COVID-19 in Oncology Patients

North Carolina Oncology Society/South Carolina Oncology Society: Joint Conference

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Disclosures and disclaimers

Charles D. Comarmond, MD, has no real or apparent financial relationships to disclose.

The views presented are those of the speaker or author and do not necessarily represent the views of the Veterans Affair or US Government.

The scientific database is dynamic (140,743 peer reviewed publications and 18,295 publications on pre-print servers [not peer reviewed])

Specific Learning Objectives

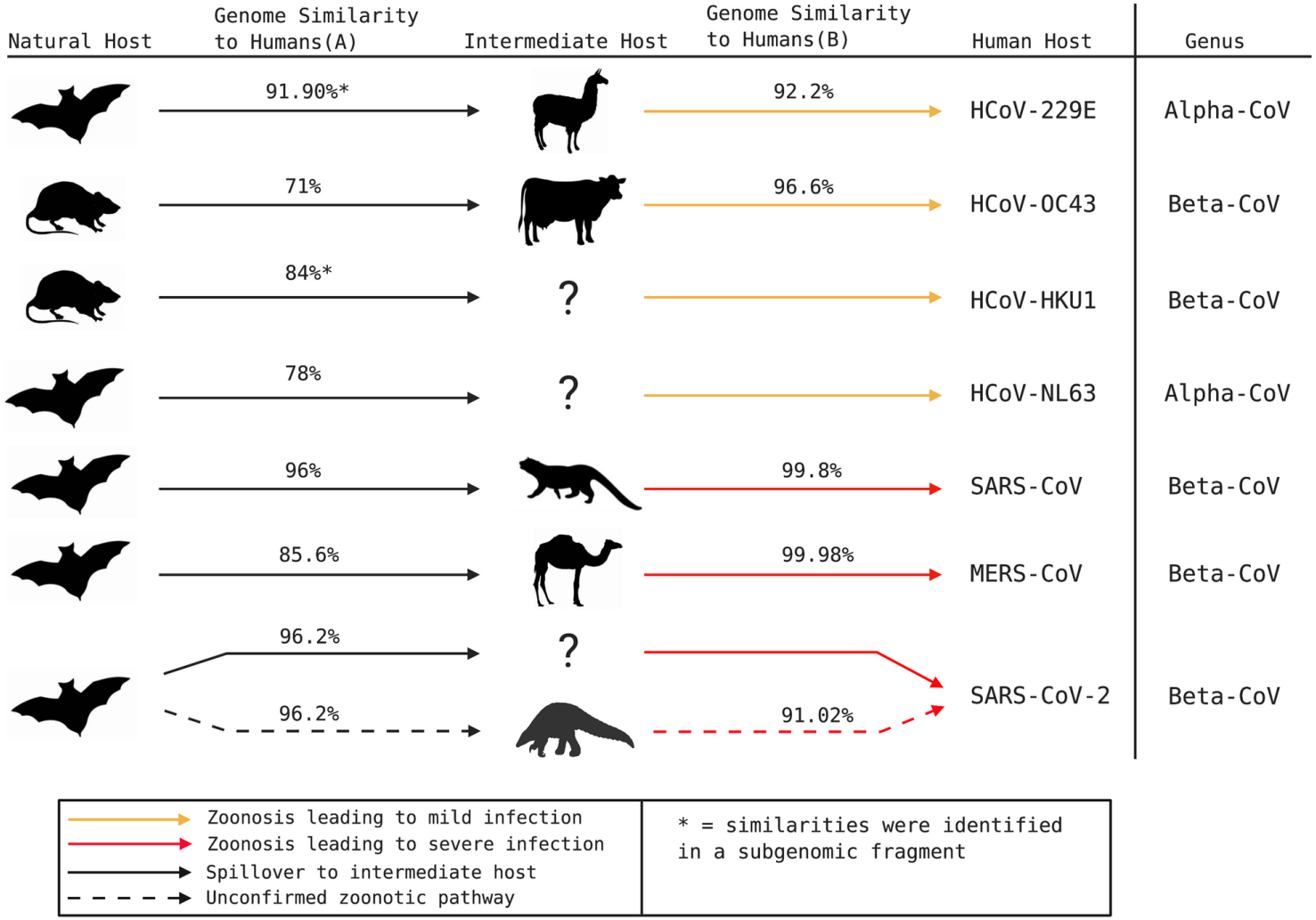
- Describe the impact of the COVID-19 pandemic on patients.

Presentation Objectives

- Epidemiology
- Basic virology and immunology
- Clinical Presentation
- Treatment strategies
- Prevention
- Future direction

Epidemiology: Origins

- There are seven established CoV known to infect humans
- Human CoV (common cold viruses) are the second most common cause of the common cold after rhinoviruses
- SARS-CoV
- MERS-CoV
- SARS-CoV-2

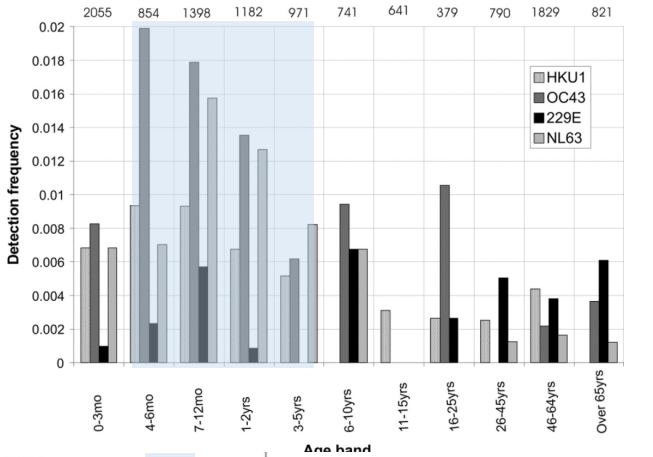


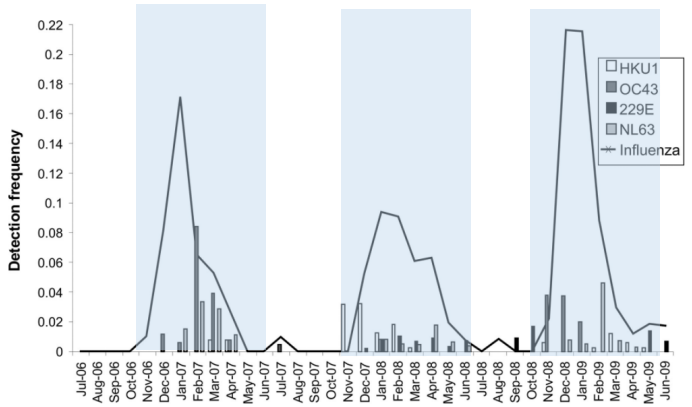
Singh et al. Virol J (2021) 18:166
https://doi.org/10.1186/s12985-021-01633-w

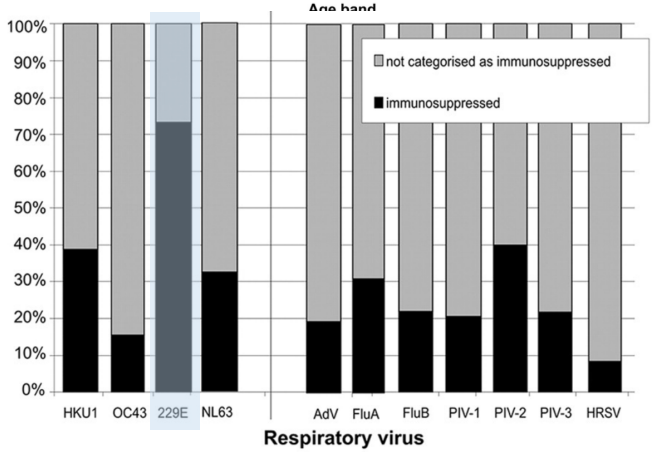
Epidemiology: HCoV comparative epidemiology

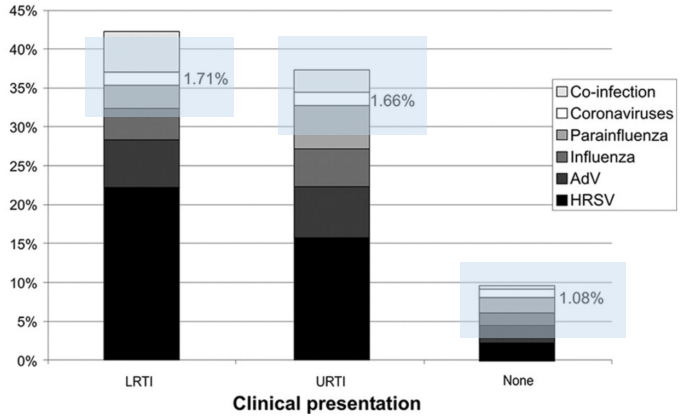
11,661 respiratory samples collected over a 3-year study period in Edinburgh, United Kingdom.

- Coronaviruses were detected in 0.3 to 0.85% of samples in all age groups.
- Marked winter seasonality between the months of December and April
- HCoV-OC43 was detected predominant in the first and third seasons and HCoV-HKU1 dominating in the second
- **70% of HCoV-229E detections were in samples from immunocompromised patients**
- Reinfection with coronaviruses HCoV-229E and HCoV-OC43 is a common occurrence







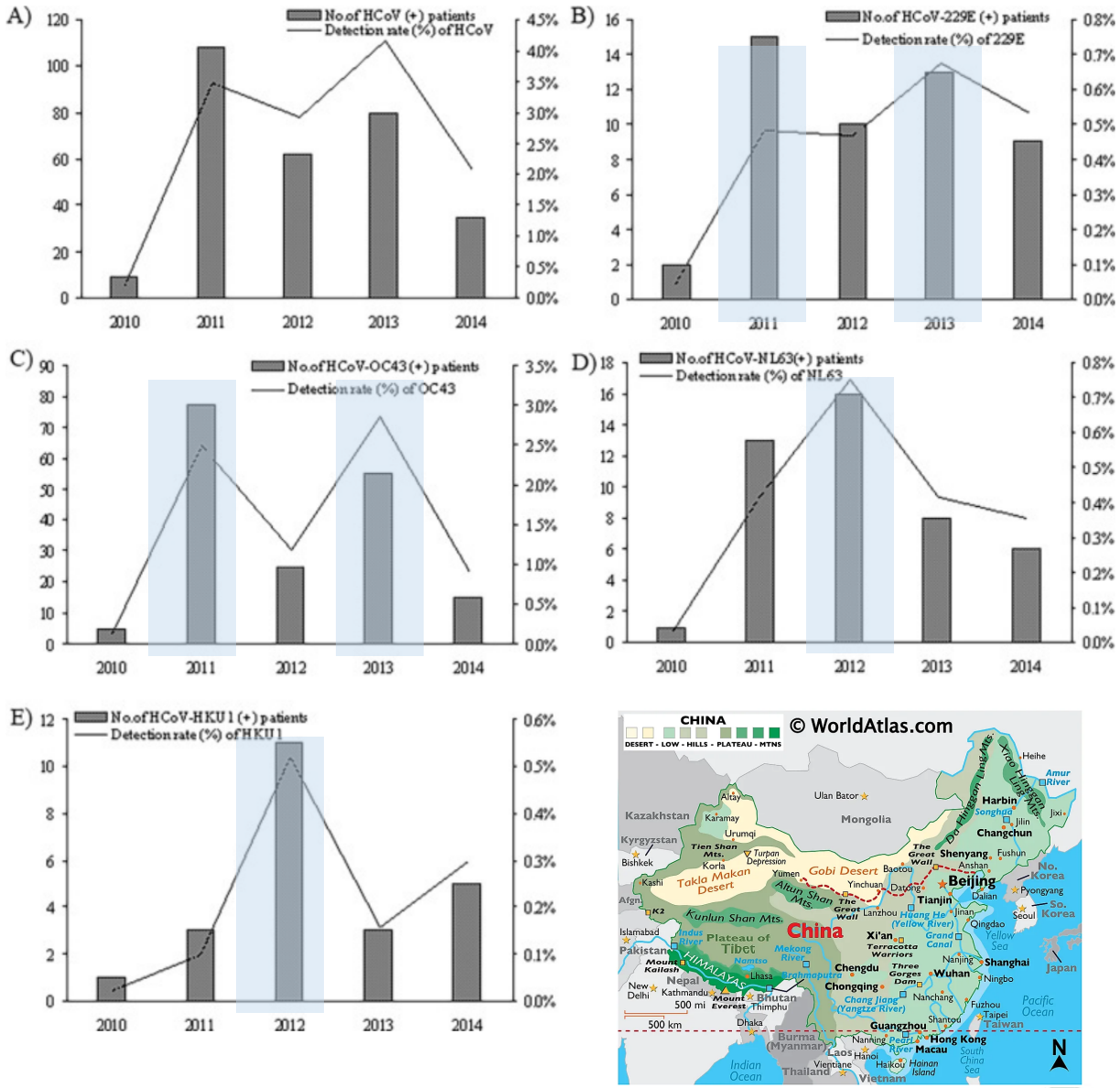


DOI:https://doi.org/10.1128/JCM.00636-10

HCoV comparative epidemiology

13048 throat/nasal swab specimens from adults and children with fever and acute upper respiratory infection symptoms in Guangzhou between July 2010 and June 2015

- HCoV was detected in 2.25% (294 positive) patients with respiratory infection symptoms
- The 5-year distribution of HCoVs during 2010–2015 shows every other year trend of epidemiology



PLoS One. 2018; 13(1): e0191789.
Published online 2018 Jan 29. doi: 10.1371/journal.pone.0191789

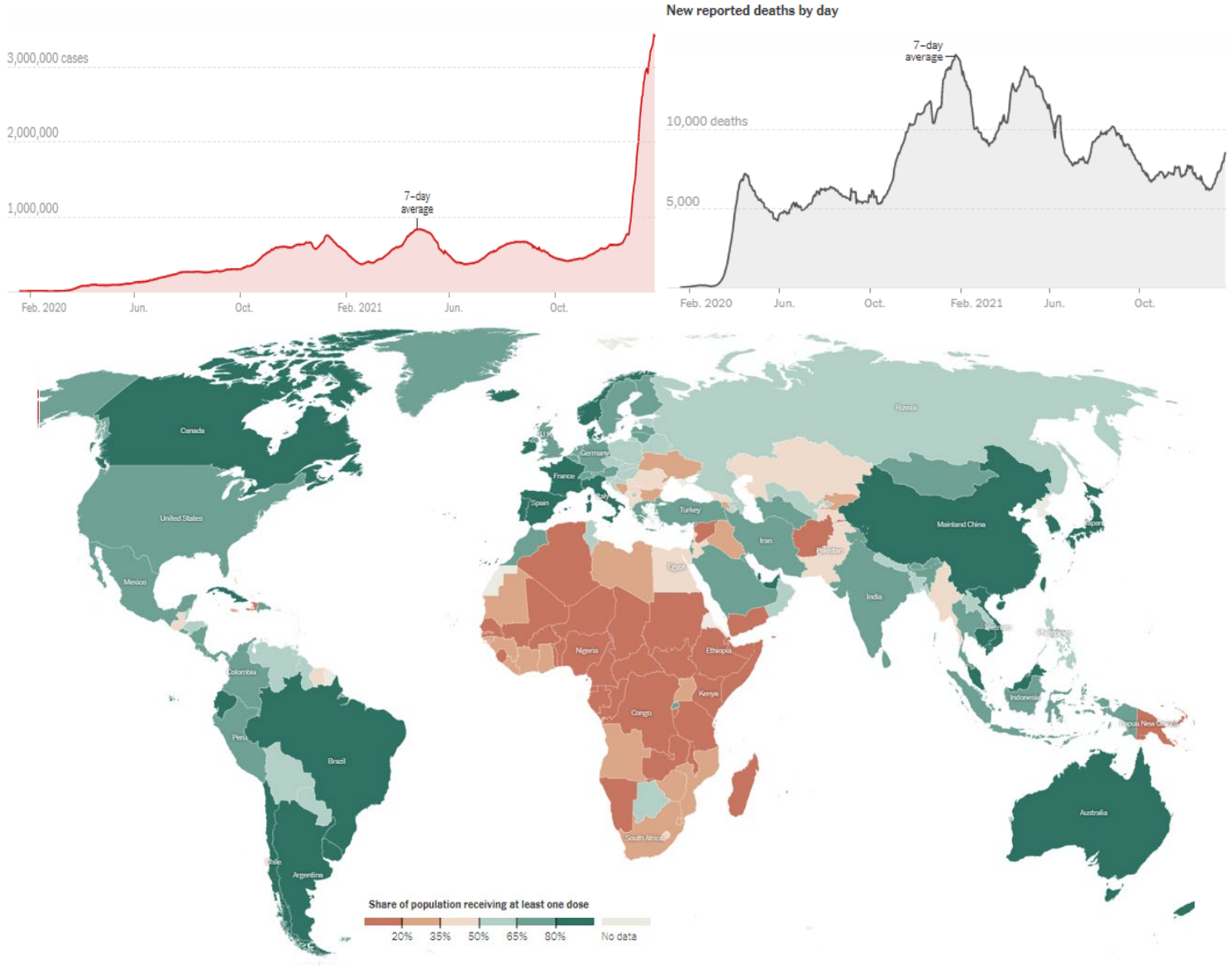
Epidemiology: Transmission

Person-to-person transmission

- **Droplet:** mainly through close-range contact (within approximately six feet or two meters) via respiratory particles
- **Contact:** Infection might also occur if a person's hands are contaminated by respiratory secretions and inoculation of mucous membranes
- **Aerosols:** SARS-CoV-2 can also be transmitted longer distances through the airborne route but the extent to which this mode of transmission has contributed to the pandemic is uncertain
- **Non-respiratory specimen:** faeces, blood, semen

Global Epidemiology

- Of 193 countries officially recognized by the UN, 189 have reported cases*
- Globally over 360 million cases
- 3.6 million new cases per day
- 5.6 million deaths
- 8500 new deaths per day
- 10 billion vaccine doses administered



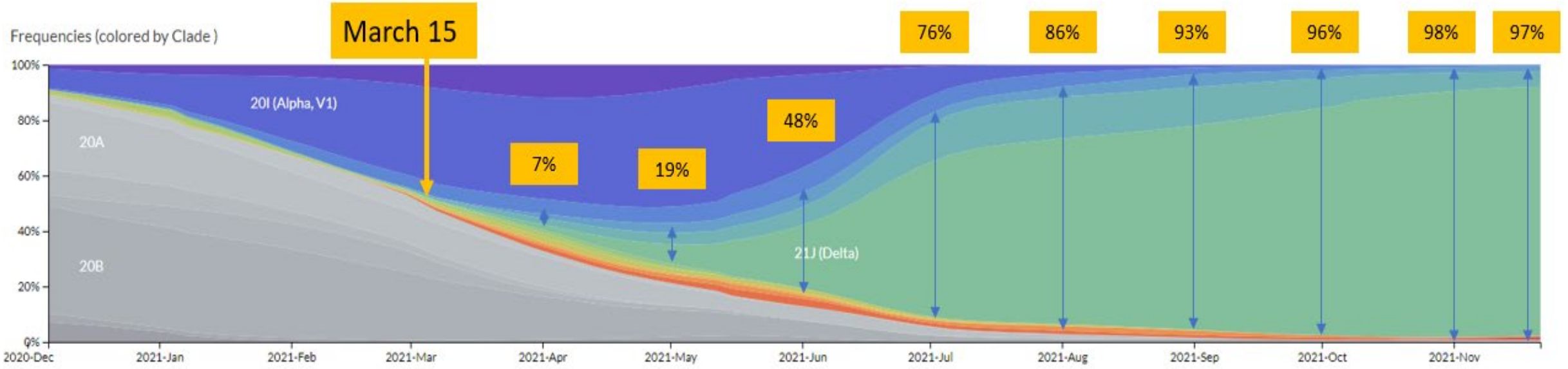
*As of January 15, 2022, North Korea, Turkmenistan, Tuvalu, Nauru have officially not reported cases

JOHNS HOPKINS UNIVERSITY & MEDICINE | CORONAVIRUS RESOURCE CENTER

The New York Times

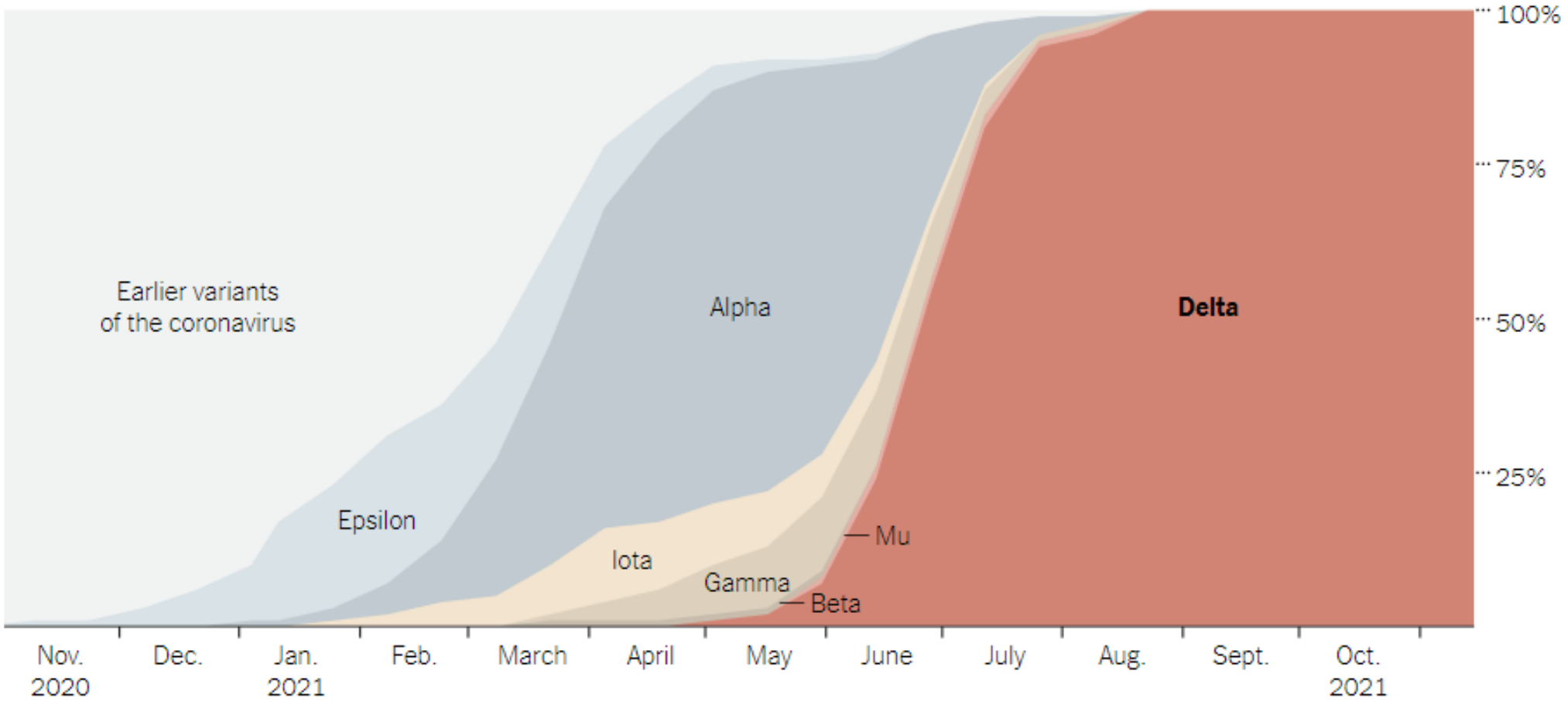
Global Epidemiology: SARS-Cov-2 Variants

Global delta variant and other variant emergence from December 2020 through December 2021



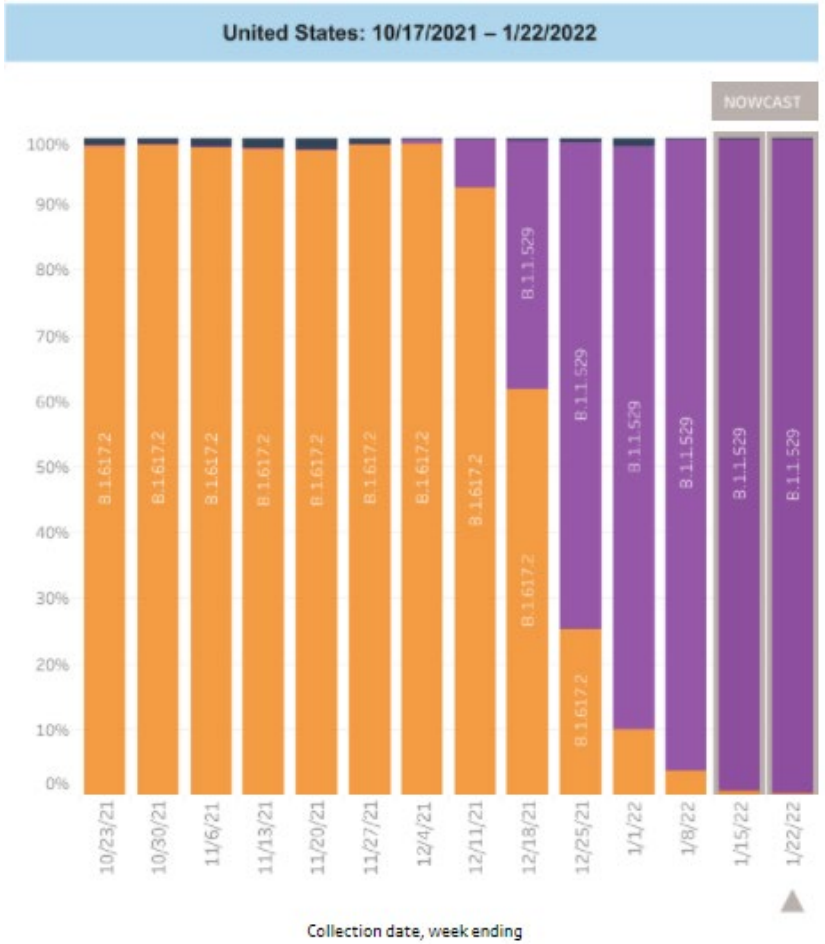
US Epidemiology: SARS-Cov-2 Variants

Variant emergence in the US



US OMICRON SARS-Cov-2 emergence

- Omicron became the dominant strain within 6 week in the US
- Estimated >100 times more transmissible than previous variants
- Estimated >500 times higher replication rate *in vitro?*
- Danish study concluded that the rapid spread of the Omicron can be ascribed to the immune evasiveness rather than an inherent increase in the basic transmissibility.



United States: 1/16/2022 – 1/22/2022 NOWCAST

USA

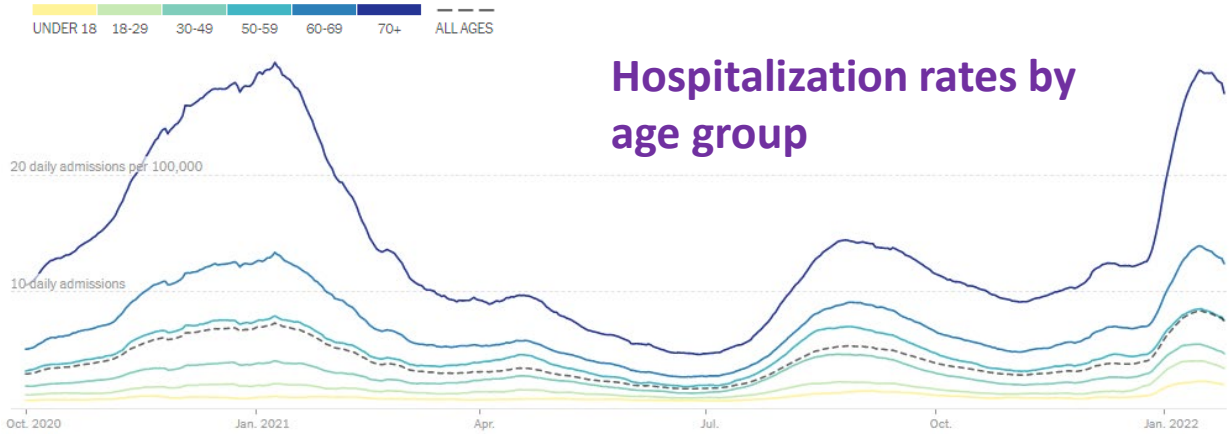
WHO label	Lineage #	US Class	%Total	95%PI
Omicron	B.1.1.529	VOC	99.9%	99.8-99.9%
Delta	B.1.617.2	VOC	0.1%	0.1-0.2%
Other	Other*		0.0%	0.0-0.0%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates.
# AY.1-AY.133 and their sublineages are aggregated with B.1.617.2. BA.1, BA.2 and BA.3 are aggregated with B.1.1.529.

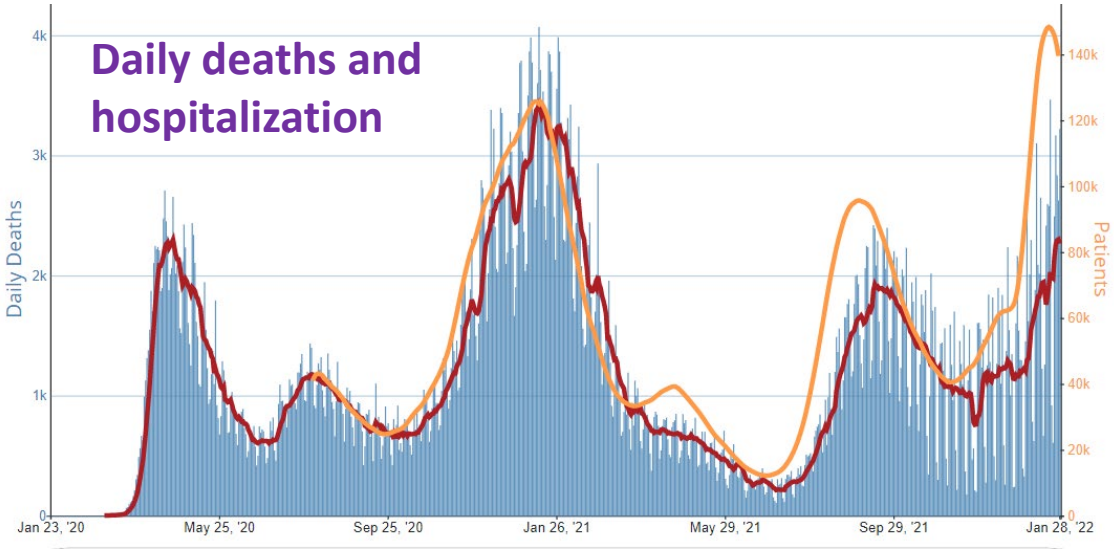
doi: https://doi.org/10.1101/2021.12.27.21268278

US Epidemiology

- Over 70 million cases cumulatively
- Over 865,000 deaths
- Daily COVID-19 hospitalizations ranging from 16,000 to 160,000



Hospitalization rates by age group

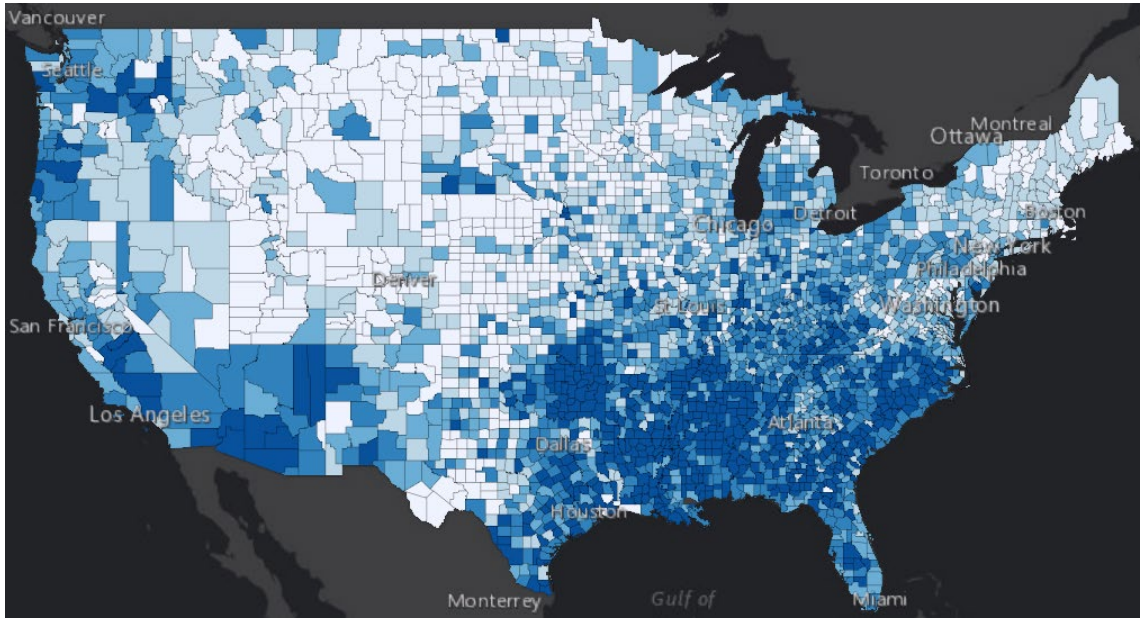


CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

The New York Times

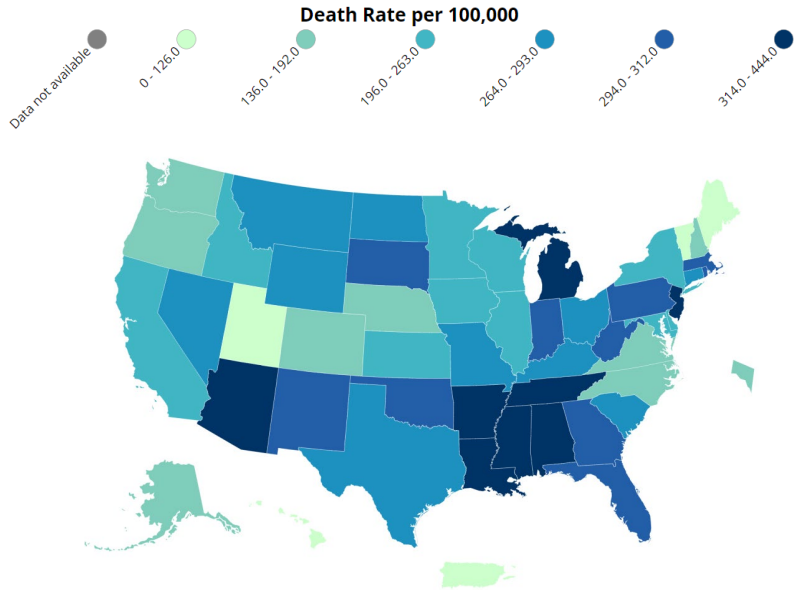
US Epidemiology

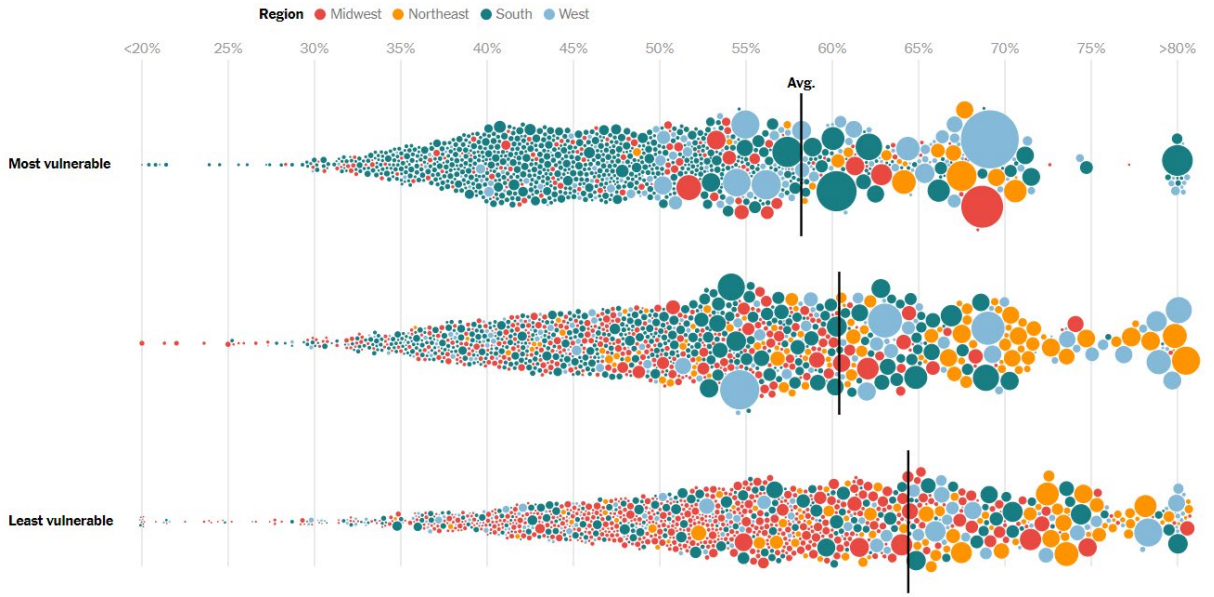
- Mortality rates vary across the United States
- Correlation between mortality rates and mortality pandemic vulnerability index
- Correlation between county social vulnerability index and vaccination rates



COVID-19 Pandemic Vulnerability Index (PVI)

Mortality

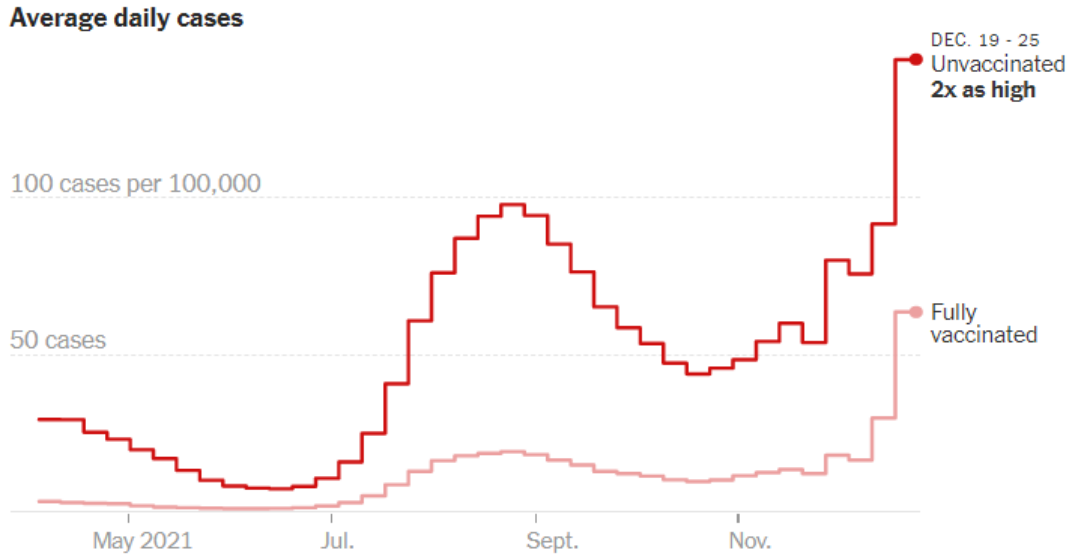


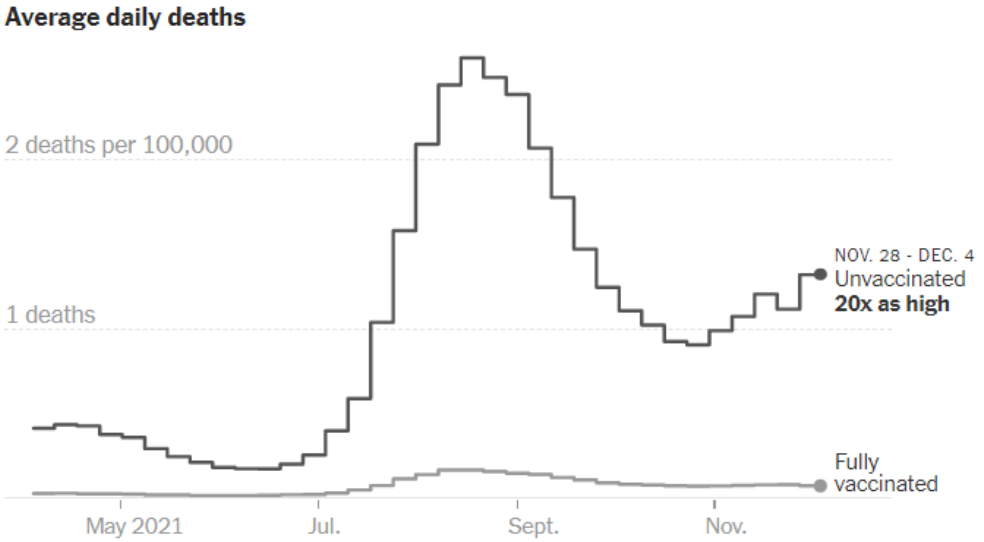


Vaccination rates by county social vulnerability

US Epidemiology

- Unvaccinated individuals are two times more likely to get infected
- Unvaccinated individuals are twenty times more likely to die from COVID-19





US Epidemiology

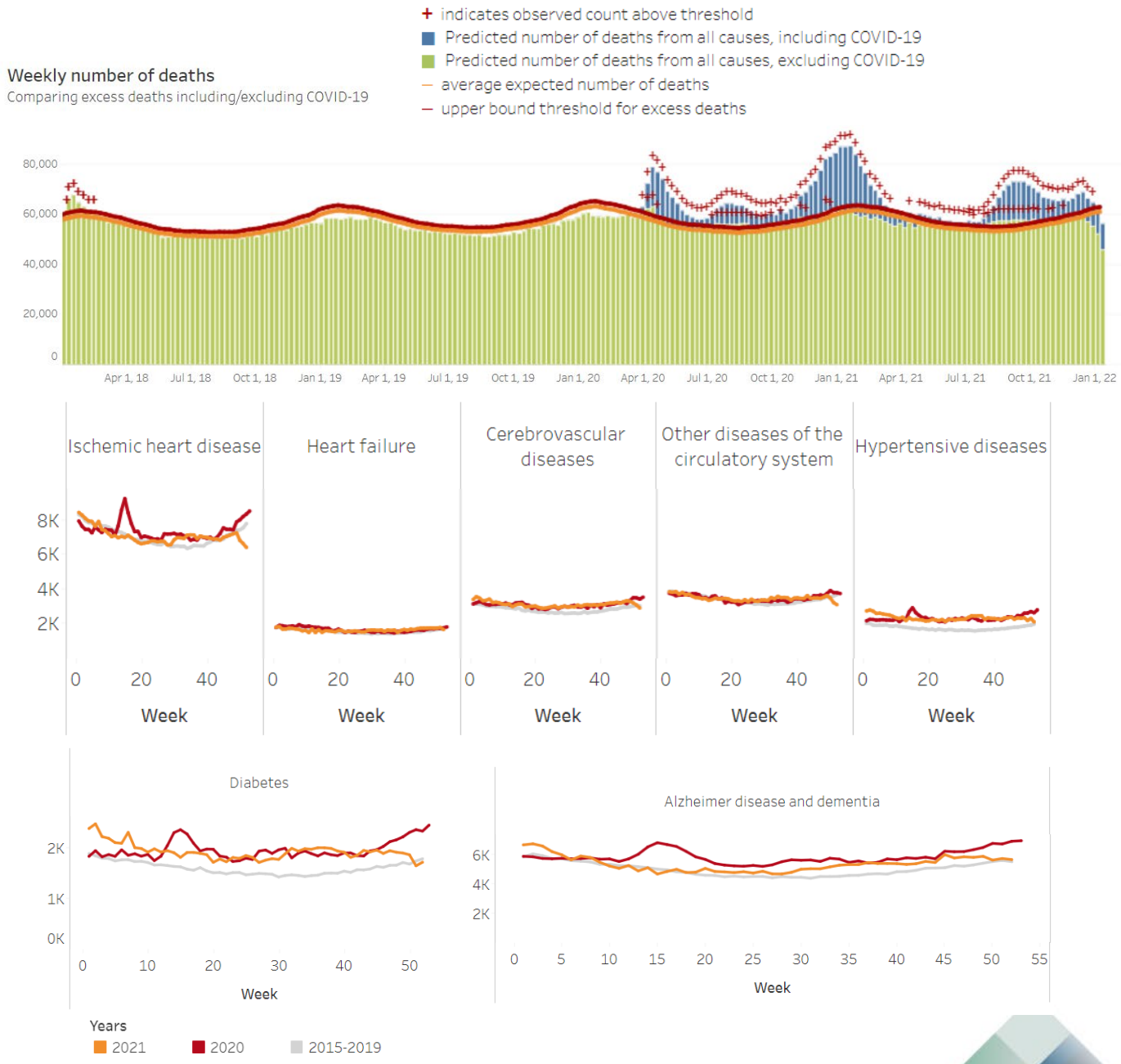
- Disproportionate Burden of COVID-19 Cases, Hospitalizations, and Deaths Among People of Color Compared to Non-Hispanic White Persons

Rate ratios compared to White, Non-Hispanic persons	American Indian or Alaska Native, Non-Hispanic persons	Asian, Non-Hispanic persons	Black or African American, Non-Hispanic persons	Hispanic or Latino persons
Cases[1]	1.6x	0.6x	1.0x	1.6x
Hospitalization[2]	3.3x	0.8x	2.6x	2.5x
Death[3]	2.2x	0.9x	1.9x	2.1x

Source: Centers for Disease Control and Prevention, 2022. Available from: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html

US Epidemiology

- Increase in the weekly expected numbers of deaths (all cause) by an average of 2% throughout the pandemic
- 202,201 all cause deaths excluding COVID
- 968,000 all cause deaths including COVID
- Chronic diseases most impacted



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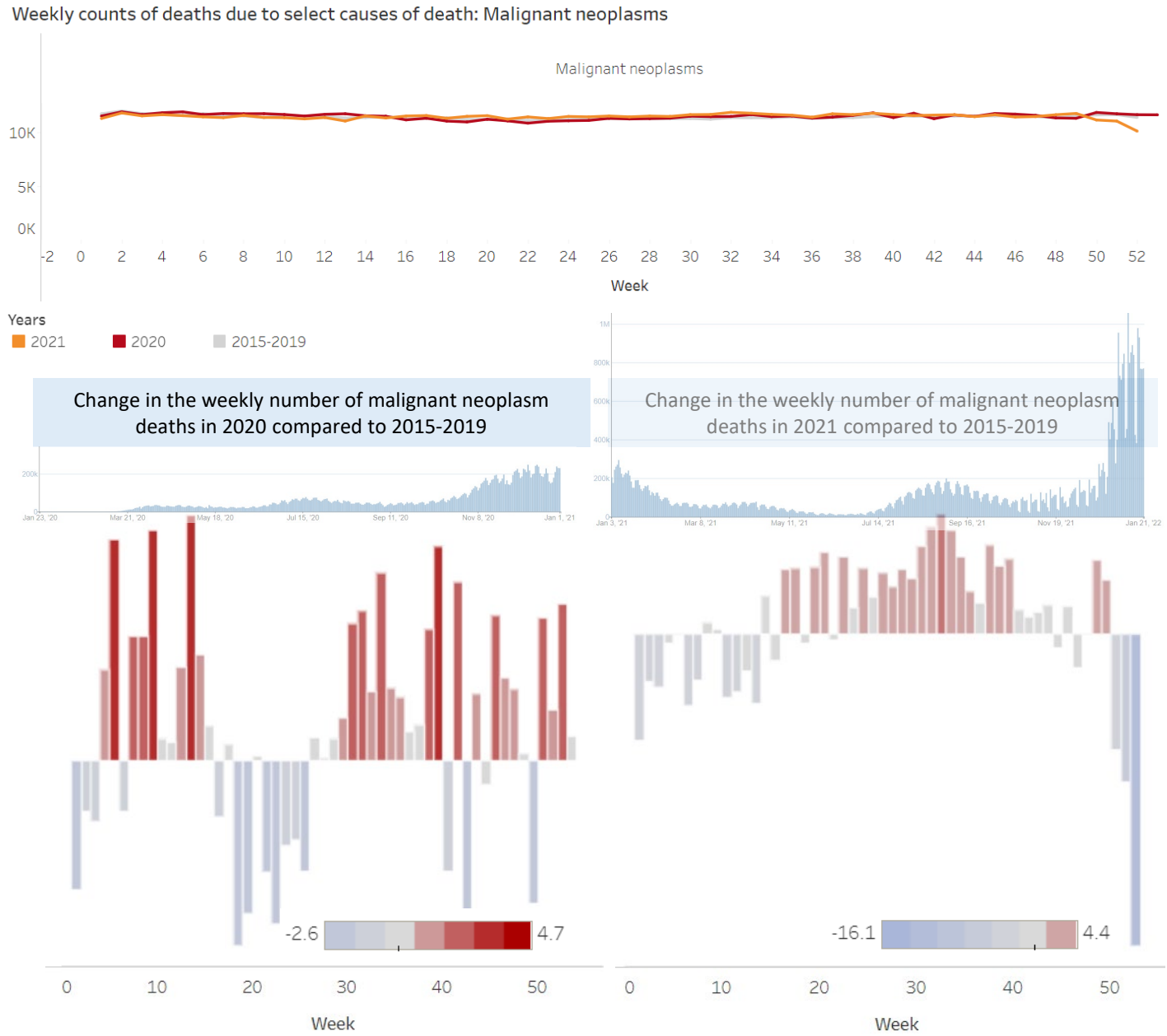
https://www.cdc.gov/nchs/nvss/vsrr/covid19/excess_deaths.htm

US Epidemiology: Oncology excess deaths

- Variable access to healthcare systems during pandemic and surges impact excess mortality in cancer patients
- Changes are more pronounced when viewing weekly changes



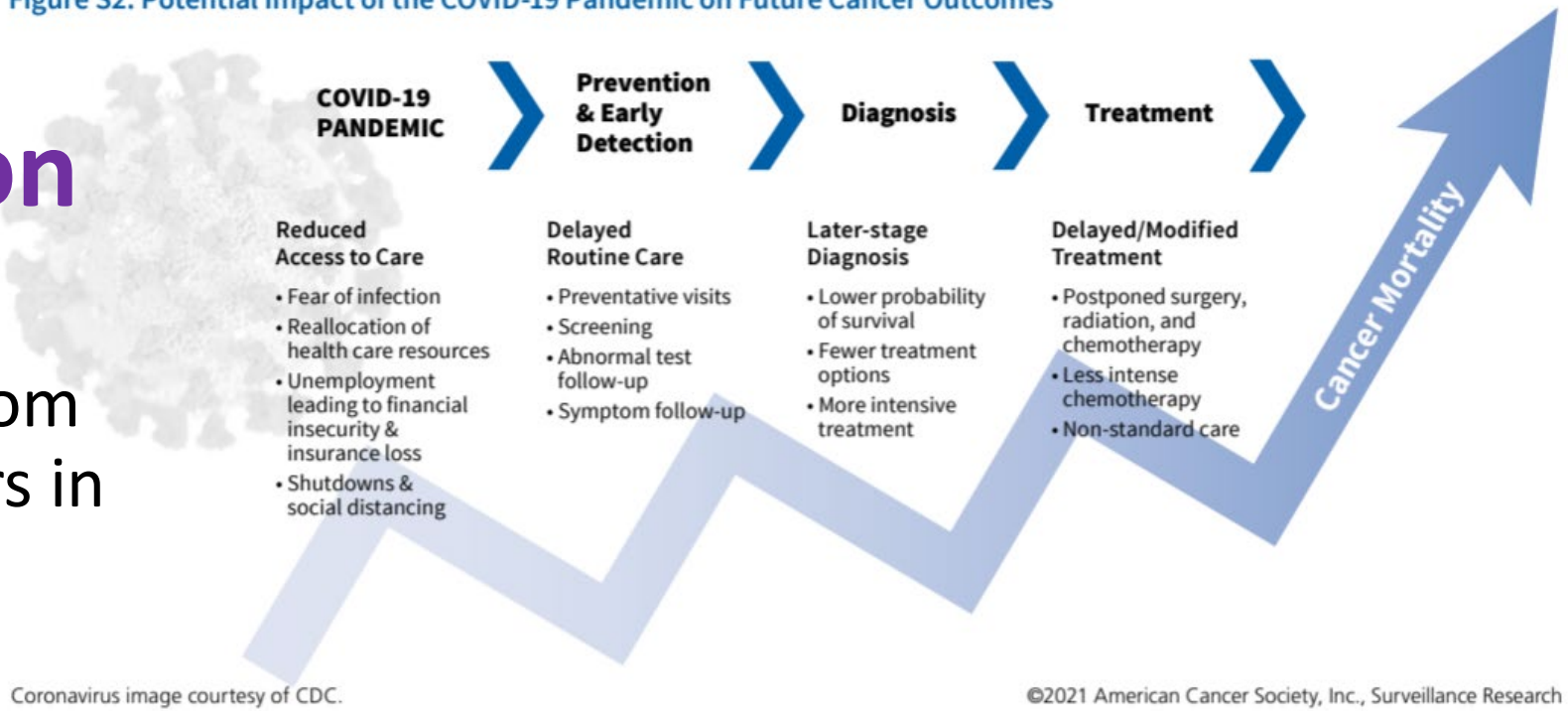
Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

https://www.cdc.gov/nchs/nvss/vsrr/covid19/excess_deaths.htm

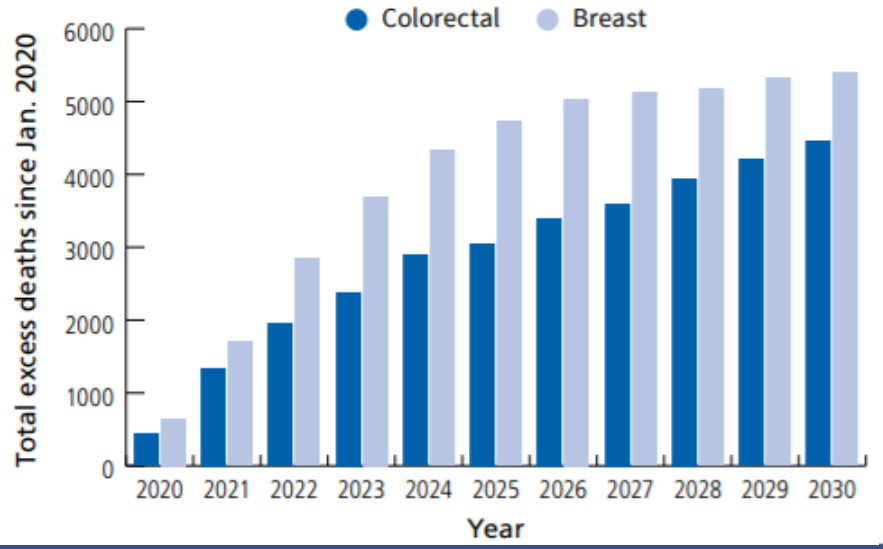
Impact on cancer care and prevention

- Anticipated increase in cumulative excess deaths from colorectal and breast cancers in the US due to the COVID-19 pandemic, 2020 to 2030
- The National Cancer Institute estimated a 1% increase in deaths from breast and colorectal cancer over the next 10 years

Figure S2. Potential Impact of the COVID-19 Pandemic on Future Cancer Outcomes

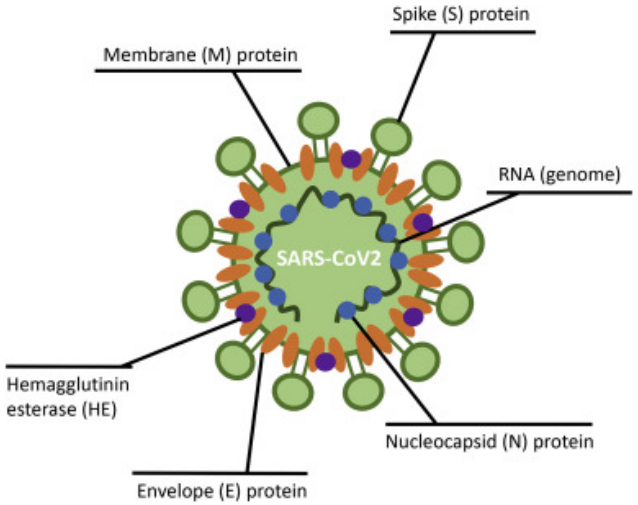


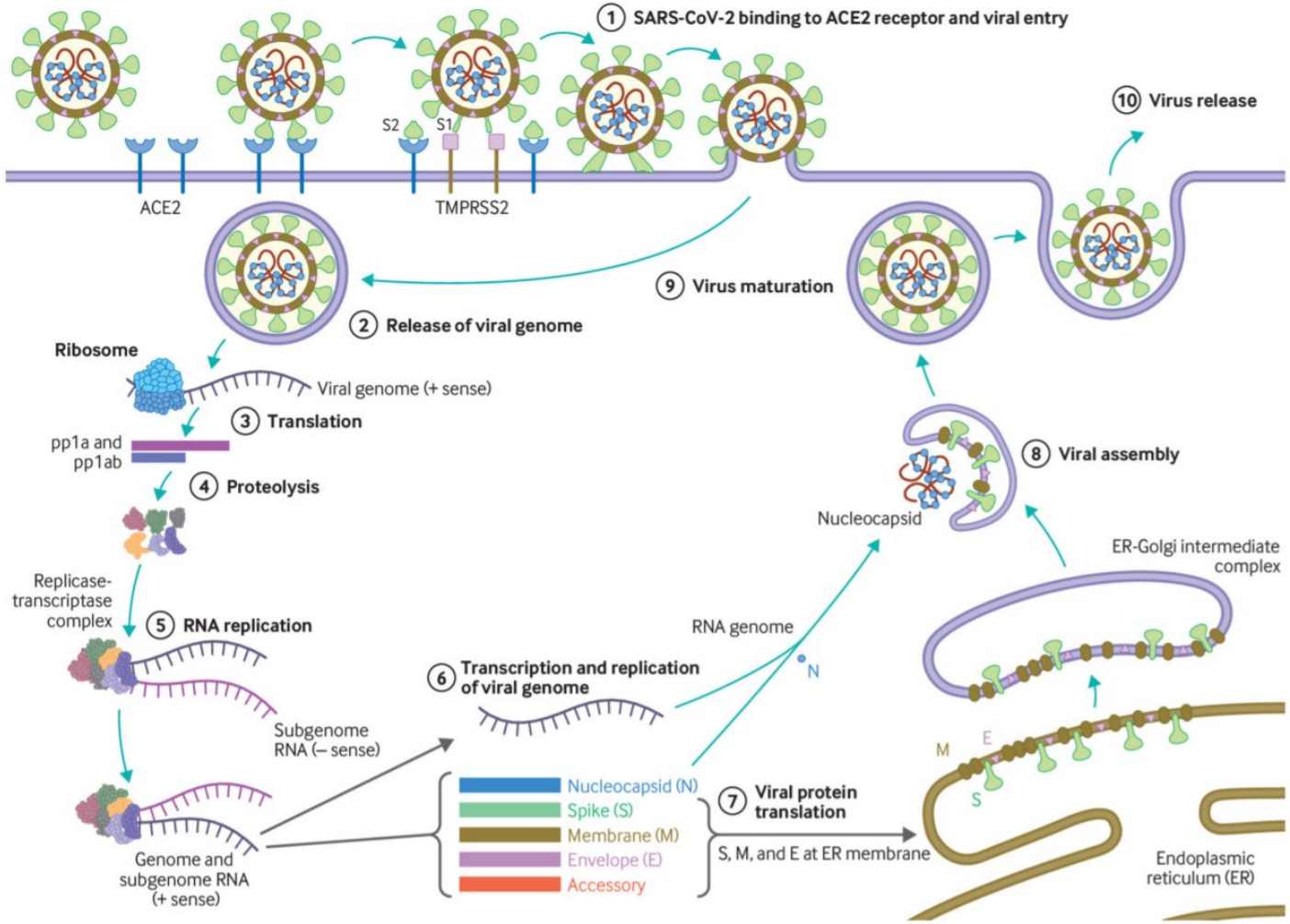
Coronavirus image courtesy of CDC.



Basic virology and immunology

- SARS-CoV-2 is an enveloped β-coronavirus, with a genetic sequence very similar to SARS-CoV-1 (80%)

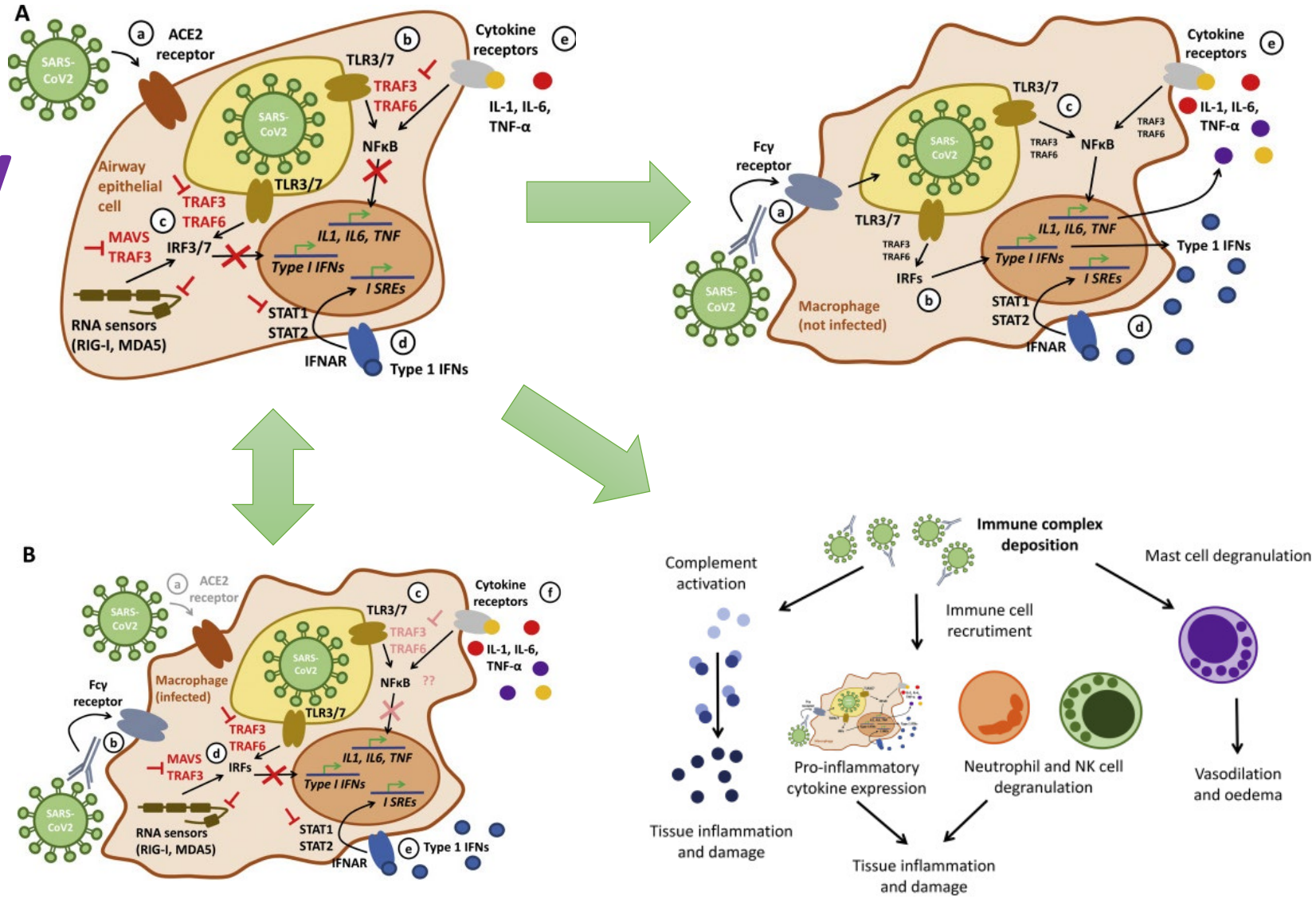




BMJ 2020; 371 doi: https://doi.org/10.1136/bmj.m3862

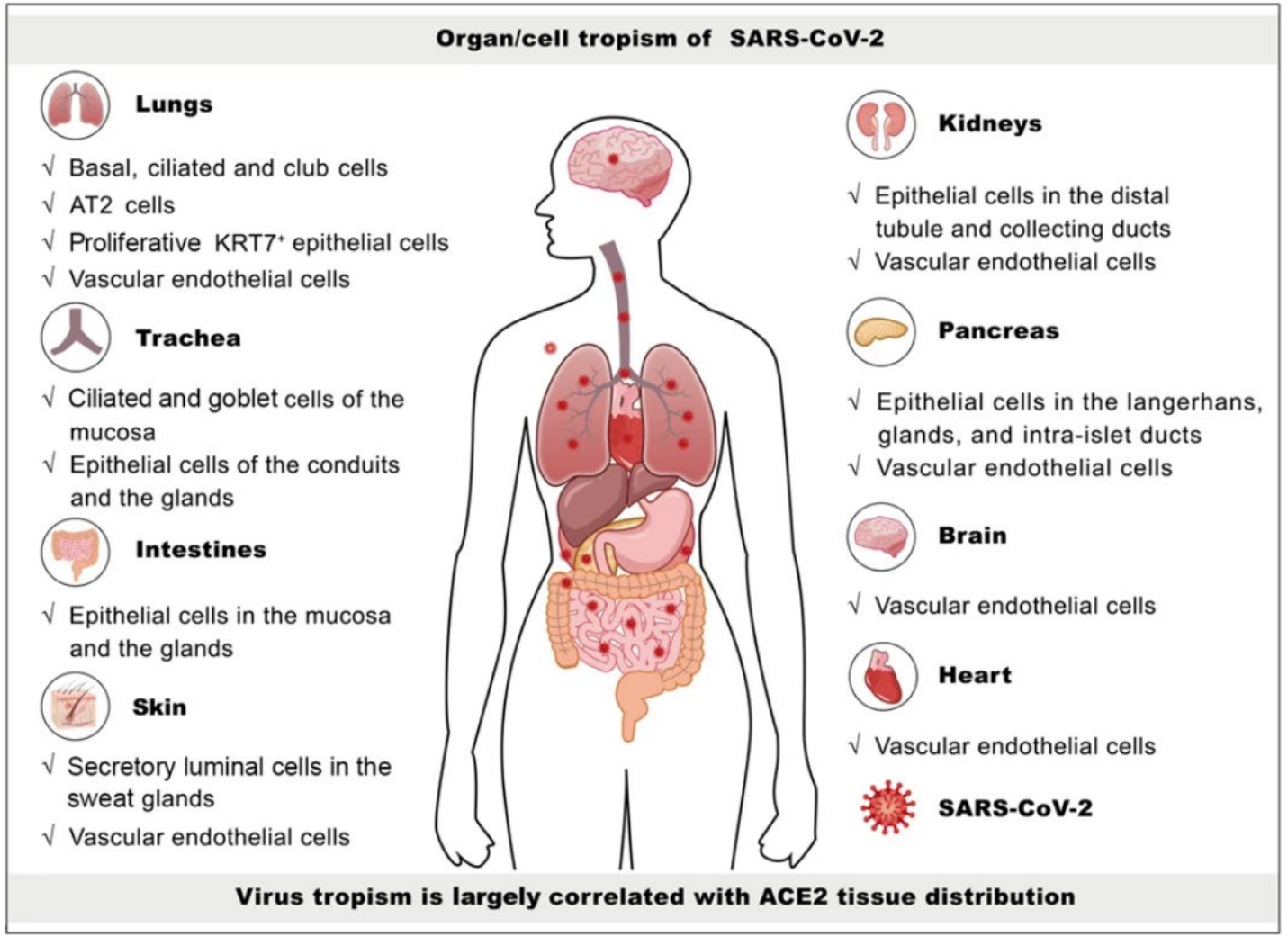
Basic virology and immunology

- Putative mechanisms of immune invasion and pro-inflammatory responses



Basic virology and immunology

- SARS-CoV-2 exploits the host angiotensin-converting enzyme 2 (ACE2) as its receptor for cell entry
- In a co-localization analysis, co-expression of ACE2 and viral antigen was observed in the lung, trachea, small intestine, kidney, pancreas and heart.



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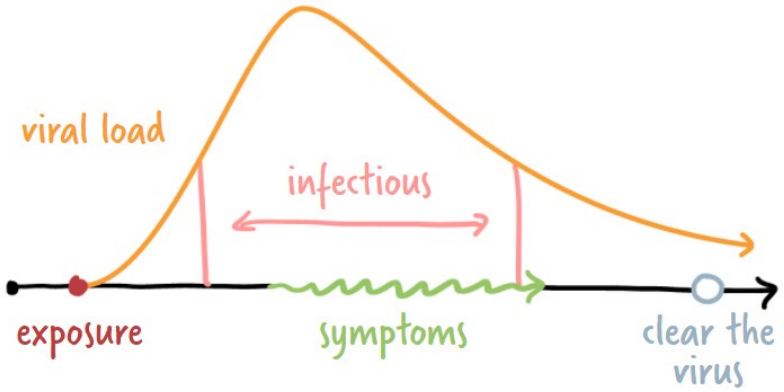
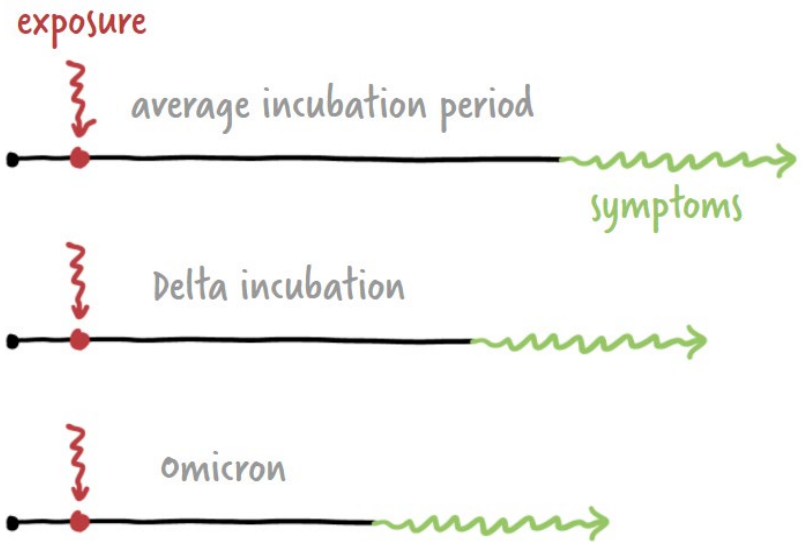
Clinical Presentation





	Asymptomatic or Presymptomatic	Mild Illness	Moderate Illness	Severe Illness	Critical Illness
Features	Positive SARS-CoV-2 test; no symptoms	Mild symptoms (e.g., fever, cough, or change in taste or smell); no dyspnea	Clinical or radiographic evidence of lower respiratory tract disease; oxygen saturation ≥94%	Oxygen saturation <94%; respiratory rate ≥30 breaths/min; lung infiltrates >50%	Respiratory failure, shock, and multiorgan dysfunction or failure
Testing	Screening testing; if patient has known exposure, diagnostic testing	Diagnostic testing	Diagnostic testing	Diagnostic testing	Diagnostic testing
Isolation	Yes	Yes	Yes	Yes	Yes
Proposed Disease Pathogenesis	Viral replication; Inflammation				
Potential Treatment	Antiviral therapy; Antibody therapy; Antiinflammatory therapy				
Management Considerations	Monitoring for symptoms	Clinical monitoring and supportive care	Clinical monitoring; if patient is hospitalized and at high risk for deterioration, possibly remdesivir	Hospitalization, oxygen therapy, and specific therapy (remdesivir, dexamethasone)	Critical care and specific therapy (dexamethasone, possibly remdesivir)

N Engl J Med 2020; 383:1757-1766
DOI: 10.1056/NEJMcp2009249

Risk Factors for Severe Covid-19

- **Cancer**
- Cerebrovascular disease
- Chronic kidney disease
- Chronic lung diseases limited to:
  - Interstitial lung disease
  - Pulmonary embolism
  - Pulmonary hypertension
  - Bronchopulmonary dysplasia
  - Bronchiectasis
  - COPD (chronic obstructive pulmonary disease)
- Chronic liver diseases limited to:
  - Cirrhosis
  - Non-alcoholic fatty liver disease
  - Alcoholic liver disease
  - Autoimmune hepatitis
- Diabetes mellitus, type 1 and type 2
- Heart conditions (such as heart failure, coronary artery disease, or cardiomyopathies)
- Mental health disorders limited to:
  - Mood disorders, including depression
  - Schizophrenia spectrum disorders
- Obesity (BMI ≥30 kg/m^2)*
- Pregnancy and recent pregnancy
- Smoking, current and former
- Tuberculosis

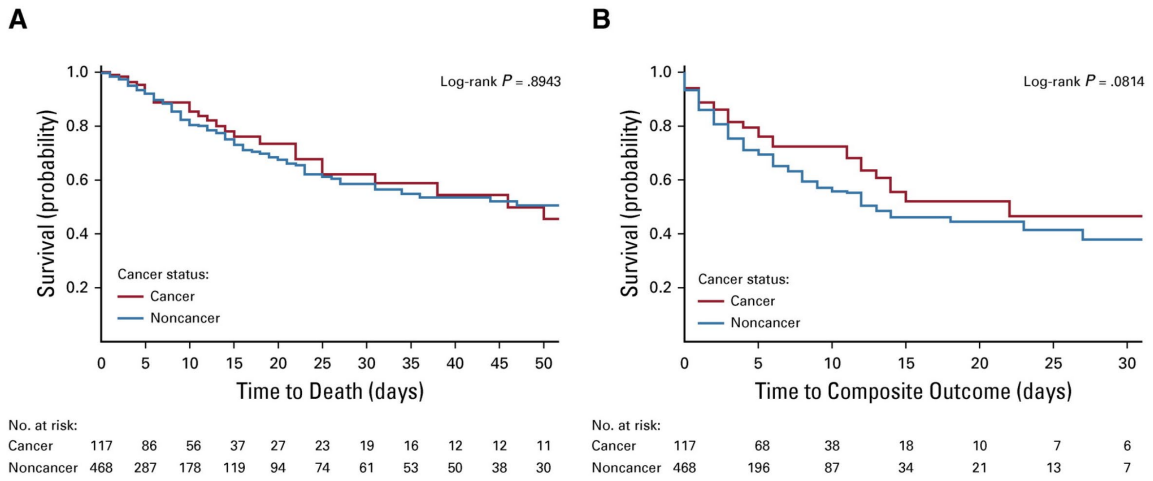
Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19: Information for Healthcare Providers (cdc.gov)

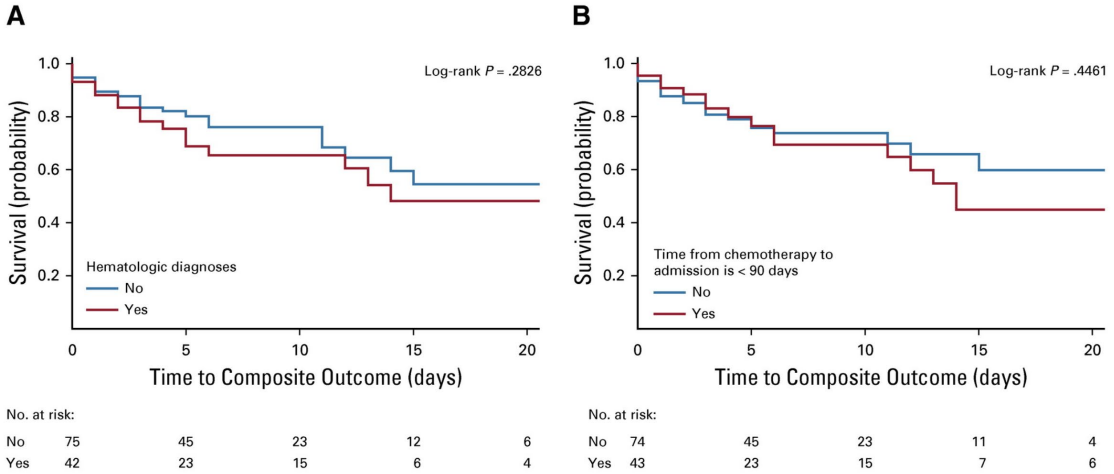
COVID-19 outcomes cancer patients

Title	Journal	Published	Findings
A systematic review and meta-analysis: the effect of active cancer treatment on severity of COVID-19	European Journal of Cancer	December 2020	Chemotherapy within the last thirty days before COVID-19 diagnosis increased the risk of death in cancer patients after adjusting for confounding variables (OR: 1.85; 95% confidence interval: 1.26–2.71)
A Systematic Review and Meta-Analysis of Cancer Patients Affected by a Novel Coronavirus	JNCI Cancer Spectrum	April 2021	38 studies and meta-analysis of 181 323 patients from 26 studies included 23 736 cancer patients. Cancer patients with COVID-19 have a higher likelihood of death (n = 165 980, OR = 2.54, 95% confidence interval [CI] = 1.47 to 4.42)
Effect of Cancer on Clinical Outcomes of Patients With COVID-19: A Meta-Analysis of Patient Data	JCO Global Oncology	June 2020	32 studies involving 46,499 patients (1,776 patients with cancer). All-cause mortality was higher in patients with versus those without cancer (2,034 deaths; RR, 1.66; 95% CI, 1.33 to 2.07; P < .0001; 8 studies with 37,807 patients). patients > 65 years of age, all-cause mortality was comparable between those with versus without cancer
Association of active oncologic treatment and risk of death in cancer patients with COVID-19: a systematic review and meta-analysis of patient data	Acta Oncologica	October 2020	Sixteen retrospective and prospective studies (3558 patients) were included in the meta-analysis. Active chemotherapy was associated with higher risk of death compared to no active chemotherapy (OR, 1.60, 95% CI, 1.14–2.23).
The risk and prognosis of COVID-19 infection in cancer patients: A systematic review and meta-analysis	Hematology/Oncology and Stem Cell Therapy	July 2020	22 studies (1018 cancer patients). The double-arm analysis showed that cancer patients had a higher risk of mortality (odds ratio [OR] = 3.23, 95% CI: 1.71–6.13)
Effects of cancer on patients with COVID-19: a systematic review and meta-analysis of 63,019 participants	Cancer Biology & Medicine	February 2021	19 retrospective studies involving 63,019 patients (2,682 patients with cancer). Mortality rate of lung cancer patients was higher than that of patients without lung cancer (RR: 1.8, 95% CI: 0.85–3.80, P = 0.02)
Immunotherapy or other anti-cancer treatments and risk of exacerbation and mortality in cancer patients with COVID-19: a systematic review and meta-analysis	Oncoimmunology	July 2020	17 studies comprising 3581 cancer patients with COVID-19. SARS-CoV-2-infected cancer patients who recently received anti-cancer treatment did not observe a higher risk of exacerbation and mortality (All p-value >0.05). Chemotherapy within 28 d increased the risk of death events (OR 1.45, 95% CI 1.10–1.91, P = .008

COVID-19 outcomes cancer patients

- Cancer patients matched 1:4 to controls without cancer
- 585 COVID-19 positives, 117 had active malignancy
- ~50% of patients with cancer were receiving therapy
- 45% of patients received cytotoxic or immunosuppressive treatment within 90 days of admission
- No statistically significant differences in morbidity or mortality (P = .894) between patients with and without cancer

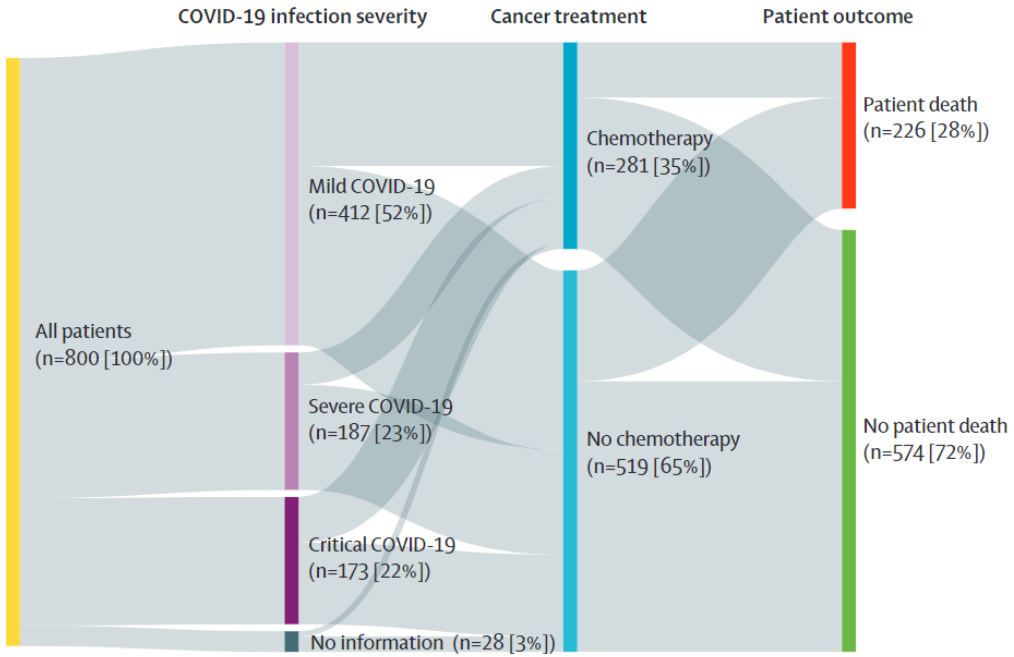




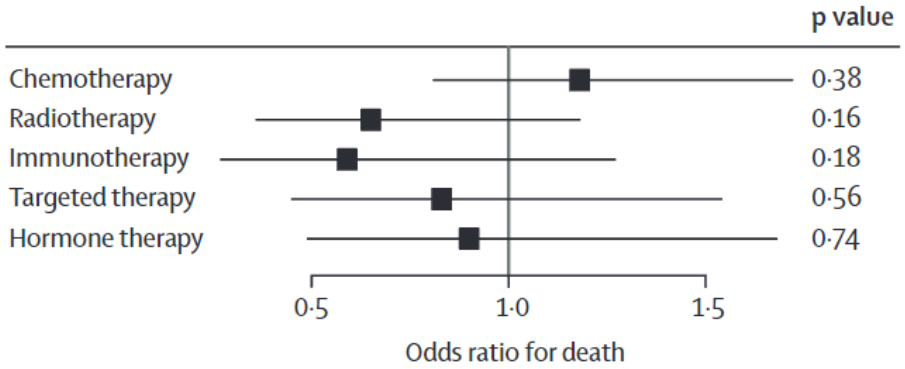
DOI: 10.1200/JCO.20.01580 Journal of Clinical Oncology 38, no. 33 (November 20, 2020) 3914-3924.

COVID-19 outcomes cancer patients

- UK Coronavirus Cancer Monitoring Project (UKCCMP)
- March 18, to April 26, 2020, 800 patients with a diagnosis of cancer and symptomatic COVID-19
- Chemotherapy in the past 4 weeks had no significant effect on mortality from COVID-19 disease
- No significant effect on mortality for patients with immunotherapy, hormonal therapy, targeted therapy, radiotherapy use within the past 4 weeks



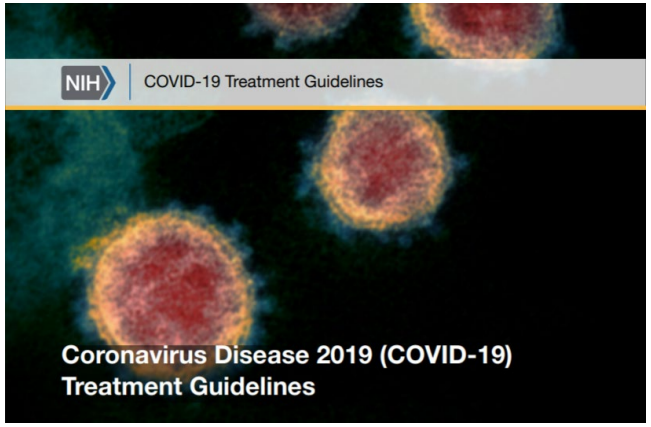
Relationship of chemotherapy use within 4 weeks of confirmed COVID-19 and mortality and severity of disease course

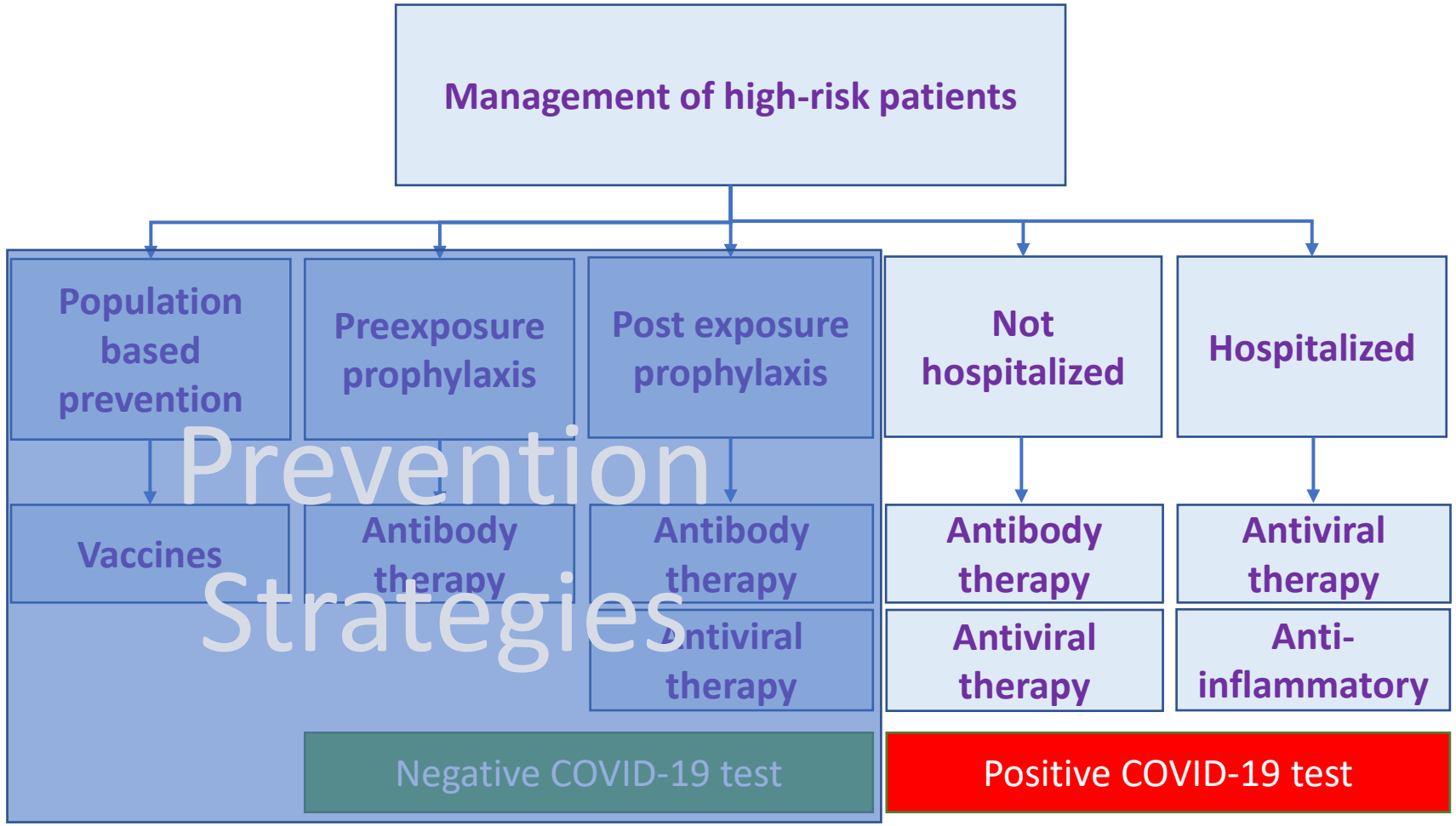


Forest plots showing effect of anticancer treatments and mortality from COVID-19

Lancet 2020; 395: 1919–26Published OnlineMay 28, 2020https://doi.org/10.1016/S0140-6736(20)31173-9

Management strategies



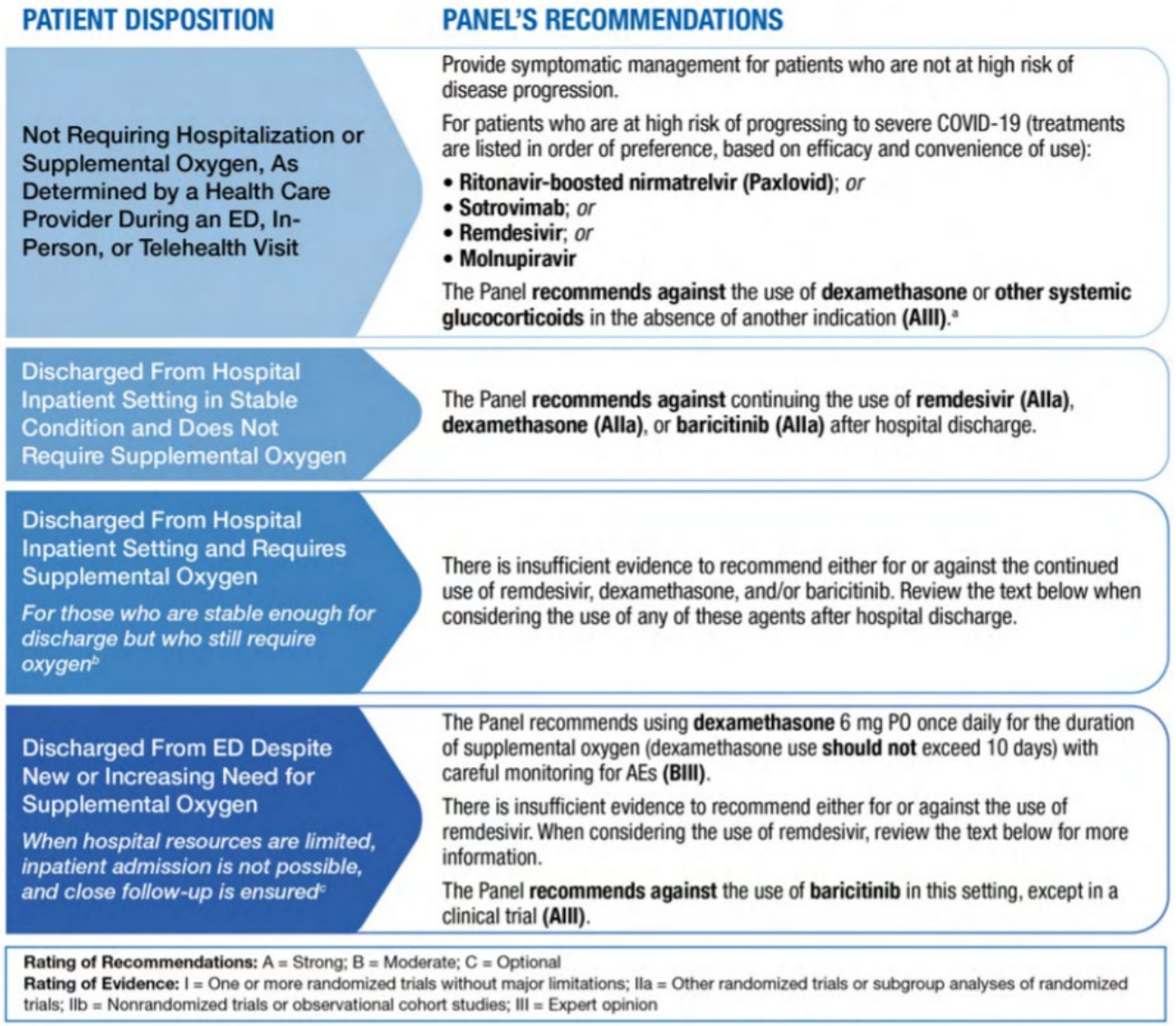


https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/whats-new/

Nonhospitalized patients

Treatment of nonhospitalized adults with laboratory-confirmed SARS-CoV-2

- Ritonavir-boosted nirmatrelvir (Paxlovid) reduced the risk of hospitalization or death by 88% compared to placebo **[EPIC-HR trial]**
- Sotrovimab demonstrated 85% relative reduction **[COMET-ICE trial]**
- Remdesivir demonstrated 87% relative reduction **[PINETREE trial]**
- Molnupiravir demonstrated 30% relative reduction **[MOVe-OUT trial]**



PATIENT DISPOSITION	PANEL'S RECOMMENDATIONS
Not Requiring Hospitalization or Supplemental Oxygen, As Determined by a Health Care Provider During an ED, In-Person, or Telehealth Visit	Provide symptomatic management for patients who are not at high risk of disease progression. For patients who are at high risk of progressing to severe COVID-19 (treatments are listed in order of preference, based on efficacy and convenience of use): • **Ritonavir-boosted nirmatrelvir (Paxlovid)**; *or* • **Sotrovimab**; *or* • **Remdesivir**; *or* • **Molnupiravir** The Panel **recommends against** the use of **dexamethasone** or **other systemic glucocorticoids** in the absence of another indication **(AIII)**.[a]
Discharged From Hospital Inpatient Setting in Stable Condition and Does Not Require Supplemental Oxygen	The Panel **recommends against** continuing the use of **remdesivir (AIIa)**, **dexamethasone (AIIa)**, or **baricitinib (AIIa)** after hospital discharge.
Discharged From Hospital Inpatient Setting and Requires Supplemental Oxygen *For those who are stable enough for discharge but who still require oxygen*[b]	There is insufficient evidence to recommend either for or against the continued use of remdesivir, dexamethasone, and/or baricitinib. Review the text below when considering the use of any of these agents after hospital discharge.
Discharged From ED Despite New or Increasing Need for Supplemental Oxygen *When hospital resources are limited, inpatient admission is not possible, and close follow-up is ensured*[c]	The Panel recommends using **dexamethasone** 6 mg PO once daily for the duration of supplemental oxygen (dexamethasone use **should not** exceed 10 days) with careful monitoring for AEs **(BIII)**. There is insufficient evidence to recommend either for or against the use of remdesivir. When considering the use of remdesivir, review the text below for more information. The Panel **recommends against** the use of **baricitinib** in this setting, except in a clinical trial **(AIII)**.

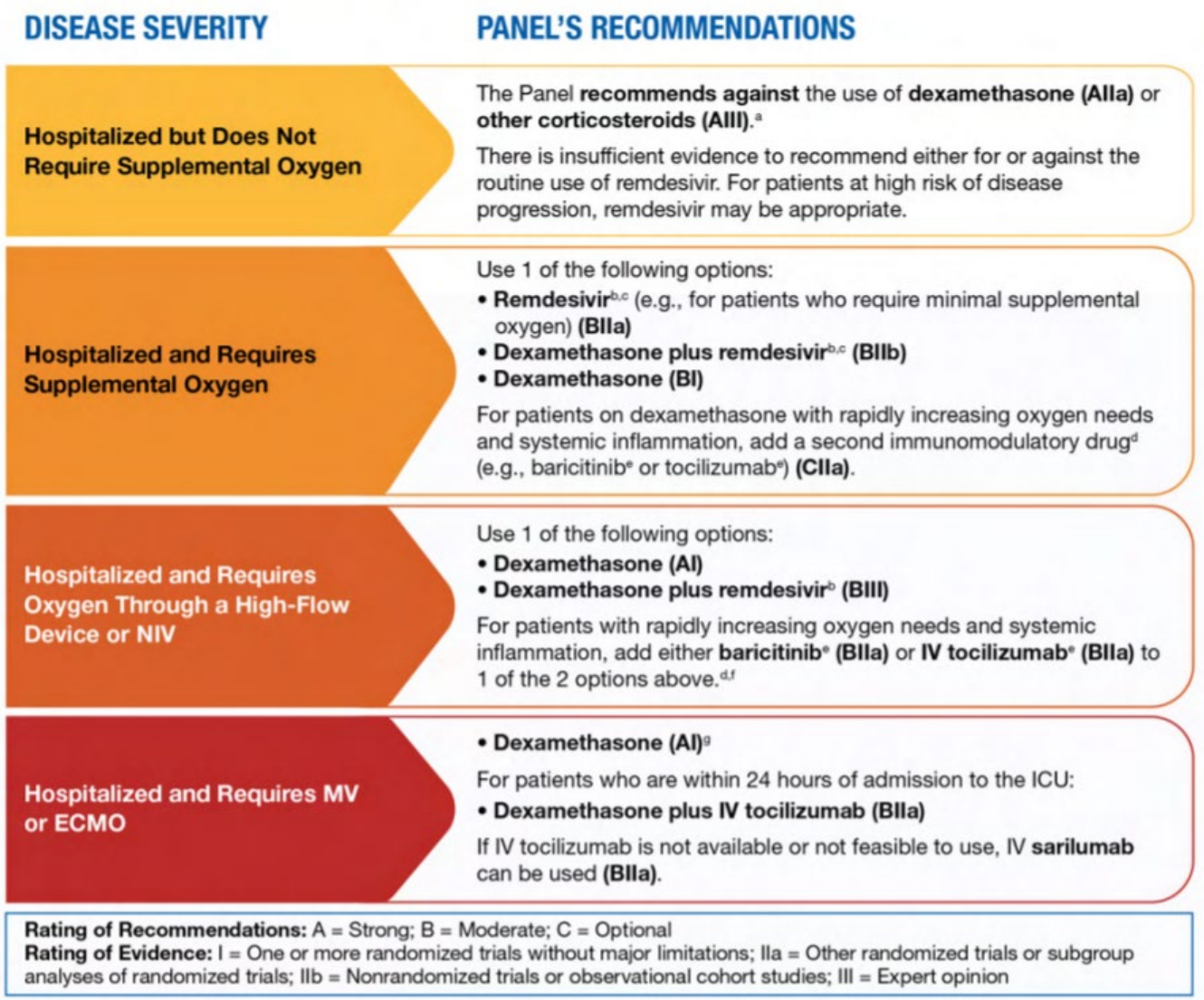
Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

*All outpatients withCOVID-19 patients who enter the healthcare system should have in-person or telehealth follow-up visit. Symptomatic treatments, including hydration, antipyretics , analgesics, and antitussives can be initiated as needed.

Hospitalized patients

Assess severity of illness

- Fewer participants in the dexamethasone arm than in the standard of care arm died within 28 days of enrollment (23.3% vs. 26.2%; rate ratio 0.82; 95% CI, 0.72–0.94). **[RECOVERY trial]**
- Fewer patients in the Remdesivir arm than in the placebo arm progressed to requiring high-flow oxygen, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) (17% vs. 24%) **[ACTT-1 trial]**



DISEASE SEVERITY	PANEL'S RECOMMENDATIONS
Hospitalized but Does Not Require Supplemental Oxygen	The Panel **recommends against** the use of **dexamethasone (AIIa)** or **other corticosteroids (AIII)**.[a] There is insufficient evidence to recommend either for or against the routine use of remdesivir. For patients at high risk of disease progression, remdesivir may be appropriate.
Hospitalized and Requires Supplemental Oxygen	Use 1 of the following options: • **Remdesivir**[b,c] (e.g., for patients who require minimal supplemental oxygen) **(BIIa)** • **Dexamethasone plus remdesivir**[b,c] **(BIIb)** • **Dexamethasone (BI)** For patients on dexamethasone with rapidly increasing oxygen needs and systemic inflammation, add a second immunomodulatory drug[d] (e.g., baricitinib[e] or tocilizumab[e]) **(CIIa)**.
Hospitalized and Requires Oxygen Through a High-Flow Device or NIV	Use 1 of the following options: • **Dexamethasone (AI)** • **Dexamethasone plus remdesivir**[b] **(BIII)** For patients with rapidly increasing oxygen needs and systemic inflammation, add either **baricitinib**[e] **(BIIa)** or **IV tocilizumab**[e] **(BIIa)** to 1 of the 2 options above.[d,f]
Hospitalized and Requires MV or ECMO	• **Dexamethasone (AI)**[g] For patients who are within 24 hours of admission to the ICU: • **Dexamethasone plus IV tocilizumab (BIIa)** If IV tocilizumab is not available or not feasible to use, IV **sarilumab** can be used **(BIIa)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

*In a post hoc analysis of deaths by Day 29, Remdesivir appeared to confer a substantial survival benefit in this subgroup (HR for death 0.30; 95% CI, 0.14–0.64)

Hospitalized patients

Rationale for Adding a Second Immunomodulatory Drug to Dexamethasone in Certain Hospitalized Patients

- REMAP-CAP trial (Sarilumab)
- COV-BARRIER trial and ACTT-2 trial (Baricitinib)
- STOP-COVID (Tofacitinib)
- EMPACTA, COVACTA, BACC Bay Tocilizumab, RCT-TCZ-COVID-19, and CORIMUNO-TOCI-1 trials (Tocilizumab)

Drug Name	Dosing Regimen	Comments
Remdesivir	RDV 200 mg IV once, then RDV 100 mg IV once daily for 4 days or until hospital discharge.	• If the patient progresses to more severe illness, complete the course of RDV. • For a discussion on using RDV in patients with renal insufficiency, see Remdesivir.
Dexamethasone	DEX 6 mg IV or PO once daily for up to 10 days or until hospital discharge.	• If DEX is not available, an equivalent dose of another corticosteroid may be used. • For more information, see Corticosteroids.
Baricitinib	Baricitinib dose is dependent on eGFR; duration of therapy is up to 14 days or until hospital discharge.	• eGFR ≥60 mL/min/1.73 m^2: Baricitinib 4 mg PO once daily • eGFR 30 to <60 mL/min/1.73 m^2: Baricitinib 2 mg PO once daily • eGFR 15 to <30 mL/min/1.73 m^2: Baricitinib 1 mg PO once daily • eGFR <15 mL/min/1.73 m^2: Baricitinib **is not recommended**.
Tofacitinib	Tofacitinib 10 mg PO twice daily for up to 14 days or until hospital discharge.	• Use as an alternative immunomodulatory drug if baricitinib is not available or not feasible to use **(BIIa)**. • eGFR <60 mL/min/1.73 m^2: Tofacitinib 5 mg PO twice daily
Tocilizumab	Tocilizumab 8 mg/kg actual body weight (up to 800 mg) administered as a single IV dose.	• In clinical trials, a third of the participants received a second dose of tocilizumab 8 hours after the first dose if no clinical improvement was observed.
Sarilumab	Use the single-dose, prefilled syringe (**not** the prefilled pen) for SQ injection. Reconstitute sarilumab 400 mg in 100 cc 0.9% NaCl and administer as an IV infusion over 1 hour.	• Use as an alternative immunomodulatory drug if tocilizumab is not available or not feasible to use **(BIIa)**. • In the United States, the currently approved route of administration for sarilumab is SQ injection. In the REMAP-CAP trial, the SQ formulation was used to prepare the IV infusion.

Prevention: PEP

Post exposure prophylaxis (PEP) in nonhospitalized adults with laboratory-confirmed SARS-CoV-2

- **Bamlanivimab 700 mg plus etesevimab 1,400 mg** associated with lower incidence of mild or worse COVID-19 than in the placebo arm (8.5% vs. 15.2%; OR 0.43; 95% CI, 0.28–0.68; P < 0.001), with an absolute risk difference of -6.6 percentage points (95% CI, -10.7 to -2.6).[BLAZE-2 trial]
- **Casirivimab 600 mg plus imdevimab 600** mg was associated with a significant reduction in risk compared to placebo (66.4% risk reduction; 36 of 753 participants [4.8%] vs. 107 of 752 participants [14.2%]; OR 0.31; 95% CI, 0.21–0.46; P < 0.0001).[COMET-ICE trial]

Summary Recommendations
• The COVID-19 Treatment Guidelines Panel (the Panel) recommends COVID-19 vaccination for everyone who is eligible according to the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices **(AI)**. • The Panel recommends using 1 of the following anti-SARS-CoV-2 monoclonal antibodies (listed alphabetically) as post-exposure prophylaxis (PEP) for people who are at high risk of progressing to severe COVID-19 if infected with SARS-CoV-2 **AND** who have the vaccination status **AND** exposure history outlined in the text below: • **Bamlanivimab 700 mg plus etesevimab 1,400 mg** administered as an intravenous (IV) infusion **(BIII)**; *or* • **Casirivimab 600 mg plus imdevimab 600 mg** administered as subcutaneous injections **(AI)** or an IV infusion **(BIII)**. • The Panel **recommends against** the use of **hydroxychloroquine** for SARS-CoV-2 PEP **(AI)**. • The Panel **recommends against** the use of other drugs for SARS-CoV-2 PEP, except in a clinical trial **(AIII)**. • The Panel **recommends against** the use of any drugs for SARS-CoV-2 pre-exposure prophylaxis (PrEP), except in a clinical trial **(AIII)**.
Rating of Recommendations: A = Strong; B = Moderate; C = Optional **Rating of Evidence:** I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

Prevention: PrEP

Pre-exposure prophylaxis in nonhospitalized adults

- Tixagevimab Plus Cilgavimab (Evusheld) for Pre-Exposure Prophylaxis for SARS-CoV-2 Infection. **77% reduction** in the incidence of RT PCR-confirmed symptomatic SARS-CoV-2 infection in the tixagevimab plus cilgavimab arm (95% CI, 46% to 90%; P < 0.001) **[PROVENT] trial**
- SARS-CoV-2 PrEP for adults and adolescents (aged ≥12 years and weighing ≥40 kg) who do not have SARS-CoV-2 infection, who have not been recently exposed to an individual with SARS-CoV-2 infection, AND who:

•Are moderately to severely immunocompromised and may have an inadequate immune response to COVID-19 vaccination (BIIa); or

• Are not able to be fully vaccinated with any available COVID-19 vaccines due to a documented history of severe adverse reactions to a COVID-19 vaccine or any of its components (AIIa).

- Single dose may be effective for pre-exposure prevention for six months

The individuals who qualify as having moderate to severe immunocompromising conditions under this EUA are those who:

• **Are receiving active treatment for solid tumors and hematologic malignancies.**

• Received a solid organ transplant and are taking immunosuppressive therapy.

• **Received a chimeric antigen receptor T cell therapy or a hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy).**

• Have a moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome).

• Have advanced or untreated HIV infection (defined as people with HIV and low CD4 T lymphocyte cell counts)

Prevention: Vaccines

- Cancer patients on active treatment should receive primary series of three doses of mRNA COVID-19 vaccine
- All patients should be strongly encouraged to receive a booster dose

Eligible For	IF YOU RECEIVED Pfizer-BioNTech	IF YOU RECEIVED Moderna	IF YOU RECEIVED Johnson & Johnson's Janssen
Additional Primary Shot	People **age 5+** who are moderately or severely immunocompromised **should** get an additional primary shot of Pfizer-BioNTech COVID-19 vaccine Given 28 days after 2nd shot	People age 18+ who are moderately or severely immunocompromised **should** get an additional primary shot of Moderna COVID-19 vaccine Given 28 days after 2nd shot	No additional primary shot is recommended at this time
Booster Shot	• Teens **ages 12–17** should only get a Pfizer-BioNTech COVID-19 vaccine booster shot • People **age 18+** should get a booster shot of either Pfizer-BioNTech or Moderna (mRNA COVID-19 vaccines) in most situations Given 5 months after additional primary shot	People **age 18+** should get a booster shot of either Pfizer-BioNTech or Moderna (mRNA COVID-19 vaccines) in most situations Given 5 months after additional primary shot	People **age 18+** should get a booster shot of either Pfizer-BioNTech or Moderna (mRNA COVID-19 vaccines) in most situations Given 2 months after 1st shot

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/immuno.html

Vaccine effectiveness in cancer patients

- 20,101 immunocompromised adults (10,564 [53%] of whom were fully vaccinated) and 69,116 immunocompetent adults (29,456 [43%] of whom were fully vaccinated).
- Effectiveness of mRNA vaccination against laboratory-confirmed COVID-19–associated hospitalization was lower **(77%)** among immunocompromised adults than among immunocompetent adults **(90%).**
- Vaccine effectiveness varied considerably among immunocompromised patient subgroups.

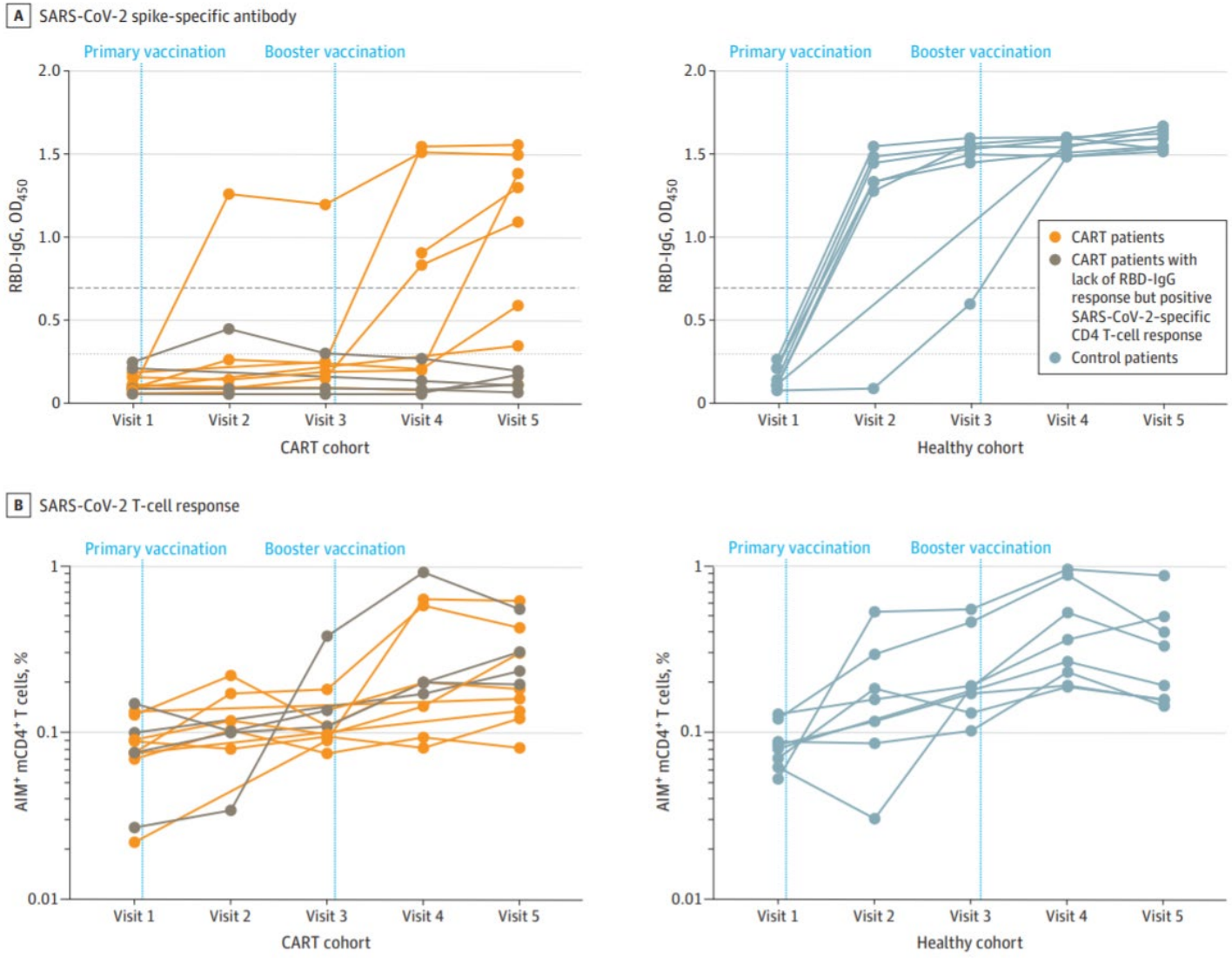
TABLE 3. Two-dose mRNA COVID-19 vaccine effectiveness* against laboratory-confirmed COVID-19–associated hospitalization† among subgroups of adults aged ≥18 years with specific types of conditions and presumed to be immunocompromised (20,101)§ — nine states,¶ January–September 2021

Condition (no. of adults)	Total	SARS-CoV-2–positive tests, no. (row %)	VE,** % (95% CI)
Solid malignancy†† (8,887)			
Unvaccinated	3,986	304 (7.6)	Ref
Vaccinated with any 2 mRNA vaccine doses§§	4,901	106 (2.2)	79 (73–84)
Vaccinated with 2 Moderna (mRNA-1273) vaccine doses§§	2,053	30 (1.5)	85 (76–91)
Vaccinated with 2 Pfizer-BioNTech (BNT162b2) vaccine doses§§	2,848	76 (2.7)	72 (62–80)
Hematologic malignancy¶¶ (2,790)			
Unvaccinated	1,156	130 (11.2)	Ref
Vaccinated with any 2 mRNA vaccine doses§§	1,634	86 (5.3)	74 (62–83)
Vaccinated with 2 Moderna vaccine doses§§	660	26 (3.9)	85 (74–92)
Vaccinated with 2 Pfizer-BioNTech vaccine doses§§	974	60 (6.2)	62 (42–75)
Rheumatologic or inflammatory disorder*** (5,024)			
Unvaccinated	2,380	383 (16.1)	Ref
Vaccinated with any 2 mRNA vaccine doses§§	2,644	123 (4.6)	81 (75–86)
Vaccinated with 2 Moderna vaccine doses§§	1,053	48 (4.6)	78 (65–86)
Vaccinated with 2 Pfizer-BioNTech vaccine doses§§	1,591	75 (4.7)	78 (69–84)
Other intrinsic immune condition or immunodeficiency††† (6,380)			
Unvaccinated	3,418	429 (12.6)	Ref
Vaccinated with any 2 mRNA vaccine doses§§	2,962	137 (4.6)	73 (66–80)
Vaccinated with 2 Moderna vaccine doses§§	1,199	42 (3.5)	81 (71–87)
Vaccinated with 2 Pfizer-BioNTech vaccine doses§§	1,763	95 (5.4)	64 (50–74)
Organ or stem cell transplant§§§ (1,416)			
Unvaccinated	607	92 (15.2)	Ref
Vaccinated with any 2 mRNA vaccine doses§§	809	80 (9.9)	59 (38–73)
Vaccinated with 2 Moderna vaccine doses§§	337	31 (9.2)	70 (46–83)
Vaccinated with 2 Pfizer-BioNTech vaccine doses§§	472	49 (10.4)	45 (13–66)

MMWR Weekly / November 5, 2021 / 70(44);1553–1559

Vaccine effectiveness in cancer patients

- Enrolled 12 patients who achieved complete remission after receiving CAR T-cell treatments (CART) that targeted either the CD19 antigen (7 patients) or the CD19 and CD22 combination (5 patients)
- Eight healthy adults were enrolled as controls.
- Immune responses to SARS-CoV-2 mRNA vaccines are induced for the majority of patients who have been treated with CAR T-cell therapies targeting B-cell lineage antigens.



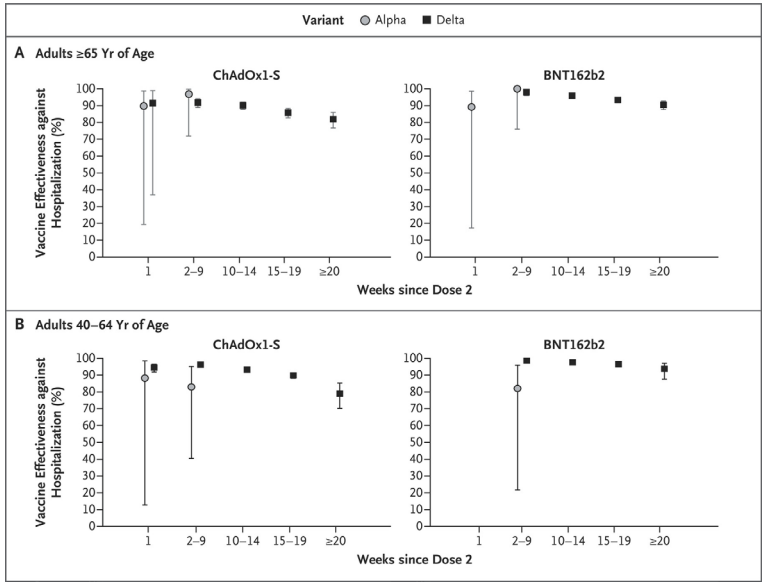
JAMA Oncol. 2022;8(1):164-167. doi:10.1001/jamaoncol.2021.6030

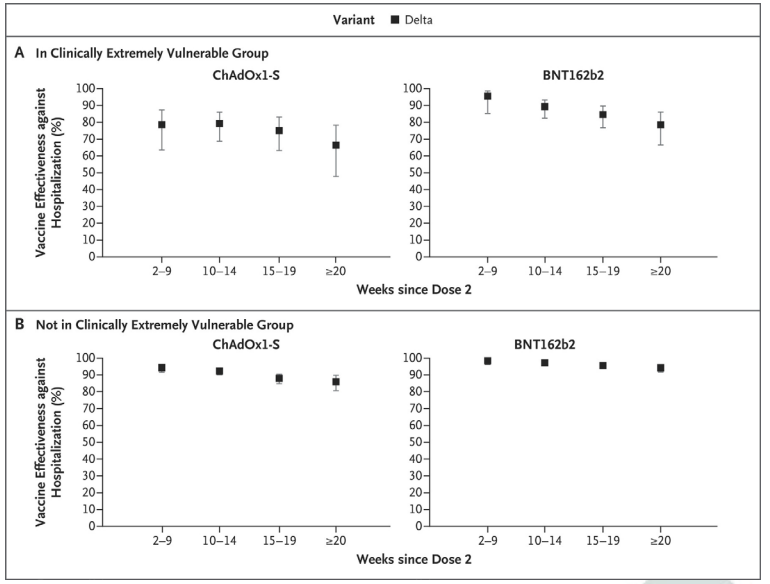
Vaccine Effectiveness against Covid-19–Related Hospitalization

- Limited waning in vaccine effectiveness against Covid-19–related hospitalization and death at 20 weeks or more after vaccination with two doses of the ChAdOx1-S or BNT162b2 vaccine

Table 3. Vaccine Effectiveness against Delta Variant–Related Death among Persons in England Who Received Two Doses of the ChAdOx1-S or BNT162b2 Vaccine, According to Weeks since Receipt of the Second Dose.

Vaccine and Age Group	Vaccine Effectiveness (95% CI)			
	2–9 Wk	10–14 Wk	15–19 Wk	≥20 Wk
	percent			
ChAdOx1-S				
≥16 Yr	95.0 (93.1–96.4)	93.7 (91.8–95.2)	90.1 (86.9–92.6)	84.8 (76.2–90.3)
≥65 Yr	94.1 (89.6–96.7)	92.9 (89.5–95.2)	87.9 (82.6–91.5)	82.1 (70.1–89.3)
BNT162b2				
≥16 Yr	98.5 (96.5–99.3)	96.0 (94.2–97.2)	94.5 (92.5–96.0)	91.9 (88.5–94.3)
≥65 Yr	97.1 (91.7–99.0)	95.1 (92.1–96.9)	93.2 (90.1–95.4)	90.2 (85.3–93.5)





January 27, 2022 N Engl J Med 2022; 386:340-350
DOI: 10.1056/NEJMoa2115481

Future Direction: PASC (Long COVID) and cancer survivorship

RECOVER
Researching COVID to Enhance Recovery

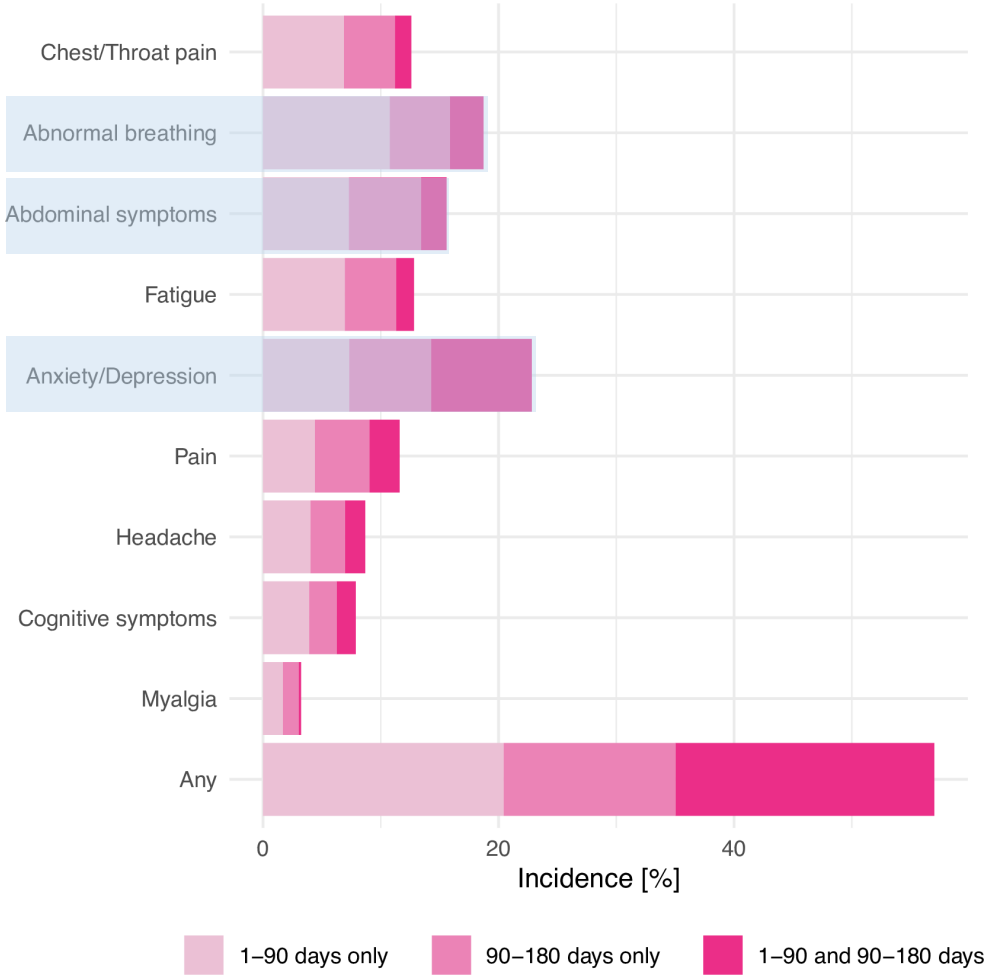
- RECOVER, a research initiative from the National Institutes of Health (NIH), seeks to understand, prevent, and treat PASC, including Long COVID.
- PASC (post-acute sequelae of SARS-CoV-2) is a term used to study the potential consequences of a SARS-CoV-2 infection.

https://recovercovid.org/

Incidence of long-COVID features

- Retrospective cohort study based on linked electronic health records (EHRs) data from 81 million patients including 273,618 COVID-19 survivors
- Among COVID-19 survivors 57% had one or more long-COVID feature recorded during the whole 6-month period and 36.55% between 3 and 6 months.

- **XX.XX% in the 1- to 180-day period; XX.XX% in the 90- to 180-day period)**
- **anxiety/depression (22.82%; 15.49%)**
- **abnormal breathing (18.71%; 7.94%)**
- fatigue/malaise (12.82%; 5.87%)
- chest/throat pain (12.60%; 5.71%)
- headache (8.67%; 4.63%)
- other pain (11.60%; 7.19%)
- **abdominal symptoms (15.58%; 8.29%)**
- myalgia (3.24%; 1.54%)
- cognitive symptoms (7.88%; 3.95%)

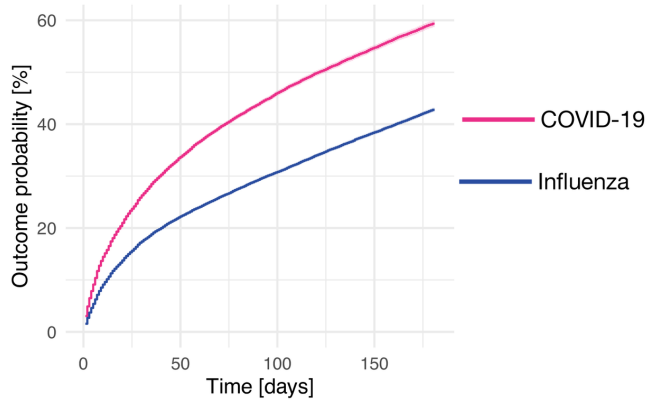


https://doi.org/10.1371/journal.pmed.1003773

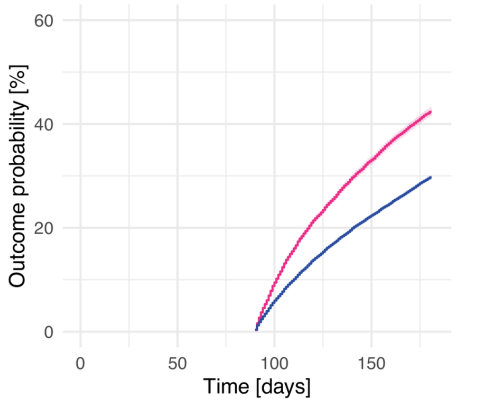
1-180 days follow-up

90-180 days follow-up

A **Any long-COVID feature** (HR 1.65, p<.0001)



B **Any long-COVID feature** (HR 1.56, p<.0001)



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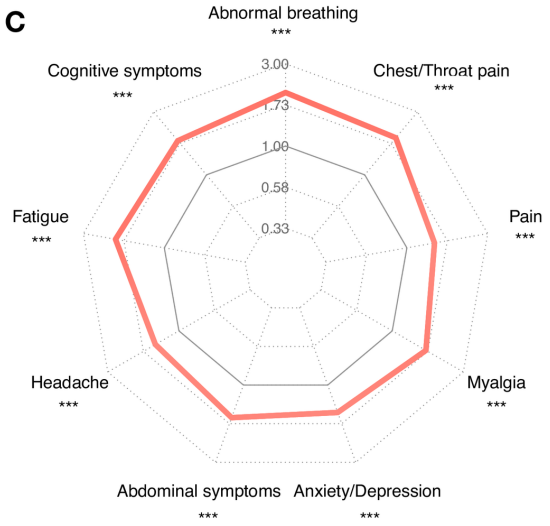

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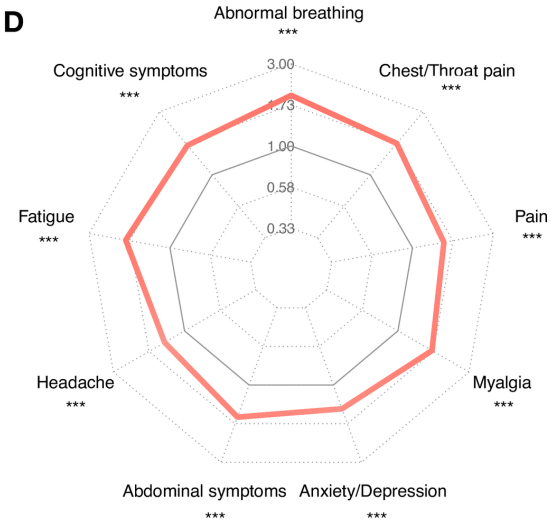
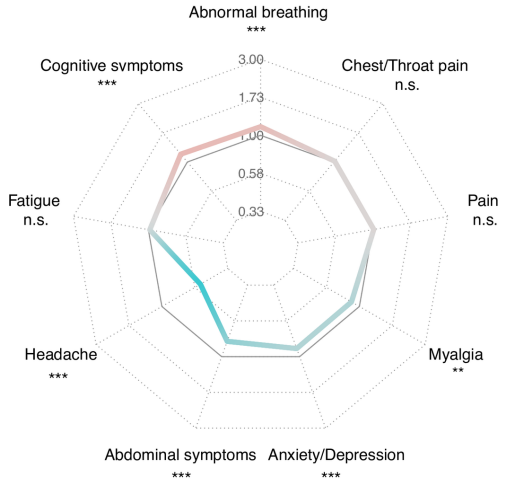
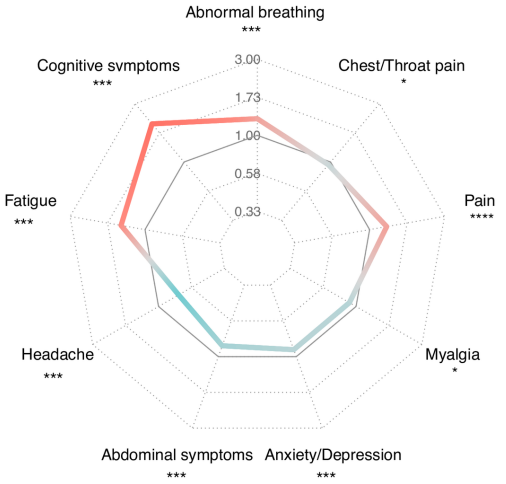


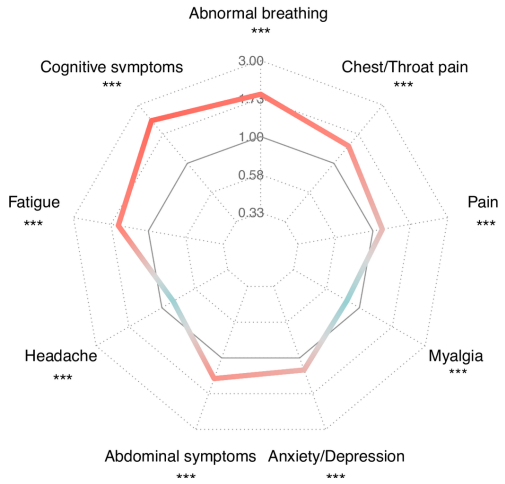
Male vs Female



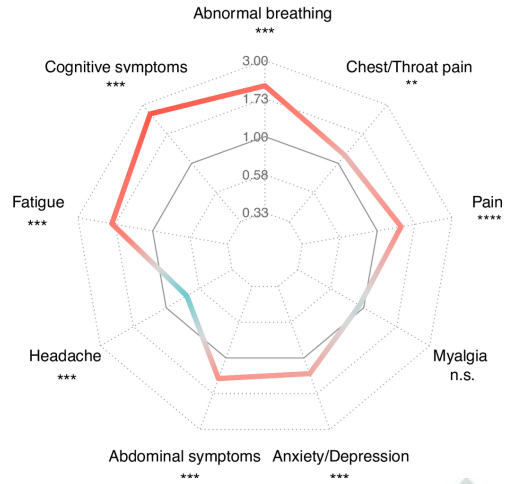
Age 45+ vs Age 10–44



Hospitalization vs No Hospitalization



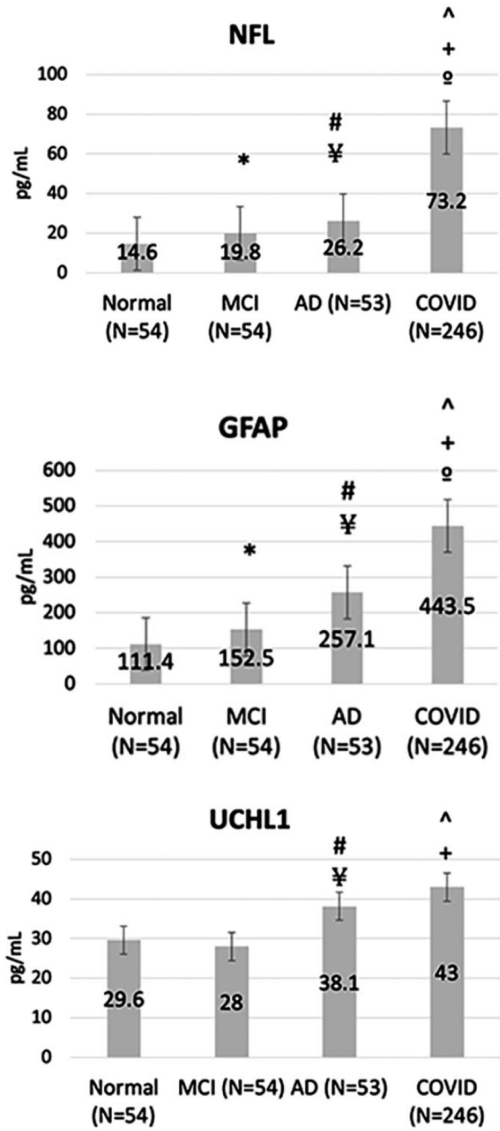
ITU admission vs No ITU admission



“Cognitive symptoms: Brain Fog”

Comparison of serum neurodegenerative biomarkers among hospitalized COVID-19 patients versus non-COVID subjects with normal cognition, mild cognitive impairment, or Alzheimer’s dementia

- Admission t-tau, p-tau181, glial fibrillary acidic protein (GFAP), neurofilament light chain (NfL), were significantly elevated inpatients with encephalopathy and in those who died in-hospital, while t-tau, GFAP, and NfL were significantly lower in those discharged home .
- NfL, GFAP, and ubiquitin carboxyterminal hydrolase L1 (UCHL1), were higher in COVID patients than in non-COVID controls with mild cognitive impairment (MCI), and Alzheimer’s disease (AD).
- Neurodegenerative biomarkers were elevated to levels observed in AD dementia and associated with encephalopathy and worse outcomes among hospitalized COVID-19 patients.



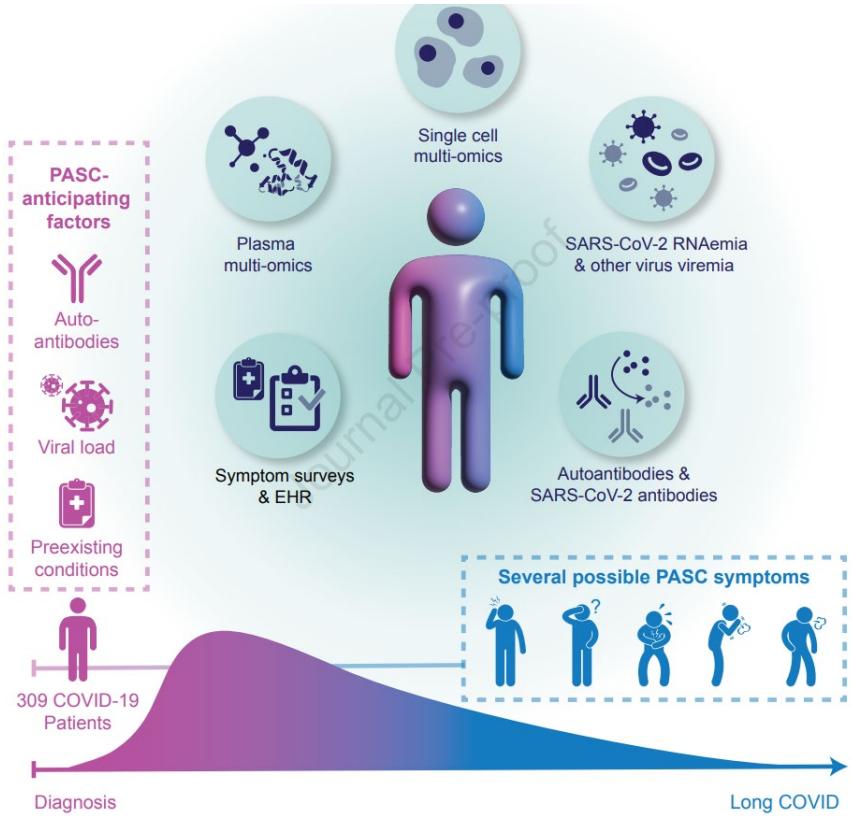
Alzheimer’s Dement.2021;1–12DOI:10.1002/alz.12556

Multiple Early Factors Anticipate Post-Acute COVID-19 Sequelae

Longitudinal investigation of 309 COVID-19 patients from initial diagnosis to convalescence (2-3 months 5 later), integrated with clinical data, and patient-reported symptoms

Four PASC-anticipating risk factors at the time of initial COVID-19 diagnosis were identified:

- **Type 2 diabetes**
- **SARS-CoV-2 RNAemia**
- **Epstein-Barr virus viremia**
- **Specific autoantibodies**



DOI: https://doi.org/10.1016/j.cell.2022.01.014

Long COVID in Cancer Patients

312 cancer patients with a median age of 57 years (18-86) at MD Anderson Cancer Center.

- The majority of patients had solid tumors (75%).
- Of the 312 patients, 188 (60%) reported long COVID-19 symptoms with a median duration of 7 months and up to 14 months after COVID-19 diagnosis.
- **A higher number of females reported a persistence of symptoms** compared to males (63% vs 37%; p=0.036)
- Fatigue (82%), sleep disturbances (78%), myalgias (67%) and gastrointestinal symptoms (61%), followed by headache, altered smell or taste, dyspnea (47%) and cough (46%)

2795 consecutive pts with COVID-19 and cancer registered to OnCovid between 01/2020 and 02/2021

- 1557 COVID-19 survivors, 234 (15%) reported sequelae including respiratory symptoms (49.6%), fatigue (41%) and cognitive/psychological dysfunction (4.3%)
- Persisting COVID-19 sequelae **were more likely found in males (p=0.0407)** aged ≥65 years (p=0.0489) with ≥2 comorbidities (p=0.0006) and positive smoking history (p=0.0004).
- Out of 473 patients who were on systemic anticancer therapy (SACT) at COVID-19 diagnosis; 62 (13.1%) permanently discontinued therapy and 75 (15.8%) received SACT adjustments, respectively.
- Discontinuations were due to worsening performance status (45.1%), disease progression (16.1%) and residual organ disfunction (6.3%). SACT adjustments were pursued to avoid hospital attendance (40%), prevent immunosuppression (57.3%) or adverse events (20.3%).
- Permanent discontinuation to be associated with an increased risk of death (HR 4.2, 95%CI: 1.62-10.7), whereas SACT adjustments did not adversely affect survival.

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Questions