1)	22 (2.4)	1 (0.6)	1 (1.5)	22 (2.1)
Cancer‖	10 (0.9)	7 (0.8)	3 (1.7)	1 (1.5)	9 (0.9)
Chronic renal disease	8 (0.7)	5 (0.5)	3 (1.7)	2 (3.0)	6 (0.6)
Immunodeficiency	2 (0.2)	2 (0.2)	0	0	2 (0.2)

Guan, et al NEJM 382;18 April 30, 2020

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COVID-19 Diagnosis

Radiologic findings					
Abnormalities on chest radiograph — no./total no. (%)	162/274 (59.1)	116/214 (54.2)	46/60 (76.7)	30/39 (76.9)	132/235 (56.2)
Ground-glass opacity	55/274 (20.1)	37/214 (17.3)	18/60 (30.0)	9/39 (23.1)	46/235 (19.6)
Local patchy shadowing	77/274 (28.1)	56/214 (26.2)	21/60 (35.0)	13/39 (33.3)	64/235 (27.2)
Bilateral patchy shadowing	100/274 (36.5)	65/214 (30.4)	35/60 (58.3)	27/39 (69.2)	73/235 (31.1)
Interstitial abnormalities	12/274 (4.4)	7/214 (3.3)	5/60 (8.3)	6/39 (15.4)	6/235 (2.6)
Abnormalities on chest CT — no./total no. (%)	840/975 (86.2)	682/808 (84.4)	158/167 (94.6)	50/57 (87.7)	790/918 (86.1)
Ground-glass opacity	550/975 (56.4)	449/808 (55.6)	101/167 (60.5)	30/57 (52.6)	520/918 (56.6)
Local patchy shadowing	409/975 (41.9)	317/808 (39.2)	92/167 (55.1)	22/57 (38.6)	387/918 (42.2)
Bilateral patchy shadowing	505/975 (51.8)	368/808 (45.5)	137/167 (82.0)	40/57 (70.2)	465/918 (50.7)
Interstitial abnormalities	143/975 (14.7)	99/808 (12.3)	44/167 (26.3)	15/57 (26.3)	128/918 (13.9)

Guan, et al NEJM 382;18 April 30, 2020

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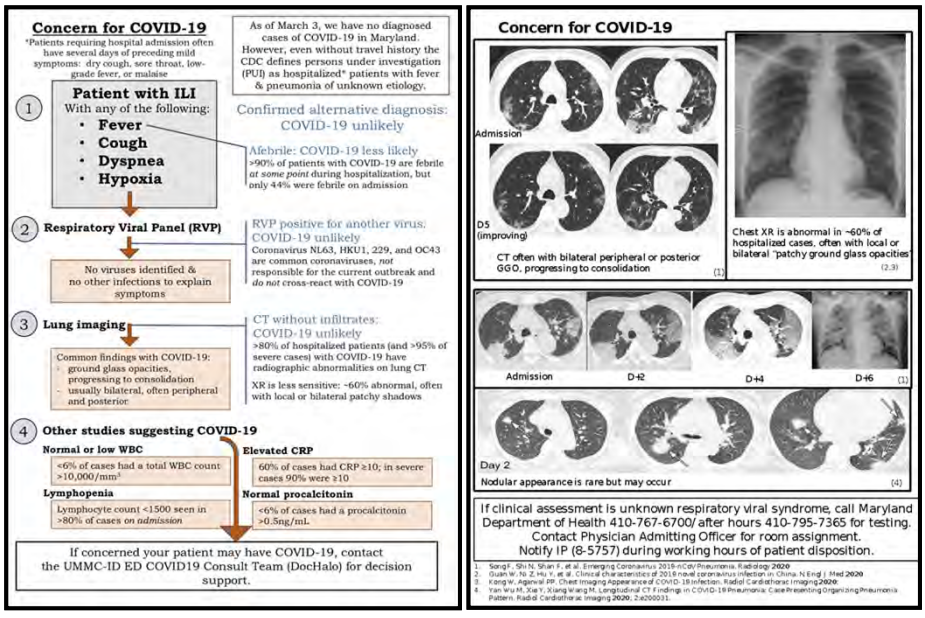
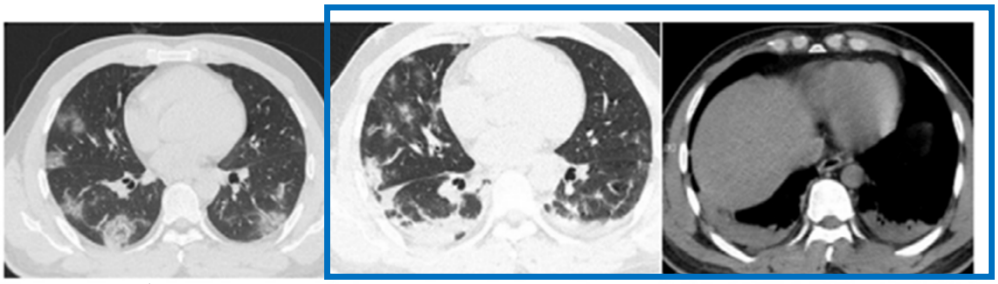
COVID-19 Diagnosis



46

COVID-19 diagnosis

- 90% of patients with COVID-19 are febrile *at some point* during hospitalization, but only 44% were febrile on admission
- 80-100% of hospitalized patients with imaging abnormalities
  - Usually bilateral, GGO progressing to consolidation, peripheral and posterior



Admission Day +5

- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA 2020 (In press).
- Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;6736:1–7.
- Song F, Shi N, Shan F, Zhang Z, Shen J, Lu H, et al. Emerging Coronavirus 2019-nCoV Pneumonia. Radiology 2020 (In press).

47

COVID-19 diagnosis

- 90% of patients with COVID-19 are febrile *at some point* during hospitalization, but only 44% were febrile on admission
- 80-100% of hospitalized patients with imaging abnormalities
  - Usually bilateral, GGO progressing to consolidation, peripheral and posterior
  - Sensitivity 97%, Specificity 25% (in a time of pandemic)

Table 2: The performance of chest CT for COVID-19 infection with RT-PCR result as reference.

	Results (n)				Test performance (%)					
	TP	TN	FP	FN	Sensitivity [95% CI]	Specificity [95% CI]	PPV [95% CI]	NPV [95% CI]	Accuracy [95% CI]	
Overall	580	105	308	21	97 (580/601) [95-98]	25 (105/413) [22-30]	65 (580/888) [62-68]	83 (105/126) [76-89]	68 (685/1014) [65-70]	

- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA 2020 (In press).
- Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;6736:1–7.
- Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, et al. Correlation of Chest CT and RT-PCR Testing in Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. Radiology 2020;2019:200642.

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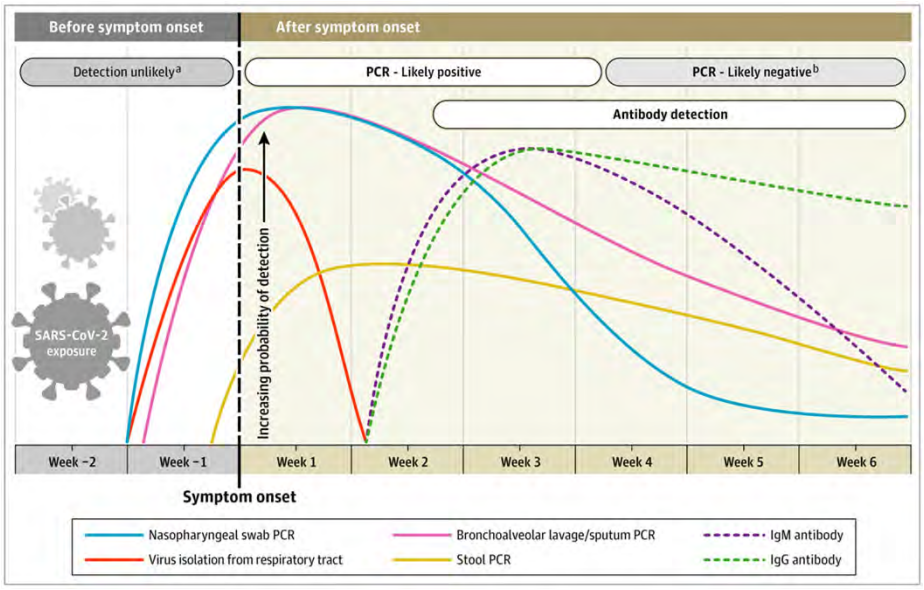
COVID-19 Diagnostics

- PCR
- Antigen
- Antibodies



Sethuraman, et al JAMA. 2020;323(22):2249-2251.

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Emergency

Use

Authorization

Not FDA approved

Most have only tested < 60 samples before gong on market

Comparison is not patient with disease vs without disease, but comparison to another assay - Positive Percent agreement (PPA), Negative Percent agreement (NPA)

50

COVID-19 Diagnostics

Methods	Targets	Source	Turn Around Time	Limit of Detection (copies/ml)	Clinical Performance
GenMark Eplex	Nucleocapsid unknown	NP	< 4 hours	750	PPA=94.4% NPA=100%
Cepheid Xpert xpress	E, N2	NP Nasal W/A	1 hour	200	PPA=100% NPA=100%
BDMax	N1, N2	NP, OP, nasal	<6 hours	100	PPA=100% NPA=97%
Roche	ORF1, E	NP, OP, Nasal	<24 days	100	PPA=100% NPA=100%
BioFire RVP2.1	S, M	NP	< 3 hours	100	PPA=98% NPA=100%
Abbott m2000	RdRp, N	NP, OP, nasal	24-48 hours	100	PPA=100% NPA=100%
MDH CDC method	N1, N2	NP, OP, sputum, BAL	24-48 hours	100	PPA=100% NPA=100%

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CC: 48yoM with diarrhea, lethargy, fevers

48yoM presents with 10 days of diarrhea, 7 days of lethargy and sinus congestion. He called his primary care physician, was evaluated for COVID with an NP swab and was negative, was treated with 7 days of amoxicillin. Did not improve, instead developed diarrhea and fevers, so he was advised to come to the ED.

Review of systems: + chills, fever, malaise/fatigue, congestion, cough, sputum production, diarrhea, dizziness.
Denies shortness of breath

Past Medical History: HTN, ESRD 2/2 FSGS s/p DDRT 2005 c/b ACR in 2007 (steroids)

Medications: MMF 360mg, tacrolimus 1.5mg, HCTZ 25mg, enalapril 10mg, allopurinol 100mg, MVI

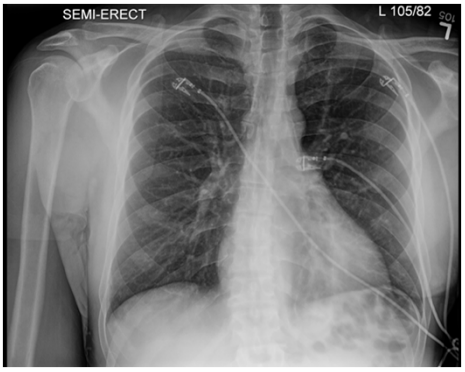
Social History: Married, works on the MARC train, two adult children (healthy), new granddaughter (1 month old)

52

CC: 48yoM with diarrhea, lethargy, fevers

Physical Exam: **T** 37.6 °C (99.7 °F) **HR** 76 **BP** 145/76 **RR** 16 **SpO2** 99%

Gen: in no distress
HEENT: normal, op clear
CV: Normal rhythm, regular, no murmurs
Pulm: Normal breath sounds, good air movement bilaterally throughout
Abd: nontender, nondistended, no rebound, no guarding
MSK: no swelling, tenderness, or deformity
Neuro: alert and oriented, grossly intact, no focal deficits



Labs:
WBC 6.2
68% pmns
21% lymphs
Hgb 10.2
Plt 155

133	104	3.18	110
4.8	20	56	

Urinalysis:
0 WBCs
0 RBCs
neg Leuk Est
neg nitrites
neg bacteria

NP Swab: negative for COVID-19

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CC: 48yoM with diarrhea, lethargy, fevers

What is the most likely diagnosis?

A. Viral upper respiratory infection, antibiotic associated diarrhea
B. Rejection
C. Transplant pyelonephritis
D. COVID-19
E. Enterovirus infection

54

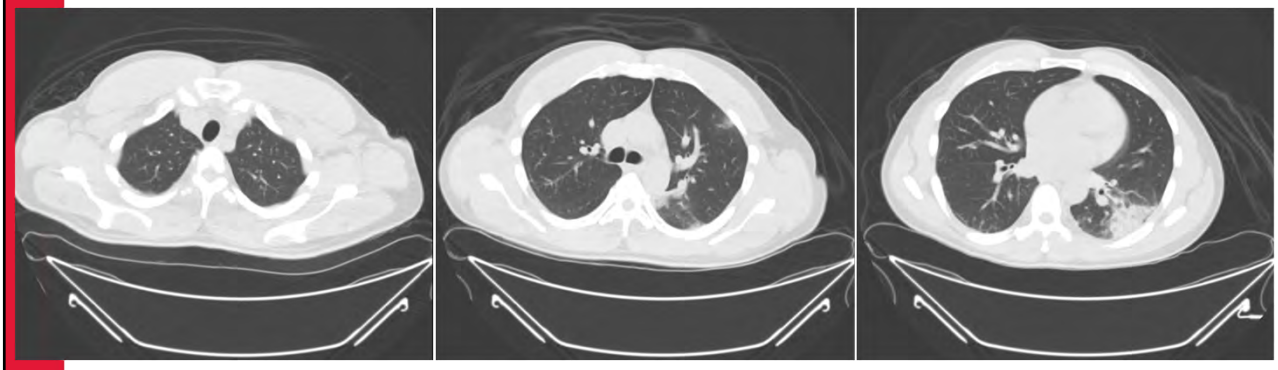
CC: 48yoM with diarrhea, lethargy, fevers

Clinical Course:

12/24 Presented to the ED with diarrhea, malaise, normal CXR, tested **COVID-19 negative** by NP swab
12/26 Febrile to 38.5, with transient shortness of breath and 1L NCO2 requirement, CT scan obtained.

55

CC: 48yoM with diarrhea, lethargy, fevers



56

CC: 48yoM with diarrhea, lethargy, fevers

What is the most likely diagnosis?

A. Viral upper respiratory infection, antibiotic associated diarrhea
B. Rejection
C. Transplant pyelonephritis
D. COVID-19
E. Enterovirus infection

57

CC: 48yoM with diarrhea, lethargy, fevers

What is the most likely diagnosis?

A. Viral upper respiratory infection, antibiotic associated diarrhea
B. Rejection
C. Transplant pyelonephritis
D. COVID-19
E. Enterovirus infection

58

CC: 48yoM with diarrhea, lethargy, fevers

Clinical Course:

12/24 Presented to the ED with diarrhea, malaise, normal CXR, **tested COVID-19 negative** by NP swab
12/26 Febrile to 38.5, with transient shortness of breath and 1L NCO2 requirement, CT scan obtained.
12/28 Febrile to 39.3, no shortness of breath, **retested negative for COVID-19 by NP swab**
12/29 Febrile to 40.1, with rigors, but shortness of breath resolved
12/30 Defervesced, evaluated by pulmonology for bronchoscopy
12/31 Underwent bronchoscopy, BAL positive for SARS-CoV-2
1/2 Discharged home off oxygen, afebrile and improving

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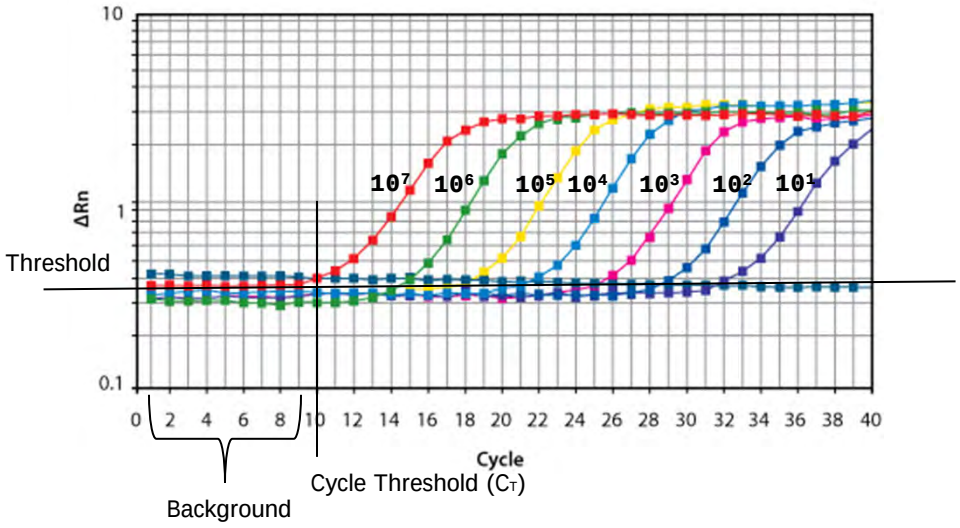
COVID-19 Diagnostics – Quantitative PCR



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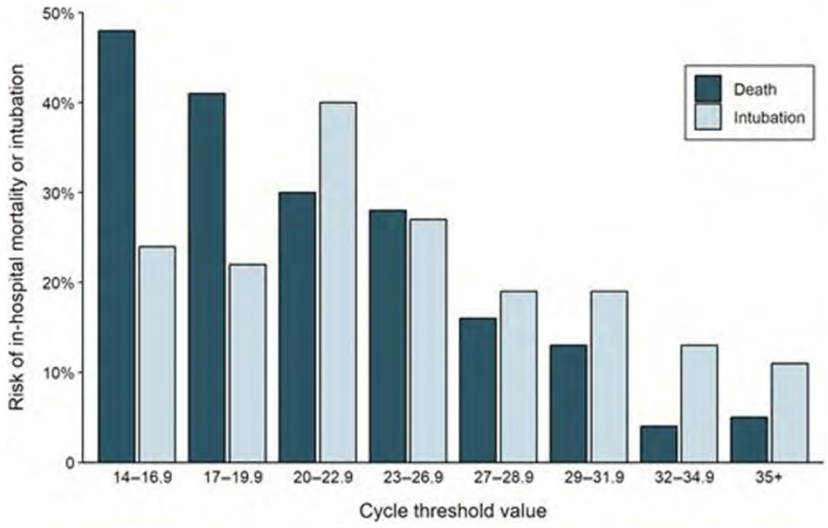
COVID-19 Diagnostics – CT Value and Mortality



Magleby et al CID June 30 2020

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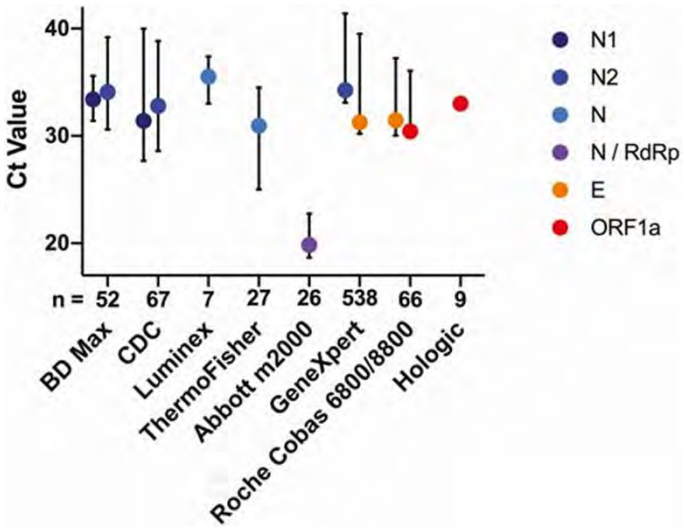
COVID-19 Diagnostics – CT Value and Caution



Factors affecting CT values

- Specimen collection method
- Specimen source
- Transport media type and volume
- Duration from specimen collection to analysis
- Days from infection to specimen collection

Rhoads et al. CID August 12, 2020

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COVID-19 Diagnostics – Performance

Table. Detection Results of Clinical Specimens by Real-Time Reverse Transcriptase–Polymerase Chain Reaction

Specimens and values	Bronchoalveolar lavage fluid (n = 15)	Fibrobronchoscope brush biopsy (n = 13)	Sputum (n = 104)	Nasal swabs (n = 8)	Pharyngeal swabs (n = 398)	Feces (n = 153)	Blood (n = 307)	Urine (n = 72)
Positive test result, No. (%)	14 (93)	6 (46)	75 (72)	5 (63)	126 (32)	44 (29)	3 (1)	0
Cycle threshold, mean (SD)	31.1 (3.0)	33.8 (3.9)	31.1 (5.2)	24.3 (8.6)	32.1 (4.2)	31.4 (5.1)	34.6 (0.7)	ND
Range	26.4-36.2	26.9-36.8	18.4-38.8	16.9-38.4	20.8-38.6	22.3-38.4	34.1-35.4	
95% CI	28.9-33.2	29.8-37.9	29.3-33.0	13.7-35.0	31.2-33.1	29.4-33.5	0.0-36.4	

From: **Detection of SARS-CoV-2 in Different Types of Clinical Specimens**

Wang et al, JAMA. 2020;323(18):1843-1844. doi:10.1001/jama.2020.3786

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COVID-19 Diagnostics – Antigen Testing

Pros

- No instrument required, Point of Care (POC)
- 20-25 minutes turn around time

Cons

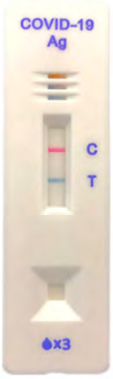
- Lower sensitivity compared to NAAT/RT-PCR
- Need confirmation testing in certain patient populations

		PCR +	PCR -
Antigen	+	173	6
	-	57	2566

True Positive	173
False Positive	6
True Negative	2566
False Negative	57

Overall percent agreement:	97.8%	
Positive agreement:	75.2%	69-81%
Negative agreement:	99.8%	
Positive predictive value:	96.6%	93-99%
Negative predictive value:	97.8%	

Scenario	Prevalence	PPV
From concordance tests	8.21%	96.6%
From all UCH tests	6.03%	95.4%
From last 7 days of all UCH tests	11.49%	97.7%



Nucleocapsid
TCID50=800

Carestart COVID-19
Antigen Testing
Kristie Johnson, PhD., D(ABMM)

64

CC: 56yoM with fevers, chills, myalgias, diarrhea

56yoM presents in March with 5 days of subjective fevers, chills, myalgias, watery diarrhea following a trip to South Carolina visiting family, where his father had an influenza-like illness, diagnosed subsequently with COVID-19.

Review of systems: + chills, fever, malaise/fatigue, diarrhea, dizziness. Denies shortness of breath

Past Medical History: NIDDM (HgbA1c 4.6), PAD, ESLD 2/2 EtOH/AIH s/p OLT 2019

Medications: tacrolimus 3mg, gabapentin 300mg, valganciclovir, ASA, MVI

Social History: Married, works as a salesman, three adult children (healthy), no tobacco, quit alcohol in June 2019

65

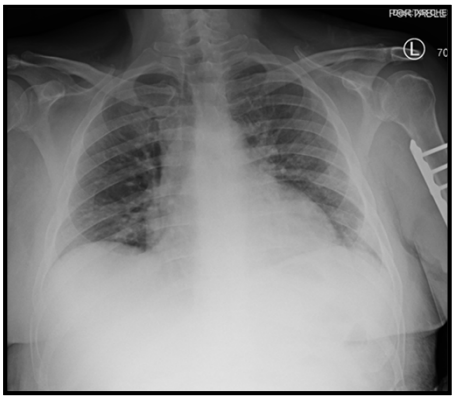
CC: 56yoM with fevers, chills, myalgias, diarrhea

Physical Exam: **T** 38.1 °C (100.6 °F) **HR** 80 **BP** 140/75 **RR** 18 **SpO2** 97%

Gen: in no distress
HEENT: normal, op clear
CV: Normal rhythm, regular, stable 3/6 systolic murmur
Pulm: Normal breath sounds, good air movement bilaterally throughout
Abd: nontender, nondistended, no rebound, no guarding
MSK: no swelling, tenderness, or deformity
Neuro: alert and oriented, grossly intact, no focal deficits

Labs: WBC 1.4 (36% pmns, 58% lymphs), Hgb 7.8, Plt 136

133	98	1.64	98
4.9	24	29	



66

CC: 56yoM with fevers, chills, myalgias, diarrhea

Clinical Course:

3/25 Presented to the ED with fevers, chills, myalgias, diarrhea, **tested COVID-19 positive** by NP swab
3/27 Developed hypoxic respiratory failure, intubated, transferred to the ICU, started azithromycin/HCQ
3/31 Started tocilizumab
4/6 Passed SBT, extubated
4/16 Discharged to home, off oxygen

<59 days pass>

5/23 Presents with dry gangrene of R great toe, planned for toe amputation, no other complaints

67

CC: 56yoM with resolved COVID-19, diabetic foot

Should you test for SARS-CoV-2 before he goes to the OR?

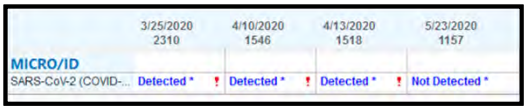
A. Yes, with PCR testing
B. Yes, with antigen testing
C. Yes, with antibody testing
D. Yes, with CT scan of chest
E. No

68

CC: 56yoM with resolved COVID-19, diabetic foot

Should you test for SARS-CoV-2 before he goes to the OR?

A. Yes, with PCR testing
B. Yes, with antigen testing
C. Yes, with antibody testing
D. Yes, with CT scan of chest
E. No



	3/25/2020 2310	4/10/2020 1546	4/13/2020 1518	5/23/2020 1157
MICRO/ID				
SARS-CoV-2 (COVID-...	Detected * !	Detected * !	Detected * !	Not Detected *

69

CC: 56yoM with fevers, chills, myalgias, diarrhea

Clinical Course:

3/25 Presented to the ED with fevers, chills, myalgias, diarrhea, **tested COVID-19 positive** by NP swab
3/27 Developed hypoxic respiratory failure, intubated, transferred to the ICU, started azithromycin/HCQ
3/31 Started tocilizumab
4/6 Passed SBT, extubated
4/16 Discharged to home, off oxygen

<59 days pass>

5/23 Presents with dry gangrene of R great toe, planned for toe amputation, no other complaints
6/2 Represents with infection at the site of his amputation, no other complaints

70

CC: 56yoM with resolved COVID-19, diabetic foot

Should you test for SARS-CoV-2 before he goes back to the OR?

A. Yes, with PCR testing
B. Yes, with antigen testing
C. Yes, with antibody testing
D. Yes, with CT scan of chest
E. No

71

CC: 56yoM with resolved COVID-19, diabetic foot

Should you test for SARS-CoV-2 before he goes to the OR?

A. Yes, with PCR testing
B. Yes, with antigen testing
C. Yes, with antibody testing
D. Yes, with CT scan of chest
E. No

	3/25/2020 2310	4/10/2020 1546	4/13/2020 1518	5/23/2020 1157	6/2/2020 1857
MICRO/ID					
SARS-CoV-2 (COVID-...	Detected * !	Detected * !	Detected * !	Not Detected *	Detected * !

72

CC: 56yoM with resolved COVID-19, diabetic foot

What's going on?

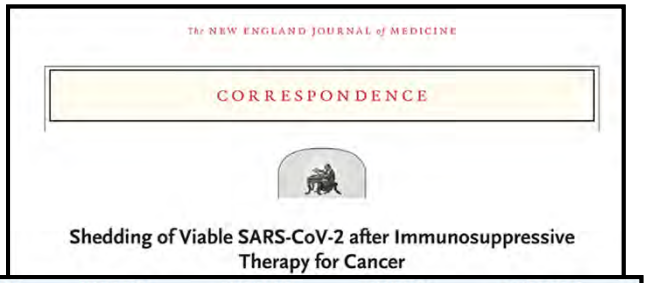
A. COVID-19 chronically infected
B. COVID-19 reinfected
C. False positive
D. 🤷‍♀️

73

CC: 56yoM with resolved COVID-19, diabetic foot

What's going on?

A. COVID-19 chronically infected
B. COVID-19 reinfected
C. False positive
D. 🤷

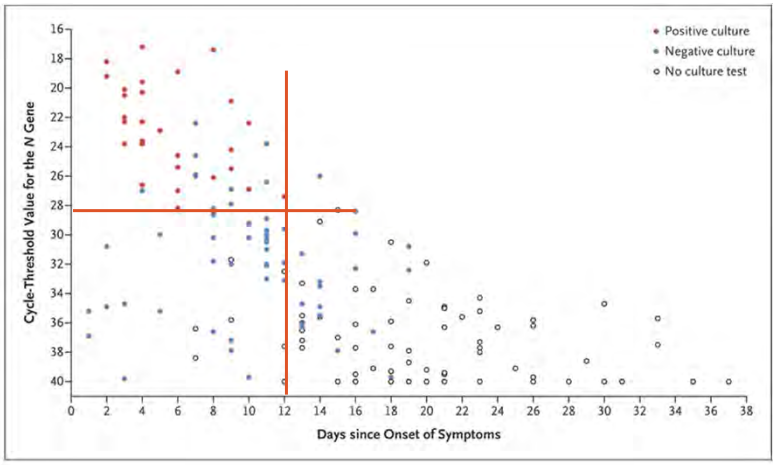


	3/25/2020 2310	4/10/2020 1546	4/13/2020 1518	5/23/2020 1157	6/2/2020 1857	6/10/2020 2211
SARS-CoV-2 (COVID-...	Detected * !	Detected * !	Detected * !	Not Detected *	Detected * !	Not Detected *
SARS-CoV-2 Antibod...						Reactive...

Aydillo, et al
December 4, 2020
N Engl J Med 2020; 383:2586-2588

74

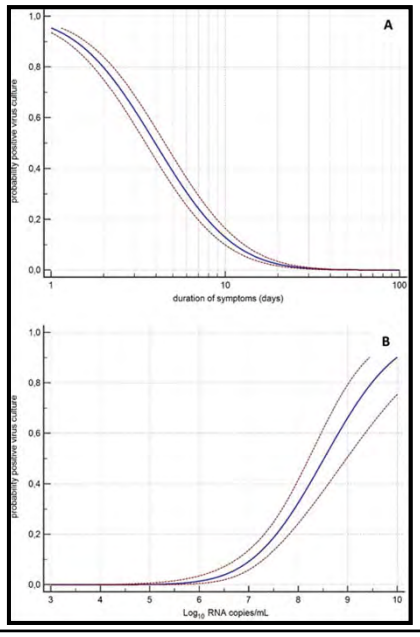
COVID-19 Diagnostics – PCR Testing

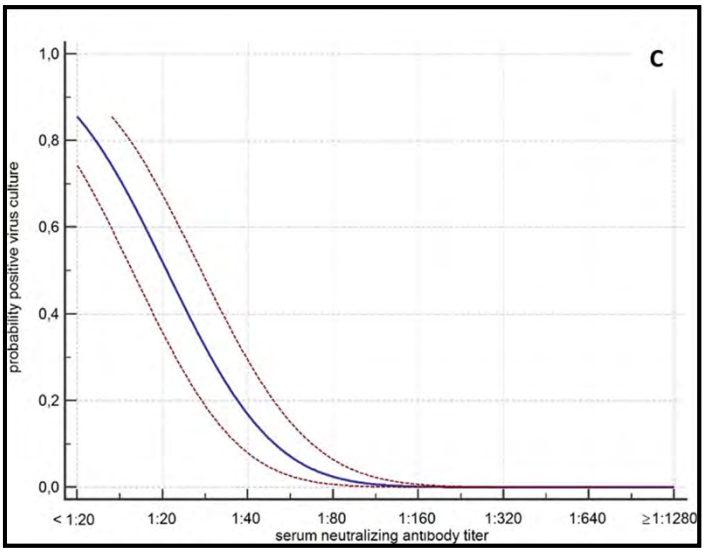


M Kim et al. N Engl J Med 2021. DOI: 10.1056/NEJMc2027040

75

COVID-19 Infectivity

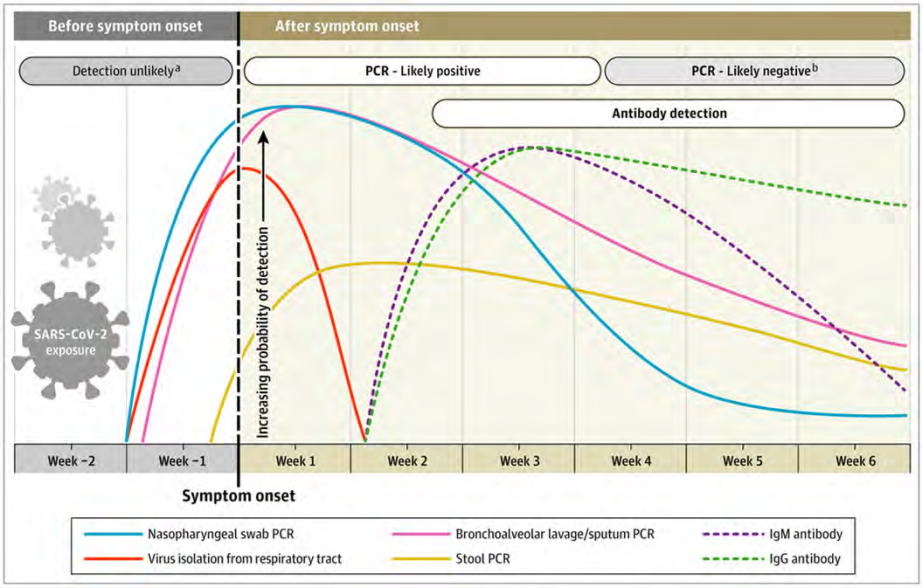




Van Kampen et al Nature Communications 2021; 12:267

76

COVID-19 Diagnostics

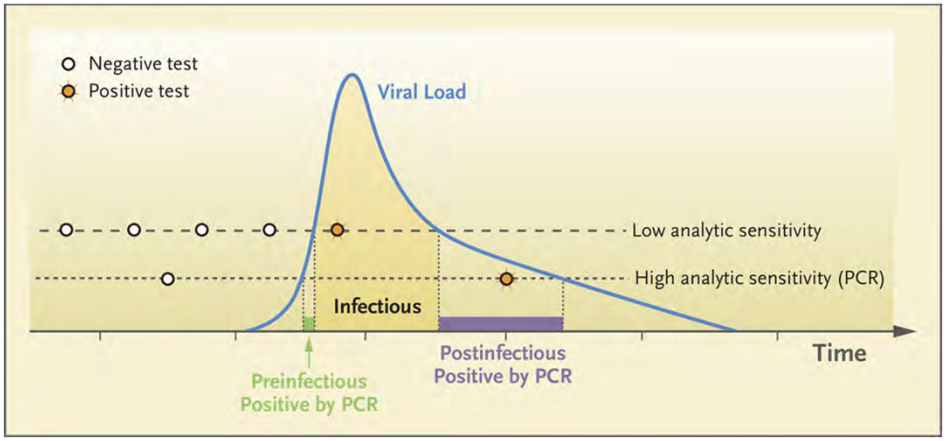


Sethuraman, et al JAMA. 2020;323(22):2249-2251.

77

COVID-19 Diagnostics – Performance

High-Frequency Testing with Low Analytic Sensitivity versus Low-Frequency Testing with High Analytic Sensitivity.



MJ Mina et al. N Engl J Med 2020;383:e120.

78

CC: 33yoW with shortness of breath

33yoW pregnant (28 weeks 2 days) presents with a 4-day history of fatigue, subjective fever, chills, diaphoresis and headache. Complained of mild cough progressing to shortness of breath. Tested positive for SARS-CoV-2. CXR negative. Admitted for three days but never required supplemental oxygen, discharged home. Re-presented to the ED two days later with worsening shortness of breath, found to be hypoxic to 80% with ambulation. Required 6-8 NCO2, transferred to UMMC for a higher level of care.

Review of systems: + fatigue, nonproductive cough, dyspnea on exertion. Denies congestion, anosmia, dysgeusia, GI symptoms

Past Medical History: Type 2 DM (HgbA1c 7.9%), G5P2022, HSV (no recent outbreaks), gestational hypertension

Medications: Insulin, metformin 100mg bid

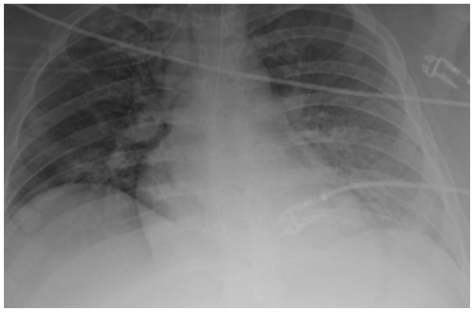
Social History: Married, 2 healthy children ages 3 and 9, no alcohol or tobacco. Husband recently with symptomatic COVID-19

79

CC: 33yoW G5P2022 with shortness of breath

Physical Exam: **T** 37.6 °C **HR** 87 **BP** 101/59 **RR** 22 **SpO2** 88% on RA; 97% HFNC

Gen: in no distress
HEENT: normal, op clear
CV: Normal rhythm, regular, no murmurs
Pulm: Normal breath sounds, good air movement bilaterally throughout
Abd: gravid, nontender
MSK: mild pedal edema, pulses intact



Labs:

SARS-CoV-2 Testing
Positive

WBC 6.0
85% pmns
12% lymphs
Hgb 11.5
Plt 252

137	110	0.43	247
4.7	11	6	

CRP 20.1 (nv ≤1 mg/dL)
LDH 606
D-dimer 580 (nv <500 ng/mL)
Ferritin 266.8 (nv 6.2-137 ng/mL)

80

CC: 33yoW G5P2022 with shortness of breath

What are we most concerned about in this pregnant woman?

A. Respiratory Failure
B. Spontaneous abortion
C. Preterm labor
D. Vertical transmission
E. Death

81

CC: 33yoW G5P2022 with shortness of breath

What are we most concerned about in this pregnant woman?

A. Respiratory Failure
B. Spontaneous abortion
C. Preterm labor
D. Vertical transmission
E. Death

82

CC: 33yoW G5P2022 with shortness of breath

Clinical Course:

11/15 Presented to OSH ED, **tested COVID-19 positive** by NP swab
11/18 Received a short course of steroids, discharged home, did not require oxygen
11/20 Re-presented to OSH ED with SOB, transferred to UMMC on HLNC
11/21 Required BiPAP
11/24 Experienced respiratory fatigue, required intubation, mechanical ventilation
Received remdesivir, canakinumab, and betamethasone for fetal lung development
MDR Acinetobacter VAP, completed 7 days of amp/sulbactam, meropenem, inhaled colistin
12/1 Extubated
12/7 Transferred back to L&D after 2 negative NP swabs
12/11 Discharged home
1/1 Delivered a healthy baby girl at 37 weeks gestation by C-section

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COVID-19 in pregnancy?

19 women in published or pre-published studies, delivering 20 babies

- All 3rd trimester
- 1 ICU admission (5%)
- 8 (42%) pre-term deliveries
  - none spontaneous
- 1 neonatal death
- No evidence of vertical transmission

	COVID-19	SARS			MERS		
Stage of pregnancy	3rd Trimester	1st trimester	2nd Trimester	3rd Trimester	1st Trimester	2nd Trimester	3rd Trimester
N	19 (20 infants)	7	5	8 (9 fetuses)	1	5	5
Women with co-morbidities	4 *(21%)*	not reported	not reported	not reported	0	2 *(40%)*	3 *(60%)*
Admitted asymptomatic	3 (16%)	0	0	0	1 *(100%)*	1 *(20%)*	0
ICU admission %	1 (5%)	1 *(14%)*	2 *(40%)*	3 *(38%)*	0	3 *(60%)*	4 *(80%)*
Maternal mortality %	0*	1 *(14%)*	1 *(20%)*	1 *(13%)*	0	1 *(20%)*	2 *(40%)*
Miscarriage or intra-uterine death	0	4 *(58%)*	1 *(20%)*	1 (1 twin) (13%)	0	1 (20%)	1 *(20%)*
Any pre-term delivery	8/19 (42%)*	not reported	2 (40%)	2 (26%)	0	1 (20%)	2 (40%)

Mullins E, Evans D, Viner R, O'Brien P, Morris E. Coronavirus in Pregnancy and Delivery: Rapid Review and Expert Consensus. MedRxiv 2020;preprint.

84

COVID-19 in pregnancy

Systematic Review of 64 pregnant women in 7 published studies:

- Symptomatic patients generally presented after 32nd week
- Presented with fever 76%, cough 29%, 22% diarrhea

- Outcomes:
  - ICU admission 9%
  - Mechanical ventilation 5%
  - Preterm delivery
    - <37 weeks 41%
    - <34 weeks 15%
  - No deaths, miscarriages, vertical transmission were not reported
    - 1 case report of vertical transmission, both mother and baby recovered

Castro at al. Covid-19 and Pregnancy: An Overview. Rev Bras Ginecol Obstet. 2020 Jul;42(7):420-426. English. doi: 10.1055/s-0040-1713408. Epub 2020 Jun 19. PMID: 32559801.
Alzamora et al. Severe COVID-19 during Pregnancy and Possible Vertical Transmission. Am J Perinatol. 2020 Jun;37(8):861-865. doi: 10.1055/s-0040-1710050. Epub 2020 Apr 18. PMID: 32305046; PMCID: PMC7356080.

85

COVID-19 in Children?

Retrospective study of 366 children with respiratory infections admitted to hospitals in Wuhan
- 23 (6.3%) Influenza A
- 20 (5.5%) Influenza B
- **6 (1.6%) SARS-CoV-2**

- No deaths

All hospitalized infants (28d to 1 year) diagnosed with COVID-19 Dec through Feb 6 in China:

→ 9 infants (7 female)

- All presumed from a family member
- 4 with fever, 2 mild URI, 1 asymptomatic, 2 unknown

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age (yr)	3	7	3	1	3	4
Sex	Female	Female	Female	Male	Female	Male
CT findings	Patchy ground-glass opacities in both lungs	NA	Patchy shadows in both lungs	Patchy shadows in both lungs	Patchy shadows in both lungs	Normal

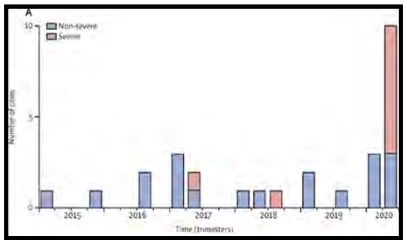
[1] Liu W, Zhang Q, Chen J, Xiang R, Song H, Shu S, et al. Detection of Covid-19 in Children in Early January 2020 in Wuhan, China. N Engl J Med 2020:2019–21.
[2] Wei M, Yuan J, Liu Y, Fu T, Yu X, Zhang Z-J. Novel Coronavirus Infection in Hospitalized Infants Under 1 Year of Age in China. JAMA 2020.

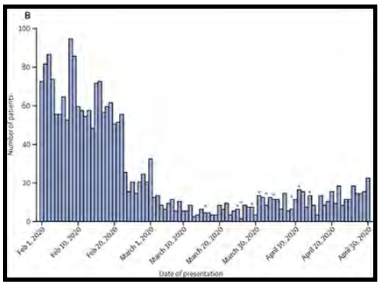
86

Post-COVID-19 in Children?

First reported in March/April 2020: children with

- cardiac dysfunction
- "multisystem inflammatory state,"
- atypical Kawasaki-like disease
- toxic shock syndrome





Reporting Multisystem Inflammatory Syndrome in Children (MIS-C)

Accessible version: https://www.cdc.gov/mis-c/hcp/index.html

Clinical Presentation

Patients with MIS-C have presented with a persistent fever, fatigue, and a variety of signs and symptoms, including multiorgan (e.g., cardiac, gastrointestinal, renal, hematologic, dermatologic, neurologic) involvement and elevated inflammatory markers. Not all children will have the same signs and symptoms, and some children may have symptoms not listed here.

MIS-C may present weeks after a child is infected with SARS-CoV-2. The child may have been infected from an asymptomatic contact and, in some cases, the child and their caregivers may not even know they had been infected.

Report possible cases of MIS-C to your local, state, or territorial health department.

Visit cdc.gov/mis-c/hcp for more information and a case report form.

Questions? Contact CDC's 24-hour Emergency Operations Center at 770-488-7100.

Case Definition

- An individual aged <21 years presenting with fever*, laboratory evidence of inflammation**, and evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); AND
- No alternative plausible diagnoses; AND
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or exposure to a suspected or confirmed COVID-19 case within the 4 weeks prior to the onset of symptoms

*Fever >38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours

**Including, but not limited to, one or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin

Additional comments:

- Some individuals may fulfill full or partial criteria for Kawasaki disease but should be reported if they meet the case definition for MIS-C.
- Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection.

Visit Information for Healthcare Providers about Multisystem Inflammatory Syndrome in Children (MIS-C) for more information about MIS-C.

CDC

cdc.gov/coronavirus

Verdoni et al Lancet V 395 (10239), June 2020; pp1771-8
http://www.cdc.gov

87

CC: 29yoM with flu-like symptoms

29yoM with a 5-day history of headache as well as 1 day of diarrhea and vomitting. Presented to the ED after his temperature was 102.5 at home.

Review of systems: + fever, nonproductive cough, headache, diarrhea, dyspnea on exertion. Denies shortness of breath, chest pain

Past Medical History: depression

Medications: none

Social History: Single, Veteran, now works in hospital administration. Social drinker, no tobacco, no drugs, sexually active with multiple partners over the past year

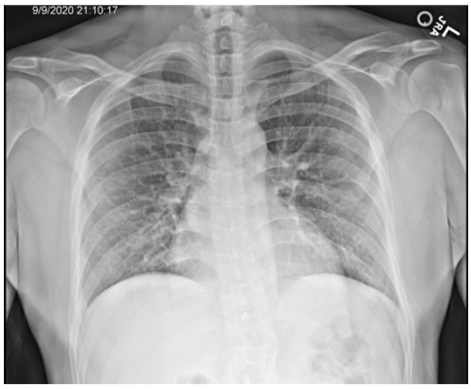
88

CC: 29yoM with flu-like symptoms

Physical Exam: **T** 38.6 °C (101.4 °F) **HR** 98 **BP** 136/85 **RR** 20 **SpO2** 99%

Gen: in no distress
HEENT: normal, op clear
CV: Normal rhythm, regular, no murmurs
Pulm: Normal breath sounds, good air movement bilaterally throughout
Abd: nontender, nondistended, no rebound, no guarding
MSK: no swelling, tenderness, or deformity

Labs: SARS-CoV-2 Testing
Negative



89

CC: 29yoM with flu-like symptoms

What should be the next step in the diagnostic work up?

A. Viral respiratory panel (including Influenza A)
B. Repeat COVID-19 testing
C. Lumbar puncture
D. HIV testing
E. Chest CT imaging

90

CC: 29yoM with flu-like symptoms

What should be the next step in the diagnostic work up?

A. Viral respiratory panel (including Influenza A)
B. Repeat COVID-19 testing
C. Lumbar puncture
D. HIV testing
E. Chest CT imaging

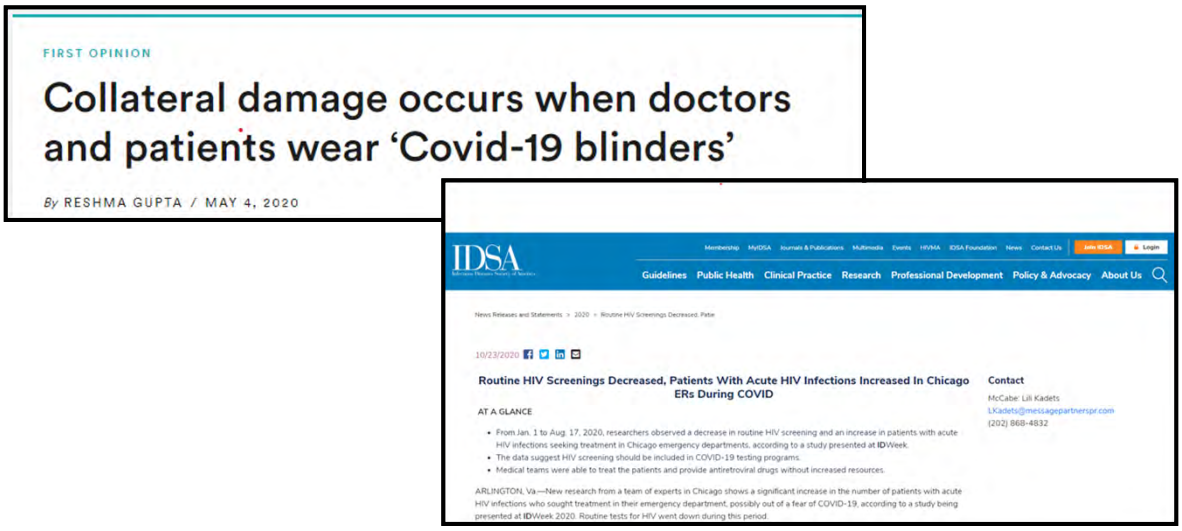
91

CC: 29yoM with flu-like symptoms

Clinical Course: Tested negative for COVID-19 twice before going to seek testing at a different facility one month later where he was diagnosed with HIV and syphilis.

92

There's more to life than COVID-19



https://www.idsociety.org/news--publications-new/articles/2020/routine-hiv-screenings-decreased-patients-with-acute-hiv-infections-increased-in-chicago-ers-during-covid/

https://www.statnews.com/2020/05/04/collateral-damage-occurs-when-doctors-and-patients-wear-covid-19-blinders/

93

Tips for Staying Safe During COVID-19

(or the next emerging infection)

Personal Hygiene & Practices

- Handwashing/Hand sanitizer
- Cough/Sneeze etiquette
- Stay home when sick
- Avoid sick contacts
- Seek medical assistance

Public Health Authorities

- Isolation/Quarantine
- Control mass gatherings/travel
- Hospitalize
  - Contact/Droplet Precautions
  - PPE
  - ICU, mech vent support
- Clear & Fast Communication
  - Prevent public panic

Diagnostics

Vaccines

Therapeutics

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THANK YOU

Meagan Deming, MD PhD
J. Kristie Johnson PhD, D(ABMM)
Wilbur Chen, MD, MS

Institute of Human Virology & Center for Vaccine Development and Global Health
University of Maryland School of Medicine

COVID-19 Providers, Patients, Researchers, First Responders and Data Fanatics

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mdeming@ihv.umaryland.edu

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SARS-CoV-2 vaccines and therapeutics

Meagan Deming, MD, PhD

February 27, 2021

Adapted from https://xkcd.com/1217/

1

Disclosures

- New data is being published (and retracted) daily. This presentation is up to date as of Feb 9, 2021. Updates from the original slide set are indicated.
- I am a sub-investigator on the following trials:
  - Recombinant S/matrix-M1 adjuvant vaccine trial (NCT04611802, Novavax)
  - mRNA-1273 vaccine trial (NCT04470427, Moderna)
  - Adaptive COVID-19 Treatment Trial (NCT04280705, NIAID)
  - Hydroxychloroquine for COVID-19 PEP (NCT04328961, Gates Foundation)
  - COVID-19 vaccine clinical study (NCT04368728, BioNtech/Pfizer)
  - CD24Fc in COVID-19 treatment (NCT04317040, OncoImmune Inc)
- I have no financial conflicts of interest

2

Objectives

At the end of this talk, you should be able to:

- Be able to state the common and uncommon clinical presentations of COVID-19 with an emphasis on the impact of age and comorbidities on outcomes

- **Review available and upcoming COVID-19 therapeutic and vaccine strategies**

Therapeutics

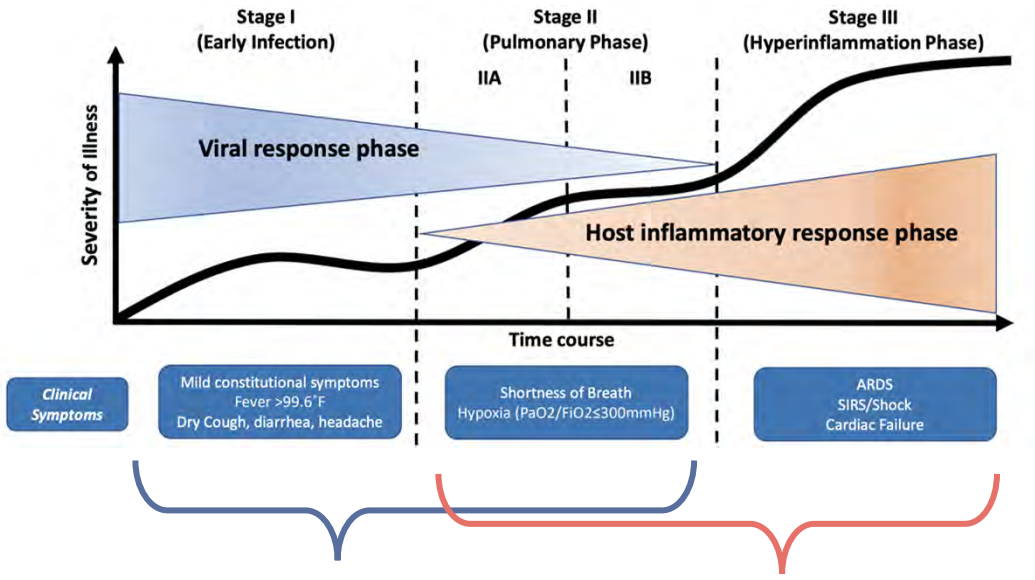
- Antivirals: Remdesivir (Veklury), monoclonals
  - In development: β-D-N4-hydroxycytidine (Molnupiravir, EIDD-2801)
- Anti-inflammatory: Dexamethasone, Baracitinib, Tocilizumab
- Ineffective: Hydroxychloroquine, Ivermectin

Vaccines

- Development process
- Available efficacy data

*slide updated since 9-Feb

3

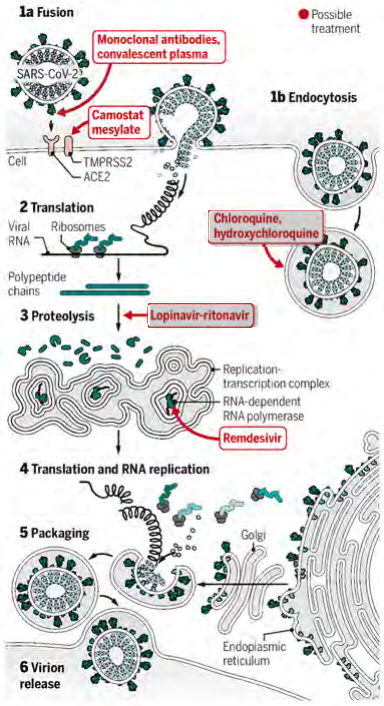


Antivirals
~days 1-10, active viral replication

Anti-inflammatory
~days 8-14 (or longer), immune dysfunction

Siddiqi JHLT 2020 doi:10.1016/j.healun.2020.03.012

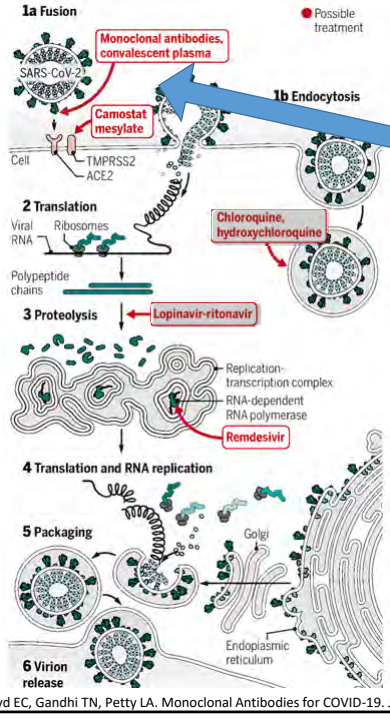
4



SARS-CoV-2 treatment options

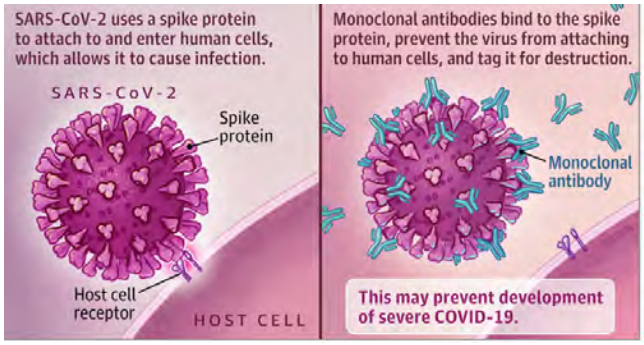
Image from: Kupferschmidt K, Cohen J. Race to find COVID-19 treatments accelerates. Science (80-) 2020.

5



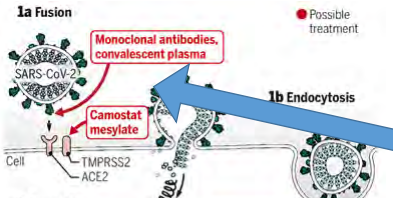
SARS-CoV-2 treatment options

Monoclonal antibodies
- Bamlanivimab (LY-CoV555)
- Casirivimab (REGN10933) and imdevimab (REGN10987)



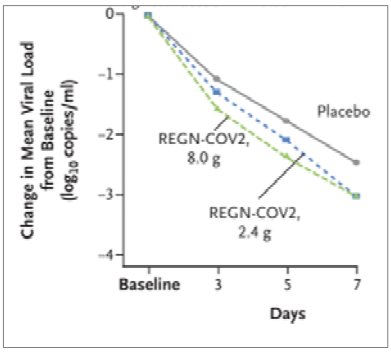
Lloyd EC, Gandhi TN, Petty LA. Monoclonal Antibodies for COVID-19. Jama 2021;2021.

6



SARS-CoV-2 treatment options

Monoclonal antibodies
- Bamlanivimab (LY-CoV555)
- Casirivimab (REGN10933) and imdevimab (REGN10987)



Outcome	LY-CoV555	Placebo	Incidence
	no. of patients/total no.		%
Hospitalization		9/143	6.3
	700 mg, 1/101		1.0
	2800 mg, 2/107		1.9
	7000 mg, 2/101		2.0
	Pooled doses, 5/309		1.6

Both EUAs issued in Nov 2020:
non-hospitalized patients with mild to moderate COVID-19 who are at high risk for progressing to severe disease and/or hospitalization

Chen P, Nirula A, Heller B, et al. SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19. N Engl J Med 2021;384(3):229–37.
Weinreich DM, Sivapalasingam S, Norton T, et al. REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19. N Engl J Med 2021;384(3):238–51.

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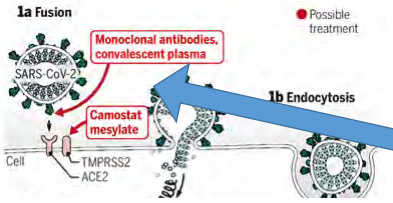

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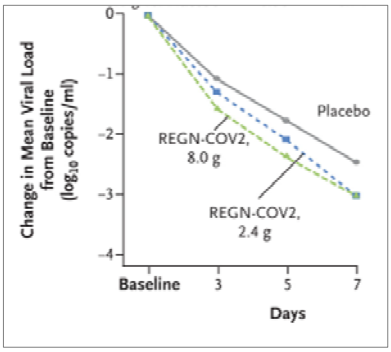

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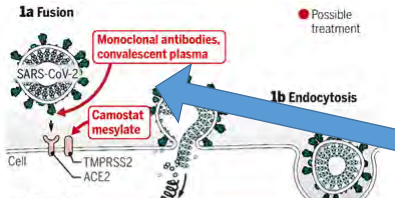

SARS-CoV-2 treatment options

Monoclonal antibodies
- Bamlanivimab (LY-CoV555)
- Casirivimab (REGN10933) and imdevimab (REGN10987)

Why not hospitalized patients?

The percentage of patients with the primary safety outcome (a composite of death, serious adverse events, or clinical grade 3 or 4 adverse events through day 5) was similar in the LY-CoV555 group and the placebo group (19% and 14%, respectively; odds ratio, 1.56; 95% CI, 0.78 to 3.10; P=0.20).

Both EUAs issued in Nov 2020:
non-hospitalized patients with mild to moderate COVID-19 who are at high risk for progressing to severe disease and/or hospitalization

Chen P, Nirula A, Heller B, et al. SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19. N Engl J Med 2021;384(3):229–37.
Wang P, Liu L, Iketani S, et al. Increased Resistance of SARS-CoV-2 Variants B.1.351 and B.1.1.7 to Antibody Neutralization. BioRxiv 2021; DOI: 10.1101/2021.01.25.428137

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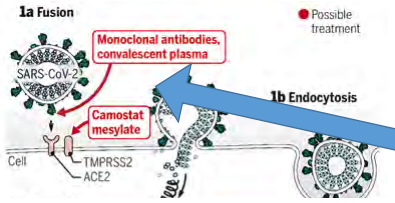
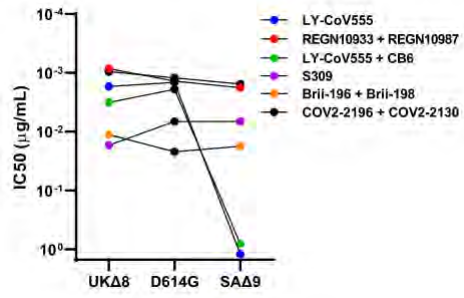


SARS-CoV-2 treatment options

Monoclonal antibodies
- Bamlanivimab (LY-CoV555) **and etesevimab** (LY-CoV016)
- Casirivimab (REGN10933) and imdevimab (REGN10987)

Two monoclonals are better than one



New EUA for Bam+Ete on Feb 9,2021
→ Phasing out Bamlanivimab alone
Non-hospitalized patients with mild to moderate COVID-19 who are at high risk for progressing to severe disease and/or hospitalization

*slide updated since 9-Feb

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10

Summary of therapeutics

Coronavirus Disease 2019 (COVID-19) Treatment Guidelines

https://www.covid19treatmentguidelines.nih.gov/

- Monoclonals:
  - Bamlanivimab (LY-CoV555) plus etesevimab (LY-CoV016)
  - Casirivimab (REGN10933) plus imdevimab (REGN10987)
  - **Before hospitalization** in patients at risk of progression
    →"As soon as possible and within 10 days of symptom onset"

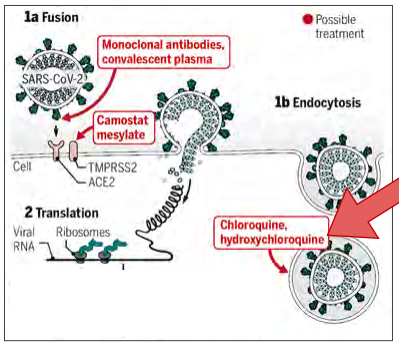
High risk is defined as patients who meet at least one of the following criteria:

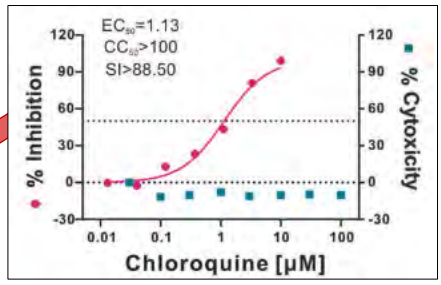
- Have a body mass index (BMI) ≥35
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥65 years of age
- Are ≥55 years of age AND have
  - cardiovascular disease, OR
  - hypertension, OR
  - chronic obstructive pulmonary disease/other chronic respiratory disease.
- Are 12 – 17 years of age AND have
  - BMI ≥85th percentile for their age and gender based on CDC growth charts, OR
  - sickle cell disease, OR
  - congenital or acquired heart disease, OR
  - neurodevelopmental disorders, for example, cerebral palsy, OR
  - a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
  - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control

*slide updated since 9-Feb

11

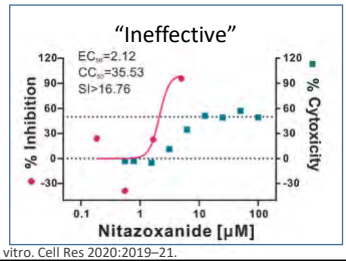
Ineffective therapies: Hydroxychloroquine





Robustly inhibits SARS-CoV-2 in cell culture

"Ineffective"



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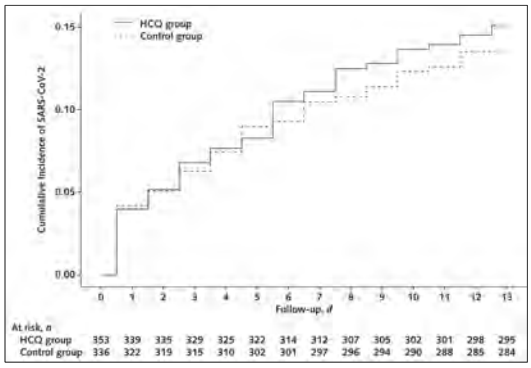


Post-exposure prophylaxis study:

- household contacts or healthcare workers exposed within the previous 4 days → **early to maximize opportunity for antiviral effect**
- Hydroxychloroquine (400 mg/d for 3 days followed by 200 mg/d for 11 days) or ascorbic acid (500 mg/d followed by 250 mg/d) as a placebo-equivalent control. → **double blind, placebo controlled**
- Daily self-administered nasal swabs for SARS-CoV-2 PCR and symptom surveys → **allowed capture of asymptomatic and symptomatic disease with objective viral outcome**

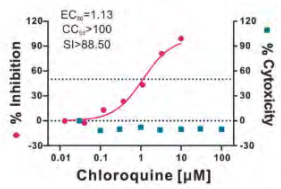
	HCQ group (n=353)	Control (n=336)
n=	53	45
Cumulative incidence % (95% CI)	15.1 (11.0-18.9)	13.5 (9.7-17.1)

Adjusted hazard ratio: 1.10 (0.73–1.66)
p >0.20

Barnabas R V., Brown ER, Bershteyn A, et al. Hydroxychloroquine as Postexposure Prophylaxis to Prevent Severe Acute Respiratory Syndrome Coronavirus 2 Infection. Ann Intern Med 2020;

13

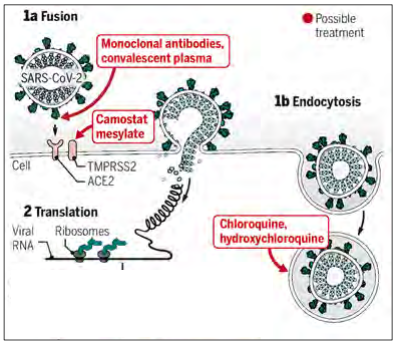
Hydroxychloroquine

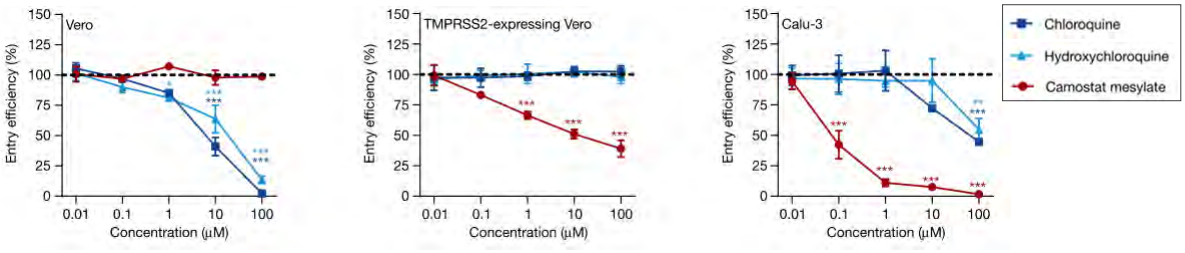


Robustly inhibits SARS-CoV-2 in cell culture → **in Vero cells**

When the co-receptor (TMPRSS2) is available (*in vivo*), SARS-CoV-2 enters by direct membrane fusion

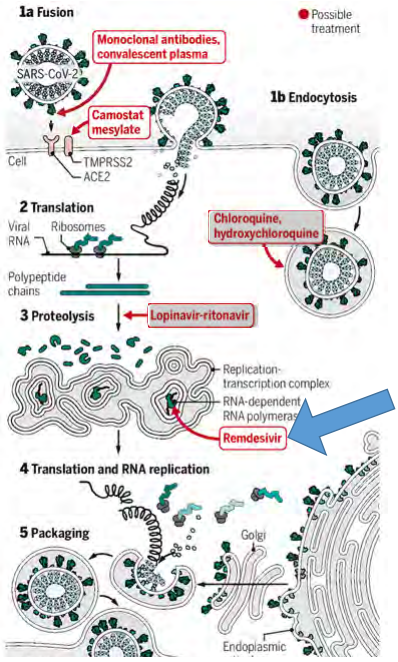
Better models give better answers



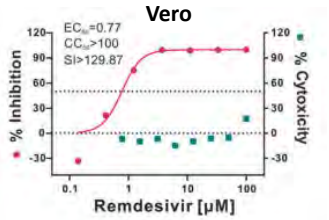


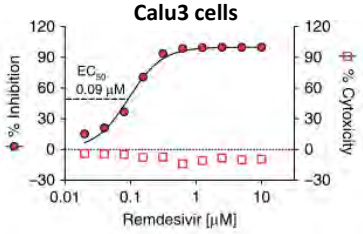
Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res 2020:2019–21.
Hoffmann M, Mösbauer K, Hofmann-Winkler H, et al. Chloroquine does not inhibit infection of human lung cells with SARS-CoV-2. Nature 2020;585(7826):588–90.

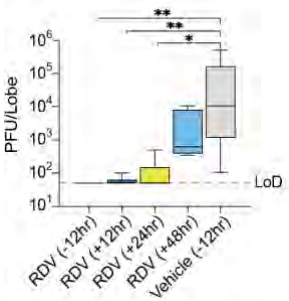
14



Remdesivir







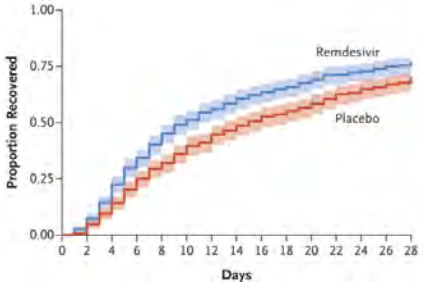
- nucleotide prodrug that inhibits viral RNA synthesis.
- EC50 against a clinical isolate of SARS-CoV-2 in primary human airway epithelial cells: 9.9 nM after 48 hours post-treatment

Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res 2020:2019–21.
Sheahan TP, Sims AC, Leist SR, et al. Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. Nat Commun 2020;11(1).
Martinez D, Schaefer A, Leist SR, et al. Early therapy with remdesivir and antibody combinations improves COVID-19 disease in mice. bioRxiv 2021;2021.01.27.428478.

15

Adaptive COVID-19 Treatment Trial

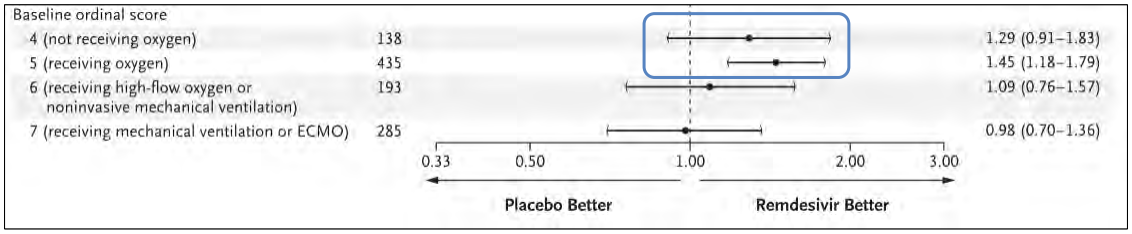
- 68 Sites, 1062 patients, **Remdesivir** vs placebo
- Primary endpoint: **time to recovery** at day 28



Overall

	Remdesivir (N=541)	Placebo (N=521)
Recovery		
No. of recoveries	399	352
Median time to recovery (95% CI) — days	10 (9–11)	15 (13–18)
Rate ratio (95% CI)†	1.29 (1.12–1.49 [P<0.001]	

5d recovery = clinical effect on disease course



1. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the Treatment of Covid-19 — Final Report. N Engl J Med 2020;383(19):1813–26.

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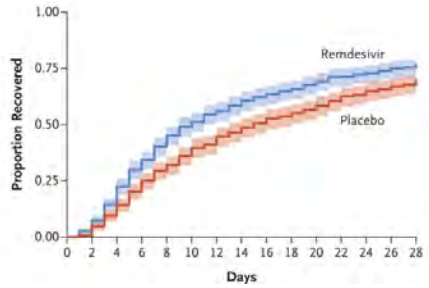


	Overall	
	Remdesivir (N=541)	Placebo (N=521)
Mortality through day 14‡		
Hazard ratio for data through day 15 (95% CI)	0.55 (0.36–0.83)	
No. of deaths by day 15	35	61
Kaplan–Meier estimate of mortality by day 15 — % (95% CI)	6.7 (4.8–9.2)	11.9 (9.4–15.0)
Mortality over entire study period‡		
Hazard ratio (95% CI)	0.73 (0.52–1.03)	
No. of deaths by day 29	59	77
Kaplan–Meier estimate of mortality by day 29 — % (95% CI)	11.4 (9.0–14.5)	15.2 (12.3–18.6)

Secondary analyses: mortality

- 5.2% mortality benefit day 15
- By day 29, 3.8% mortality benefit

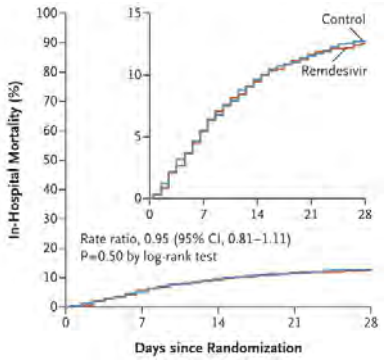
Not powered to evaluate mortality

1. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the Treatment of Covid-19 — Final Report. N Engl J Med 2020;383(19):1813–26.

17

WHO Solidarity trail

- Randomized, no placebo, **open label**
- hydroxychloroquine, Lopinavir, interferon beta-1a, and Remdesivir
  - 1st 3 discontinued for futility
  - 2750 patients were assigned to receive remdesivir
- Primary objective: in-hospital mortality
  - low flow or high flow oxygen: 12.2% vs 13.8%, Risk ratio 0.85 (0.66–1.09)
  - Ventilated: 43% vs 37.8%, risk ratio 1.20 (0.8-1.8)
- Limitations that may bias towards null:
  - unblended allocation
  - no requirement for PCR confirmed SARS-CoV-2 or pulmonary imaging findings
  - if discharged considered alive



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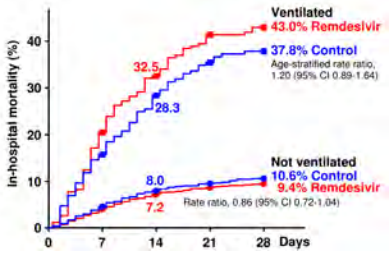
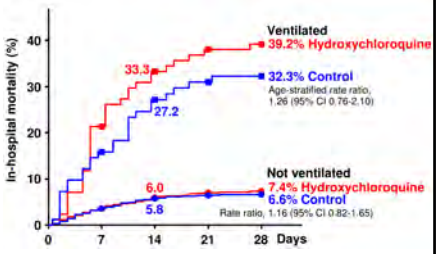
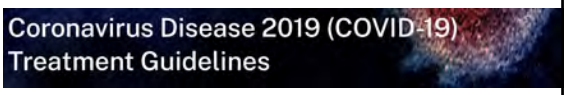




Bigger may not be better

19

Summary of therapeutics



https://www.covid19treatmentguidelines.nih.gov/

- Monoclonals:
  - Bamlanivimab (LY-CoV555) plus etesevimab (LY-CoV016) and the combination Casirivimab (REGN10933) plus imdevimab (REGN10987)
  - **Before hospitalization** in patients at risk of progression
- Antivirals: Remdesivir (Veklury) approved Oct 2020
  - adults and pediatric patients >12 years
  - 200mg day 1, 100mg up to 9 additional days
  - **Use early** (before high flow oxygen or mechanical ventilation)

Not therapeutic:
- **Hydroxychloroquine**
- **Lopinavir/ritonavir**

20

Ineffective therapies: Ivermectin


Antiviral Research 178 (2020) 104787

Contents lists available at ScienceDirect

Antiviral Research

journal homepage: www.elsevier.com/locate/antiviral

The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 *in vitro*

Leon Caly[a], Julian D. Druce[b], Mike G. Catton[b], David A. Jans[b], Kylie M. Wagstaff[b,*]

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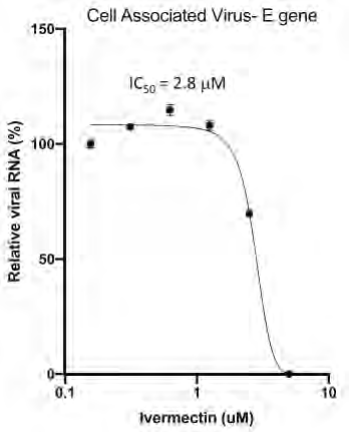

- HIV, Dengue, West Nile Virus, Venezuelan equine encephalitis virus, influenza…
- **Mechanism**? Inhibition of nuclear import of host and viral proteins via the importin (IMP) α/β1 heterodimer…
- IC50 determined to be approximately 2 µM

Caly L, Druce JD, Catton MG, Jans DA, Wagstaff KM. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 *in vitro*. Antiviral Res 2020;178(March):3–6.
Frieman M, Yount B, Heise M, Kopecky-Bromberg SA, Palese P, Baric RS. Severe Acute Respiratory Syndrome Coronavirus ORF6 Antagonizes STAT1 Function by Sequestering Nuclear Import Factors on the Rough Endoplasmic Reticulum/Golgi Membrane. J Virol 2007;81(18):9812–24.

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- **Mechanism**? Inhibition of nuclear import of host and viral proteins via the importin (IMP) α/β1 heterodimer…
- IC50 determined to be approximately 2 µM

Host-directed agent
Viruses are dependent on cellular machinery, this is blocking key cellular processes.

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Ineffective therapies: Ivermectin

The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 *in vitro*

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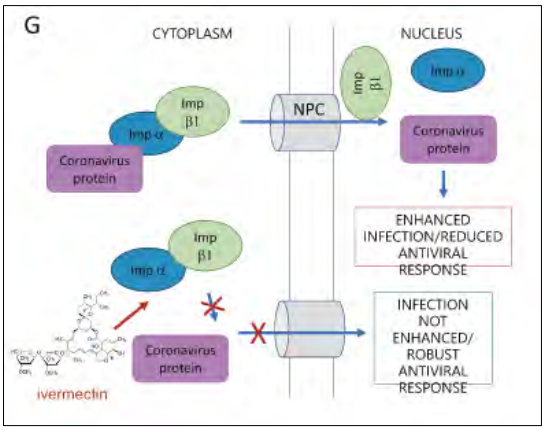
[2] Australian Discovery Institute, Monash University, Clayton, Vic. 3800, Australia

Mechanism? Inhibition of nuclear import of host and viral proteins via the importin (IMP) α/β1 heterodimer

- No SARS-CoV-2 proteins are imported into the nucleus.
- The opposite: SARS-CoV proteins sequester nuclear import proteins to prevent activation of innate antiviral responses (STAT1)



Caly L, Druce JD, Catton MG, Jans DA, Wagstaff KM. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 *in vitro*. Antiviral Res 2020;178(March):3–6.
Frieman M, Yount B, Heise M, Kopecky-Bromberg SA, Palese P, Baric RS. Severe Acute Respiratory Syndrome Coronavirus ORF6 Antagonizes STAT1 Function by Sequestering Nuclear Import Factors on the Rough Endoplasmic Reticulum/Golgi Membrane. J Virol 2007;81(18):9812–24.

23

Ineffective therapies: Ivermectin

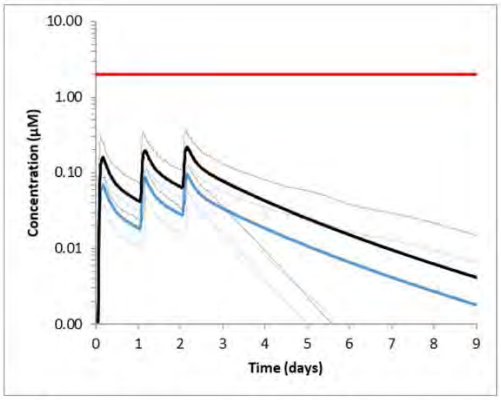


Fig. 1. Simulated mean concentration-time profile of ivermectin in plasma (black line) and lung tissue (blue line) following 600 μg/kg dose daily for 3 days. The 5th and 95th percentiles are also shown. The red-line is the IC_{50} (2μM) against SARS-CoV-2 determined *in vitro* by Caly et al. (2020).

- HIV, Dengue, West Nile Virus, Venezuelan equine encephalitis virus, influenza… → likely cell toxicity
- **Mechanism**? Inhibition of nuclear import of host and viral proteins via the importin (IMP) α/β1 heterodimer… → not applicable
- IC50 determined to be approximately 2 μM

Unachievable therapeutic concentration

Caly L, Druce JD, Catton MG, Jans DA, Wagstaff KM. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 *in vitro*. Antiviral Res 2020;178(March):3–6.
Bray M, Rayner C, Noël F, Jans D, Wagstaff K. Ivermectin and COVID-19: A report in Antiviral Research, widespread interest, an FDA warning, two letters to the editor and the authors' responses. Antiviral Res 2020;178(April):1–3.

24

Ineffective therapies: Ivermectin

- HIV, Dengue, West Nile Virus, Venezuelan equine encephalitis virus, influenza… → gumming up cell processing
- **Mechanism**? Inhibition of nuclear import of host and viral proteins via the importin (IMP) α/β1 heterodimer… → not applicable
- IC50 determined to be approximately 2 μM → not achievable

Some clinical studies showed no benefits or worsening of disease after ivermectin use,[11-14] whereas others reported shorter time to resolution of disease manifestations attributed to COVID-19,[15-18] greater reduction in inflammatory markers,[16,17] shorter time to viral clearance,[11,16] or lower mortality rates in patients who received ivermectin than in patients who received comparator drugs or placebo.[11,16,18] However, most of the studies reported to date had **incomplete information and significant methodological limitations, which make it difficult to exclude common causes of bias**.

https://www.covid19treatmentguidelines.nih.gov/

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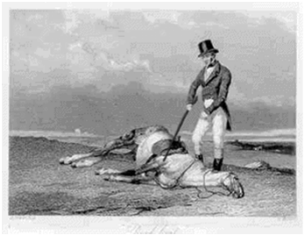
Ineffective therapies: Ivermectin



- HIV, Dengue, West Nile Virus, Venezuelan equine encephalitis virus, influenza… → gumming up cell processing
- **Mechanism**? Inhibition of nuclear import of host and viral proteins via the importin (IMP) α/β1 heterodimer… → not applicable
- IC50 determined to be approximately 2 μM → not achievable

FDA Letter to Stakeholders: Do Not Use Ivermectin Intended for Animals as Treatment for COVID-19 in Humans

MARCH 25, 2020

Man Dies, Wife Hospitalized From Ingesting Fish Tank Cleaner to Prevent COVID-19

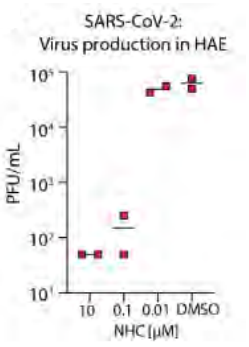
By Tom Rosenthal

Self-medication by a Phoenix-area couple in their 60s with chloroquine phosphate in the mistaken belief the additive, commonly used by aquariums to clean fish tanks, was a prophylactic for COVID-19 resulted in the husband's death and his spouse in critical care, according to officials.

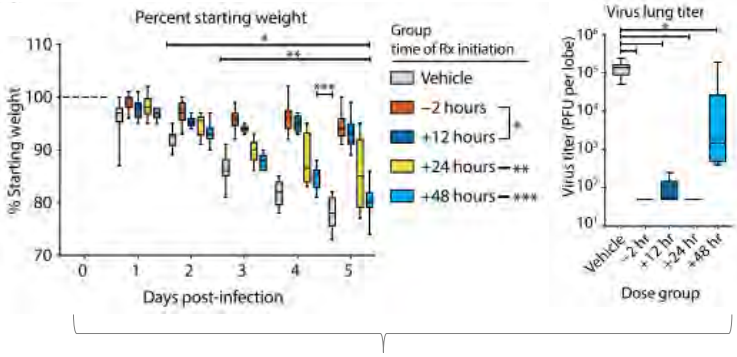
26

Upcoming therapeutics

- β-D-N4-hydroxycytidine (NHC, EIDD-2801)
  - orally bioavailable ribonucleoside analog with broad-spectrum antiviral activity against multiple coronaviruses



Human airway epithelial cells

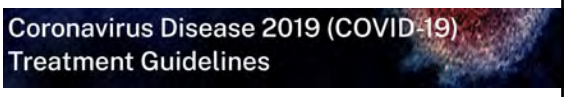


Mouse model

Sheahan TP, Sims AC, Zhou S, et al. An orally bioavailable broad-spectrum antiviral inhibits SARS-CoV-2 and multiple endemic, epidemic and bat coronavirus. Sci Transl Med 2020;12(541):1–151.

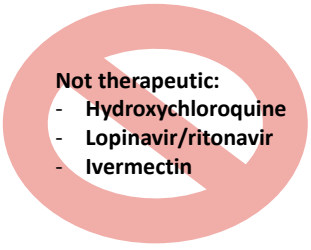
27

Summary of therapeutics



https://www.covid19treatmentguidelines.nih.gov/

- Antivirals: Remdesivir (Veklury) approved Oct 2020
  - adults and pediatric patients >12 years
  - 200mg day 1, 100mg up to 9 additional days
  - No difference in 5 vs 10d course if not mechanically vented (start with 5d course)
  - Check renal function before and monitor hepatic function during therapy
- Ongoing trials: Molnupiravir (EIDD-2801), phase2



Not therapeutic:
- **Hydroxychloroquine**
- **Lopinavir/ritonavir**
- **Ivermectin**

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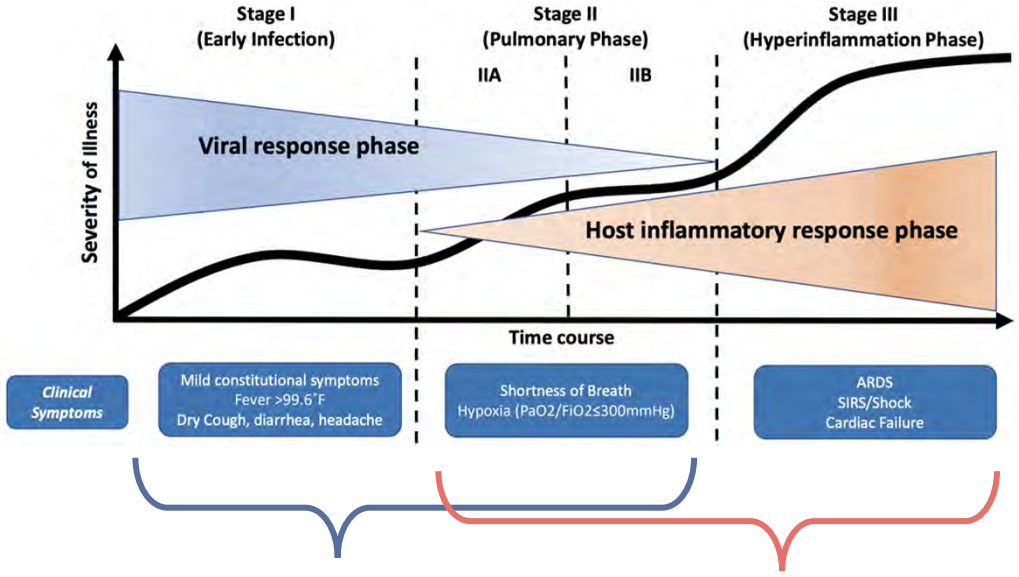

Antivirals
~days 1-10, active viral replication

Anti-inflammatory
~days 8-14 (or longer), immune dysfunction

Siddiqi JHLT 2020 doi:10.1016/j.healun.2020.03.012

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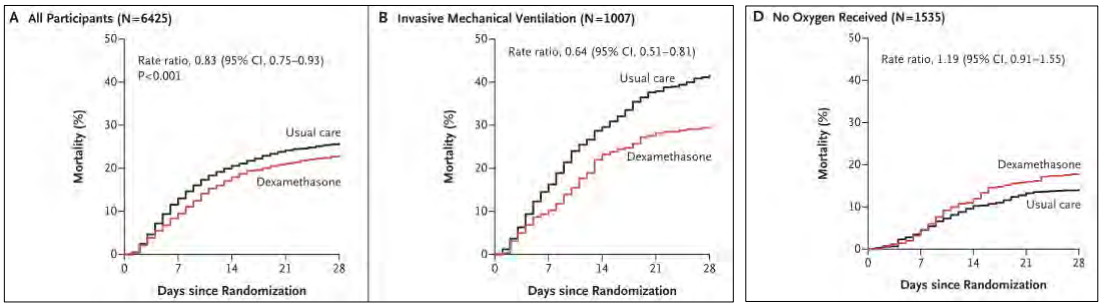
Dexamethasone

Steroid intended to reduce the immune-mediated inflammatory organ injury

Outcome	Dexamethasone (N=2104)	Usual Care (N=4321)	Rate or Risk Ratio (95% CI)*
	no./total no. of patients (%)		
Primary outcome			
Mortality at 28 days	482/2104 (22.9)	1110/4321 (25.7)	0.83 (0.75–0.93)



Recommended for hospitalized patients on oxygen or requiring mechanical ventilation
6mg daily up to 10 days

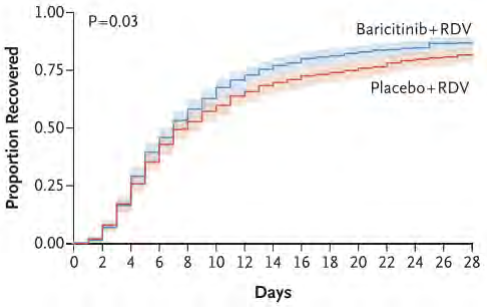
The RECOVERY Collaborative Group. Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report. N Engl J Med 2020;1–11.

30

ACTT-2: Baricitinib

Baracitinib: oral Janus kinase (JAK) inhibitor

- 1,033 hospitalized patients with COVID-19 and evidence of pneumonia.
- Randomized 1:1 to receive baricitinib 4 mg orally or placebo for up to 14 days
- both groups also received remdesivir for up to 10 days



Slight improvement in time to recovery (1 day)
EUA approval → Only for rare situations where corticosteroids cannot be used.

	Baricitinib (N=515)	Placebo (N=518)
Recovery		
No. of recoveries	433	406
Median time to recovery (95% CI) — days	7 (6–8)	8 (7–9)
Rate ratio (95% CI)†	1.16 (1.01–1.32 (P=0.03))	

Kalil AC, Patterson TF, Mehta AK, et al. Baricitinib plus Remdesivir for Hospitalized Adults with Covid-19. N Engl J Med 2020;1–13.

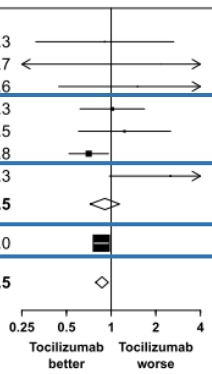
31

Tocilizumab

Recombinant humanized anti-IL-6 receptor monoclonal antibody

	Deaths / Patients randomised (%)		Observed−Expected		Ratio of death rates, RR (95% CI)
	Tocilizumab	Usual care	(O−E)*	Var(O−E)	
COR−IMUNO TOCI	7/64 (10.9)	8/67 (11.9)	−0.3	3.3	0.91 (0.31−2.65)
RCT−TCZ−COVID−19	2/60 (3.3)	1/66 (1.5)	0.6	0.7	2.17 (0.22−21.3)
BACC Bav	9/161 (5.6)	(3/82) x2† (3.7)	1.0	2.6	1.51 (0.44−5.13)
COVACTA	58/294 (19.7)	(28/144) x2† (19.4)	0.3	15.3	1.02 (0.62−1.68)
EMPACTA	26/249 (10.4)	(11/128) x2† (8.6)	1.6	7.5	1.23 (0.60−2.52)
REMAP−CAP	98/353 (27.8)	142/402 (35.3)	−14.2	40.8	0.71 (0.52−0.96)
TOCIBRAS	14/65 (21.5)	6/64 (9.4)	3.9	4.3	2.51 (0.97−6.50)
Subtotal: 7 trials	**214/1246 (17.2)**	**241/1307 (18.4)**	**−7.2**	**74.5**	**0.91 (0.72−1.14)**
RECOVERY	596/2022 (29.5)	694/2094 (33.1)	−48.2	316.0	0.86 (0.77−0.96)
All trials	**810/3268 (24.8)**	**935/3401 (27.5)**	**−55.4**	**390.5**	**0.87 (0.79−0.96) p=0.005**

Heterogeneity between RECOVERY and previous trials: χ^2_1=0.2



Horby PW, Campbell M, Staplin N, et al. Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): preliminary results of a randomised, controlled, open-label, platform trial. medRxiv 2021;19. DOI: 10.1101/2021.02.11.21249258

*slide added since 9-Feb

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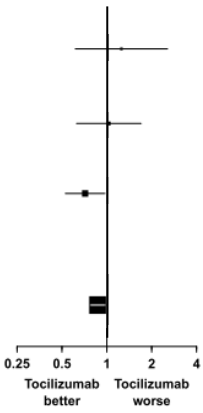
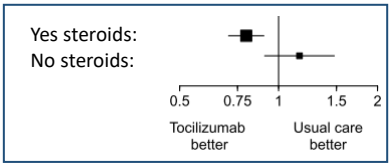
Tocilizumab

recombinant humanized anti-IL-6 receptor monoclonal antibody

Trial Name	N	median CRP (range)	Mechanically vented?	Corticosteroids?
EMPACTA	389	136 (**2.5**-2776)	**none** excluded CPAP, BIPAP, MV	80% toci; 87% control
COVACTA	438	150 (**1.1**-446)	26 v 31% simple O2 32 v 27% icu or noninvasive 38 v 38% MV or ECMO	**19% in toci,** **29% in control**
REMAP-CAP	895	136 (79–208)	29 v 27% HFNC 42 v 42% noninvasive 29 v 30% MV	83% each arm
RECOVERY	4116	143 (107-203)	19 vs 22% just O2 36 vs 40% noninvasive **47 vs 48% mech vent**	82% each arm**



**no benefit if not on steroids



1. Salama C, Han J, Yau L, et al. N Engl J Med 2021;384(1):20–30.
2. Gordon AC, Mouncey PR, Al-beidh F, et al. N Engl J Med 2021;1–12.
3. Rosas IO, Bräu N, Waters M, et al. N Engl J Med 2020;1–14.
4. Horby PW, Campbell M, Staplin N, et al. medRxiv 2021;. DOI: 10.1101/2021.02.11.21249258

*slide added since 9-Feb

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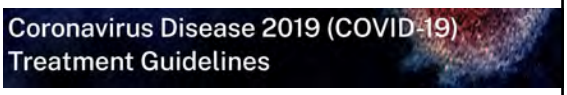
Summary of therapeutics



Monoclonals:

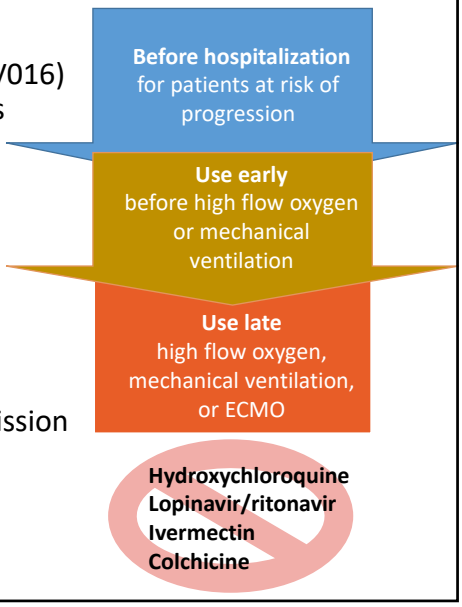
- Bamlanivimab (LY-CoV555) plus etesevimab (LY-CoV016) and the combination Casirivimab (REGN10933) plus imdevimab (REGN10987)

Antivirals:

- Remdesivir (Veklury) approved Oct 2020

Anti-inflammatory:

- Dexamethasone - 6mg daily, up to 10 days
- Baracitinib - only if corticosteroids contraindicated
- ±Tocilizumab - not responding to steroids, ICU admission



*slide updated since 9-Feb
https://www.covid19treatmentguidelines.nih.gov/

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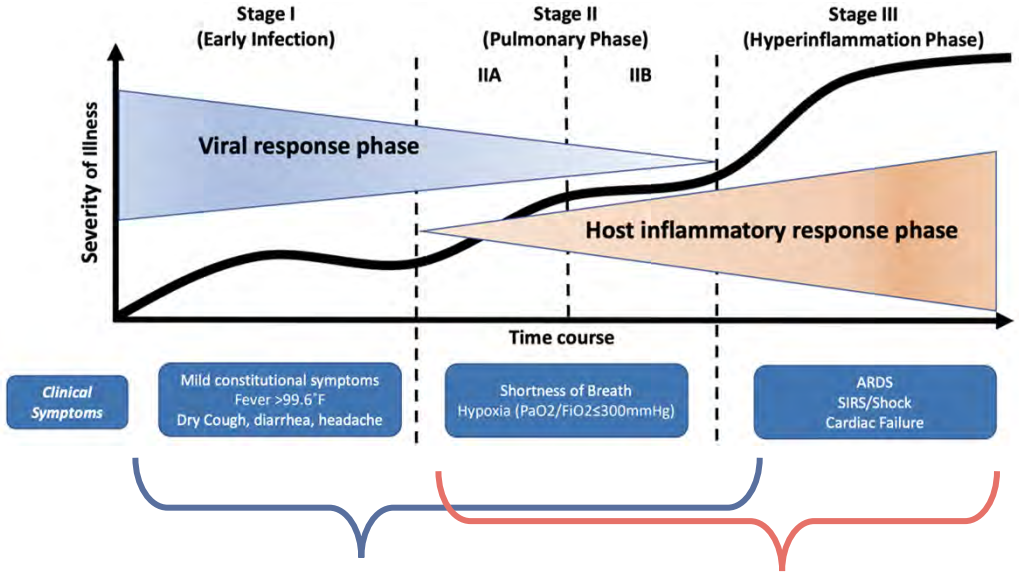

Monclonals, then Remdesivir if hospitalized
~days 1-10, active viral replication

Dexamethasone, then Tocilizumab if worsening
~days 8-14 (or longer), immune dysfunction

Siddiqi JHLT 2020 doi:10.1016/j.healun.2020.03.012

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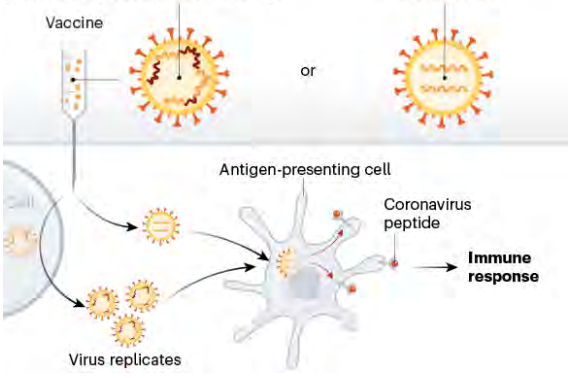
Vaccine strategies – whole virus

Weakened virus
A virus is conventionally weakened for a vaccine by being passed through animal or human cells until it picks up mutations that make it less able to cause disease. Codagenix in Farmingdale, New York, is working with the Serum Institute of India, a vaccine manufacturer in Pune, to weaken SARS-CoV-2 by altering its genetic code so that viral proteins are produced less efficiently.

Inactivated virus
In these vaccines, the virus is rendered uninfectious using chemicals, such as formaldehyde, or heat. Making them, however, requires starting with large quantities of infectious virus.



Callaway E. The Race for Coronavirus Vaccines. Nature 2020;580:576–7.

Attenuated virus

Examples: MMR (measles, mumps, rubella), intranasal flu, oral polio, chickenpox

Advantages: all antigens of the virus included at all stages of the virus life cycle

Disadvantages: Attenuated/weakened virus = long production time (years) to develop the virus and make sure it's safe.

Inactivated virus:

Examples: Hepatitis A, rabies

Advantages: all antigens of the virus included, no replication associated risk

Disadvantages: need large quantities of virus, inactivation may alter structure of some key proteins

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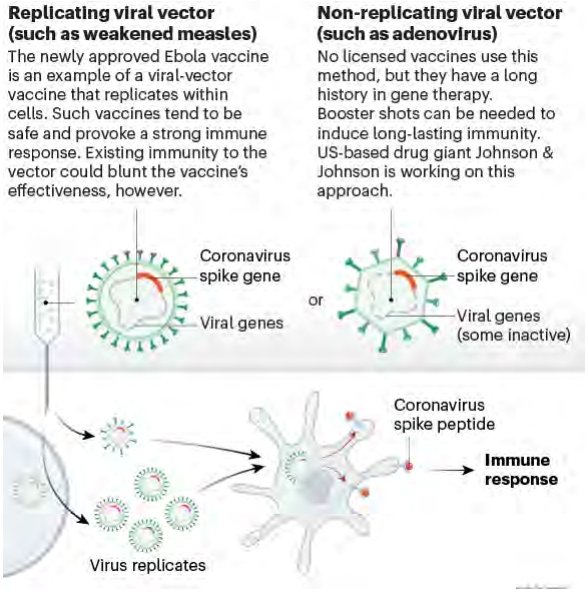
Vaccine strategies – vectored vaccines



Callaway E. The Race for Coronavirus Vaccines. Nature 2020;580:576–7.

Vectored Vaccines (adenovirus)

Examples: none yet for adenovirus; Ebola for measles vectored (MVA)

Advantages: rapid production, include key proteins

Disadvantages: pre-existing population immunity can reduce efficacy

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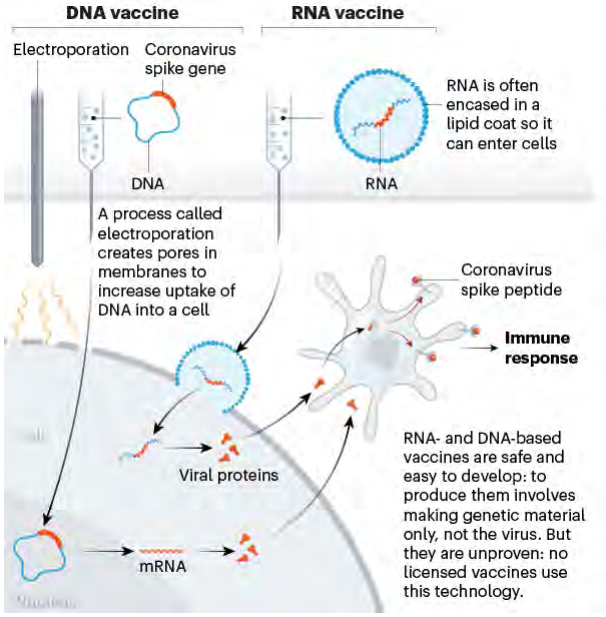
Vaccine strategies – nucleic acid vaccines



RNA and DNA vaccines

Examples: none before SARS-CoV-2

Advantages: very rapid production

Disadvantages: require delivery systems to get into cells (electroporation for DNA, lipid nanoparticles for mRNA). No prior approved vaccines, so scaling was a concern.

Callaway E. The Race for Coronavirus Vaccines. Nature 2020;580:576–7.

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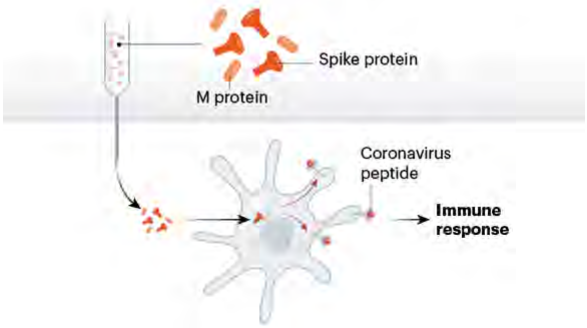
Vaccine strategies – protein vaccines

Protein subunits

Twenty-eight teams are working on vaccines with viral protein subunits — most are focusing on the virus's spike protein or a key part of it called the receptor binding domain. Similar vaccines against the SARS virus protected monkeys against infection but haven't been tested in people. To work, these vaccines might require adjuvants — immune-stimulating molecules delivered alongside the vaccine — as well as multiple doses.



Recombinant protein

Examples: Hepatitis B, shingles

Advantages: well-studied

Disadvantages: need large production of the protein; needs an adjuvant to stimulate the immune response

Callaway E. The Race for Coronavirus Vaccines. Nature 2020;580:576–7.

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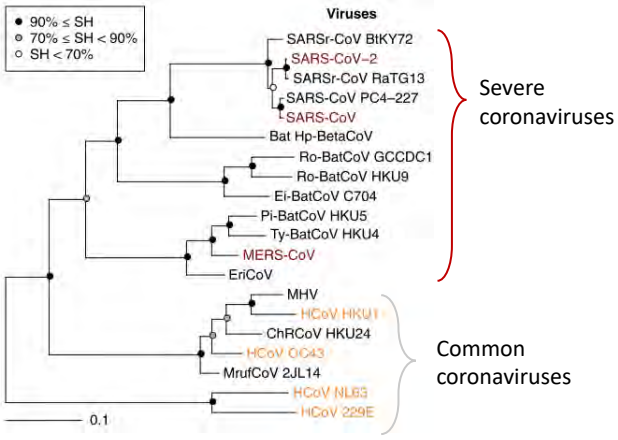
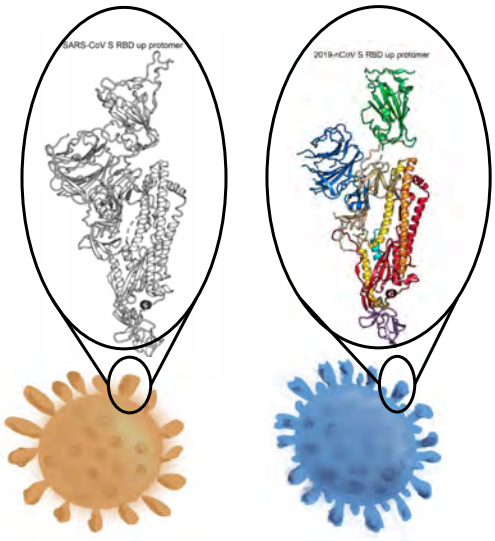
Spike glycoprotein



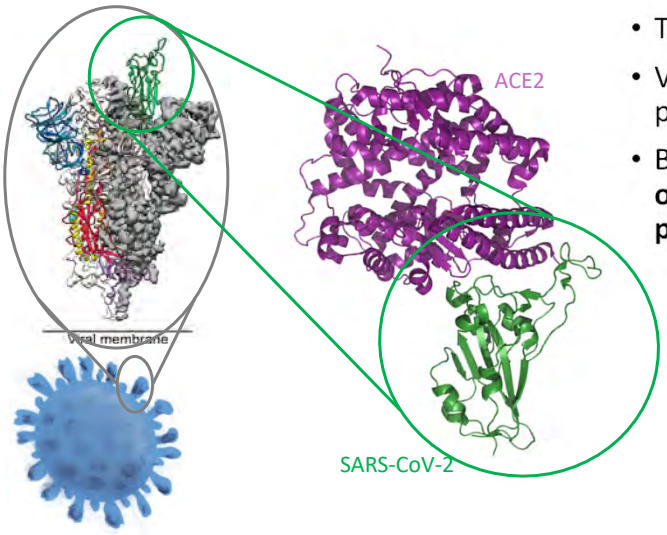


Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nat Microbiol 2020;5(March).

Wrapp D, Wang N, Corbett K, et al. Cryo-EM Structure of the 2019-nCoV Spike in the Prefusion Conformation. Science (80-) 2020;1–9.

40

Spike glycoprotein

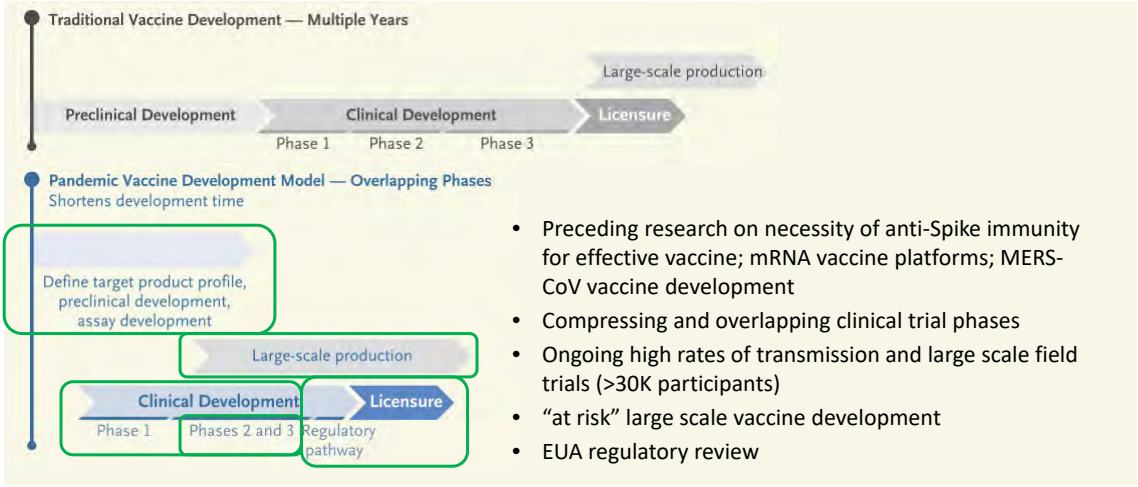


- Target of neutralizing antibodies
- Vaccines against spike protect non-human primates from SARS-CoV-2 challenge
- Based on SARS-CoV, immune responses to **other proteins (nucleocapsid) are not protective** and may enhance disease

Wrapp D, Wang N, Corbett K, et al. Cryo-EM Structure of the 2019-nCoV Spike in the Prefusion Conformation. Science (80-) 2020;1–9.

41

Accelerated vaccine development strategy



- Preceding research on necessity of anti-Spike immunity for effective vaccine; mRNA vaccine platforms; MERS-CoV vaccine development
- Compressing and overlapping clinical trial phases
- Ongoing high rates of transmission and large scale field trials (>30K participants)
- "at risk" large scale vaccine development
- EUA regulatory review

Deming ME, Nelson ML, Robb M, Cohen MS, Neuzil KM. Accelerating Development of SARS-CoV-2 Vaccines — The Role for Controlled Human Infection Models. N Engl J Med 2020;63(1):1969–73.

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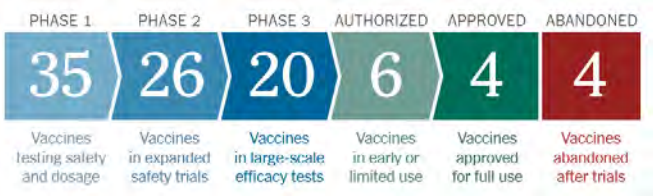
Accelerated vaccine development strategy



Vaccine strategies	Timeline	Caveats	Farthest development
RNA or DNA	Weeks	Need delivery systems (e.g. lipid nanoparticles), scaling	2 EUA Approved (Pfizer, Moderna)
Vectored	Weeks	Pre-existing immunity (AdV)?	EUA submitted (Janssen)
Protein	Months-year	Adjuvant dependent	Phase 3 trials with interim results
Killed	Months-year	Possible immunopathogenesis?	2 Approved in Russia, China
Attenuated	Year(s)	Lots of safety testing required	Phase 1

https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html; accessed 2/7/21

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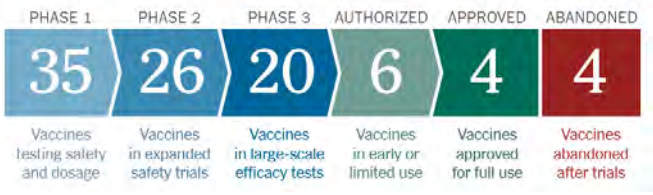
Accelerated vaccine development strategy



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https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html; accessed 2/7/21

*slide updated since 9-Feb

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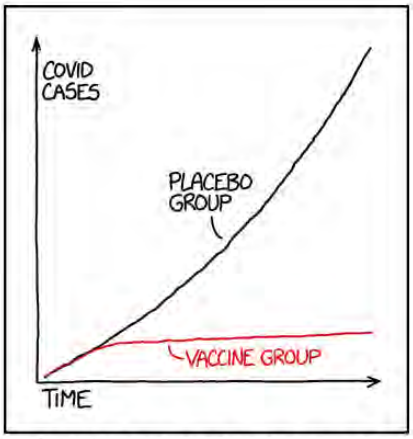
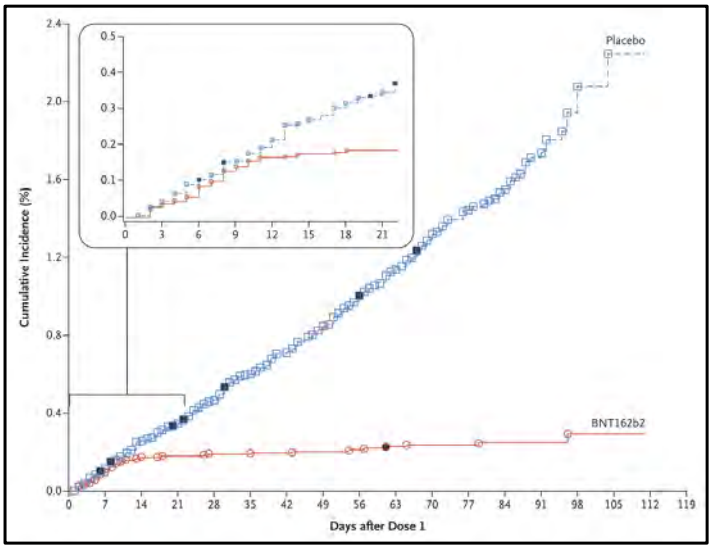
Vaccines



Pfizer (BNT162b2) efficacy: **95.0%** (7d from dose #2)

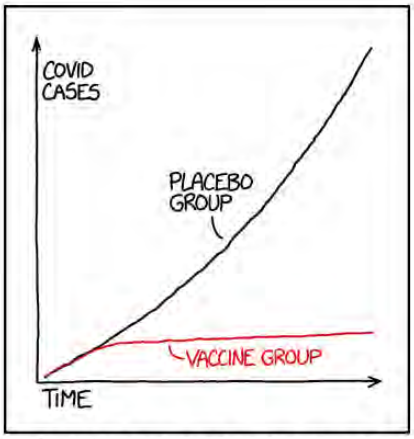


https://xkcd.com/2400/

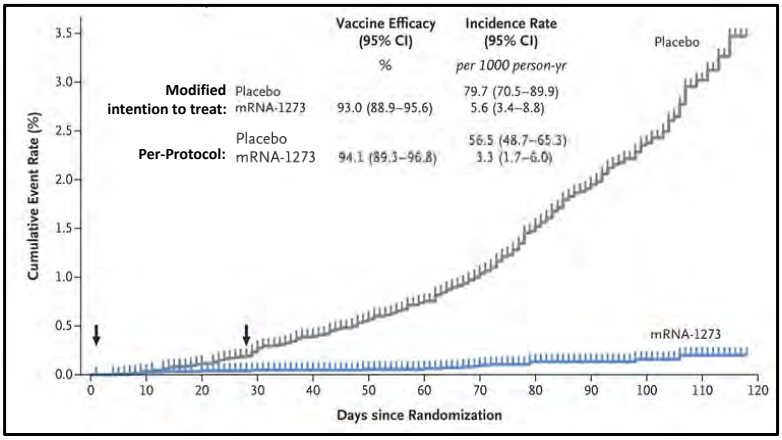
Polack FP, Thomas SJ, Kitchin N, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med

45

Vaccines



Moderna (mRNA-1273) efficacy: **94.1%** (14d from dose #2)



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Baden LR, El Sahly HM, Essink B, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med 2020;384(5):403–16. 3. J

46

Vaccines: efficacy

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AstraZeneca	ChAdOx1-nCoV-19	62.1% (standard dose)[5] now less than 25% in S.Africa?	100% (10 hospitalized/1 death in control, 0 in vaccine)

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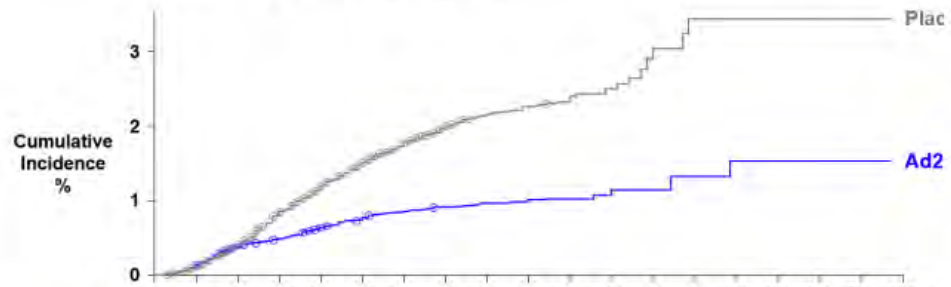
47

Figure 12: Cumulative Incidence of Molecularly Confirmed Moderate to Severe/Critical COVID-19 Cases with Onset at Least 1 Day after Vaccination up to Day 126, Full Analysis Set (Study COV3001)



Note: Severe cases are marked as blue or grey circles on the graphs.

Vaccines and Related Biological Products Advisory Committee. COVID-19 Vaccine Ad26.COV2.S. 2021;Available 2/24/2021. https://www.fda.gov/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-february-26-2021-meeting-announcement#event-materials

48

Vaccines: efficacy

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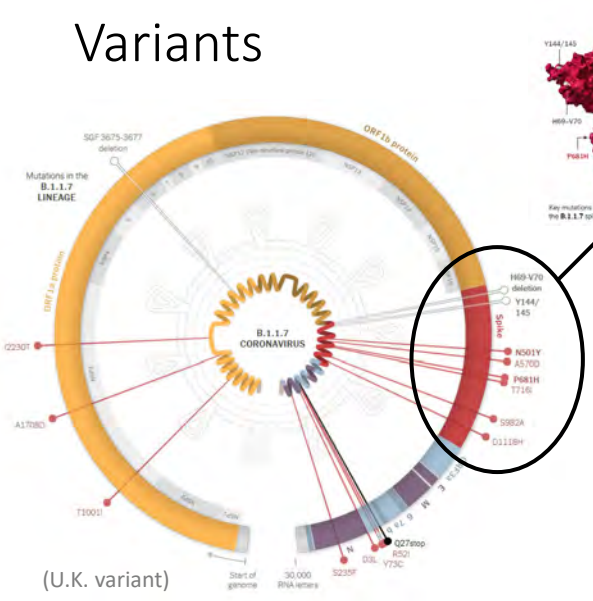
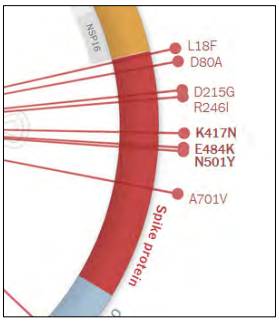
49

Variants

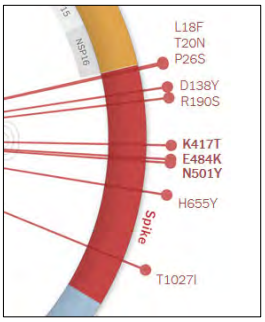


https://www.nytimes.com/interactive/2021/health/coronavirus-variant-tracker.html

- RNA viruses accumulate substitutions
- Some of these substitutions happen to improve viral fitness (and may emerge multiple times, independently)
- If these changes sufficiently alter the structure of the spike, the immune system may not be able to 'recognize' the new variants



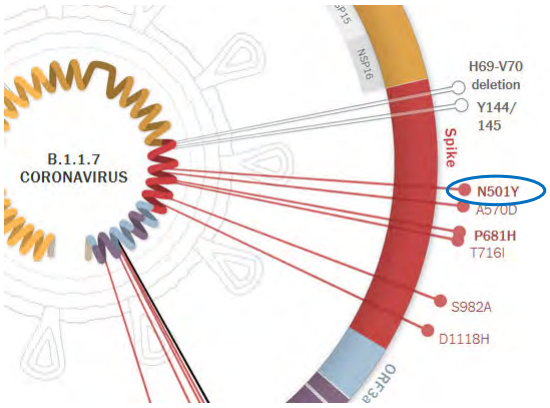
B.1.351, S.Africa variant

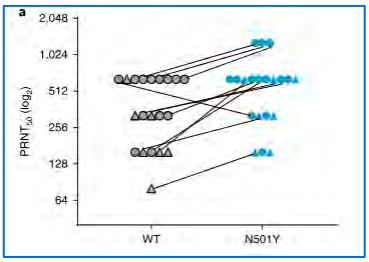


P1, Brazil variant

50

Variants



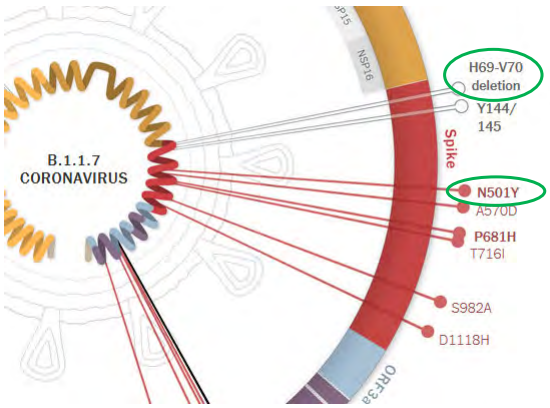


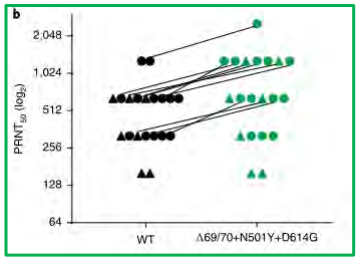
N501Y
- U.K. and most S.Africa and Brazil
- Increases binding to ACE2
- Same or better neutralization

Xie X, Liu Y, Liu J, et al. Neutralization of SARS-CoV-2 spike 69/70 deletion, E484K, and N501Y variants by BNT162b2 vaccine-elicited sera. Nat Med 2021;https://doi.org/10.1038/s41591-021-01270-4.

51

Variants





N501Y
- U.K. and most S.Africa and Brazil
- Increases binding to ACE2
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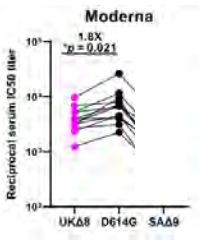
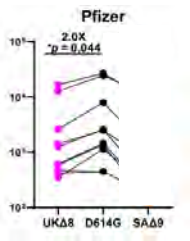
Deletion69/70
- U.K.
- Slight shape change to Spike
- Same or better neutralization





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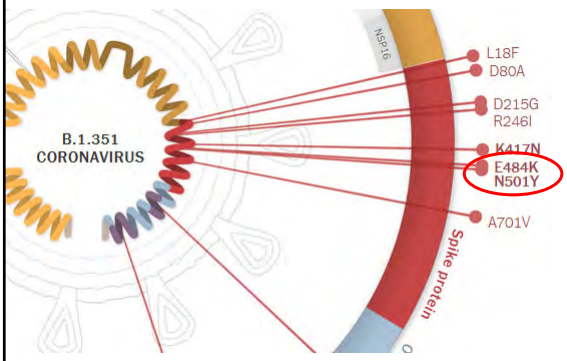
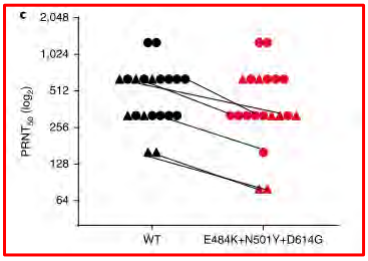
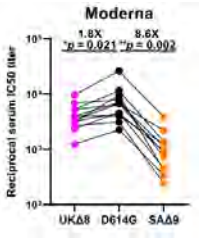
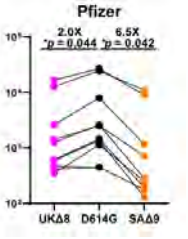
Variants









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- U.K. and most S.Africa and Brazil
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- Same or better neutralization

E484K
- S.Africa and Brazil, now a few in U.K.
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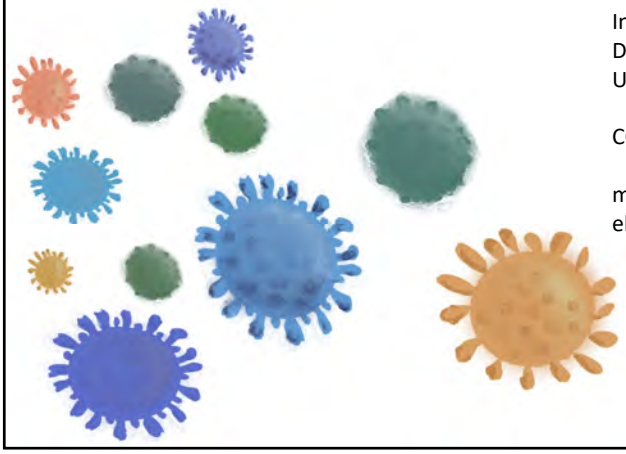
Thank You



Eleanor Wilson, MD, MPH

Institute of Human Virology & Center for Vaccine Development and Global Health,
University of Maryland School of Medicine

COVID-19 Researchers

mdeming@ihv.umaryland.edu
eleanor.wilson@ihv.umaryland.edu

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Coronavirus Disease 2019 (COVID-19) Epidemiology Update - Maryland

Maryland Department of Health

Infectious Disease Epidemiology and Outbreak Response Bureau

February 27, 2021

1

Objectives

- Summarize COVID-19 in Maryland and in the world
- Identify State COVID treatment resources
- Identify State COVID vaccination resources
- List 3 websites with important resources

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COVID-19 - The Pandemic

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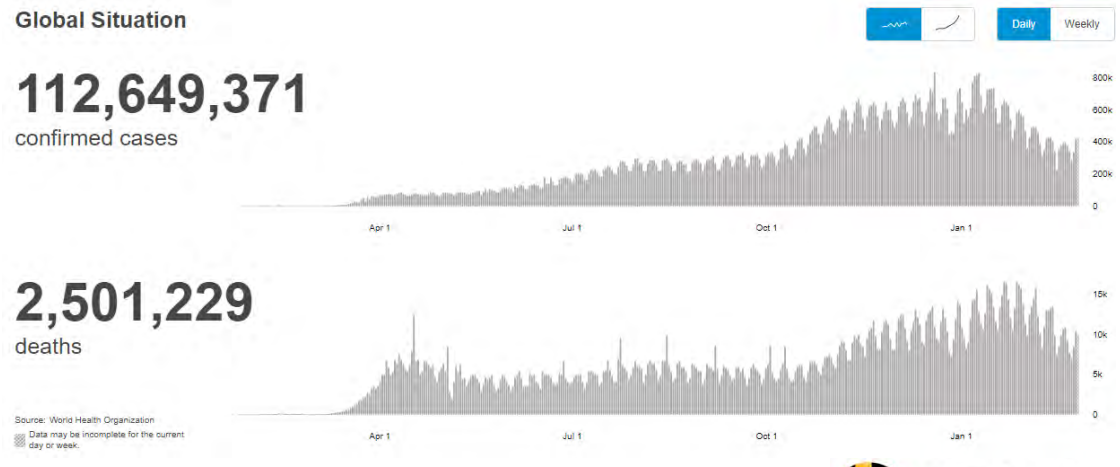
3

Worldwide: COVID-19



Source: https://covid19.who.int/ , accessed February 26th, 2021

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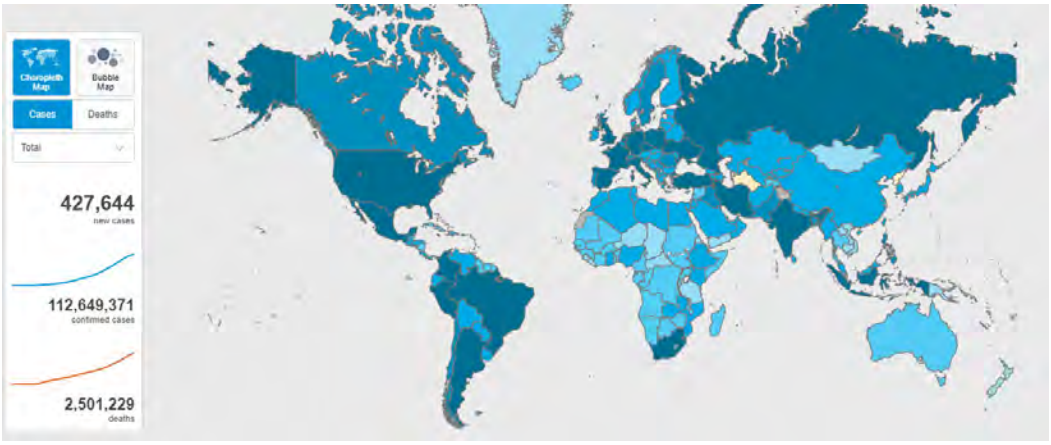
Worldwide: COVID-19



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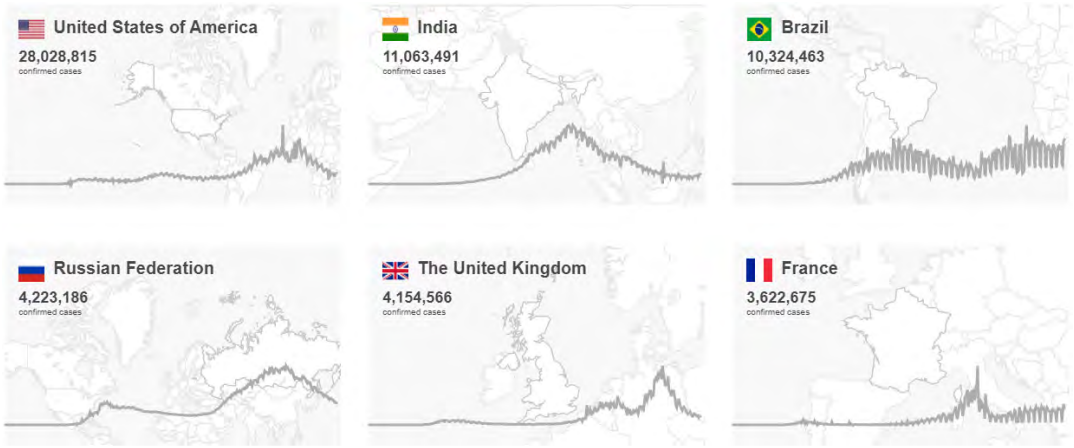
Worldwide: COVID-19



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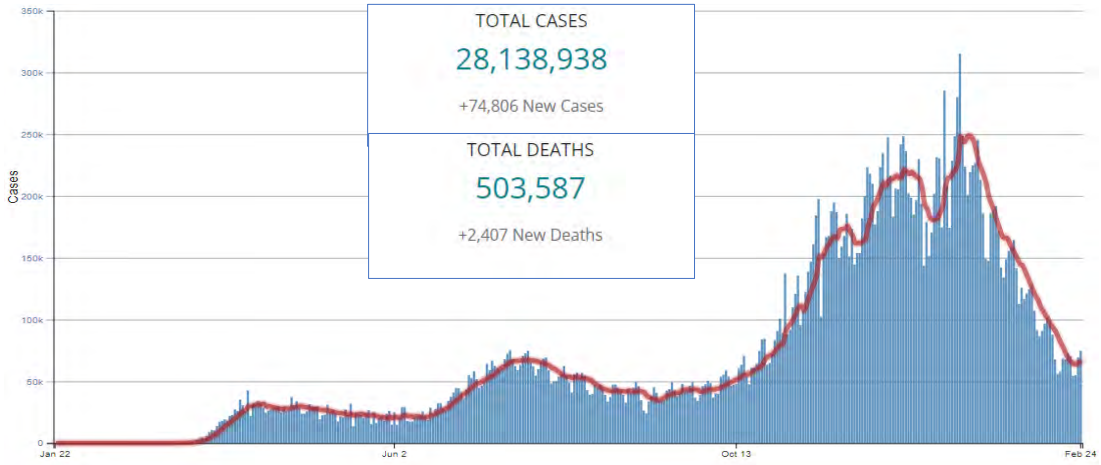
Daily US Trends in COVID-19 Cases



Source: CDC, https://www.cdc.gov/covid-data-tracker/index.html#trends, accessed February 26th, 2021

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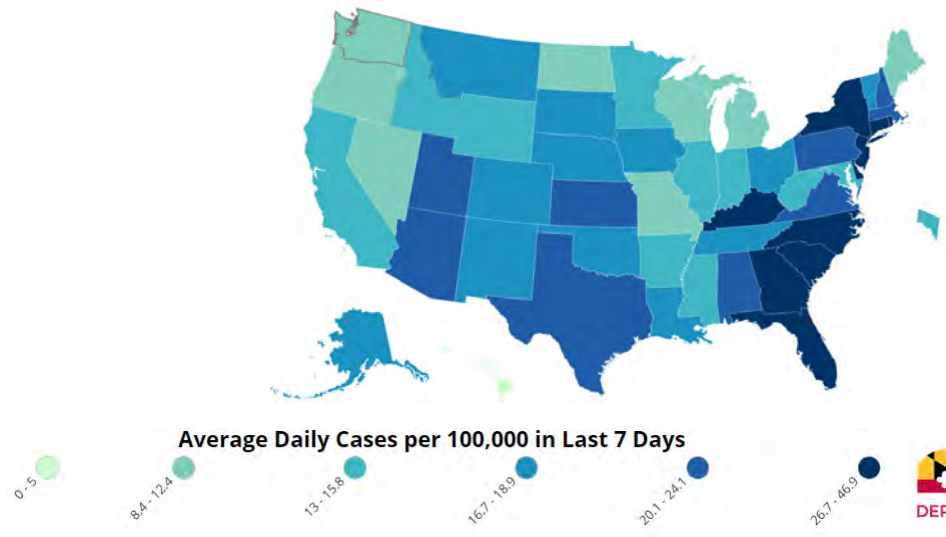
US: COVID-19

Source: CDC, https://covid.cdc.gov/covid-data-tracker/#cases_casesper100klast7days accessed February 26, 2021



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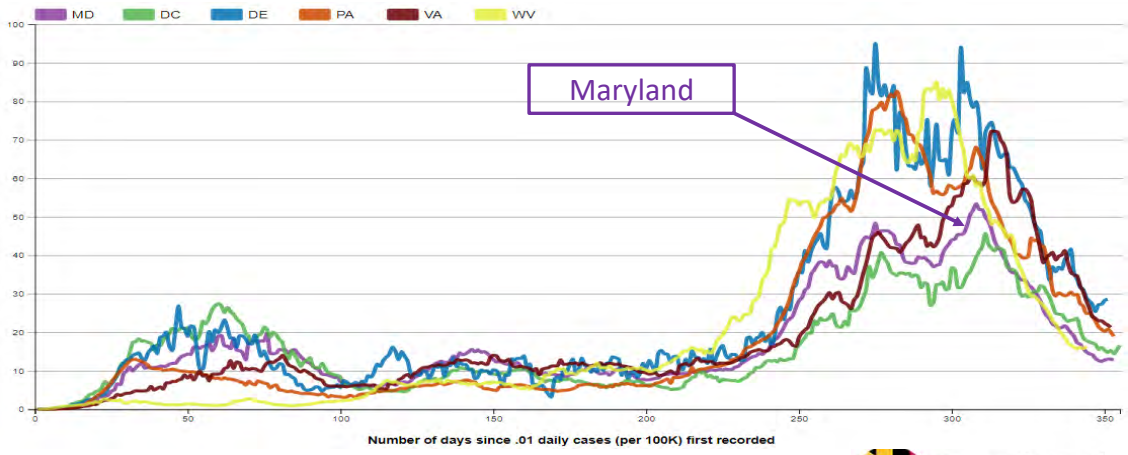
US: COVID-19

Source: CDC, https://covid.cdc.gov/covid-data-tracker/#compare-trends_newcasesper100k accessed February 26, 2021



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COVID-19 - Maryland

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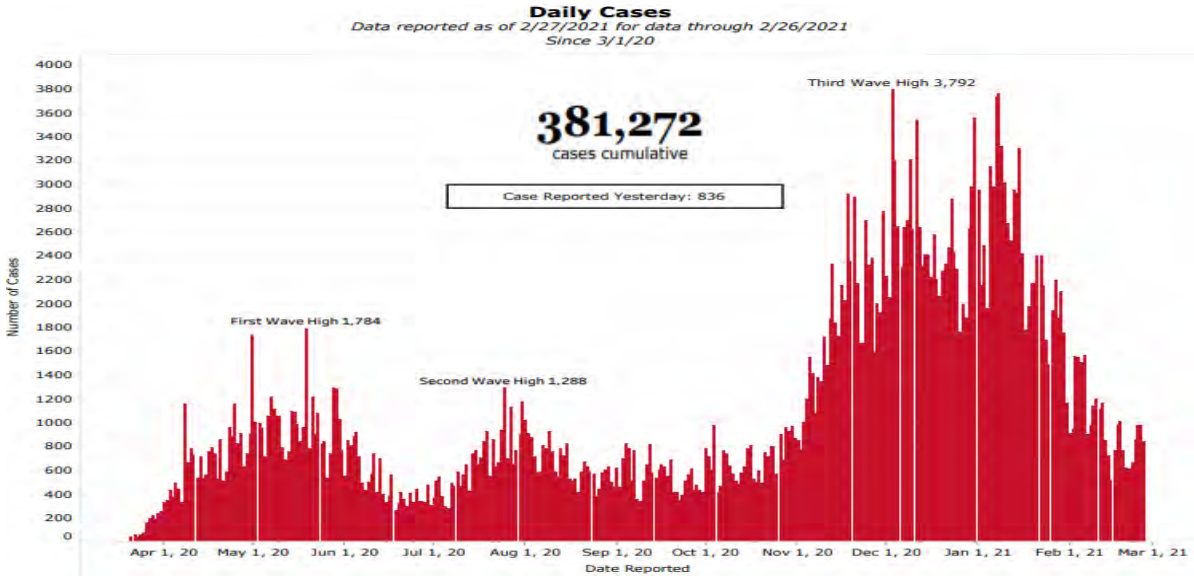
10

Maryland: COVID-19 Cases



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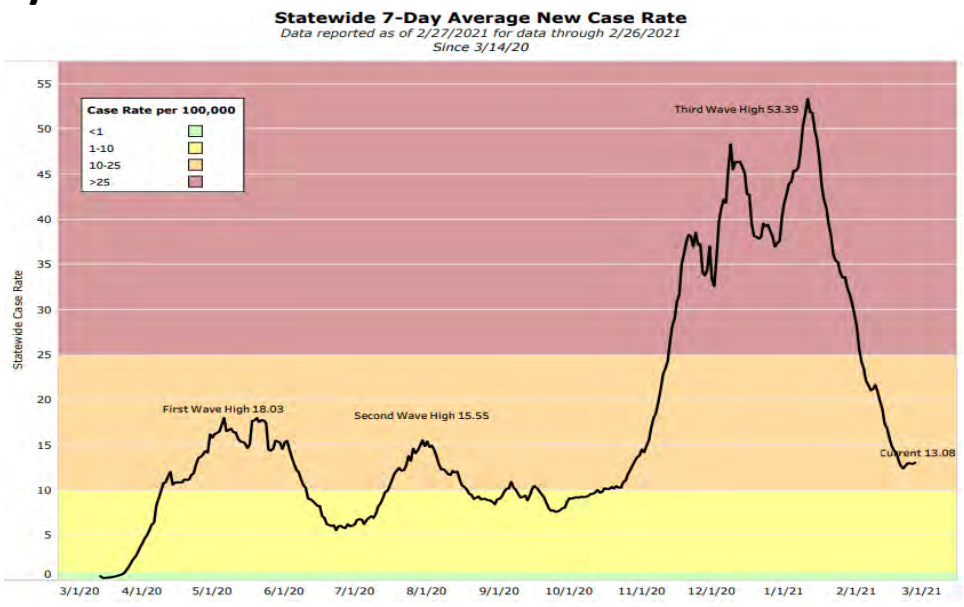
Maryland: COVID-19 Cases



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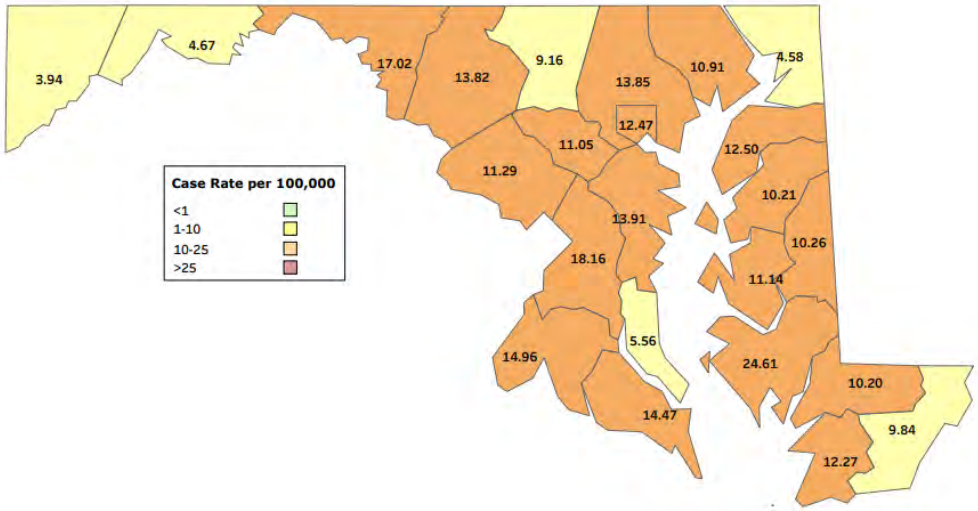
Maryland: COVID-19 Cases



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Maryland: COVID-19 Cumulative Cases: 381,272

Gender	Cum. Cases	% of Cum. Cases
F	199,491	52%
M	181,781	48%

Age Group	Cum. Cases	% of Cum. Cases
<18	42,358	11%
18-64	286,141	75%
65+	52,773	14%

Region	Cum. Cases	% of Cum. Cases
NCR	162,112	43%
BMA	162,436	43%
Southern	8,747	2%
Eastern Shore	27,359	7%
Western	20,618	5%

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Maryland: COVID-19: Age Distribution

10-Year Age Breakdowns (New and Cumulative):

Age Groups	New Cases	% of New Cases	Cum. Cases	% of Cum. Cases
0-9	60	7%	18,969	5%
10-19	114	14%	36,540	10%
20-29	173	21%	69,262	18%
30-39	138	17%	65,501	17%
40-49	99	12%	57,814	15%
50-59	116	14%	57,501	15%
60-69	84	10%	38,945	10%
70-79	32	4%	22,112	6%
80+	20	2%	14,628	4%

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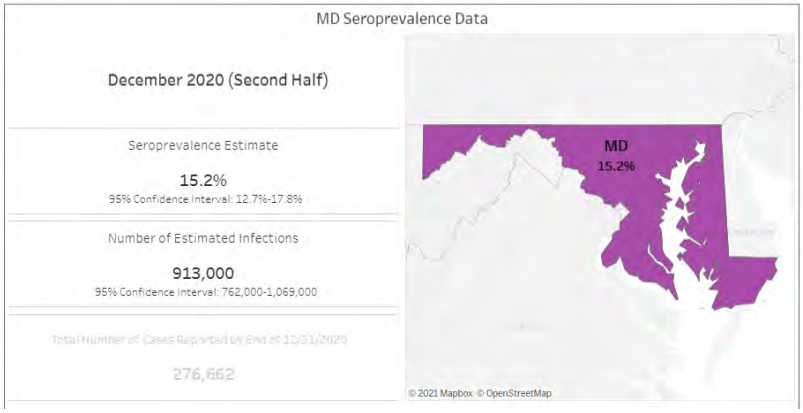
Maryland: COVID-19 Seroprevalence



https://covid.cdc.gov/covid-data-tracker/#national-lab, Accessed 2/23/21

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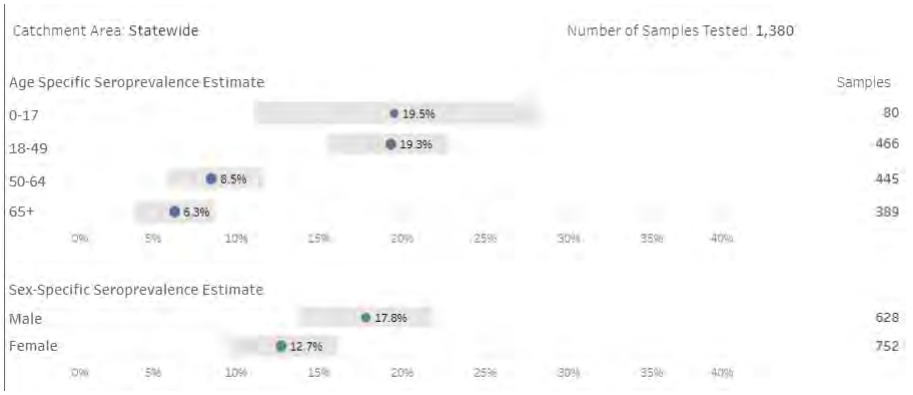
Maryland: COVID-19 Seroprevalence



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COVID-19 – Maryland - Severity

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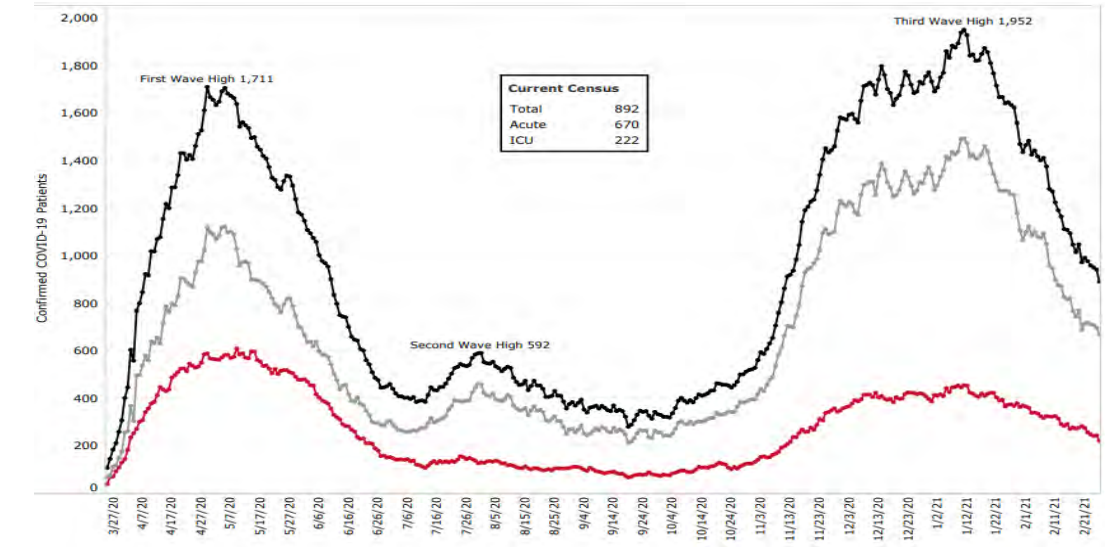
18

Maryland: COVID-19 Hospitalizations



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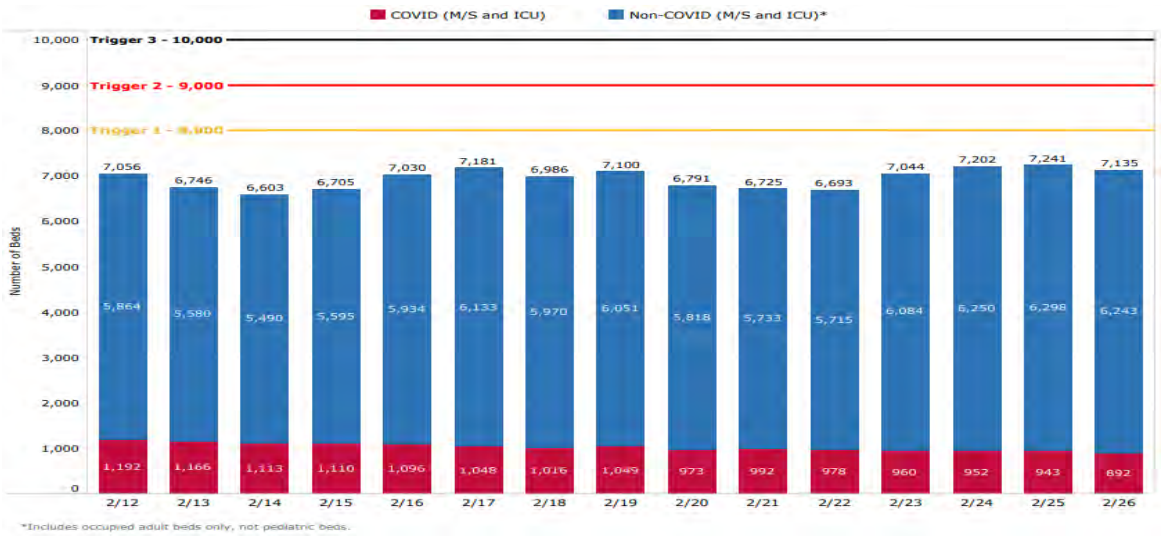
Maryland: COVID-19 Hospitalizations



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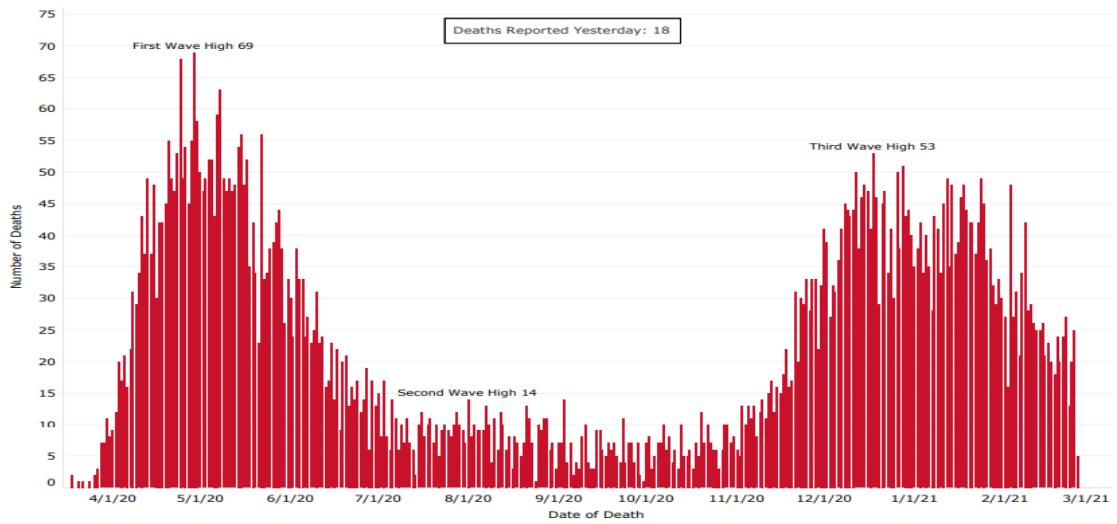
Maryland: COVID-19 Deaths: 7,674



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Maryland: COVID-19 Deaths

Age Group	Number	% of Total	Cases
0-9 yrs	3	0%	5%
10-19 yrs	6	0%	10%
20-29 yrs	34	0%	18%
30-39 yrs	74	1%	17%
40-49 yrs	206	3%	15%
50-59 yrs	577	8%	15%
60-69 yrs	1,217	16%	10%
70-79 yrs	1,958	26%	6%
80+ yrs	3,597	47%	4%

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Maryland: COVID-19 Deaths

Race/Ethnicity	Deaths (n)	% of All Deaths
White	3,933	52
African-American	2,643	36
Hispanic	704	9
Asian	265	3
Other	75	1
Unknown	54	1

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Variant COVID Strains

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Variant COVID Strains

- Viruses change constantly through mutation
- New variants emerge over time
- Variants can be a concern if the if the new strain:
  - Transmits more efficiently
  - Causes more severe illness
  - Demonstrates resistance to treatments (like monoclonal antibody treatment)
  - Evades protection provided by vaccination
  - Is not detected by current tests

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Current Variant COVID Strains of Concern

- B.1.1.7 (aka “the UK variant”)
- B.1.135 (aka “the South African variant”)
- P.1 (aka “the Brazilian variant”)

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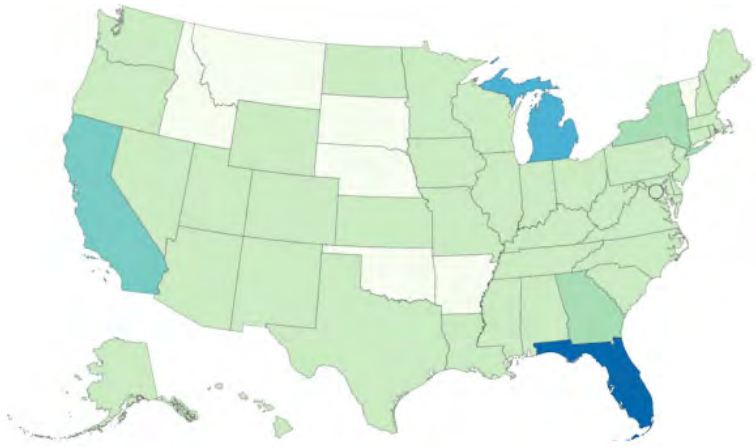
B.1.1.7 ("UK Variant")



- Total US B.1.1.1.7 cases = 2,102
- 45 states reporting at least 1 case
- States with highest counts: FL (504), MI (336), CA (204)
- Maryland: 68 cases

Source: CDC, https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant-cases.html, accessed February 26, 2021

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B.1.351 ("South African Variant")

- Total B.1.351 cases = 49
- 15 states reporting at least 1 case
- South Carolina: 21
- North Carolina: 3
- Virginia: 3
- Maryland: 9 cases

Source: CDC, https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant-cases.html, accessed February 26, 2021

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P.1 ("Brazilian Variant")

- Total P.1 cases = 6
- 5 states reporting at least 1 case
- Minnesota: 2
- Oklahoma: 1
- Florida: 1
- Alaska: 1
- Maryland: 1 case

Source: CDC, https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant-cases.html, accessed February 26, 2021

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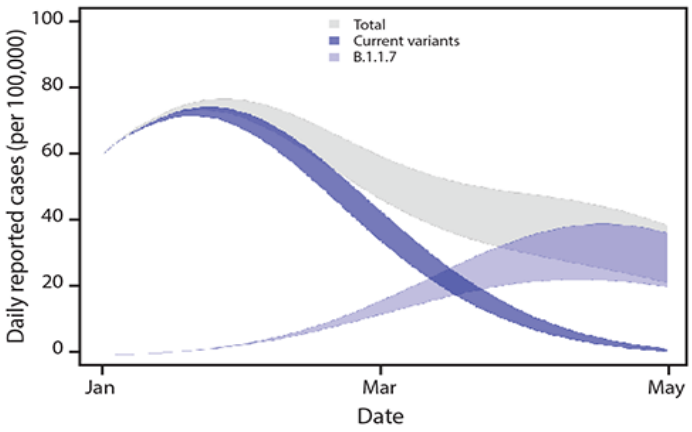
Variant COVID Strains



Source: CDC, https://www.cdc.gov/mmwr/volumes/70/wr/mm7003e2.htm accessed February 11, 2021

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Variant COVID Strains

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State COVID Treatment Resources

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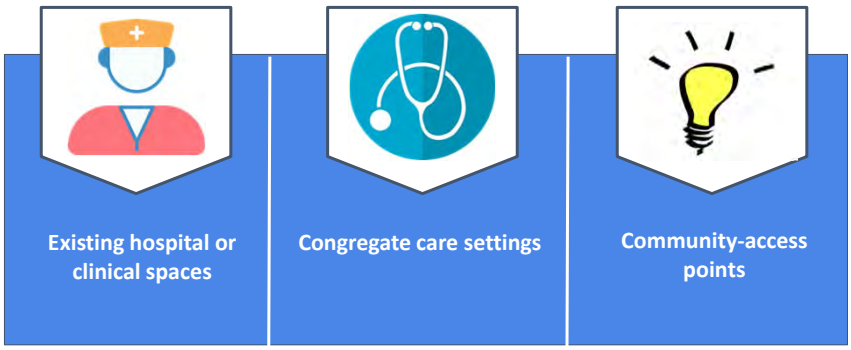
COVID-19 Therapeutics

Three-pronged Approach



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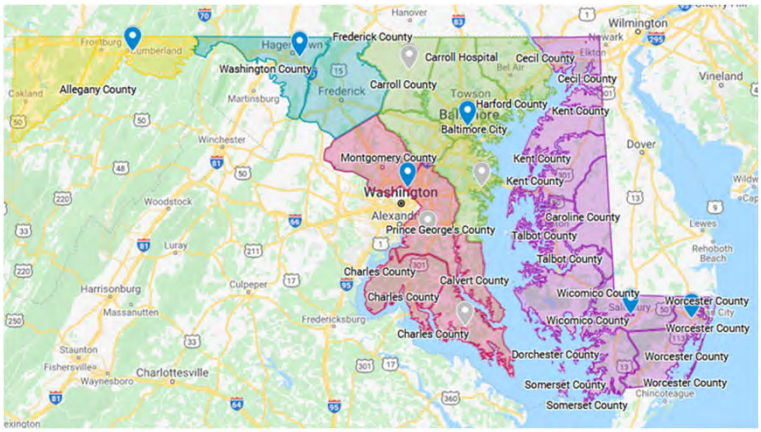
COVID-19 Therapeutics

Regional Hospital-based Infusion Sites



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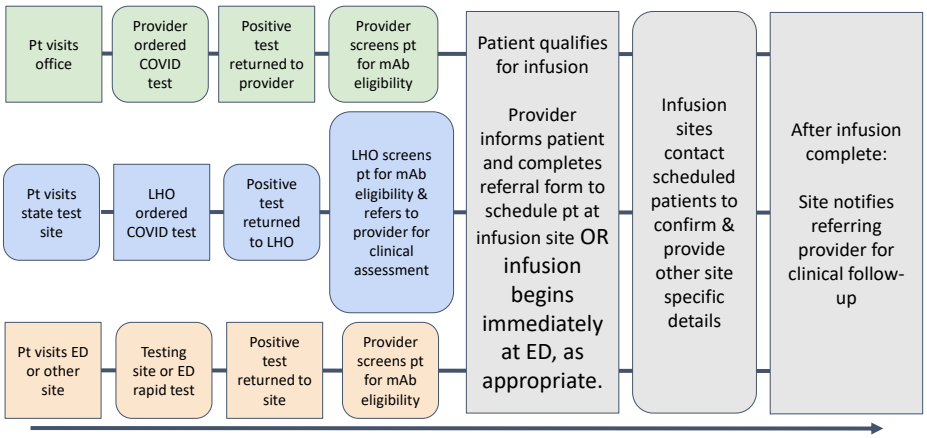
COVID-19 Therapeutics

Referral Pathway for Infusion Centers



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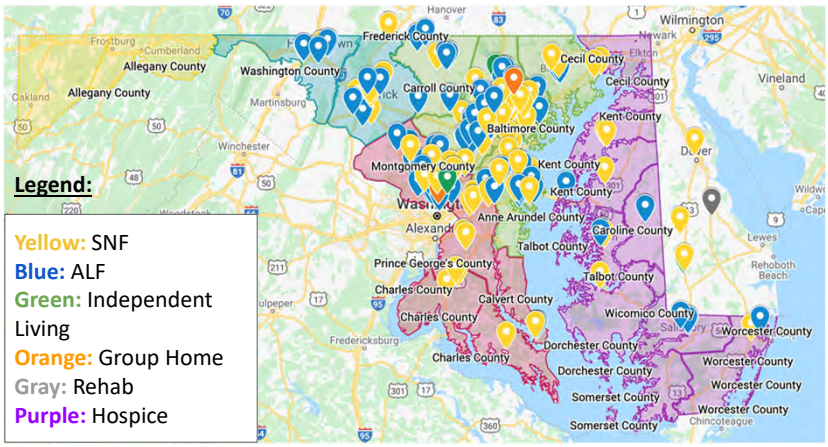
COVID-19 Therapeutics

LTC Facilities Served by Partner Pharmacies



Link

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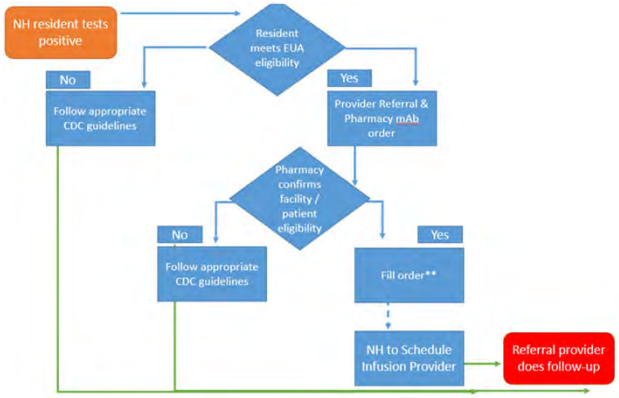
COVID-19 Therapeutics

Nursing Home Referral Pathway

Figure 5. Referral Pathway for nursing home partners to order and receive treatment



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COVID-19 Therapeutics

Process for Prescribing/Ordering

1. Screen resident with positive COVID-19 test for eligibility criteria in EUA (PCR or antigen)
2. Contact prescriber to order using your LTC pharmacy intake/ ordering form
3. Review mAb information with patient and provide appropriate "Fact Sheet for Patients"
4. Pharmacy reviews referral/order and confirms patient eligibility
5. Pharmacy and/or NH coordinate mAb delivery, supplies, and staff capable of administering infusion *Note: NH may use separate infusion provider*
6. mAbs are delivered to NH, administered to patient, and patient is observed for at least 1 hour
7. NH schedules follow-up with PCP
8. Report any adverse events

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COVID-19 Therapeutics

Site Administration Checklist

- ❑ Identify dedicated space and plan to manage patient flow
- ❑ Ensure dedicated source of supplies
- ❑ Assign sufficient personnel to meet expected demand
  - ❑ Identify staff (internal/external) with appropriate competencies for mAb administration
- ❑ Prepare for drug administration process
  - ❑ Pre-visit: Clear treatment and monitoring plan
  - ❑ Treatment
  - ❑ Post-treatment
- ❑ Ensure process for reimbursement in place
- ❑ Prepare for reporting needs

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Source: Operation Warp Speed Therapeutics: Monoclonal Antibody Playbook for outpatient administration (Version 2.0)

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COVID-19 Therapeutics

Staffing Needs

Role	Needed skills/ profile
Patient Intake	Scheduling and administrative skills
Drug preparation	Pharmacist or pharmacy technician trained in IV preparation
Infusion: Start IV	Nurse or other HCP trained to begin an IV
Infusion: Administer infusion	Nurse or other HCP trained in administering an IV
Infusion monitoring	Nurse or other HCP trained in vital sign monitoring
Post infusion observation	Nurse or other HCP trained in vital sign monitoring
Patient release	Administrative skills
Cleaning	Person trained in COVID cleaning / disinfection

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Source: Operation Warp Speed Therapeutics: Monoclonal Antibody Playbook for outpatient administration (Version 2.0)

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COVID-19 Therapeutics

Communication Needs

Education Essential to Inform and Reduce Hesitancy

- For Medical Directors and Attending Providers
- For Facility Administrators
- For Nursing Leads and Directors
- For Staff
- For Resident and their POAs

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COVID-19 Therapeutics

Next Steps

- Build out regional subsidiary sites
- Expand allocation and distribution to nursing homes partners
- Leverage long-term care pharmacy chain partnerships for distribution of mAbs to additional nursing home populations

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State COVID Vaccination Resources

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Planning for Vaccination Response

The Maryland COVID-19 Vaccination Plan:

- The Plan is based on the CDC COVID-19 Vaccination Interim Playbook for Jurisdiction Operations.
- As the supply of available vaccine increases, distribution will expand, increasing access to vaccination services for a larger population.

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Phased Approach

- Phase 1
  - Vaccination of critical populations
  - Limited availability of vaccine
- Phase 2
  - Begins when Phase 1 populations have been given a chance at being vaccinated
  - Focus on those at increased risk of severe illness / complications and essential functions of society
- Phase 3
  - Vaccination of the general public
  - Vaccination efforts continue until every Marylander who wants a vaccine is able to get one

****We do not wait for a phase to finish for the next phase to start****

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Plan Components

Key Components of the Plan:

- Provider Enrollment
- Vaccine Ordering and Distribution
- Vaccine Administration
- Communication and Outreach

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Provider Enrollment

- Providers interested in administering COVID-19 vaccine must register with the MDH immunization information system, ImmuNet.
- MDH will work through partners to encourage providers to enroll to ensure that there are sufficient vaccination providers to reach all Marylanders

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Vaccine Ordering and Distribution

- Providers may now register in ImmuNet
- Registered providers who are eligible to receive vaccine place their COVID-19 vaccine orders in the ImmuNet system
- Vaccine are shipped directly to the provider from CDC's distributor
- MDH works with providers to track inventory and administration of vaccine and to ensure that if two doses are required, people receive same product each time.

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Vaccine Administration

- The State is working with federal partners, local hospital systems, local health departments, and pharmacies to administer vaccine to Phase 1 priority groups.
- Once vaccine is widely available (Phase 2), Marylanders will be able to receive vaccinations through their health care provider or at a pharmacy (similar to a flu shot).
- Eventually, any Maryland resident that wants to be vaccinated will be able to receive a vaccine.
- Health equity considerations are crucial to ensure access across all populations.

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Communication and Outreach

Communication and Sharing of Information is key to the success of the COVID-19 Vaccination Program. The MDH GOVAX program aims to improve the following issues:

- Some groups may be more hesitant to vaccinate than others.
- Messaging will need to provide facts about the vaccine(s), instill confidence, and encourage vaccination.
- Outreach efforts will need to be culturally competent and take into account the needs of different populations throughout the state.

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Federal / State Vaccination Partnerships

- Pharmacy Partnership for Long-Term Care (LTC) Program
  - LTC Part A (NHs)
  - LTC Part B (ALFs, other LTCF)
  - CVS, Walgreens
- Federal Pharmacy Transfer Program
  - Giant, Walmart, Safeway, Rite-Aid, Martin's
  - Launched Jan 25
- Federal Retail Pharmacy Partnership Program
  - CVS, Walgreens
  - Launched Feb 11

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Vaccine Access-Related Questions:

mdh.covidvax@maryland.gov

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Maryland: COVID Vaccinations

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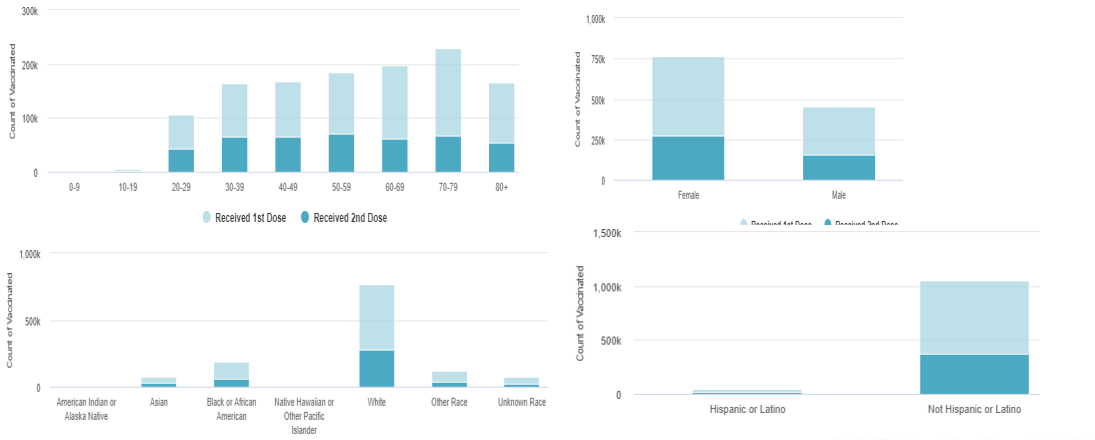
Maryland: COVID Vaccinations



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Web Resources:

https://coronavirus.maryland.gov/

https://www.covid19treatmentguidelines.nih.gov/

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

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Questions?

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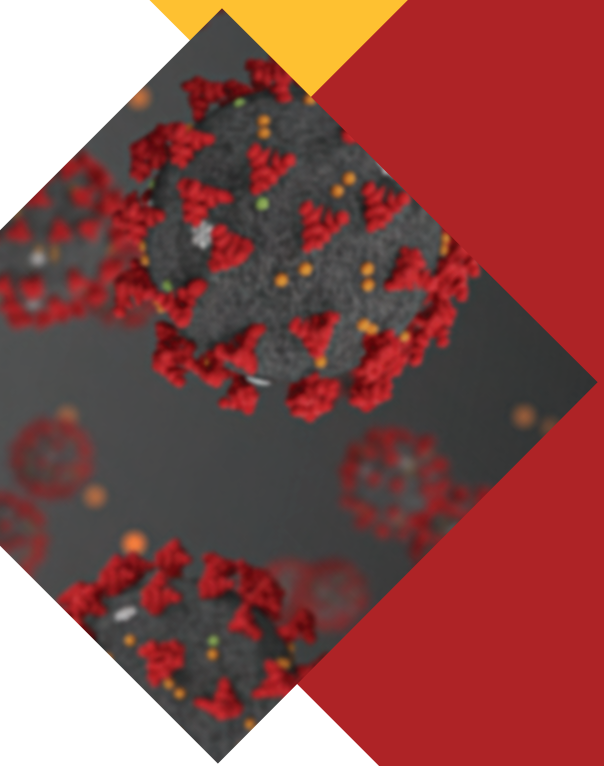
Notes:



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https://mmcp.health.maryland.gov/pap/pages/paphome.aspx