COVID-19: Fundamentals and Looking Ahead

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Outline

- SARS-CoV-2 in Context and State of the Pandemic
- Transmission and the Hierarchy of Controls
- Diagnosis, Disease, and Treatment
- Variants and vaccines
- (Something amazing)
- Looking ahead





CONTEXT





Coronaviruses

- Large, enveloped, RNA viruses; 4 genera (alpha, beta, delta and gamma)
 - Alpha and beta infect humans
 - HCoV 229E, NL63, OC43, and HKU1 are endemic and cause 15-30% of common cold syndromes
- Reservoirs: bats, multiple other animals
- Until 2002 not seen as too important given mild illness, then:
 - Severe Acute Respiratory Syndrome (SARS): 2002 2003
 - Middle East Respiratory Syndrome (MERS): 2012 current
 - SARS-CoV-2/COVID-19: 2019 current





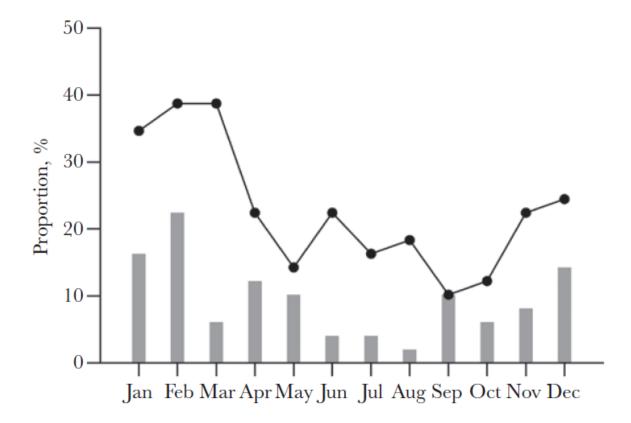
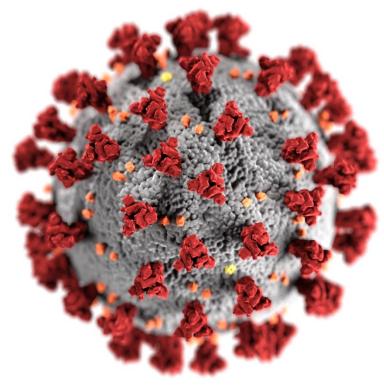


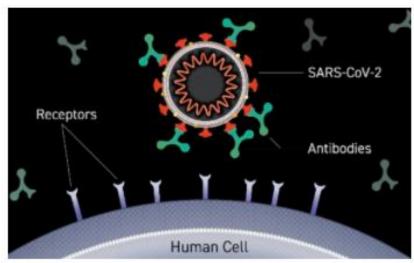
Figure 2. Monthly distribution of human coronavirus (HCoV) infection worldwide. The bar indicates the proportion of the peaks in HCoV infection per observation period. The line indicates the proportion of studies that reported more than 5% of specimens that tested positive for HCoV.

Sangshin P et al, Open Forum Infectious Diseases, Volume 7, Issue 11, November 2020, ofaa443, https://doi.org/10.1093/ofid/ofaa443







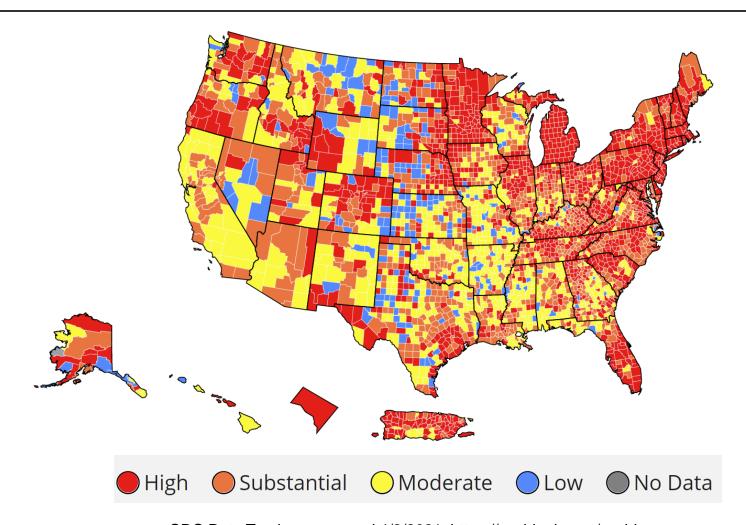


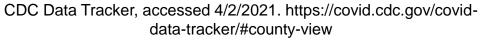
CDC and NIH.





State of the Pandemic











Massachusetts Department of Public Health | COVID-19 Dashboard Trends: 7-day Averages Over Time

Released on: April 3, 2021
Data as of: April 2, 2021
Caution: recent data may be incomplete

Navigation

Today's Overview

Overview Trends

COVID-19 Cases

COVID-19 Testing

Hospitalization

COVID-19 Deaths

Higher Ed & LTCF

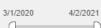
Patient Breakdown

City and Town

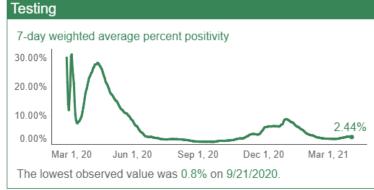
Resources

Data Archive

Date Filter











For details on the definitions of each indicator please see the corresponding tab for that indicator. All data included in this dashboard are preliminary and subject to change. Data Sources: COVID-19 Data provided by the Bureau of Infectious Disease and Laboratory Sciences and the Registry of Vital Records and Statistics; Created by the Massachusetts Department of Public Health, Bureau of Infectious Disease and Laboratory Sciences, Office of Integrated Surveillance and Informatics Services.

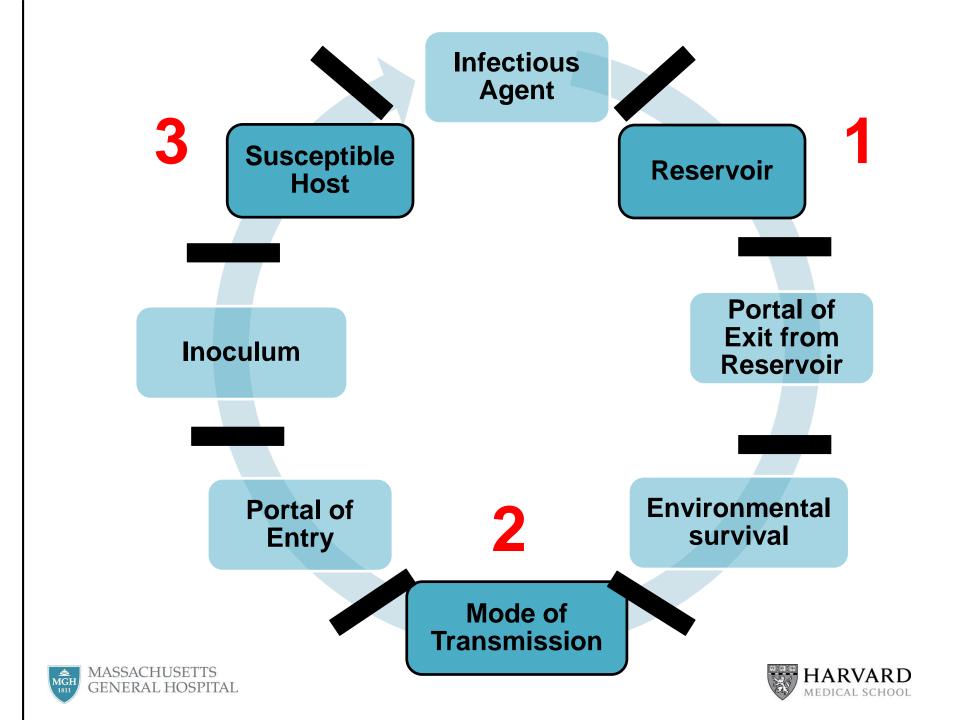




TRANSMISSION AND THE HIERARCHY OF CONTROLS







Factors that influence risk of exposure > infection

- Duration of interaction
- Distance between source and exposed
- Type of activities
- Use of barriers (mask use by source and exposed)
- Stage of infection (time since onset) of the source
- Inoculum
- Source factors: asymptomatic, symptomatic, severity of symptoms





Figure 2. Number of Contacts, Secondary Cases, and Secondary Clinical Attack Rate by the Time of First Exposure

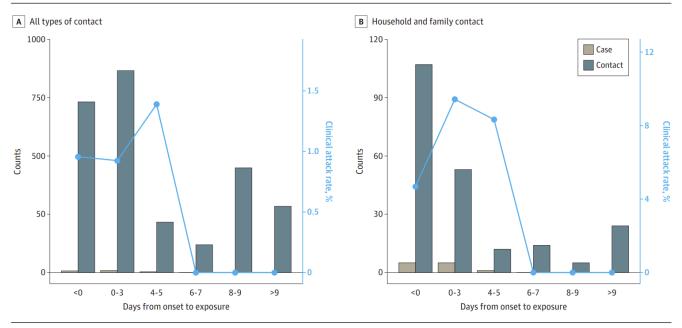


Table 3. Risk for Symptomatic COVID-19 Infection Among the 2761 Close Contacts, Simultaneously Stratified by Exposure Setting and Time From Symptom Onset of the Index Case to First Day of Exposure

	Household		Nonhousehold family		Health care		Othersa	
First day of exposure, d	Case/contact, No.	Attack rate, % (95% CI) ^b	Case/contact No.	,Attack rate, % (95% CI) ^b	Case/contact, No.	Attack rate, % (95% CI) ^b	Case/contact, No.	Attack rate, % (95% CI) ^b
<0	4/100	4.0 (1.6-9.8)	1/10	10.0 (1.8-40.4)	2/236	0.8 (0.2-3.0)	0/389	0 (0-1.0)
0-3	2/39	5.1 (1.4-16.9)	3/15	20.0 (7.0-45.2)	3/150	2.0 (0.7-5.7)	0/663	0 (0-0.6)
4-5	1/6	16.7 (3.0-56.4)	0/6	0 (0-39.0)	1/38	2.6 (0.5-13.5)	1/166	0.6 (0.1-3.3)
6-7	0/4	0 (0-49.0)	0/10	0 (0-27.8)	0/17	0 (0-18.4)	0/88	0 (0-4.2)
8-9	0/2	0 (0-65.7)	0/3	0 (0-56.1)	0/110	0 (0-3.3)	0/334	0 (0-1.1)
>9	0/0	NC	0/24	0 (0-13.8)	0/146	0 (0-2.6)	0/114	0 (0-3.3)

Abbreviations: COVID-19, coronavirus disease 2019; NC, not calculable.

^a Others include friends, airline crew members and passengers, and other casual

contacts.





^b Secondary clinical attack rate.

Transmission of SARS-CoV-2 in Community Settings

Setting	Attack Rate	Reference
Contact tracing	391 cases with 3,410 close contacts → 127 infections 3.7% (overall) • 10.3% (household) 890 asymptomatic contacts with high risk exposures; secondary attack rates: • Boxing stadiums 111/129 (86%) • Nightclubs 34/187 (18.2%)	Luo, Annals of Internal Medicine, 2020. Doung-ngern, Emerg Infect Dis, 2020
Hair salon	2 cases with 138 exposed clients → no secondary cases	Hendrix, MMWR, 2020
Child care centers	 Contact tracing Rhode Island 6/1/2020-7/31/2020 29/666 day cares with total of 52 cases over 2 months 20/29 single case, no secondary transmission 5/29 more than one case, no secondary transmission 4/29 child care centers where secondary transmission could not be ruled out (all with violations of regulations) 	Link-Gellis, MMWR, 2020





In-person school: minimal transmission with mitigation measures in place

Setting	What they found	Reference
Sweden, March 1- June 30, 2020	Follow up of children aged 1-16 years and preschool/school teachers Low incidence of severe COVID-19 among children (15 out of 1.95 million or 1 per 130,000) Among teachers: 10 preschool and 20 schoolteachers with severe COVID-19 (19 per 100,000); compared to other occupations, adjusting for sex and age, no difference for preschool teachers and lower risk for school teachers	Ludvigsson, NEJM, 2021.
Norway, August 28- November 11,2020	Follow up in children age 5-13 in two counties in Norway, during time of high community prevalence. Contact tracing of 13 cases, of which 12 were infected in the household; 2/234 child contacts infected, 1/58 adult contacts; no secondary cases	Brandal, Eurosurveillance, 2020
North Carolina, August 15- October 23, 2020	11 of 56 school districts; 90,000 K-12 students 3Ws: wear a mask, wait 6 feet, wash hands; daily symptom monitoring and temp checks; rest per each district 773 cases of community-acquired; 32 acquired within schools No child to adult transmission	Zimmerman et al, Pediatrics, 2021
Wisconsin, August 31- November 29,2020	17 schools; K-6: 8 schools, 1,529 in person; 7-19: 9 schools, 3,347 in person); 12.4% virtual learners; mask mandate, provided with 2-3 layer cloth masks, distance, hygiene, cohorting Total cases: 133 students, 58 staff; 7 (3.7%) attributed to within school transmission; no transmission between cohorts, 3 of 7 within a single class; incidence was 37% LESS than in the community at the time	Falk, MMWR, 2021





Risk of infection in hospital settings: nosocomial exposures to infected patient

Study	HCW exposed	HCW infections attributed to exposure	%
Ng, <i>Annal</i> s 2020	41	0	0.0%
Burke, <i>MMWR</i> 2020	222	0	0.0%
Heinzerling MMWR 2020	121	3	2.5%
Ghinai , <i>Lancet</i> 2020	75	0	0.0%
Cheng, JAMA IM 2020	698	6	0.9%
Baker, <i>ICHE</i> 2020	43	2	4.7%
Bayes, <i>ICHE</i> 2020	292	7	2.4%
Klompas, <i>Annals</i> 2021	385	11	2.9%
	1877	29	1.1%

And with the advent of universal pandemic precautions (surgical mask and eye protection) exposures should be infrequent/rare.





Serological studies support risk is not related to healthcare occupation

- Belgium; > 3000 HCP
 - Having a household contact with suspected COVID-19 was associated with seropositivity
- Emory Health (Atlanta); > 10,000 HCP
 - Community contact with a person known or suspected to have COVID-19, community COVID-19 incidence, Black race
- 4 health centers in the US; > 24,000 HCP
 - Community COVID-19 contact and community COVID-19 cumulative incidence were associated with seropositivity

Steensels et al., JAMA. 2020 Jul 14;324(2):195-197. doi: 10.1001/jama.2020.11160; Baker JM, et al. Ann Intern Med. 2021 Jan 29. doi: 10.7326/M20-7145; Jacob JT, et al. JAMA Netw Open. 2021 Mar 1;4(3):e211283. doi: 10.1001/jamanetworkopen.2021.1283





Summary of what we know about transmission

- Mainly transmitted through close, sustained contact with infected individuals (closest contacts with highest attack rates are household contacts; spouses> others)
 - Asymptomatic infection occurs
 - Pre-symptomatic infection occurs
 - Attack rate higher when exposed to someone early in their illness
- Non-pharmaceutical interventions (masking, distance, hygiene) are effective: seen in many studies
- Outbreaks and superspreading events associated with lack of masking, close, prolonged contact, enclosed spaces (weddings, parties, restaurants, eating)





Table. Studies of the Effect of Mask Wearing on SARS-CoV-2 Infection Risk^a

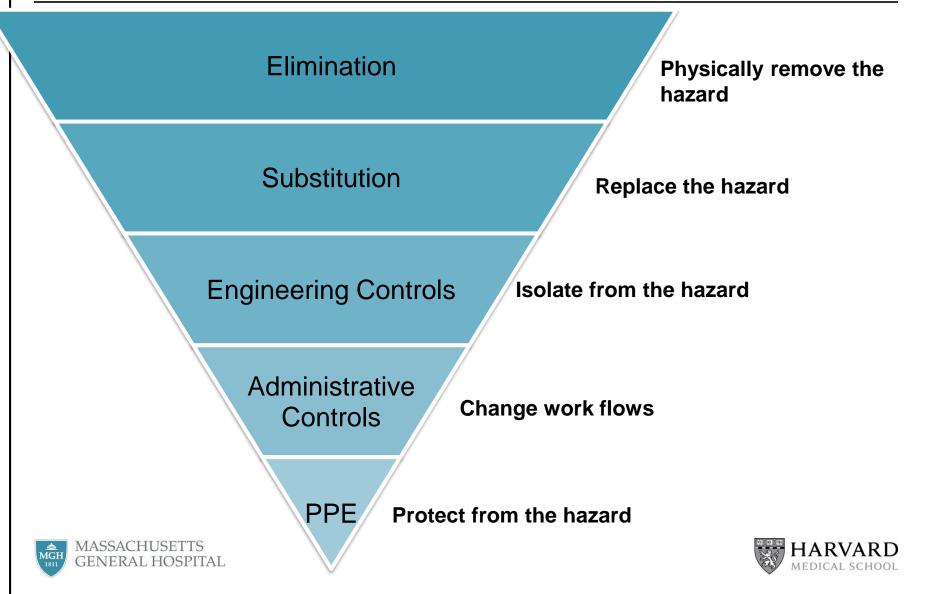
Source	Location	Population studied	Intervention	Outcome
Hendrix et al	Hair salon in Springfield, Missouri	139 Patrons at a salon with 2 infected and symptomatic stylists	Universal mask wearing in salon (by local ordinance and company policy)	No COVID-19 infections among 67 patrons who were available for follow-up
Payne et al	USS Theodore Roosevelt, Guam	382 US Navy service members	Self-reported mask wearing	Mask wearing reduced risk of infection by 70% (unadjusted odds ratio, 0.30 [95% CI, 0.17-0.52])
Wang Y et al	Households in Beijing, China	124 Households of diagnosed cases comprising 335 people	Self-reported mask wearing by index cases or ≥1 household member prior to index case's diagnosis	Mask wearing reduced risk of secondary infection by 79% (adjusted odds ratio, 0.21 [95% CI, 0.06-0.79])
Doung-ngern et al	Bangkok, Thailand	839 Close contacts of 211 index cases	Self-reported mask wearing by contact at time of high-risk exposure to case	Always having used a mask reduced infection risk by 77% (adjusted odds ratio, 0.23 [95% CI, 0.09-0.60])
Gallaway et al	Arizona	State population	Mandatory mask wearing in public	Temporal association between institution of mask wearing policy and subsequent decline in new diagnoses
Rader et al	US	374 021 Persons who completed web-based surveys	Self-reported mask wearing in grocery stores and in the homes of family or friends	A 10% increase in mask wearing tripled the likelihood of stopping community transmission (adjusted odds ratio, 3.53 [95% CI, 2.03-6.43])
Wang X et al	Boston, Massachusetts	9850 Health care workers (HCWs)	Universal masking of HCWs and patients in the Mass General Brigham health care system	Estimated weekly decline in new diagnoses among HCWs of 3.4% after full implementation of the mask wearing policy
Mitze et al	Jena (Thuringia), Germany	City population aged ≥15 y	Mandatory mask wearing in public spaces (eg, public transport, shops)	Estimated daily decline in new diagnoses of 1.32% after implementation of the mask mandate
Van Dyke et al	Kansas	State population	Mandatory mask wearing in public spaces	Estimated case rate per 100 000 persons decreased by 0.08 in counties with mask mandates but increased by 0.11 in those without
Lyu and Wehby	15 US states and Washington, DC	State populations	Mandatory mask wearing in public	Estimated overall initial daily decline in new diagnoses of 0.9% grew to 2.0% at 21 days following mandates
Karaivanov et al	Canada	Country population	Mandatory mask wearing indoors	Estimated weekly 25%-40% decline in new diagnoses following mask mandates

^a See the Supplement for the complete table.





Prevention of Transmission: The Hierarchy of Controls



DIAGNOSIS, DISEASE, AND TREATMENT





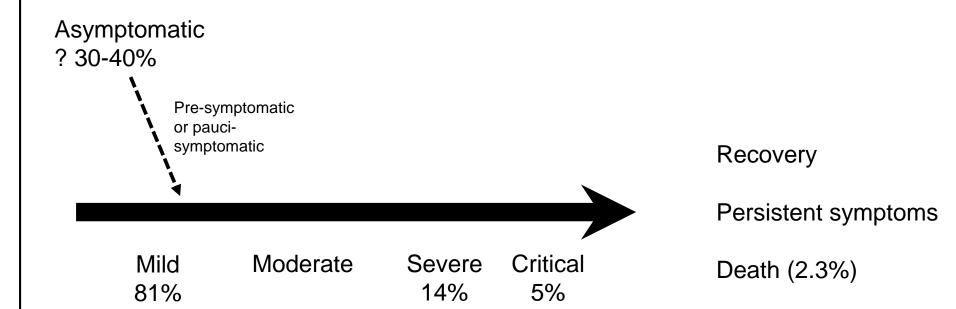
Who and what?

- Who should be tested?
 - Anyone with symptoms consistent with COVID-19, regardless of vaccination status or prior infection
 - Asymptomatic
 - Unvaccinated: known exposure*
 - Other asymptomatic populations per public health
- What type of test?
 - Viral tests: PCR or antigen
 - PCR finds virus fragments, "gold standard"
 - Antigen tests finds virus protein, less sensitive than PCR
 - Antibody tests (serology tests)- looks for past infection
- Interpretation
 - Active infection (infectious)
 - Past infection (non-infectious)
 - False pos, false neg





Wide spectrum of disease







Severe disease

- Defined
 - Hospital admission
 - Intensive care unit admission
 - Ventilator support
 - Death
- Age- very strong predictor
- Medical conditions
 - At increased risk
 - May be at increased risk





Risk of hospitalization and death associated with increasing age

Rate ratios compared to 5-17 year olds¹

	0—4 years	5—17 years	18—29 years	30—39 years	40—49 years	50—64 years	65—74 years	75—84 years	85+ years
Cases ²	<1x	Reference group	3x	2x	2x	2x	2x	2x	2x
Hospitalization ³	2x	Reference group	7x	10x	15x	25x	35x	55x	80x
Death ⁴	2x	Reference group	15x	45x	130x	400x	1100x	2800x	7900x

All rates are relative to the 5—17-year age category. Sample interpretation: Compared with 5—17-year-olds, the rate of death is 45 times higher in 30—39-year-olds and 7,900 times higher in 85+-year-olds. Compared with 18—29-year-olds, the rate of hospitalization is 8 times higher in 75—84-year-olds (55 divided by 7 equals 7.9).





Risk factors for severe disease

- Cancer
- Chronic kidney disease
- Chronic lung diseases
- Dementia and other neurological disorders
- Diabetes (1 or 2)
- Down Syndrome
- Heart conditions, such as heart failure, coronary artery disease, or cardiomyopathies
- HIV infection
- Immunocompromised state Liver disease
- Overweight and obesity
- Pregnancy
- Sickle cell disease or thalassemia
- Smoking, current or former
- Solid organ or blood stem cell transplant
- Stroke or cerebrovascular disease
- Substance use disorders





What to do with this information?

- Vaccine allocation
- Therapeutic decisions
- Decisions re admission, monitoring
- Working to mitigate risk





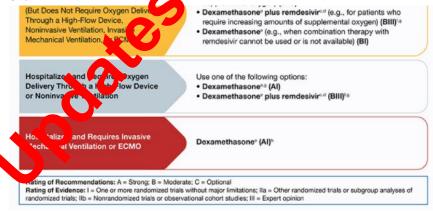
Therapeutic management

- Early stage: prior to immune response, disease mediated by viral replication
- Later stage: immune/inflammato ry response



Based on the available evidence, the Panel has determined the ollowing:

The Panel recommends the use of bamlaniving 1,700 mg to a setesevimab 1,400 mg for the treatment of outpatients with mild to moderate COVID-191 (ho a part high risk of clinical progression as defined by the EUA criteria (see below) (BIIa). Treatment how the started as soon as possible after the patient has received a positive result on a SARS-CoV-2 a pigen or nucleic acid amplification test and within 10 days of symptom onset (see the Panel's ranchale for this recommendation below).

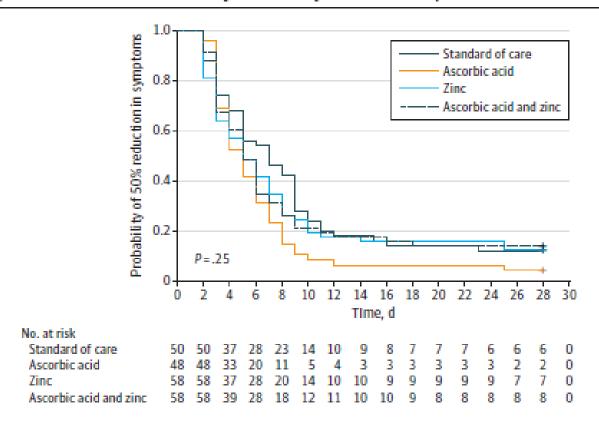






Zinc and Vitamin C: no effect

Figure 3. Kaplan-Meier Curves for the Primary End Point by Treatment Group



Thomas S, Patel D, Bittel B, et al. *JAMA Netw Open.* 2021;4(2):e210369. doi:10.1001/jamanetworkopen.2021.0369





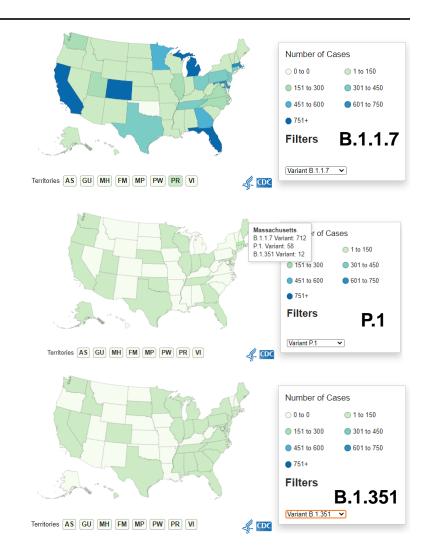
VARIANTS





Variant SARS-CoV-2: what do we know?

- Viruses constantly change through mutation, and new variants of a virus are expected to occur over time
 - Sometimes new variants emerge and disappear
 - Other times, new variants emerge and persist.
- Multiple variants have been documented in the United States and globally during this pandemic
- Questions:
 - Transmissibility
 - Severity of disease
 - Escape from natural immunity
 - Effectiveness of vaccines
 - Effectiveness of therapies







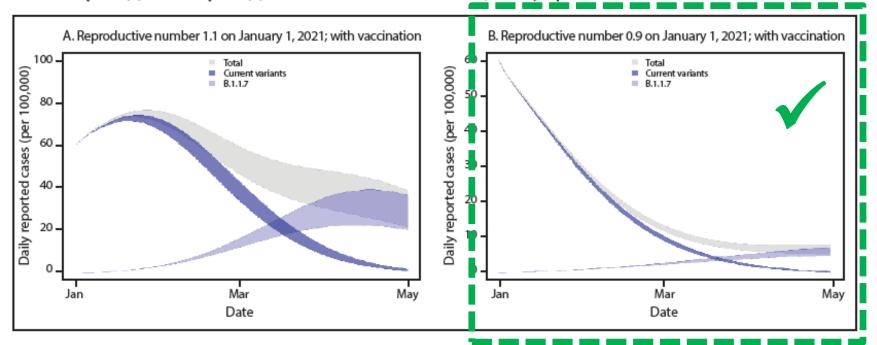
Estimated impact of B117 in the US: yes community vaccination (1m/day)



Morbidity and Mortality Weekly Report January 15, 2021

Emergence of SARS-CoV-2 B.1.1.7 Lineage —
United States, December 29, 2020–January 12, 2021
Sunner E. Gilovo, ROV. Palous field RDV. Decem R. McCome RDV. Modet A. Johanner, RDV.
John T. Brosh RDV. And McAll RDV. Hald J. Some, RDV. State Eng. RDV. Robota S. Johnson, RDV.

FIGURE 2. Simulated case incidence trajectories* of current SARS-CoV-2 variants and the B.1.1.7 variant, † assuming community vaccination and initial R_t = 1.1 (A) or initial R_t = 0.9 (B) for current variants — United States, January–April 2021



R_t= 1.1 mitigation, but increasing transmission

R_t= 0.9
decreasing transmission



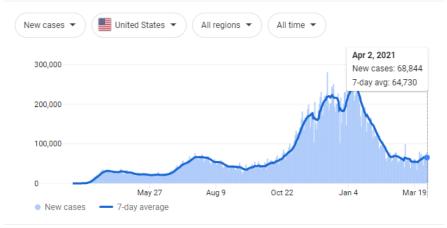


Daily change



Each day shows new cases reported since the previous day $\,\cdot\,$ Last updated: 2 days ago Source: <u>JHU CSSE COVID-19 Data</u> $\,\cdot\,$ <u>About this data</u>

Daily change



Each day shows new cases reported since the previous day $\,\cdot\,$ Last updated: 20 hours ago Source: The New York Times $\,\cdot\,$ About this data





Vaccines: an elimination strategy

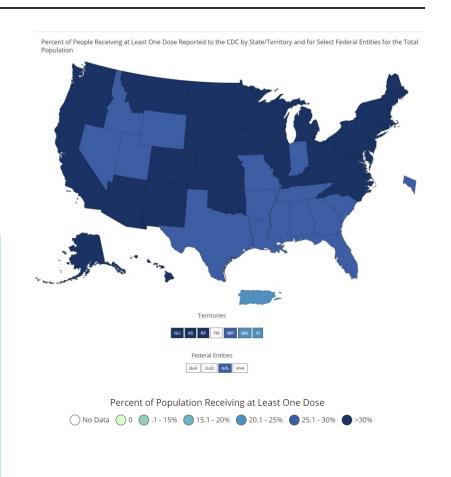
Total Vaccine Doses

Delivered 207,866,645

Administered 161,688,422

Learn more about the distribution of vaccines.

People Vaccinated	At Least One Dose	Fully Vaccinated
Total	104,213,478	59,858,146
% of Total Population	31.4%	18%
Population ≥ 18 Years of Age	103,517,359	59,650,494
% of Population ≥ 18 Years of Age	40.1%	23.1%
Population ≥ 65 Years of Age	41,007,245	29,904,535
% of Population ≥ 65 Years of Age	75%	54.7%







CDC | Data as o: Apr 3 2021 12:28PM ET

Vaccines

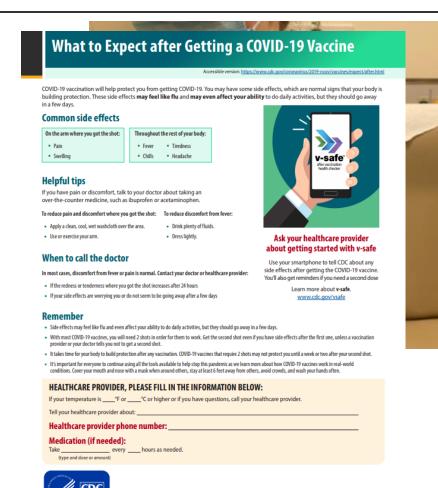
- 3 FDA approved vaccines
 - Pfizer (2 shots, 21 days apart)
 - Moderna (2 shots, 21 days apart)
 - Johnson & Johnson/Janssen (1 shot)
- Highly effective at preventing severe disease and hospitalization
- Emerging data on preventing transmission
- Emerging data on efficacy against variants
- Emerging data on safety and efficacy in children





What to expect

- Before
- In the clinic
- Afterwards
 - Local injection site reaction
 - Pain, redness
 - · Can be delayed
 - Systemic effects
 - Fatigue
 - Aches
 - Headache
 - Fever
 - Self-limited



cdc.gov/coronavirus





Vaccines—future considerations

- Booster doses
 - Annual
 - 1 vs 2
 - Inclusion of variants
- Age range
- Long-term



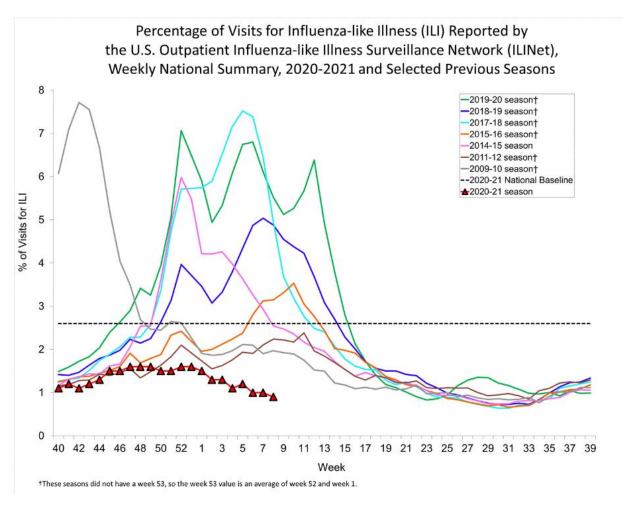


SOMETHING AMAZING HAPPENED TO FLU





The twindemic that never happened









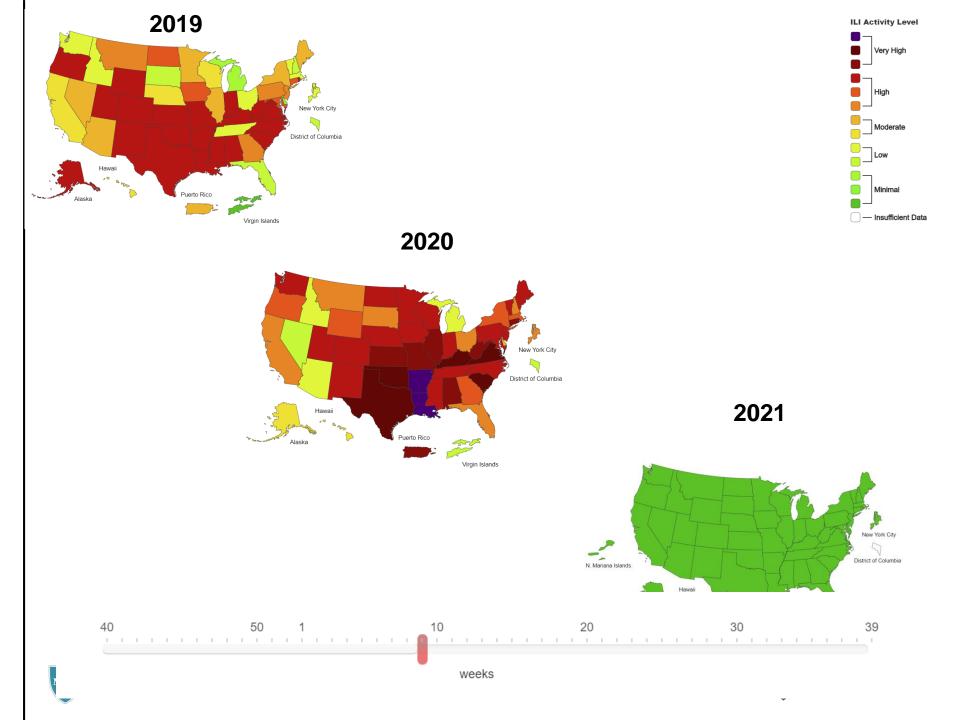
% samples testing positive for influenza

- Since September 2020, CDC reports:
 - public health labs: 196/336,133 (0.1%)
 - clinical labs: 1543/693,603 (0.2%)
- Also MIA: RSV, adenovirus, endemic coronaviruses, parainfluenza
- At MGH, during the 2020-2021 respiratory virus season, we have tested ~28K samples for influenza and have identified:

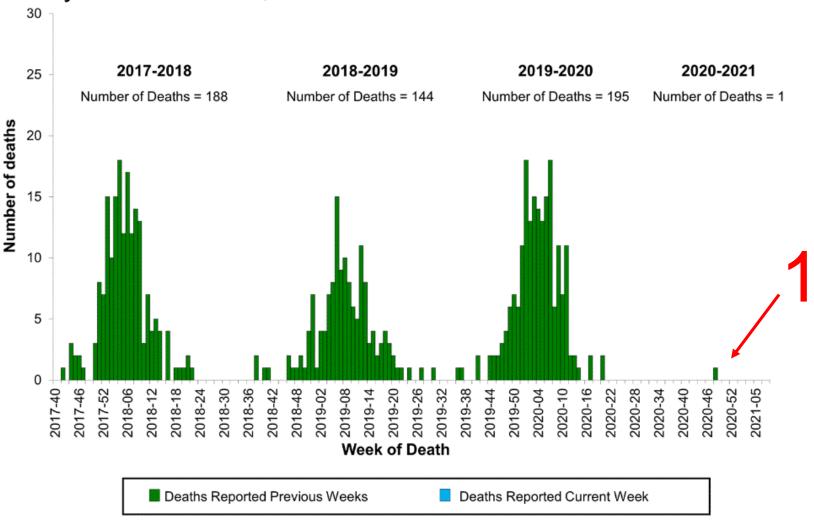








Influenza-Associated Pediatric Deaths by Week of Death, 2017-2018 season to 2020-2021 season







Why?

- All the same mitigation measures we have been using against COVID-19 work against flu and other respiratory viruses
 - Decreased interactions including travel
 - Staying home when sick
 - Masking, distance, hygiene
- Community immunity for routine respiratory viruses
- Vaccination coverage
 - Ramped up flu vaccination campaigns (adult vaccination 42%→ 52%)
- Other reasons...





SUMMARY





Summary

- Fundamentals about transmission inform interventions— both in healthcare and in our communities
- Looking ahead
 - Will there be another surge, will COVID-19 fade, or will we experience smoldering transmission with periodic blips?
 - Sustaining vigilance
 - Potential impact of variants





What will support success?

- Vigilance
 - Masking, hygiene, distance/density, staying home when sick
- Vaccines
 - Excellent news overall!
 - Much to learn
 - We will figure it out







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THANK YOU



