OCTOBER 2022

COVID-19 Updates

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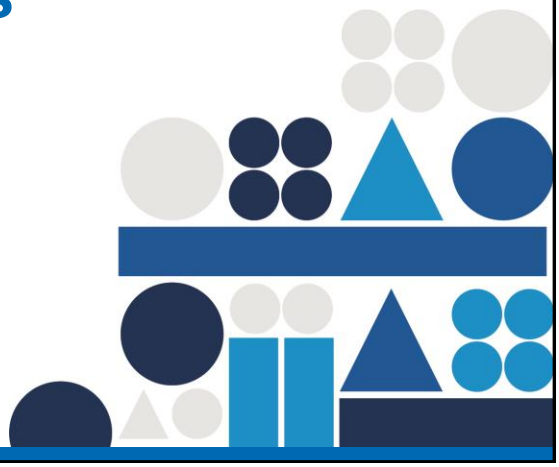

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Disclosures

Former consultant for Sequiris

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Objectives

By the end of this talk you should be able to:

1. Discuss the current epidemiology of SARS-CoV-2
2. Outline important similarities and differences between SARS-CoV-2 and influenza
3. Summarize testing and treatment guidelines
4. Understand current COVID-19 vaccination recommendations

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The current state of the pandemic

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"A marathon runner does not stop when the finish line comes into view. She runs harder, with all the energy she has left. So must we. We can see the finish line. We're in a winning position. But ***now is the worst time to stop running****"*

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Epidemiology and Clinical Characteristics of influenza and SARS-CoV-2

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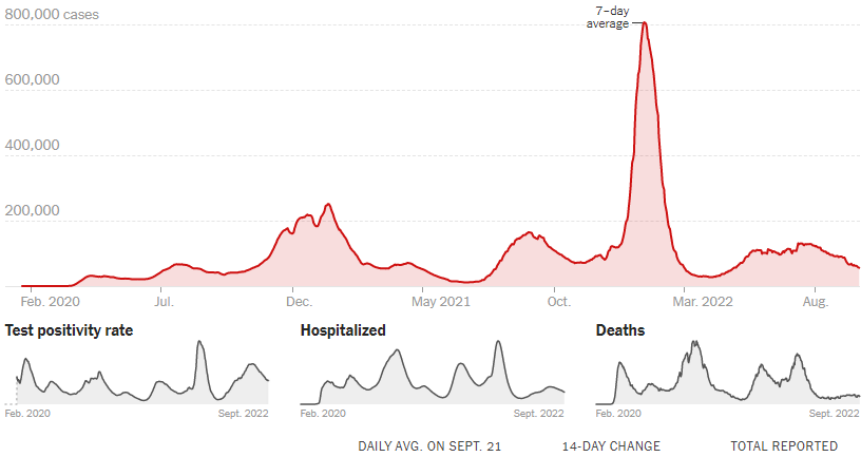
COVID in the US



Likely to be a gross underestimate given more at home testing not reported to states

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Source: New York Times Map and Case Count

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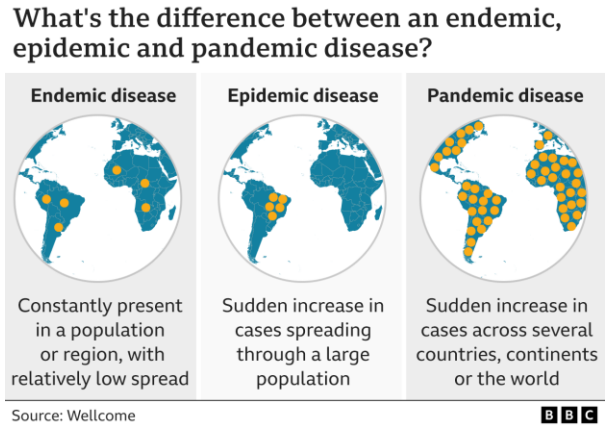
What is the future of the pandemic?

- Early phase of the pandemic, experts considered end once herd immunity was reached
- Persisted due to rapidly evolving variants
- Rather than being eliminated, SARS CoV2 will become endemic
- Difficult to predict when this shift will happen



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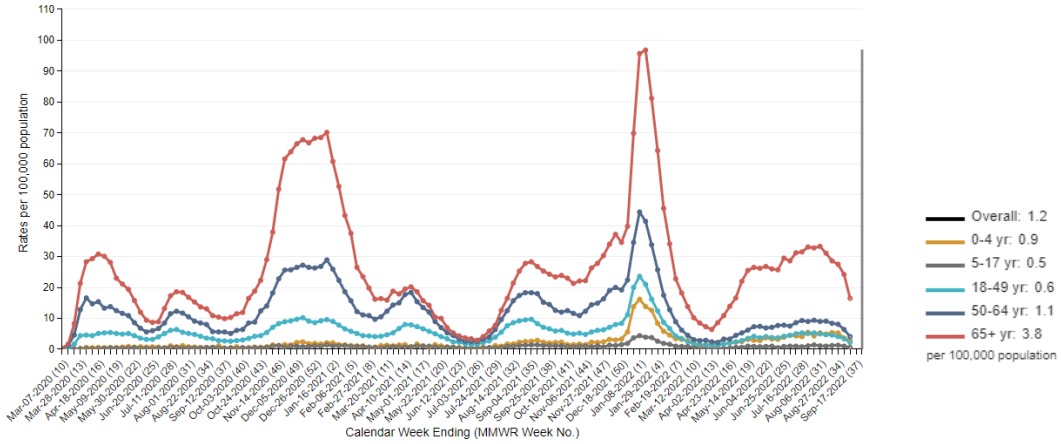
COVID-19 hospitalizations rates in the US



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https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html

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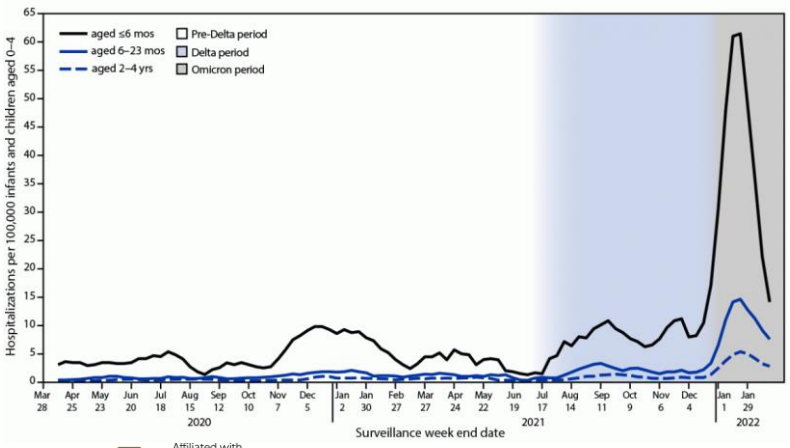
Hospitalization rates in infants and children



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Marks, MMWR Morb Mortal Wkly Rep 2022;71:429–436

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Shi et al. MMWR Morb Mortal Wkly Rep 2022;71:574-581

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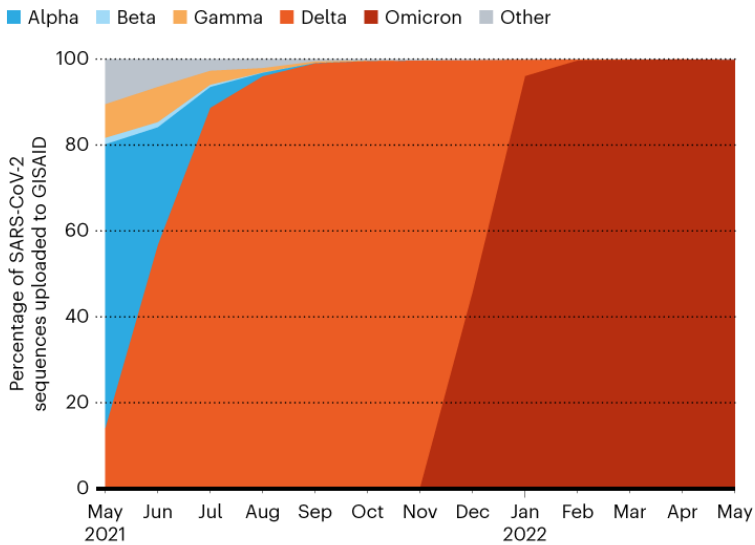
Variant Definitions

Classification	
Variant being monitored	α,β.γ,δ,ε,η,ι,κ,μ,ζ
Variant of interest	None currently
Variant of concern	Omicron B.1.1.529, BA.1, BA.1.1, BA.2, BA.3, BA.4 and BA.5
Variant of high consequence	None



©nature

https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-classifications.html

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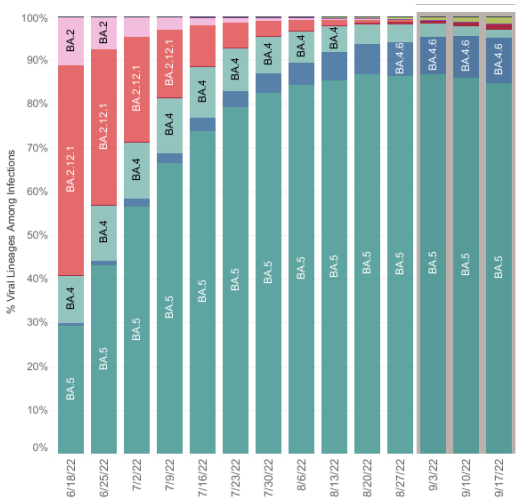
Current variants



- In US predominant variant BA.5
- BA.5 - growth and transmission advantage over BA.2.12.1 (additional spike mutation) and more severe disease in animal models
- BA.4/BA.5 4X more resistant to 3 vaccine doses, increasing risk of breakthrough infections
- BA.2.75 – first detected in India, more transmissible, greater concerns for immune escape (currently ~1.3%)

https://covid.cdc.gov/covid-data-tracker/#variant-proportions;
https://www.biorxiv.org/content/10.1101/2022.05.26.493539v1.full.pdf

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Clinical Characteristics

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High Risk medical conditions

Age	**> 65 years**
	Asthma, ILD, PE, bronchiectasis, pulmonary hypertension, bronchiectasis, COPD, CF, TB
	e.g. heart failure, coronary artery disease, or cardiomyopathies
	Cirrhosis, non-alcoholic fatty liver disease, alcoholic liver disease, autoimmune hepatitis, chronic kidney disease
	Diabetes type 1 and 2, **obesity**
	ADHD, CP, Congenital malformations, developmental disabilities, learning disabilities, spinal cord injuries, dementia, cerebrovascular disease
	**Primary immunodeficiencies**, **malignancy**, **SOT, HSCT HIV**, immunosuppressive medications
	Pregnancy and recent pregnancy

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Source: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html

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Persons at high risk for COVID-19

Race/ethnicity	Black/African American, American Indian/Alaska Native, Hispanic/Latinx
Mental Health Disorders	Mood disorders including depression, schizophrenia spectrum disorders
Behavioral factors	Physical inactivity Smoking, current and former
Medical complexity	**Medical complexity with technology dependence**

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https://www.cdc.gov/flu/highrisk/index.htm
https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html

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Risk for COVID-19 infection, hospitalization and death by race and ethnicity

Rate ratios compared to White, Non-Hispanic persons	American Indian or Alaska Native	Asian	Black or African American	Hispanic or Latinx persons
Cases	1.5x	0.8x	1.1x	1.5x
Hospitalization	3.0x	0.8x	2.3x	2.2x
Death	2.1x	0.8x	1.7x	1.8x

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Source: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html 18

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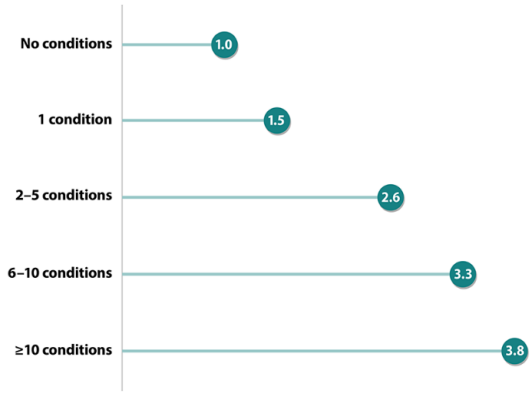
Death risk ratio for COVID-19 increases as number of comorbid conditions increases



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Kompaniyets L, Pennington AF, Goodman AB, Rosenblum HG, Belay B, Ko JY, et al. Underlying Medical Conditions and Severe Illness Among 540,667 Adults Hospitalized With COVID-19, March 2020–March 2021 19

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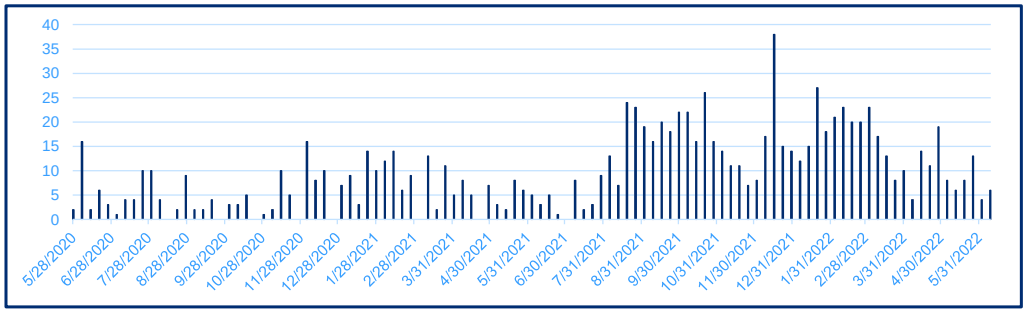
COVID-19 deaths in children



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https://downloads.aap.org/AAP/PDF/AAP%20and%20CHA%20-%20Children%20and%20COVID-19%20State%20Data%20Report%206.23.22%20FINAL.pdf?_ga=2.135341941.578427903.1656981628-255427512.1651171206

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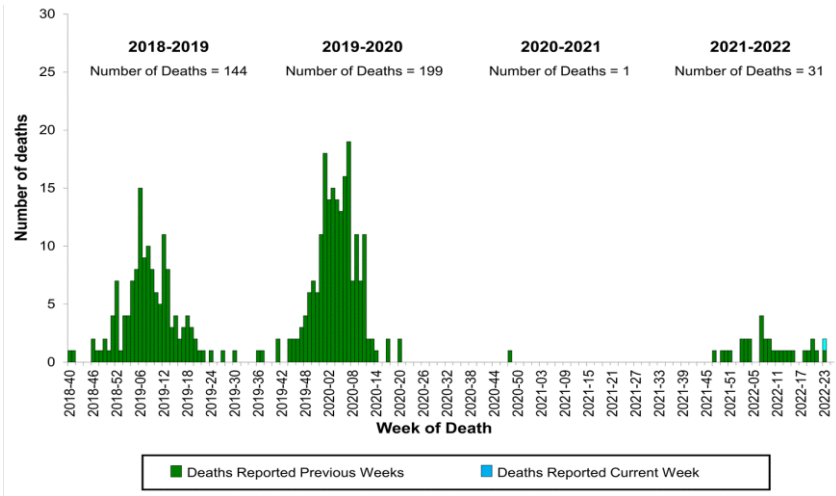
Influenza deaths in children



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https://www.cdc.gov/flu/weekly/index.htm

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Limited distinctive clinical characteristics- influenza vs COVID-19

	COVID-19	Influenza
Common symptoms	Fever (50%), non-productive cough (38%) most common	Fever, cough, rhinorrhea most common
Other symptoms	Muscle aches, nasal congestion, headache, loss of appetite, shortness of breath	Muscle aches, nasal congestion, headache, loss of appetite, shortness of breath
Loss of taste and smell	Loss of smell/Loss of taste highly associated	Loss of smell reported in influenza
Gastrointestinal symptoms	Abdominal pain, diarrhea, vomiting more common than flu	Nausea, vomiting and diarrhea more common in pre-school aged children

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Welge-Lussen, Adv Otorhinolaryngol 2006; CDC COVID-19 website; Song et al JAMA Network Open 2020 Sep 1;3(9):e2020495
Rao S et al. "Influenza" P, in: Kendig and Chernick's Disorders of the Respiratory Tract in Children, 9th Edition; AAP influenza Pedialink website

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Complications of COVID-19 and influenza in children

Influenza	COVID-19
Cytokine storm, cardiorespiratory failure, ARDS	Inflammatory response, cardiorespiratory failure, ARDS
	MIS-C
Myocarditis (cardiac symptoms in 5-10% of adults, less frequent in children)	Cardiac dysfunction, myocarditis (12.6-17.6 cases per 100,000), arrhythmias
DIC (1% hospitalized patients)	Thromboembolic events (2.1% of hospitalized children)
AKI (lower incidence, 25-30% overall)	AKI 12% to 44% of hospitalized children
Reye's syndrome, febrile seizures, encephalitis, acute necrotizing encephalitis, encephalopathy	Neurologic involvement 30% to 40% of hospitalizations- severe encephalopathy, stroke, demyelinating conditions, cerebral edema, and Guillain-Barré syndrome,
Secondary bacterial infection	Less commonly seen than in influenza

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Testing

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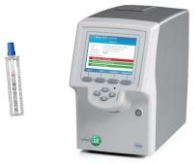
Testing



Point of care tests

PCR NAAT DIA RIDT

Decreasing sensitivity

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Source: Google images

Whom to test depends on how results will affect clinical management and public health considerations

- Turnaround time of tests
- Patient's illness severity
- Disease prevalence
- Availability of other ancillary test results
- Co-morbidities, risk factors
- Public health and infection control considerations
- Duration of symptoms
- Types of testing available

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Hanson et al CID 2020
Rao S. Curr Opin Infect Dis. 2014 Aug;27(4):342-7

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Whom to test depends on how results will affect clinical management and public health considerations

- Turnaround time of tests
- Patient's illness severity
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- Availability of other ancillary test results
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- **Public health and infection control considerations**
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Hanson et al CID 2020
Rao S. Curr Opin Infect Dis. 2014 Aug;27(4):342-7

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COVID-19 – Antigen testing

- Cochrane review
- 64 studies Europe and North America, 24,087 nose or throat samples
- 16 antigen tests and five molecular tests
- Antigen test- identified COVID-19 infection in an average of 72% symptomatic and 58% of asymptomatic people
- Most accurate - first week after symptoms first developed (78% detection)
- In test negative, antigen tests correctly ruled out infection in 99.5% of people with symptoms and 98.9% of people without symptoms

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Dinnes J et al. Cochrane Database of Systematic Reviews 2021, Issue 3. Art. No.: CD013705.

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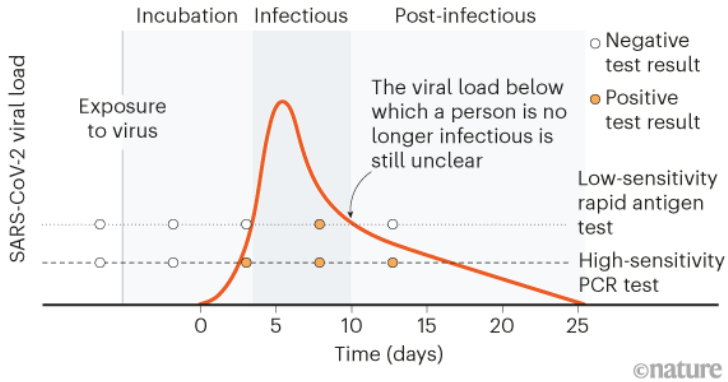
COVID-19 – molecular testing vs antigen testing



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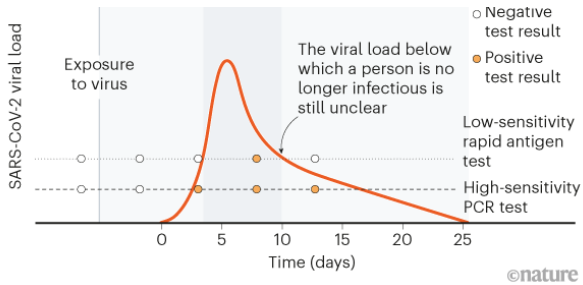
COVID-19 – molecular testing vs antigen testing

Serial testing 24-36 hrs apart preferred with rapid tests

Similar sensitivity when VL high, but more variable when VL is low



Under-reporting to state, one study showed that 1 in 3 reported results

Test positive by PCR 1-2 days before antigen test

Most research in controlled settings, need more real-world studies

More likely to be contagious if positive antigen test

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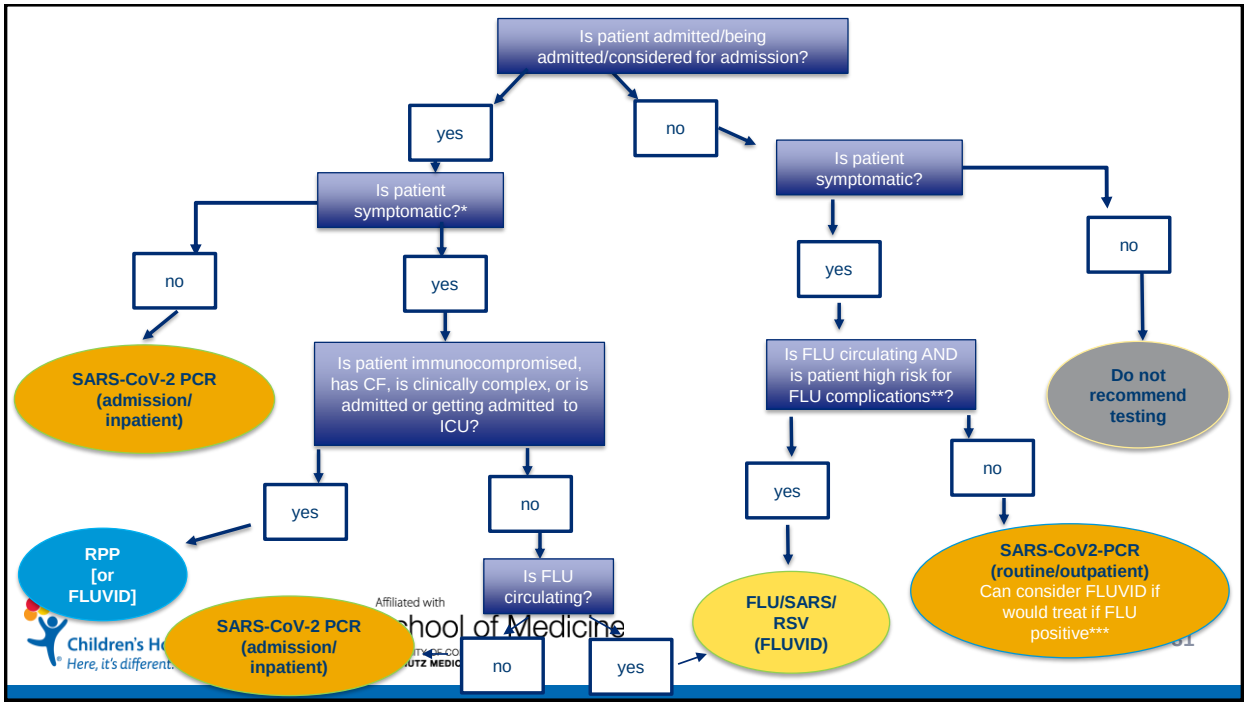

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COVID-19 treatment

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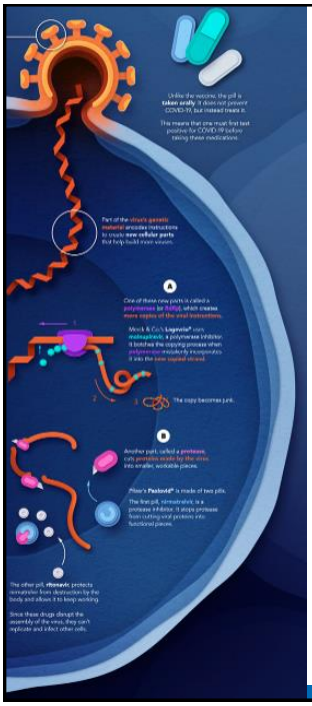

Antivirals and monoclonal antibodies against SARS-CoV-2- how they work

- **Monoclonal Antibodies e.g. bebtelovimab**
- **Remdesivir**
- **Molnupiravir**
- **Nirmatrelvir/ritonavir**

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https://www.visualcapitalist.com/visualizing-how-covid-19-antiviral-pills-and-vaccines-work-at-the-cellular-level/

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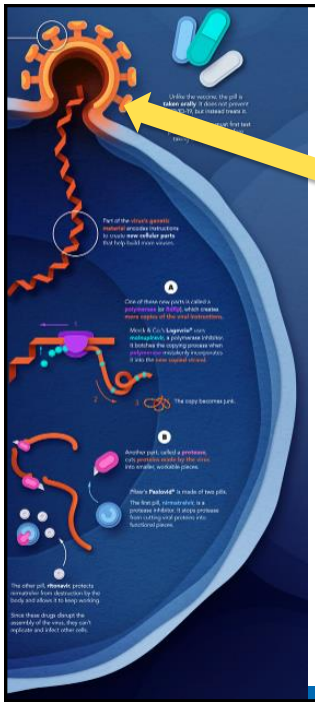


Antivirals against SARS-CoV-2- how they work

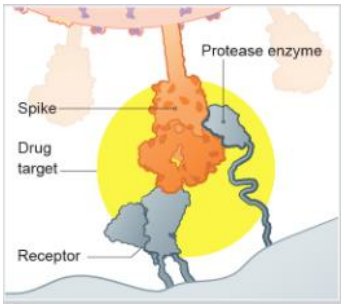
Monoclonal Antibodies e.g. bebtelovimab

Remdesivir

Molnupiravir

Nirmatrelvir/ritonavir

Bind to spike protein
Neutralize ability to attach to host cell



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https://jamanetwork.com/journals/jama/fullarticle/2776307

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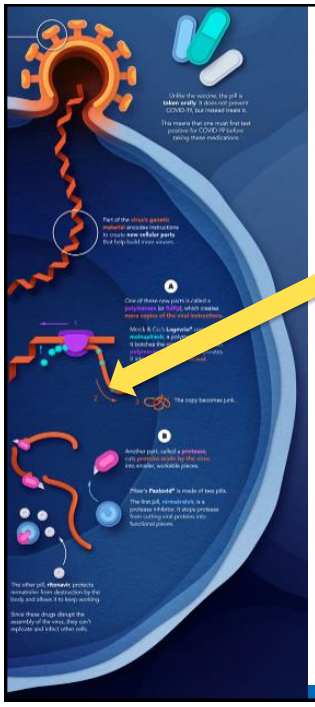


Antivirals against SARS-CoV-2- how they work

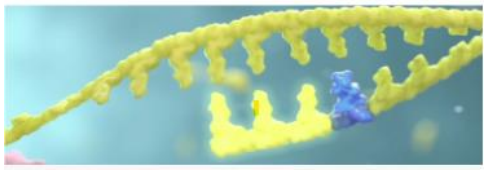
Monoclonal Antibodies

Remdesivir- nucleotide prodrug

Molnupiravir

Nirmatrelvir/ritonavir

Resembles RNA building blocks binds to RNA polymerase and terminates RNA transcription



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https://www.vekluryhcp.com/

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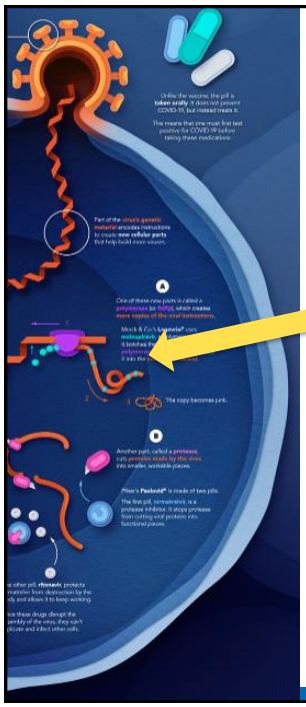
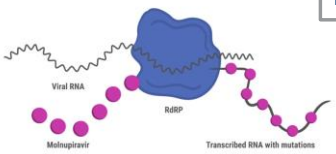


Antivirals against SARS-CoV-2- how they work

Monoclonal Antibodies
Remdesivir
Molnupiravir- RNA analogue
Nirmatrelvir/ritonavir

Incorporates into RNA, many mutations create faulty proteins



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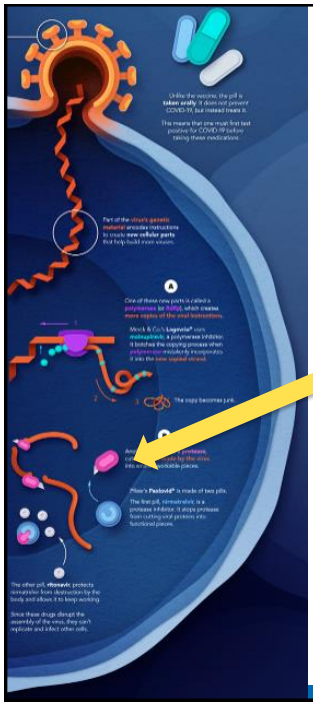
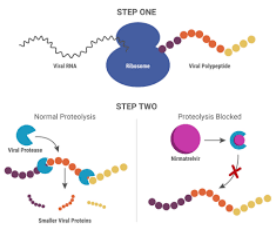


Antivirals against SARS-CoV-2- how they work

Monoclonal Antibodies
Remdesivir
Molnupiravir
Nirmatrelvir/ritonavir- protease inhibitor

Prevents proteases from cutting proteins into functional pieces



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COVID-19 treatment

Not recommended | Recommended for certain patients | Recommended all patients

	Asymptomatic	Mild/Moderate	Severe	Critical
Definition	*No symptoms of acute COVID-19*	*No oxygen or baseline home oxygen*	*New or increased oxygen requirement*	*Rapidly worsening and/or new or increasing requirement for non-invasive/invasive ventilation, shock or multi-organ failure*
Antiviral Treatment	No treatment	Paxlovid first line for high risk Remdesivir 2nd line Molnupiravir if ≥ 18 yrs for high risk	Remdesivir	Remdesivir
Monoclonal antibodies	Not routinely recommended	Bebtelovimab for high risk as second line	Not authorized for IP use by EUA	Not authorized for IP use by EUA
Steroids	No treatment	Not recommended	Dexamethasone	Dexamethasone
Immuno-modulatory therapy	Not recommended	Not recommended	Not recommended	Tociluzimab, Anakinra, etc.

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Remdesivir Efficacy

Inpatient Trial- ACTT-1

- Phase 3 trial of 1062 hospitalized adult patients (mild, moderate or severe COVID-19)
- 5 day course of treatment
- Median time to recovery 10 days vs 15 days with placebo, recovery rate ratio: 1.29 (95% CI 1.12-1.49; p < 0.001), even faster recovery if started within 10d symptom onset

Outpatient Trial- PINETREE

- Phase 3 trial of 562 non hospitalized adult patients
- 3-day course of remdesivir
- 87% lower risk of hospitalization or death by day 28 compared with placebo (hazard ratio, 0.13; 95% CI 0.03 to 0.59; p=0.008)

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Gottlieb R et al. N Engl J Med 2022; 386:305-315
Beigel JH et al. N Engl J Med 2020;383(19):1813-1826

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Remdesivir

Mild-moderate	Severe	Critical
• 3 day course in those with with high risk medical conditions who are unable to take nirmatrelvir + ritonavir	• Treat in those with significant or rapidly increasing oxygen requirement • Consider in those with high risk medical conditions	• Treat all critical patients with high risk medical conditions • Consider in those without high risk medical conditions

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Remdesivir- inpatient treatment

- Available for pts >3.5 kg
- Most effective if started within 10 days of symptom onset, treatment for 5 days
- Dosing: < 40 kg: 5mg/kg IV once daily X1, then 2.5 mg/kg IV once daily X4 days
- > 40 kg and adults: 200 mg IV once daily X1, then 100 mg IV once daily
- Monitoring: LFT and Cr at baseline, then LFTs daily
- Side effects: transaminitis, nausea, increased PT, hypersensitivity reactions

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https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/remdesivir/

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Remdesivir – outpatient treatment

- Approved for use in infants ≥ 28 days and older and at least 3 kg
- 3-day treatment course
- Ideally start within 7 days
- Outpatient dosing: 200 mg on day one followed by 100 mg on days 2 and 3. Pediatric dosing for those < 12 yrs and ≥ 3kg and < 40kg is 5 mg/kg on day 1 and 2.5 mg/kg on days 2 and 3
- Monitoring: baseline LFTs, sCr
- Need to be monitored ~ 1 hour post infusion
- SE: elevated LFTs, hypersensitivity

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https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/remdesivir/

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Steroids

RECOVERY trial – Open-Label RCT of Dexamethasone in Hospitalized Patients With COVID-19 in the United Kingdom

- Hospitalized adults, dexamethasone for 7 days
- All-cause mortality at 28 days: All patients: 23% in DEX arm vs. 26% in SOC arm (age-adjusted rate ratio 0.83; 95% CI, 0.75–0.93; *P* < 0.001)
- Greatest effect for those receiving mechanical ventilation
- No effect for those hospitalized who did not require oxygen.

CoDEX Trial- Open-Label RCT of Dexamethasone in Patients With Moderate or Severe ARDS and COVID-19 in Brazil

- Received MV within 48 hrs of ARDS, 20mg dexamethasone for 5 days then 10mg IV daily for 5 days or until ICU d/c
- Mean number of days alive and free from MV by Day 28: 7 in DEX arm vs. 4 in SOC arm (*P* = 0.04)

Improved clinical outcomes and ↓ mortality in hospitalized patients with COVID-19 on supplemental oxygen, not recommended if no supplemental oxygen

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https://www.covid19treatmentguidelines.nih.gov/tables/systemic-corticosteroids-data/

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Steroids

Mild-moderate	Severe	Critical
• Not recommended	• Treat in those with significant or rapidly increasing oxygen requirement • Consider in those with high risk medical conditions, greater than 10 days into illness course, have COVID-related inflammation	• Treat all critical patients

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Steroid Dosing

COVID-19 croup	Dexamethasone 0.6 mg/kg orally once
COVID-19 asthma exacerbation	Dexamethasone 0.6 mg/kg one dose per day for 48 hrs or prednisone 2mg/kg/day in 2 divided doses for 5 days
COVID-19 bronchiolitis	Not routinely recommended
COVID-19 other	Dexamethasone 0.1 mg/kg/dose once daily for up to 10 days or until discharge (whichever comes first)

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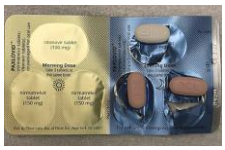
Nirmatrelvir/Ritonavir



- High risk, mild to moderate COVID, ≥ 12 years of age and weigh ≥ 40 kg
- IDSA guidelines suggest ≤ 5 days of symptom onset
- Dosing: 300 mg nirmatrelvir + 100 mg ritonavir bid X 5 days (3 tabs bid)
- Renal adjustment required, not recommended for GFR < 30 mL/min or severe hepatic impairment
- Only available as oral tablets, crushing not recommended
- Drug interactions common – may require dose adjustment
- Contraindicated with drugs that are highly dependent on CYP3A for clearance and with drugs that are potent CYP3A inducers

Management of Drug Interactions With Nirmatrelvir/Ritonavir (Paxlovid®): Resource for Clinicians

IDSA Infectious Diseases Society of America

IDSA COVID-19 TREATMENT AND MANAGEMENT GUIDELINE PANEL ON BEHALF OF THE INFECTIOUS DISEASES SOCIETY OF AMERICA

FACT SHEET FOR HEALTHCARE PROVIDERS: EMERGENCY USE AUTHORIZATION FOR PAXLOVID™

https://www.fda.gov/media/155050/download

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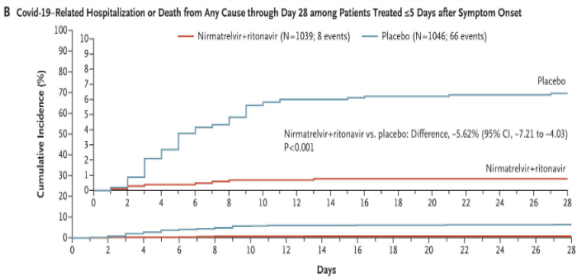
Nirmatrelvir/Ritonavir Efficacy

- EPIC-HR study –Phase 2/3 randomized, double-blind study of unvaccinated non-hospitalized adults with COVID-19, n = 2246
- 89% RR reduction in hospitalization/death among adults within 3 days of symptom onset, and 88% within 5 days of treatment onset, lower viral load
- No deaths in treatment group
- Adverse events treatment
- (25%) and placebo groups (24%)
- Dysgeusia, diarrhea, and vomiting
- Safety and effectiveness not established in pediatric patients
- EPIC-PEDS Pediatric trial underway



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Hammond et al. N Engl J Med 2022; 386:1397-1408

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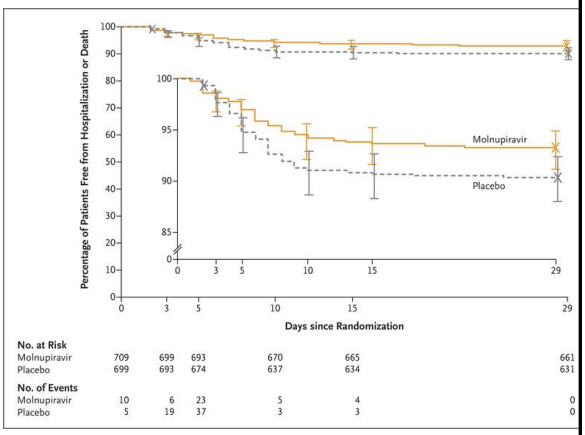
Molnupiravir

- For those 18 yrs of age and older
- Treat within 5 days of symptom onset
- Dosing: 800 mg (4 capsules) po bid for 5 days
- Efficacy: 30% RR reduction in hospitalization/death
- No drug interactions reported, no need for lab monitoring
- Not recommended in pregnancy (fetal toxicity, bone/cartilage toxicity); contraception precautions if sexually active
- Efficacy in MOVe-OUT Trial – rate of hospitalization or death 31% lower compared with placebo



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Bernal et al. N Engl J Med 2022; 386:509-520

Bebtelovimab

- High risk, mild to moderate COVID, ≥ 12 years of age and weigh ≥ 40 kg alternative COVID-19 treatment options not accessible
- Consider if unable to take pills, drug-drug interactions
- Ideally within 7 days of symptom onset
- Dosing: 175 mg IV once over at least 30 seconds, need to monitor for 1 hour post infusion
- Most common adverse reactions are infusion-related reactions (0.3%), pruritus (0.3%), and rash (0.8%)
- No drug interactions
- Infusion related reactions observed in clinical trials 24 hrs after injection (unclear if progression of COVID-19 or direct effect of infusion)

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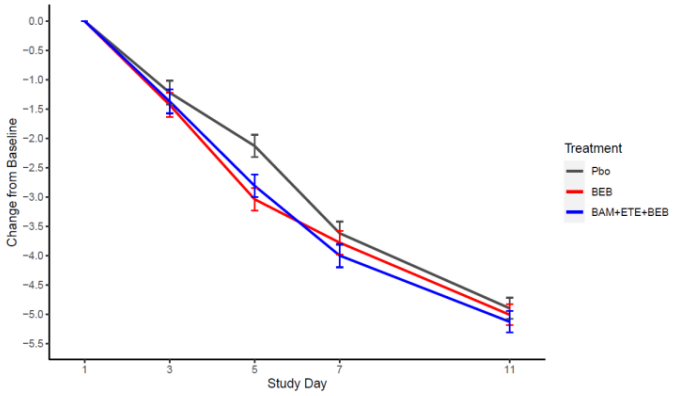
https://www.covid19treatmentguidelines.nih.gov/therapies/anti-sars-cov-2-antibody-products/summary-recommendations/

Bebtelovimab efficacy in clinical trials

- Phase 2 portion of BLAZE-4 trial (randomized, single dose clinical trial evaluating treatment of mild-moderate COVID-19 prior to omicron)
- Primary endpoint- viral load by day 7
- 34% (95% CI: -15%, 62%) relative reduction in persistently high viral load
- Failed to show or to exclude a beneficial effect on hospitalizations (RR: 1.02; 95% CI: 0.15, 7.16;)
- Median time to sx resolution 6 days compared with 8 days for placebo
- 85% RR reduction in hospitalization or death among prior mAbs studied



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https://www.medrxiv.org/content/10.1101/2022.03.10.22272100v1.full
https://www.fda.gov/media/156152/download

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Antithrombotic therapy

- Not recommended in non critically ill patients
- Insufficient evidence to recommend either for or against in critically ill patients with COVID-19
- Not recommended to continue VTE prophylaxis after hospital discharge
- Insufficient evidence to recommend either for or against continuing anticoagulation after hospital discharge unless another indication for VTE prophylaxis exists.

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https://www.covid19treatmentguidelines.nih.gov/therapies/antithrombotic-therapy/

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MIS-C

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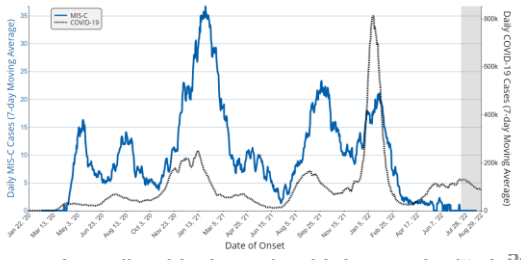
MIS-C: multi-inflammatory syndrome in children

- <21 yrs, fever, inflammation, involvement of at least 2 organ systems requiring hospitalization (no alternative diagnosis, and evidence of infection/exposure)
- Coronary artery aneurysms occur in over 8% of patients
- Post-infectious syndrome occurring 3-6 weeks after mild or asymptomatic SARS-CoV-2 infection
- Children 6-12 years of age
- Estimates 3 in 10,000 children in the US What triggers MIS-C in certain children remains unknown
- Cases of MIS-C decreasing over time (differences in inflammatory response a/w each variant, enhanced host immunity after infection and vaccination)



Source: https://covid.cdc.gov/covid-data-tracker/#mis-national-surveillance

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MIS-C evaluation

- CBC with differential (absolute lymphocyte count < 1000, platelets < 150,000)
- CRP (CRP >3 mg/dL)
- Complete metabolic profile (Na less than 130, Cr elevated for age or greater than 1.5X baseline, LFTs 2X upper limit of normal for age)
- ESR (greater than 40mm/hr)
- Rainbow draw

- pro-BNP, troponin
- SARS-CoV-2 serology, PCR
- Urinalysis
- Other labs based on severity and need to rule out other causes
- Echo

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MIS-C management at CHCO

- First line therapy- inFLIXimab followed by IVIG
- Pre-treat with acetaminophen and diphenhydramine
- Low dose aspirin

- Second line therapy- repeat dose of infliximab
- Corticosteroids (IV methylprednisolone)
- Anakinra

- Influenza vaccine prior to discharge, no live vaccines for 11 months

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Prevention

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Tixagevimab plus cilgavimab

- EUA for tixagevimab with cilgavimab
- ≥ 12 years of age and ≥ 40 kilograms
- Pre-exposure prophylaxis if vaccine unlikely to work or if unable to get vaccinated
  - moderate to severely compromised immune systems and may not mount an adequate immune response to COVID-19 vaccination **or**
  - history of severe adverse reactions to a COVID-19 vaccine and/or component(s)
- 300 mg of tixagevimab and 300 mg of cilgavimab - two separate consecutive intramuscular (IM) injections every 6 months
- Higher dosing to overcome potential resistance to Omicron

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Timeline of vaccination in children

December 2020	BNT162b2 (Pfizer-BioNTech) ≥ 16 years
May 2021	BNT162b2 (Pfizer-BioNTech) 12-15 years
October 2021	BNT162b2 (Pfizer-BioNTech) 5-11 years
December 2021	BNT162b2 (Pfizer-BioNTech) booster 16-17 years
January 2022	BNT162b2 (Pfizer-BioNTech) booster 12-15 years
May 2022	BNT162b2 (Pfizer-BioNTech) booster 5-11 years
June 2022	Moderna 6 months-17 years
July 2022	Novavax 12 years of age and older
September 2022	Bivalent booster vaccines 12 years and older

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How well do vaccines work in children?

Pfizer's Covid-19 vaccine had 100% efficacy for 12-15 year olds, 88% efficacy in children 6-11 years of age, and 80.3% efficacy in children under 5 years old (3 doses)

Moderna vaccine efficacy for children between 6 months and 2 years of age was 43.7%, and 37.5% for 2-6 year olds (note 2 doses and during omicron wave)

Study in Singapore, VE was 65.3% against all PCR confirmed infection and 82.7% against hospitalizations

Study in US, VE was 68% against hospitalizations and 79% against critical illness during omicron

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N Engl J Med 2022; 386:1899-1909;

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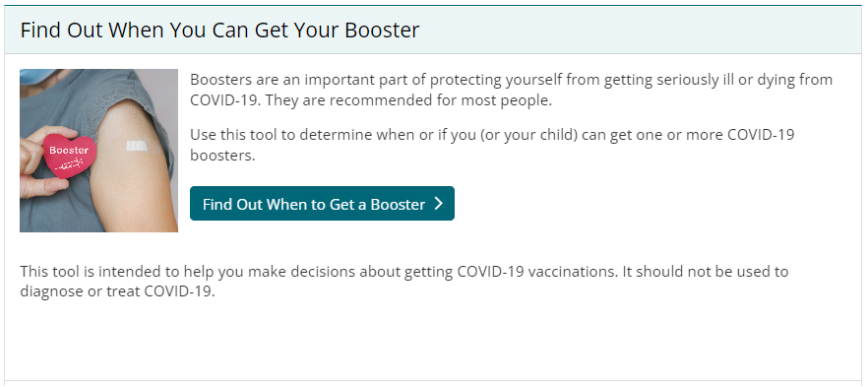
Vaccine information



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https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html?s_cid=11747:cdc%20up%20to%20date%20vaccine:sem.ga:p:RG:GM:gen:PTN:FY22

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Take home points

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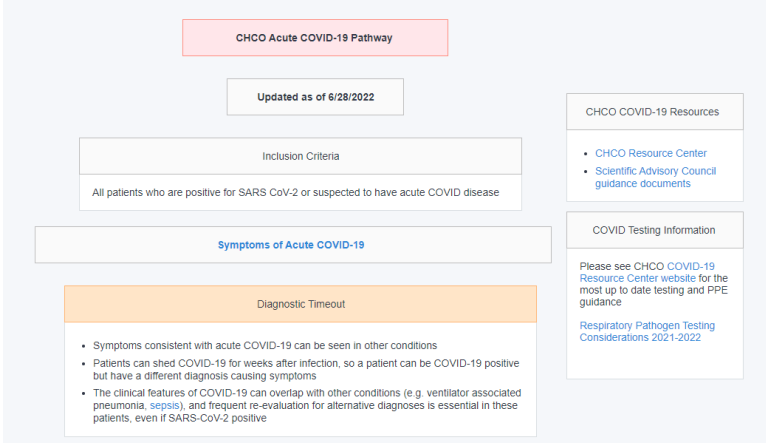
Resources

https://www.childrenscolorado.org/health-professionals/clinical-resources/clinical-pathways/

- Acute COVID-19
- MIS-C
- Cardiac Evaluation for post COVID-19 return to play



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Resources

Children's Hospital Colorado COVID-19 Clinical Pathways: https://www.childrenscolorado.org/health-professionals/coronavirus-professional-resources/clinical-guidance-practice-resources/covid19-clinical-pathways/

NIH Treatment guidelines: https://www.covid19treatmentguidelines.nih.gov/

IDSA Treatment Guidelines: https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/

Pharmacy locator for ritonavir-boosted nirmatrelvir: https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com/

IDSA drug interactions: https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/management-of-drug-interactions-with-nirmatrelvirritonavir-paxlovid/

Quarantine and Isolation recommendations: https://www.cdc.gov/coronavirus/2019-ncov/your-health/quarantine-isolation.html

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Thank you

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Extra slides

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Vaccine recommendations

6 months to 4 years of age	1st dose (monovalent) 2nd dose 3-8 weeks after first dose (mono or biv) 3rd dose at least 8 weeks after second dose (mono or biv Pfizer only) Up to date – 2 weeks after third dose for Pfizer, 2 weeks after second dose for Moderna
5 to 11 years of age	1st dose (monovalent) 2nd dose 3-8 weeks after first dose (mono or biv) 3rd dose at least 5 months after second dose (mono or biv Pfizer only) Up to date – immediately after third dose for Pfizer, 2 weeks after second dose for Moderna

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Vaccine recommendations

12-17 years of age	1st dose (monovalent) 2nd dose 3-8 weeks after first dose (mono or biv) 3rd dose at least 8 weeks after second dose or last booster, and can only be Pfizer-BioNTech biv Booster doses- can be different from primary series Up to date- after most recent booster recommendation

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How to make a strong vaccine recommendation

- Normalize the process - *We routinely provide flu vaccines to our patients in our clinic/hospital*
- Use presumptive language - *We can take care of your child's flu vaccine during this visit/hospital stay.*
- Be respectful of their concerns- *Do you mind if I ask why you are not wanting your child to receive the flu vaccine today?*
- Tailor the discussion to address concerns - *Thanks for letting me know about your concerns. I've been thinking a lot about this and we get a lot of education about influenza vaccines- would it be alright if I shared some of this information with you?*
- Find common ground - *I know you are a wonderful parent, and you want to do what's best for your child. We also want to do everything possible to keep your child as healthy as possible, and vaccination is one of those ways.*

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