Infectious Diseases update with an emphasis on COVID

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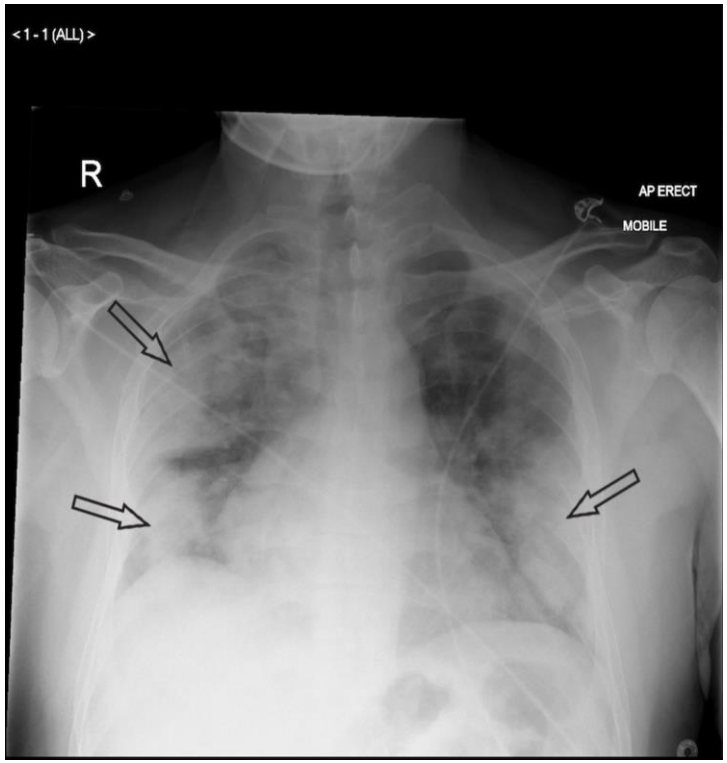
Disclosures

- I have no relevant relationships with ineligible companies* to disclose within the past 24 months

Learning Objectives

- Discuss updates in the prevention and treatment of mild COVID-19 for non-hospitalized patients
- Discuss best practices in the management of hospitalized patients with COVID-19
- Review the antibiotic recommendations for postoperative wound infections

Severe COVID-19

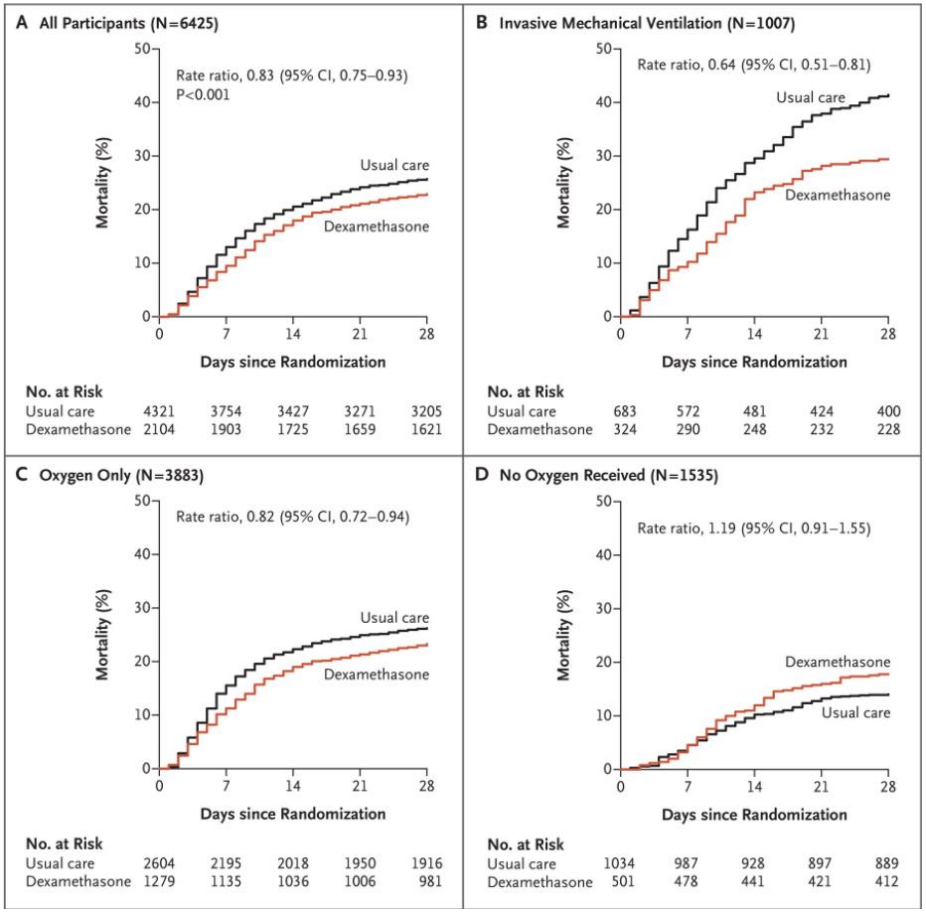


- 65 year male, CKD, BMI- 35, CAD, hospitalized with COVID-19, RR-24, on 4l by NC, hospitalized

- Recommendations:
- **Remdesivir** IV X 5 days- if given early
- **Dexamethasone** 6 mg IV/PO for up to 10 days or until hospital discharge
- Or **dexamethasone** alone
- Consider Tocilizumab/Baricitinib if increasing O2 requirement within first 24 hours

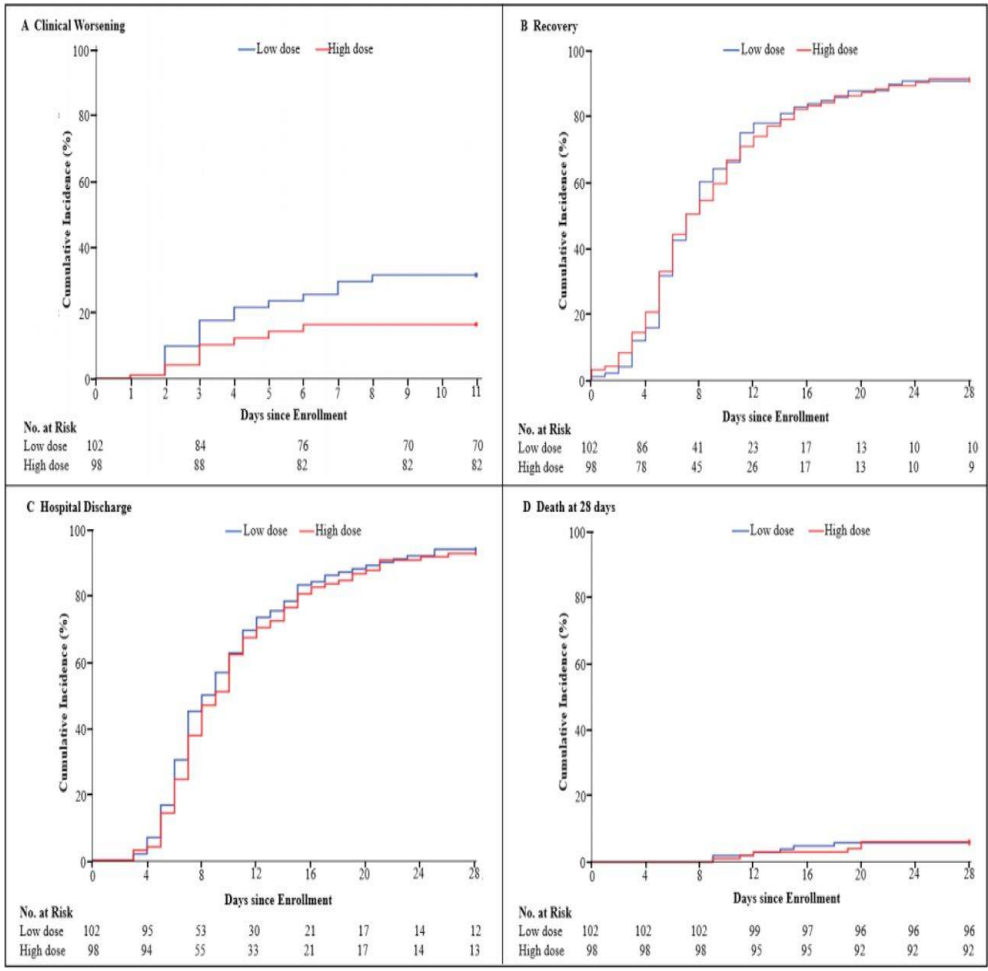
Corticosteroids- Recommendations based on RECOVERY Trial

- **Yes** in hospitalized, critically ill patients
  - Odds of mortality at 28 days is 34% lower in the dexamethasone group
- **Yes** in hospitalized patients with severe COVID-19
  - 28-day mortality - 17% lower
- **No** in hospitalized patients without hypoxemia
- Dose
  - Dexamethasone 6 mg IV or PO for 10 days (or until discharge if earlier)
    - Or Equivalent total daily doses of alternative glucocorticoids



Dexamethasone low dose vs high dose

- **Low or High Dose Dexamethasone (HIGHLOWDEXA)**
- Randomized to receive
  - Low dose dexamethasone
    - (6 mg once daily for 10 days)
  - Or high dose dexamethasone
    - (20 mg once daily X 5 days, followed by 10 mg once daily X 5 days)



Tocilizumab- Studies showing benefit in patients with worsening Oxygen requirements

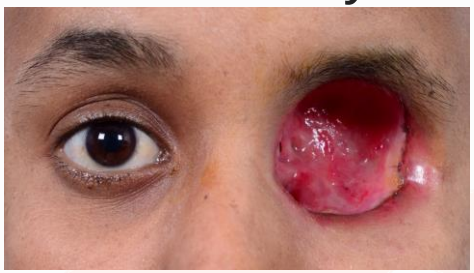
- RECOVERY
  - 2000 patients in Toci arm vs 2000 in standard of care arm
    - Reduction in mechanical ventilation 12% vs 15%
    - Reduction in 28 day mortality if given with steroids
      - 27% vs 33%
- REMAP-CAP Trial (n =800)
    - IL-6 antagonist started within 24 hours of ICU admission
    - Reduced mortality in IL-6 arm

NIH guidance on anticoagulation- *January 5, 2022*

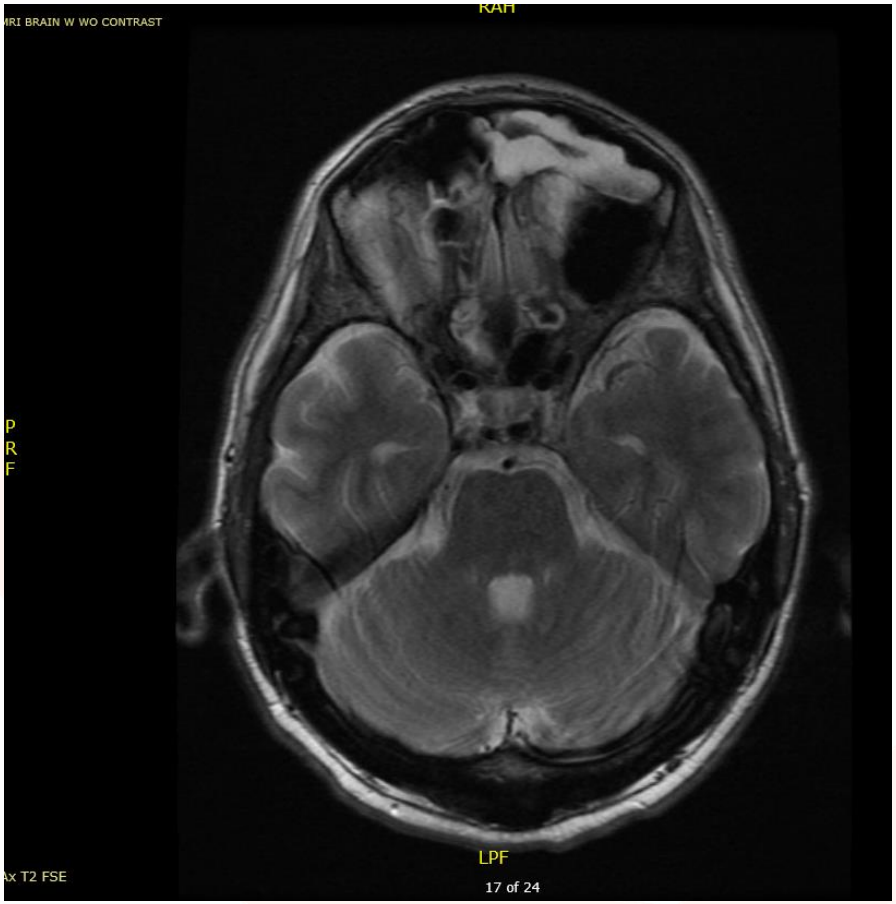
- Hospitalized, Nonpregnant Adults Who Require Low-Flow Oxygen and Are Not Receiving ICU Level of Care
- Panel recommends using therapeutic-dose heparin for
  - Patients who have a D-dimer above the upper limit of normal
  - Require low-flow oxygen
  - Have no increased bleeding risk or contraindications
  - Treatment should continue for 14 days or hospital discharge,
  - Do not use therapeutic-dose oral anticoagulants
- Anticoagulation for patients in ICU or on high flow Oxygen
  - The Panel recommends **against** the use of intermediate-dose and therapeutic-dose anticoagulation for VTE prophylaxis
  - Use prophylactic-dose heparin as VTE prophylaxis

Other Infectious complications in patients with COVID-19

- **Fungal infections:**
- 50-year-old healthy male, no comorbidities
- COVID in August 2021- received steroids and tocilizumab
- 3 weeks later developed fungal sinusitis
- Progressive orbital involvement led to left eye exenteration



- This is not his picture but similar!
- 6 months later has had 5 sinus surgeries and is still on antifungals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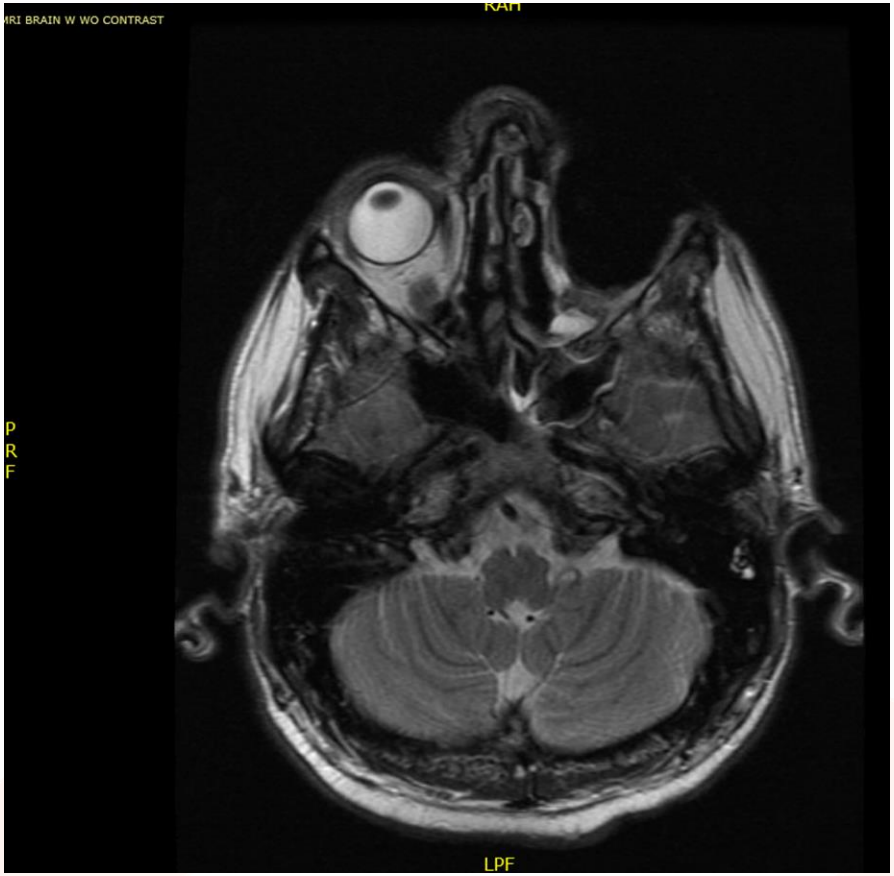
MRI BRAIN W WO CONTRAST
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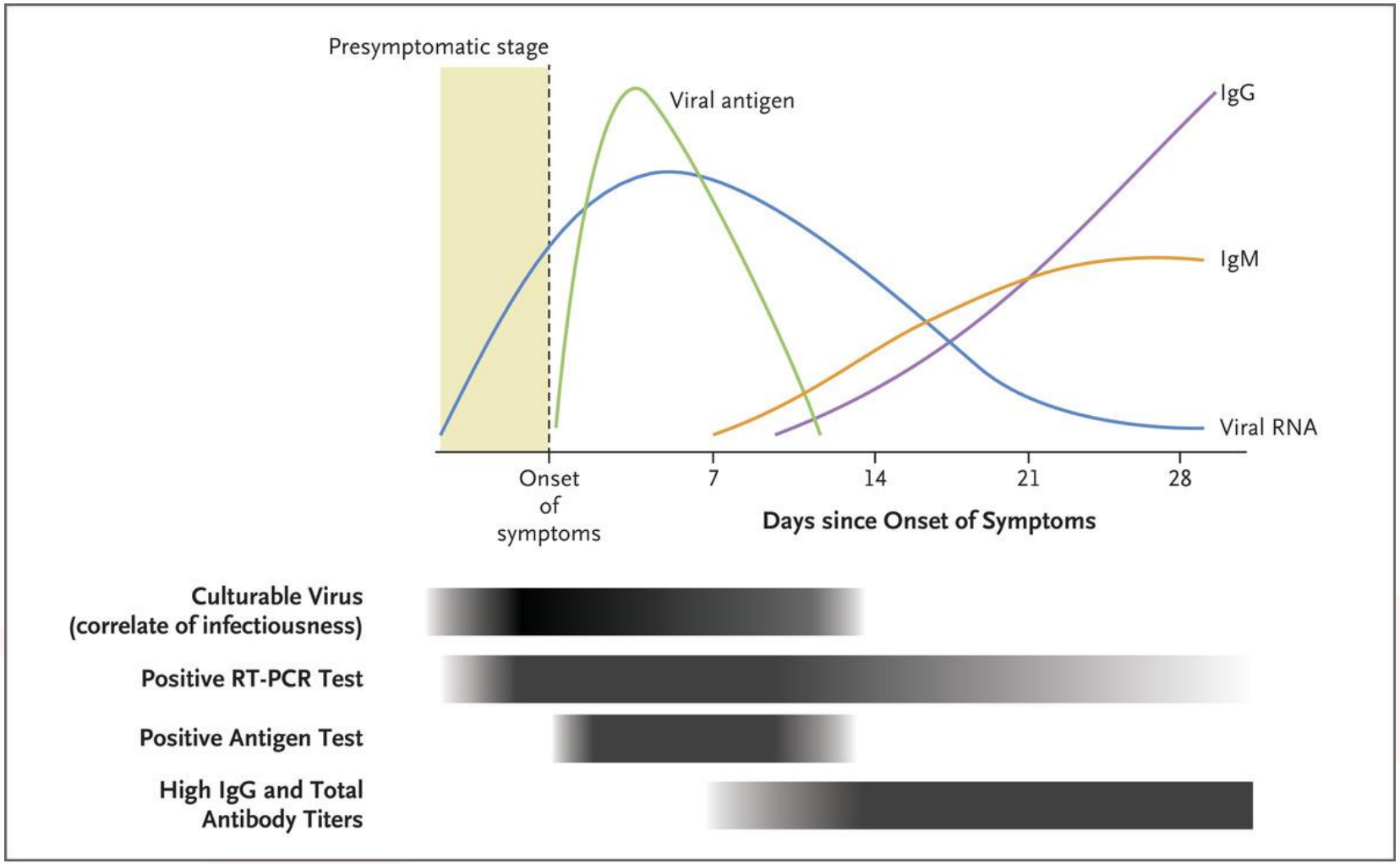
Risk Factors for Severe COVID-19 Among Fully Vaccinated

- 1,228,664 persons, 465 Health Care Facilities, United States
- Aged ≥18 Years, December 2020–October 2021
  - Severe COVID-19 associated outcomes-0.015%
  - Death- 0.0033%
- Risk factors for severe outcomes
  - Age ≥65 years
  - Immunosuppressed
  - Six other underlying conditions : diabetes, immunosuppression, chronic liver, lung, heart or neurological disease
- 78% of those who died had 4 or more of these conditions

DOI: http://dx.doi.org/10.15585/mmwr.mm7101a4external icon

Pathophysiology and Timeline of Viremia, Antigenemia, and Immune Response during Acute SARS-CoV-2 Infection.



PK Drain. N Engl J Med 2022;386:264-272.

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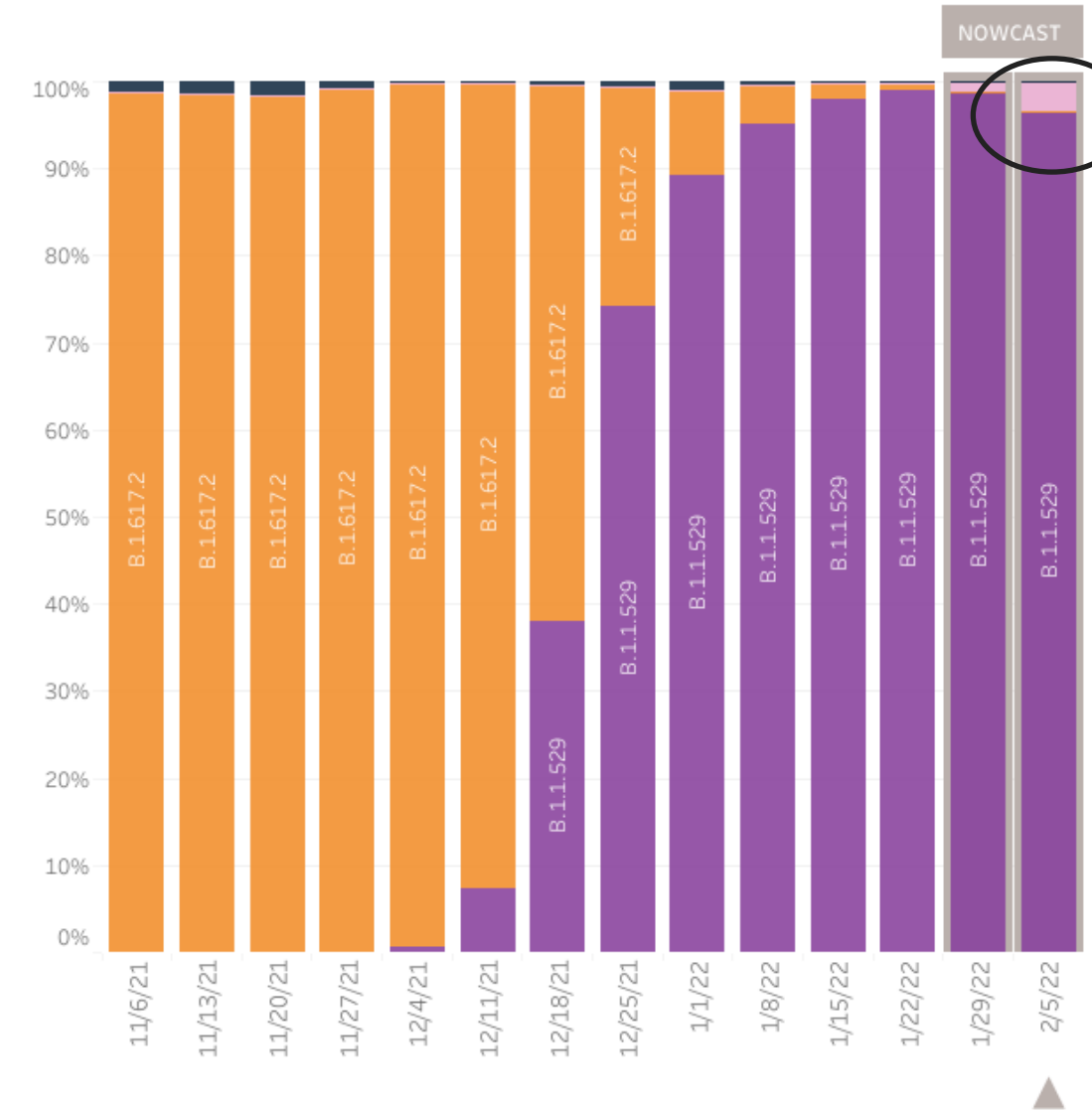
Diagnostic Tests

- Clinical performance of diagnostic SARS-CoV-2 testing depends on:
  - Viral load and the time since exposure or symptom onset
  - Specimen type, swab technique, transport conditions
  - sample preparation and signal amplification
- Nucleic acid amplification tests :
  - NAATs are highly sensitive and accurate
  - Remain positive for weeks to months after infection
- Rapid diagnostic tests (RDTs) ; Antigen-based assays
  - remain positive for 5 - 12 days after symptom onset
  - Perform better in persons with a high viral load which correlates with disease severity and death

United States: 10/31/2021 – 2/5/2022



United States: 1/30/2022 – 2/5/2022 NOWCAST

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	B.1.1.529	VOC	96.4%	93.2-98.2%
	BA.2	VOC	3.6%	1.8-6.8%
Delta	B.1.617.2	VOC	0.0%	0.0-0.0%
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 and BA.3 are aggregated with B.1.1.529.

BA.2 lineage

- Original Omicron is BA.1 (B.1.1.529)
- BA.1 and BA.2 differ by approximately 40 mutations.
- BA. 2 nicknamed the “stealth omicron”
  - Not because it is “harder to detect”
  - “Stealth”:because it does not exhibit the S gene target failure that distinguishes Omicron from other variants
  - Need to do genotyping to identify the variant
- No evidence that it causes more severe disease, but there is evidence for increased transmissibility

Transmissibility : Omicron vs. Delta vs. Omicron BA.2

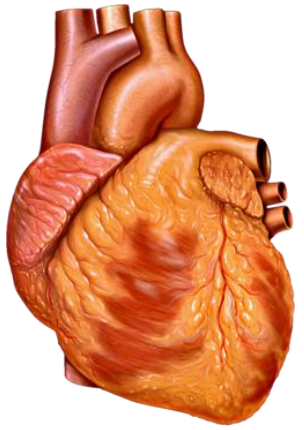
- Studies from Denmark:
- Secondary attack rate (SAR) among household members
  - Omicron- 31%
  - Delta-21%
  - **Omicron BA.2- 39%**

- Unvaccinated about the same risk as vaccinated w/o booster
- Does the Booster reduce infection from Omicron?
  - Works for Omicron BA.1
  - Not so much for BA.2

Comments (6)

Transmission of SARS-CoV-2 Omicron VOC subvariants BA.1 and BA.2: Evidence from Danish Households

Long-term cardiovascular outcomes of COVID-19

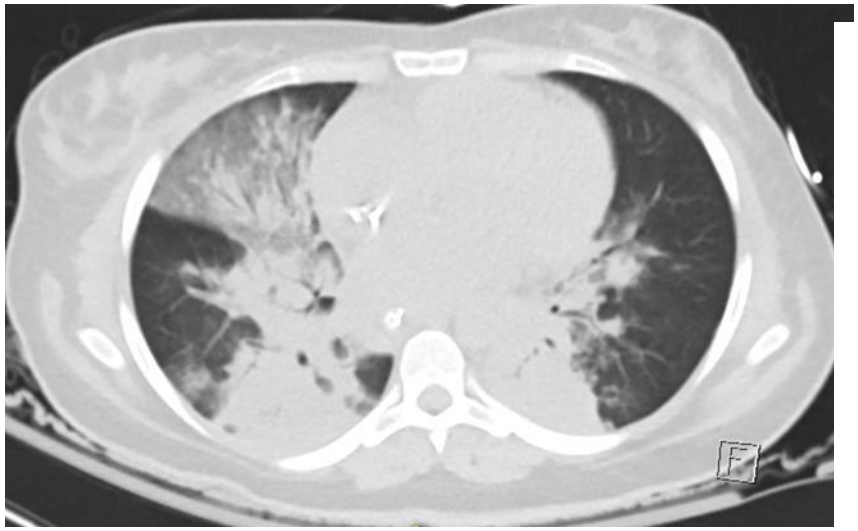


- Veterans Affairs
- COVID-19- 153,760 patients
- Without COVID-19:
  - 5,637,647 (contemporary controls) and 5,859,411 (historical controls)
- > 30 d after infection, COVID-19 cases at increased risk of:
  - Cerebrovascular disorders
  - Dysrhythmias
  - Ischemic & non-ischemic heart disease
  - Pericarditis/myocarditis, heart failure and thromboembolic disease
  - Reports of increased risk of out-of-hospital cardiac arrest

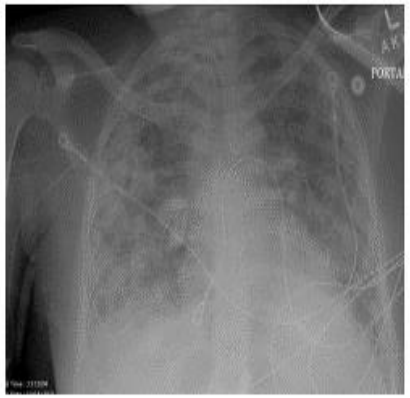
  72% higher risk of CHF even at 12 months
- Even in non-hospitalized cases with mild-moderate disease

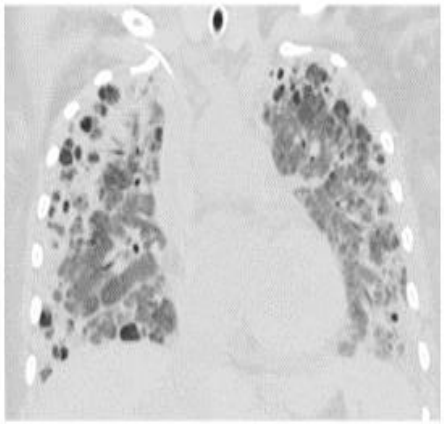
https://www.nature.com/articles/s41591-022-01689-3#MOESM1

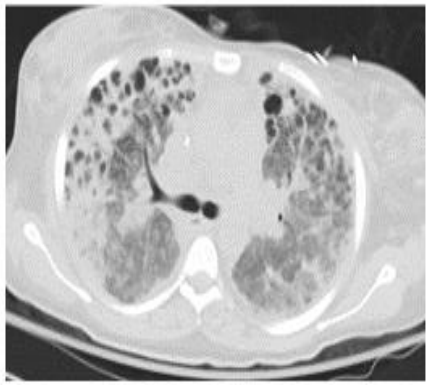
- **Long Haul COVID in the Lung**
- Young patient with Diabetes, Admitted 3 months ago with COVID,

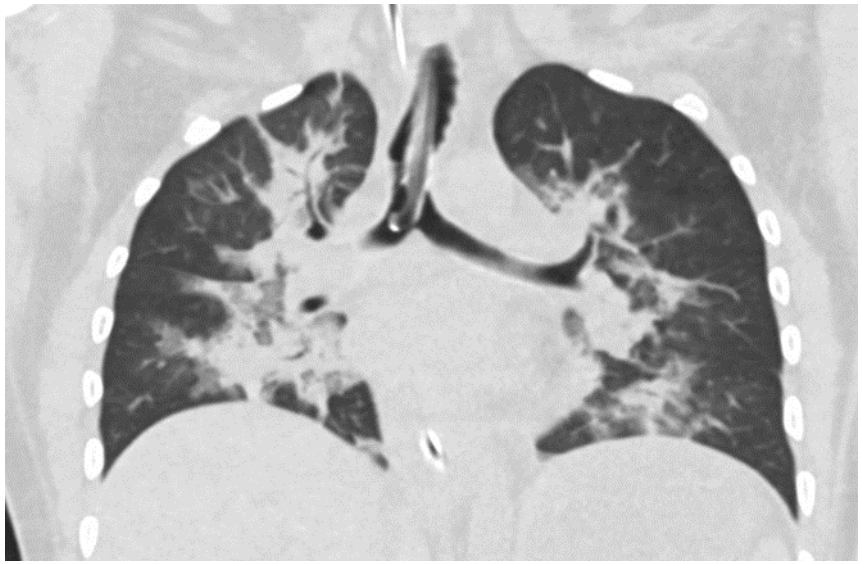


Same patient 3 months later
Long Haul COVID lung

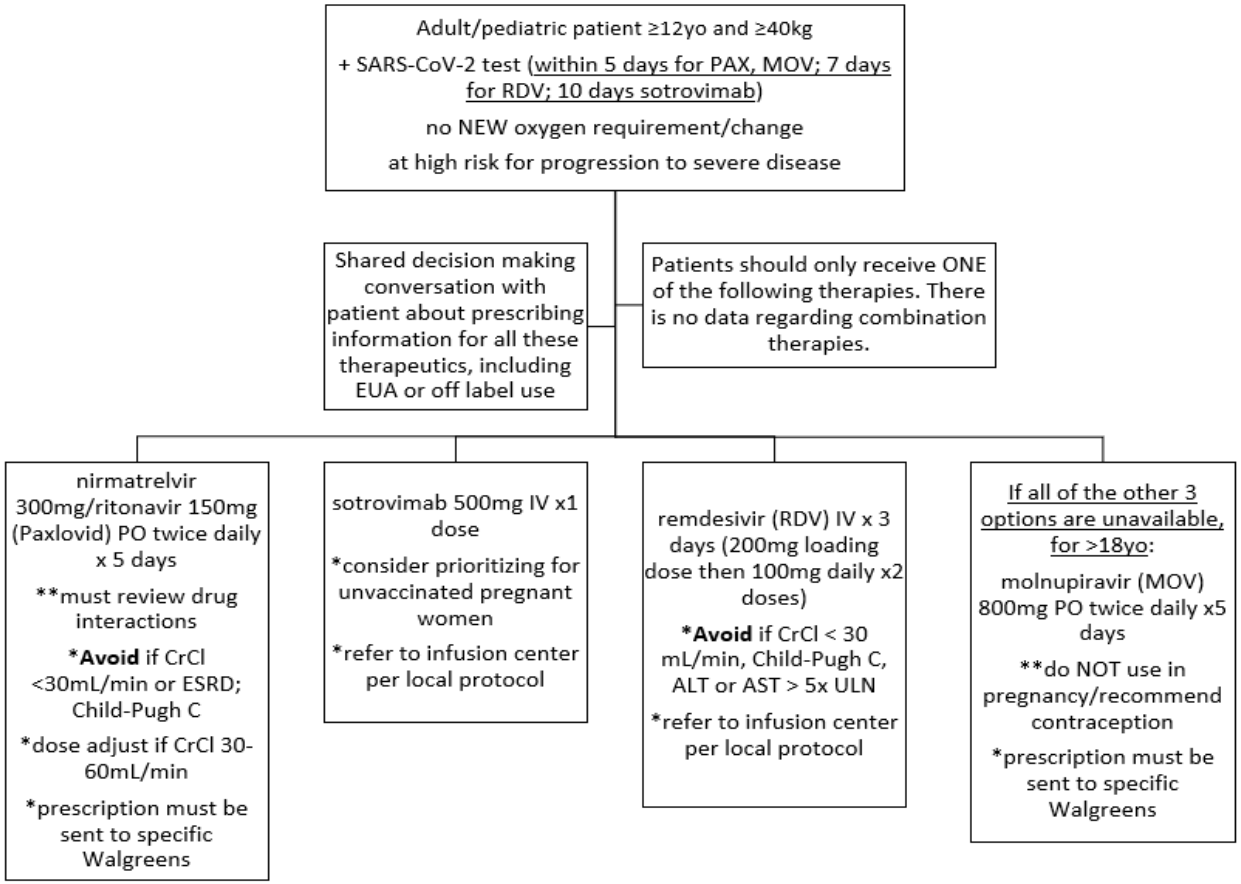








South Carolina Outpatient COVID-19 Therapeutics Consensus Guidance



Prioritize: Clinicians should screen and prioritize patients at the highest risk of clinical progression.

Risk Prioritization Tiers:

Tier 1A: Immunocompromised individuals *Pregnant persons, unvaccinated

Tier 1B: Unvaccinated individuals at the highest risk of severe disease, meeting at least one of the following: ≥ 75 years; ≥ 65 years with any clinical risk factors, Pregnant persons, partially vaccinated

Tier 2: Unvaccinated individuals at risk of severe disease not included in Tier 1 AND meeting at least one of the following: ≥ 65 years; < 65 years with any clinical risk factors; Preganant persons, fully vaccinated (with booster)

Tier 3: Vaccinated individuals at high risk of severe disease

Tier 4: *Vaccinated individuals at risk of severe disease (anyone ≥65 years or anyone <65 with clinical risk factors)

Current COVID-19 Therapeutics

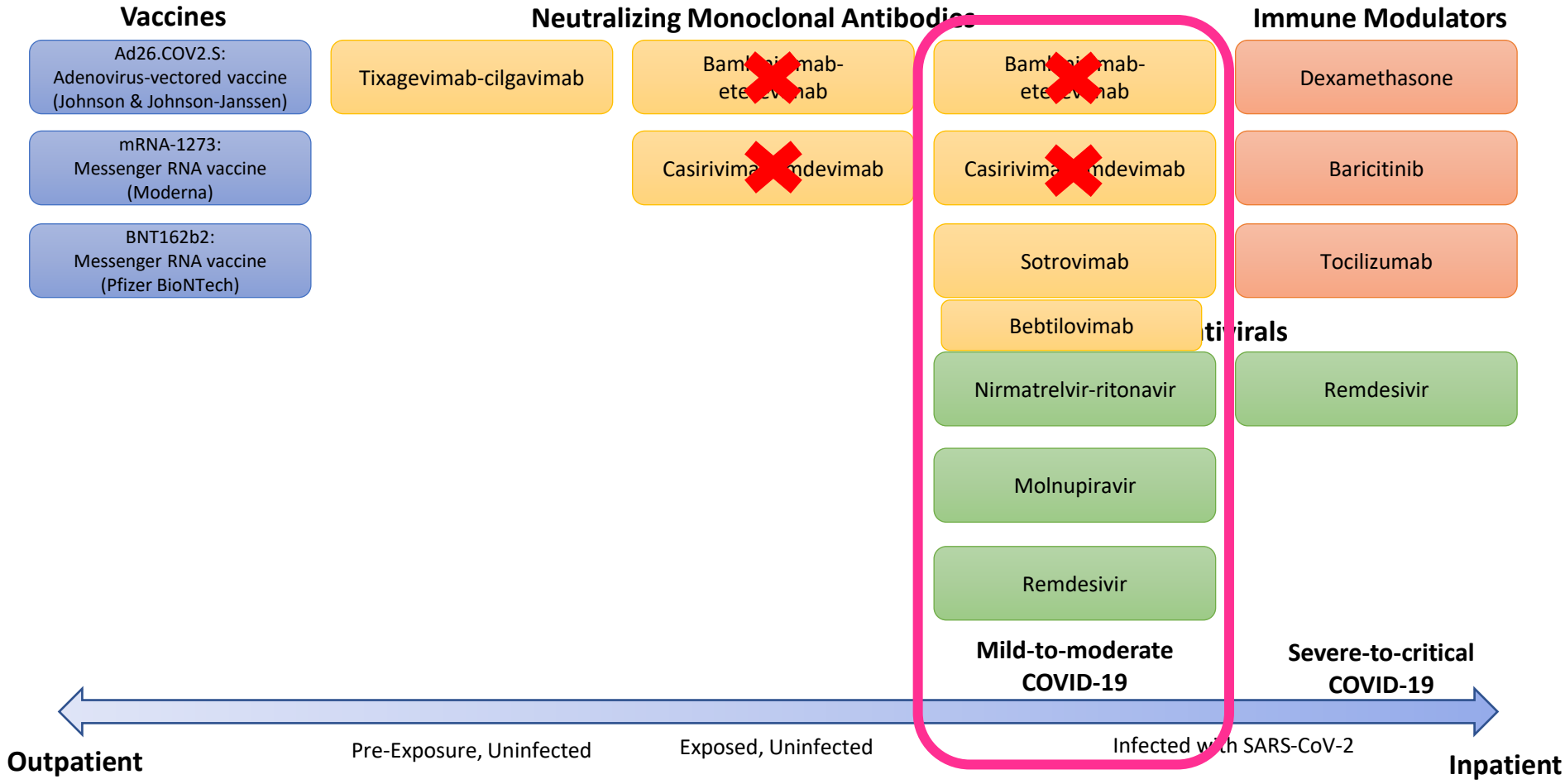


Figure adapted from Heil EL, Kottilil S. NEJM. 2021 Dec 22. doi: 10.1056/NEJMe2118579.

Efficacy of Antibodies and Antiviral Drugs against Covid-19 Omicron Variant; NEJM- January 26, 2022

Table 1. Efficacy of Monoclonal Antibodies and Antiviral Drugs against SARS-CoV-2 Variants in Vitro.*

Monoclonal Antibody or Antiviral Drug	SARS-CoV-2 Variant					
	SARS-CoV-2/UT-NC002-1T/Human/2020/Tokyo (A)	SARS-CoV-2/UT-HP127-1Nf/Human/2021/Tokyo (Alpha/B.1.1.7)	hCoV-19/USA/MD-HP01542/2021 (Beta/B.1.351)	hCoV-19/Japan/TY7-503/2021 (Gamma/P.1)	hCoV-19/USA/WI-UW-5250/2021 (Delta/B.1.617.2)	hCoV-19/Japan/NC928-2N/2021 (Omicron/B.1.1.529)
Neutralization activity of monoclonal antibody — ng/ml†						
LY-CoV016, etesevimab	18.19±9.10	150.38±83.51	>50,000	>50,000	15.37±9.78	>50,000
LY-CoV555, bamlanivimab	4.69±1.43	2.65±1.30	9554.88±926.53	1601.65±896.02	641.73±324.79	>50,000
REGN10987, imdevimab	3.05±0.93	1.87±1.60	2.17±1.30	1.04±0.68	3.95±1.78	>50,000
REGN10933, casirivimab	2.79±1.87	2.74±1.84	757.13±287.91	187.69±128.88	2.89±1.78	14,110.70±1782.13
COV2-2196, tixagevimab	1.92±0.28	1.34±0.67	18.98±1.42	6.56±1.56	4.05±2.60	1299.94±406.58
COV2-2130, cilgavimab	7.70±2.20	3.60±1.62	10.03±3.05	4.00±2.70	12.76±2.93	443.87±167.96
S309, sotrovimab precursor	27.33±3.24	44.91±22.76	100.98±22.27	28.38±1.86	111.43±58.22	373.47±159.49
LY-CoV016 plus LY-CoV555	12.60±1.91	15.26±3.98	>10,000	2545.04±625.72	10.28±3.33	>10,000
REGN10987 plus REGN10933	3.53±0.66	1.55±0.78	5.18±1.45	2.11±0.48	1.91±0.79	>10,000
COV2-2196 plus COV2-2130	3.42±0.92	1.94±0.34	10.30±1.17	1.79±0.87	5.50±2.75	255.86±45.31
Viral susceptibility to drug — μM‡						
GS-441524§	1.04±0.32	0.83±0.19	0.63±0.20	0.91±0.33	1.12±0.20	1.28±0.42
EIDD-1931¶	0.51±0.14	0.95±0.17	0.60±0.21	0.41±0.13	0.83±0.41	0.43±0.08
PF-00835231‖	18.45±7.35	10.56±5.85	14.20±4.34	9.40±3.28	14.81±5.24	12.71±3.00

New Monoclonal Antibody: Bebtelovimab

- EUA granted on basis of lab data: binds and neutralizes all currently known VOC including Omicron and BA.2
- Limited clinical data: Rates of COVID-19 hospitalization and death through Day 29 were lower in bebtelovimab given alone or with other mAb compared to placebo rates reported in prior trials of other mAb in high-risk patients
- Give within 7 days of symptom onset
- Single IV infusion over 30 seconds followed by 1 hour observation
- Can be used for in-patient who tests positive but hospitalized for a non-COVID reason
- SC will receive 895 patient courses this week plus 1000 doses of Sotrovimab - might consider Sotrivimab preferable

Evusheld

- Pre-exposure prophylaxis (PrEP) for immunocompromised
- Long acting antibody cocktail that may prevent infection for upto 1 year
  - PROVENT Phase III pre-exposure prophylaxis trial
- Results:
  - Reduced risk of developing symptomatic COVID-19 by 77%

Evusheld

Risk Assessment Criteria (Check the applicable box. Must m

Oncology

☐ Receipt of autologous hematopoietic stem cell transplant (HSCT) in past 6 months OR receipt of allogenic HSCT in past 12 months

☐ Allogeneic HSCT within past 1-3 years OR autologous HSCT within past 6-12 months

☐ Received CAR-T cell therapy

☐ Patients receiving rituximab therapy in past 12 months for treatment of non-Hodgkins lymphoma (NHL) or chronic lymphocytic leukemia (CLL) AND age ≥ **65 years**

☐ Patients receiving rituximab therapy in past 12 months for treatment of NHL or CLL AND age **< 65 years**

☐ Any HSCT patient currently on treatment for graft-versus-host disease

☐ Patients on therapy for acute lymphoblastic leukemia, acute myelogenous leukemia, or myelodysplastic syndrome AND age ≥ **65 years**

☐ On therapy for acute lymphoblastic leukemia, acute myelogenous leukemia, or myelodysplastic syndrome, age **< 65 years**

☐ Patients with multiple myeloma, other lymphomas (including cutaneous T-cell lymphoma) or chronic leukemias, myeloproliferative neoplasms, aplastic anemia, or Castleman's disease

☐ Curative adjuvant cytotoxic chemotherapy in past 6 months

☐ Lung cancer on treatment

☐ Non-curative intent on cytotoxic chemotherapy

Non-Oncology

☐ Patients receiving anti-CD20/CD52/B-cell depleting therapy (e.g. rituximab, ocrelizumab, ofatumumab, alemtuzumab) for a non-oncology indication within the past 12 months (date of last infusion_____)

☐ Severe primary immunodeficiency (CVID, agammaglobulinemia, CGD, SCID, Wiskott-Aldrich, DiGeorge, Dock 8 or Stat 3 deficiency, hypogammaglobulinemia requiring IVIG replacement)

☐ HIV positive with CD4 < 200 and not on therapy

☐ HIV positive, controlled on therapy, and receipt of COVID-19 vaccine is not recommended

☐ Active treatment with high-dose corticosteroids (i.e., ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), antimetabolites, tumor-necrosis (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory

Solid Organ Transplant

☐ Lung transplant recipients

☐ Any solid organ transplant recipient within 12 months of transplant or rejection treatment with antithymocyte globulin or alemtuzumab

☐ Any solid organ transplant recipient ≥ 65 years old having completed primary vaccination series + booster

☐ All abdominal transplant recipients within 5 years of transplant and on antimetabolite or immunosuppressive drugs

☐ Solid organ transplant on antimetabolite (renal within 9 months, liver within 6 months) or Solid organ transplant on belatacept or heart transplant recipients

Interval between monoclonal antibody and vaccine

Passive Antibody Products

Current guidance

Defer COVID-19 vaccination for:

- 30 days if product used for post exposure prophylaxis
- 90 days if product used for treatment
- No guidance for pre-exposure prophylaxis

Revised guidance

- No recommended deferral period
- However, tixagevimab/cilgavimab (EVUSHELD™) should be deferred for at least two weeks after vaccination

Paxlovid - (**nirmatrelvir/ritonavir)**

- Pfizer- Novel drug- SARS-CoV-2-3CL protease inhibitor.
- EPIC-HR (patients at High risk of severe disease)
  - Randomized, double-blind study
  - Clinical trial sites across North and South America, Europe, Africa, and Asia
  - < 5 days from symptom onset period
  - Mild to moderate symptoms

- Results:
  - 2246 patients
  - **Paxlovid- 0 deaths, 0.8 % hospitalization**
  - **Placebo- 12 deaths, 6.3% hospitalization**
  - **89% reduction**
  - Relative benefit similar at 3 and 5 days from symptom onset
  - 10 fold reduction in viral load

Paxlovid (nirmatrelvir/ritonavir)

- **Contraindicated – drugs that are CYP3A inducers** and can lower Paxlovid plasma concentrations, loss of antiviral response, risk for resistance emergence
- Cannot start Paxlovid immediately after discontinuing CYP3A inducer:
  - Anticonvulsant: carbamazepine, phenobarbital, phenytoin
  - Antimycobacterials: rifampin
  - Herbal products: St. John's Wort (*hypericum perforatum*)

  List not comprehensive – see Fact Sheet for Providers
- Risk of HIV-1 resistance to HIV protease inhibitors

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

Molnupiravir (Lagevrio)

- Incorporated into the viral RNA, prevents viral propagation
- Four 200 mg capsules every 12 hours X 5 days
  - Named after Thor's hammer: Mjölnir
- Age 18 and older (no peds)
- Start within 5 days of symptom onset
- No drug interactions identified
- No dose adjustment for renal or hepatic impairment
- Contraindicated in pregnancy
- Caution in women of child bearing age and sexually active men

Outpatient Remdesivir

- Intravenous (IV) remdesivir is FDA-approved for treatment of COVID-19 in hospitalized adult and pediatric patients
- Remdesivir is expected to be active against omicron variant
- PINETREE study – Published NEJM , December 2021
  - Remdesivir for ouptaient treatment of patients with mild to moderate COVID-19 to prevent progression
- FDA approved on January 21, 2022 for outpatient use
- Dosing:
  - Remdesivir 200 mg IV on Day 1; 100 mg once daily on Days 2& 3
  - Should be initiated within 7 days of symptom onset
  - Logistical constraints as it is an IV infusion

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Early Remdesivir to Prevent Progression to Severe Covid-19

DOUBLE-BLIND, RANDOMIZED, CONTROLLED TRIAL

562
Outpatients with Covid-19,
<7 days from symptom onset and with
≥1 risk factor for disease progression

Covid-related hospitalization or death from any cause by day 28

N=279	N=283
Intravenous Remdesivir, 3 days	Placebo
0.7% (2 patients)	5.3% (15 patients)

HR, 0.13; 95% CI, 0.03–0.59 (P=0.008)

Remdesivir resulted in an 87% lower risk of Covid-related hospitalizations or death than placebo and had an acceptable safety profile.

R.L. Gottlieb et al. 10.1056/NEJMoa2116846

Fluvoxamine

- Lancet Global Health, October 27, 2021, TOGETHER Trial
  - Placebo controlled adaptive platform trial in Brazil, 11 sites
- < 7 days of symptoms
  - Fluvoxamine 100 mg PO BID X 10 days
- Absolute risk reduction- 5%
- Relative Risk Reduction 32%
- However:
  - No difference in time to symptom resolution
  - No difference in hospitalization
  - No difference in mortality
- Too many limitations in the study be able to recommend it

	Intention-to-treat analysis			Modified intention-to-treat analysis		
	N	n (%)	Relative risk (95% BCI)	N	n (%)	Relative risk (95% BCI)
Fluvoxamine	741	79 (11%)	0·68 (0·52–0·88)	740	78 (11%)	0·69 (0·53–0·90)
Placebo	756	119 (16%)	1 (ref)	752	115 (15%)	1 (ref)

BCI=Bayesian credible interval.

Table 2: Proportion of primary outcome events and relative risk of hospitalisation defined as either retention in a COVID-19 emergency setting or transfer to tertiary hospital due to COVID-19 for patients allocated fluvoxamine versus placebo

	Number enrolled	Composite of Hospitalization or ED obs > 6 hours	Deaths	
Fluvoxamine	746	11%	17	100 mg PO twice daily X 10 days
Placebo	756	16%	25	

Inhaled corticosteroids for non hospitalized patients

- Budesonide Trials

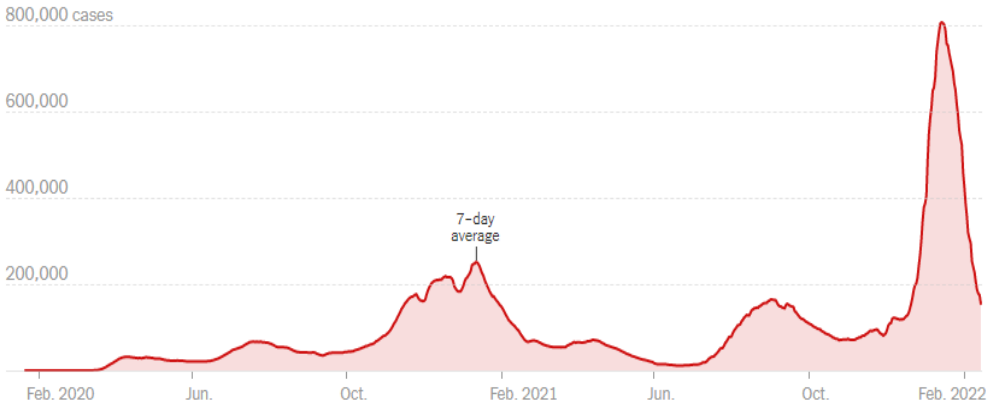
	Time from onset of symptoms	Budesonide dose	Hospitalized	
			Budesonide	Placebo
PRINCIPLE	6 days	800mcg BID	6.8%	8.8%
STOIC	3 days	800 mcg BID	1%	14%

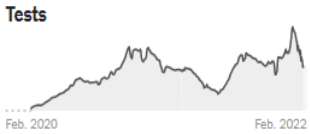
- Inhaled Ciclesonide has also been evaluated but no clear benefit

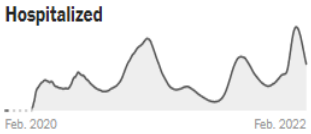
As we approach a million deaths in the US lets take a moment to reflect

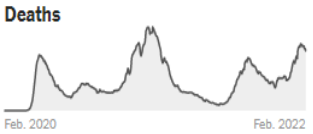
- Deaths in US
  - WWII- 291,000
  - Spanish flu of 1918- 675,000
- By December 2020 Covid was the leading cause of death in the US
  - Had overtaken heart disease and cancer

The true heroes



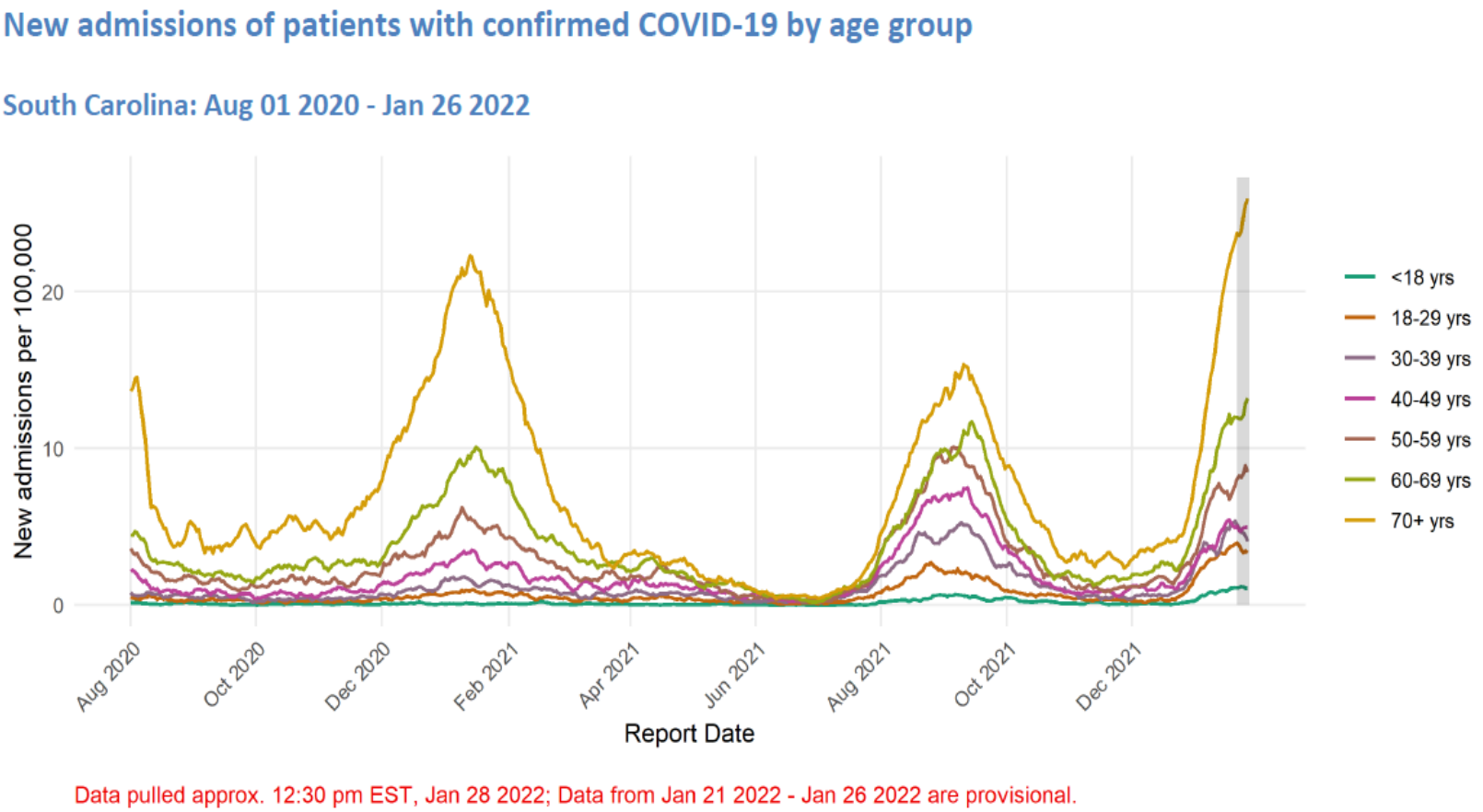




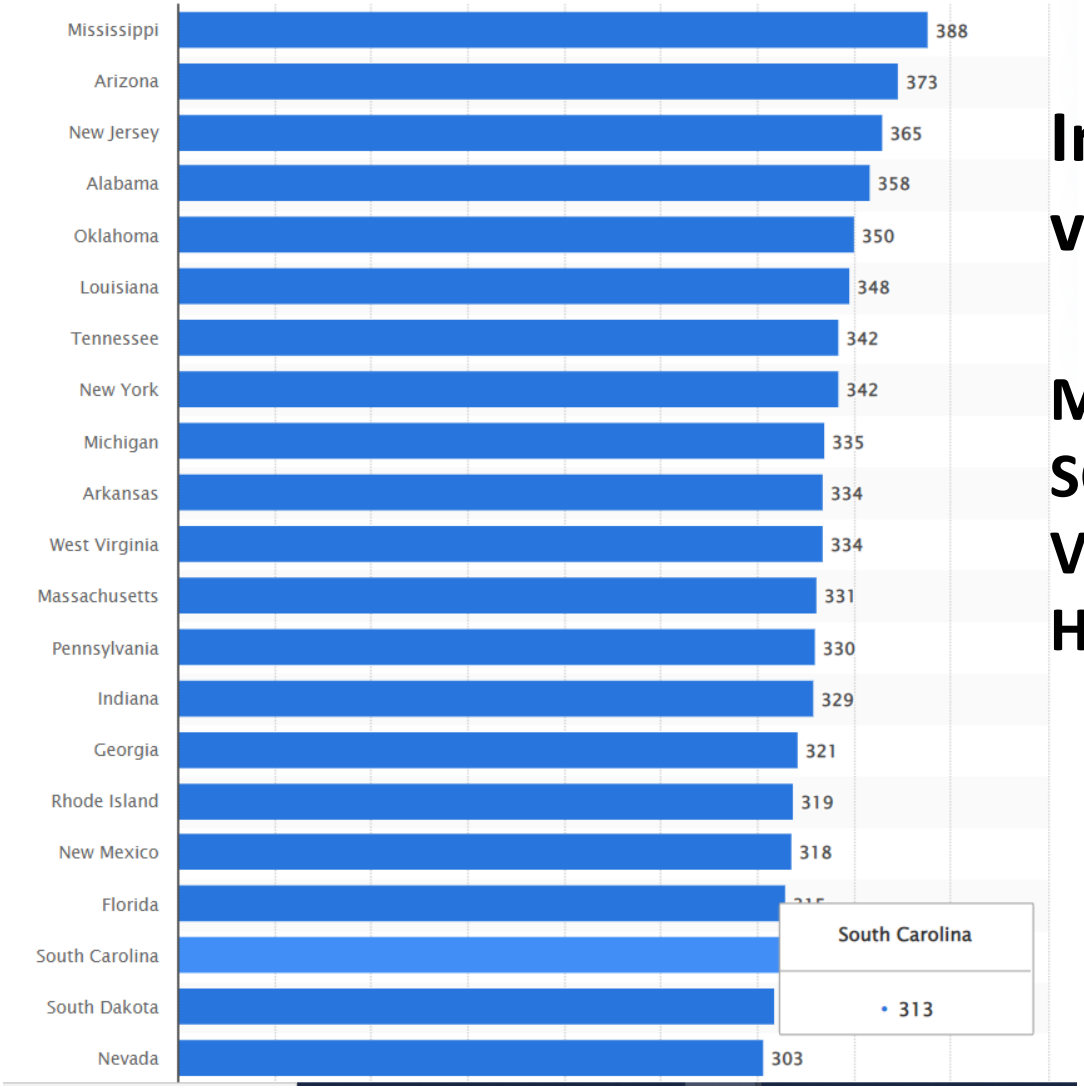


	DAILY AVG. ON FEB. 14	14-DAY CHANGE	TOTAL REPORTED
Cases	154,912	-66%	77,835,989
Tests	1,309,278	-31%	—
Hospitalized	89,158	-36%	—
In I.C.U.s	16,761	-31%	—
Deaths	2,400	-6%	920,959

Hospitalizations by age breakdown- South Carolina



Death rates by state



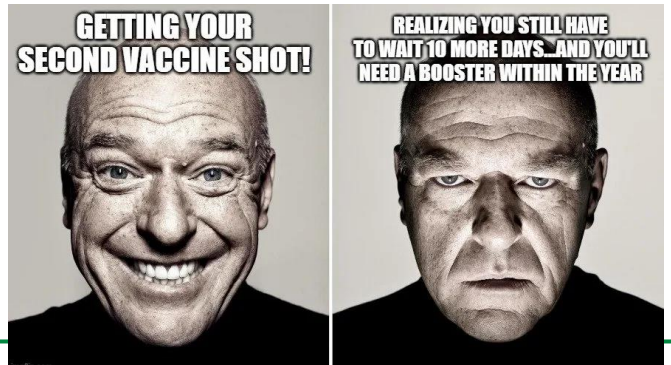
Inverse correlation with vaccination rates

MS-388/100K (50.5% vax)
SC-313/100K (56% vax)
VT-91/100K (79.8% vax)
HI-89/100K (76.6% Vax)

https://www.statista.com/statistics/1109011/coronavirus-covid19-death-rates-us-by-state/

Reminder about current booster recommendations

Previous Vaccine	Who	When	Which
Pfizer-BioNTech	≥ 12 years	> 5 months after completing primary series	Pfizer-BioNTech or Moderna are preferred Teens 12–17 years old may only get a Pfizer-BioNTech COVID-19 vaccine booster
Moderna	≥ 18 years	> 5 months after completing primary series	Pfizer-BioNTech or Moderna (mRNA COVID-19 vaccines) are preferred in
Johnson & Johnson's Janssen	≥ 18 years	> 2 months after	Pfizer-BioNTech or Moderna (mRNA COVID-19 vaccines) are preferred in



MMWR- January 28, 2022

- Effectiveness of a Third Dose of Pfizer–BioNTech and Moderna Vaccines in Preventing COVID-19 Hospitalization
- Study period: August 19–December 15, 2021
  - 3000 Adults admitted to 21 hospitals in 18 states included
  - Median age - 62 years; 49% - female; 36% immunocompromised

	Hospitalized Immunocompetent	Hospitalized immunocompromised
Two doses	82%	69%
Three doses	97%	88%

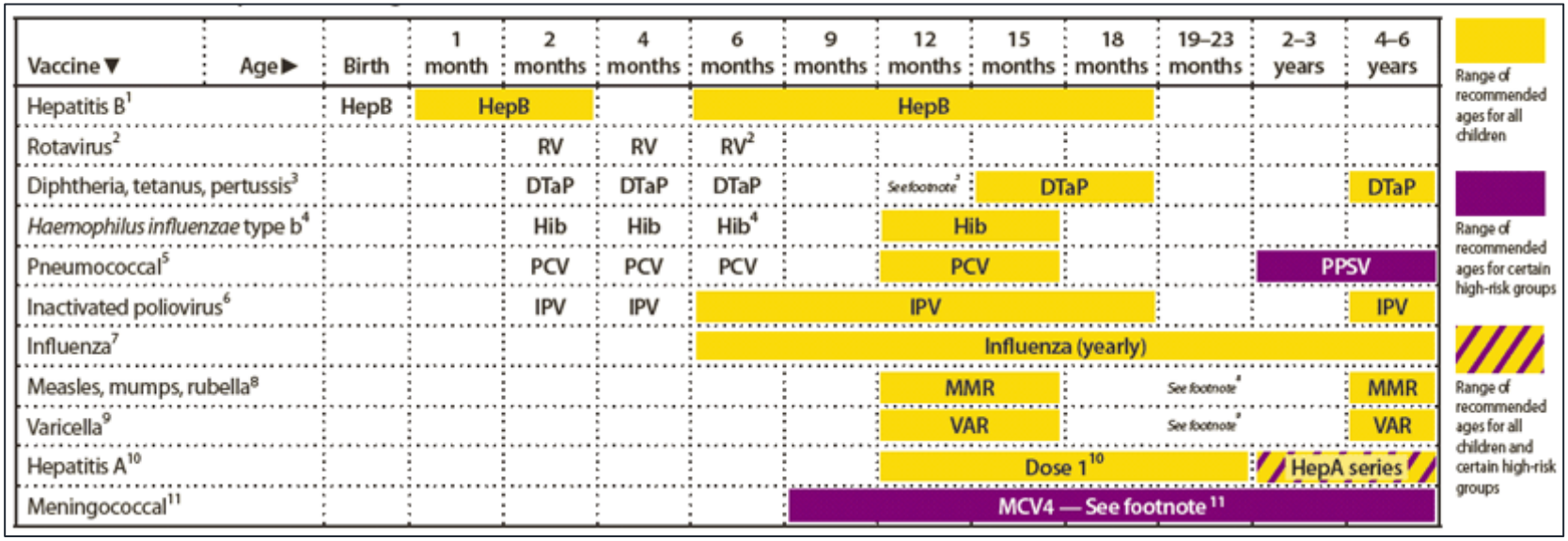
How about the 4th "booster for immunecompromised?

REVISED COVID-19 Vaccination Schedule for People Who Are Moderately or Severely Immunocompromised

Vaccine	Vaccination Schedule				
Pfizer-BioNTech (ages 5 years and older)	1st dose	2nd dose (21 days after 1st dose)	3rd dose (at least 28 days after 2nd dose)		Booster dose* (at least 3 months after 3rd dose)
Moderna (ages 18 years and older)	1st dose	2nd dose (28 days after 1st dose)	3rd dose (at least 28 days after 2nd dose)		Booster dose* (at least 3 months after 3rd dose)
Janssen (ages 18 years and older)	1st dose	Additional dose† (at least 28 days after 1st dose)		Booster dose* (at least 2 months after additional dose)	

*Any COVID-19 vaccine can be used for the booster dose in people ages 18 years and older, though mRNA vaccines are preferred. For people ages 12–17 years, only Pfizer-BioNTech can be used. People ages 5–11 years should not receive a booster dose.
†Only Pfizer-BioNTech or Moderna COVID-19 Vaccine should be used

Many vaccines require boosters



Vaccine ▼ / Age ►	Birth	1 month	2 months	4 months	6 months	9 months	12 months	15 months	18 months	19–23 months	2–3 years	4–6 years
Hepatitis B[1]	HepB	HepB			HepB							
Rotavirus[2]			RV	RV	RV[2]							
Diphtheria, tetanus, pertussis[3]			DTaP	DTaP	DTaP		See footnote[3]	DTaP				DTaP
Haemophilus influenzae type b[4]			Hib	Hib	Hib[4]		Hib					
Pneumococcal[5]			PCV	PCV	PCV		PCV				PPSV	
Inactivated poliovirus[6]			IPV	IPV	IPV							IPV
Influenza[7]					Influenza (yearly)							
Measles, mumps, rubella[8]							MMR		See footnote[8]			MMR
Varicella[9]							VAR		See footnote[9]			VAR
Hepatitis A[10]							Dose 1[10]				HepA series	
Meningococcal[11]						MCV4 — See footnote[11]						

Range of recommended ages for all children

Range of recommended ages for certain high-risk groups

Range of recommended ages for all children and certain high-risk groups

VACCINE ▼ / AGE GROUP ►	19–21 years	22–26 years	27–49 years	50–59 years	60–64 years	≥65 years
Influenza[2,*]	1 dose annually					
Tetanus, diphtheria, pertussis (Td/Tdap)[3,*]	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 years					Td/Tdap[3]
Varicella[4,*]	2 doses					
Human papillomavirus (HPV)[5,*] Female	3 doses					
Human papillomavirus (HPV)[5,*] Male	3 doses					
Zoster[6]					1 dose	
Measles, mumps, rubella (MMR)[7,*]	1 or 2 doses			1 or 2 doses		
Pneumococcal (polysaccharide)[8,9]	1 or 2 doses					1 dose
Meningococcal[10,*]	1 or more doses					
Hepatitis A[11,*]	2 doses					
Hepatitis B[12,*]	3 doses					

Vaccine 6 months – 4 years

- ~ 18 million children ages 6 months - 4 years in the US
- Vaccine:
  - Different color cap (maroon)
  - Different dose (3 mcg/0.2mL); Different diluent added (2.2mL)
- Pfizer-BioNTech is postponing its rolling application to the FDA
- Vaccines for this age group will not be available in the coming weeks
- Pfizer wants to wait for its data on a three-dose series of the vaccine
- Three doses "may provide a higher level of protection in this age group.“
- Data on the third dose is expected in early April

Kaiser Family Foundation surveys

Figure 5

Three In Ten Parents Say They'll Get Their Child Under The Age Of Five Vaccinated ASAP When A COVID-19 Vaccine Is Authorized For Their Age Group

Thinking about your child under the age of 5, once there is a COVID-19 vaccine authorized and available for your child's age group, do you think you will…?

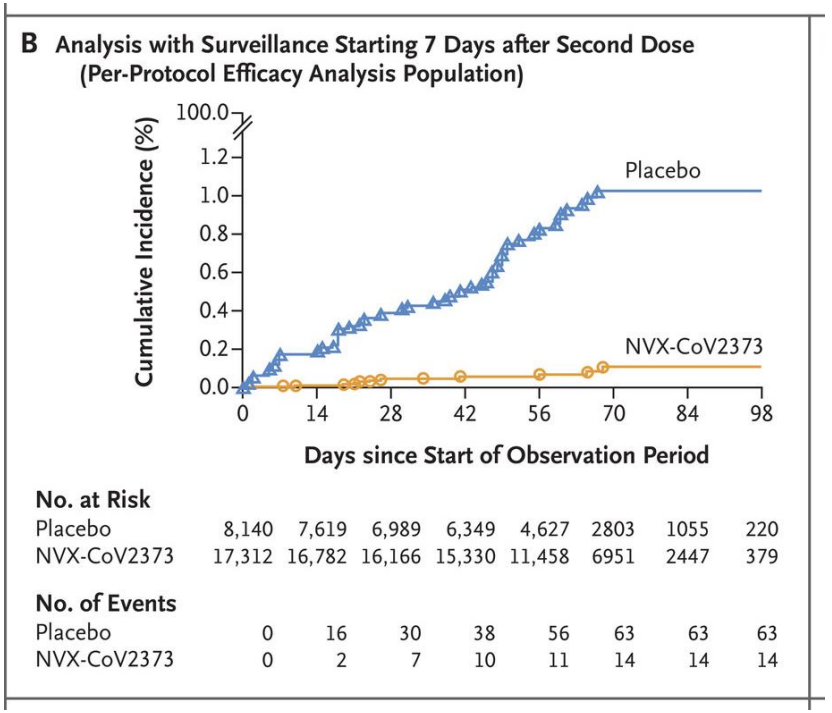
NOTE: Among parents or guardians of children under the age of 5. See topline for full question wording.
SOURCE: KFF COVID-19 Vaccine Monitor

KFF COVID-19 Vaccine Monitor

https://www.kff.org/coronavirus-covid-19/poll-finding/kff-covid-19-vaccine-monitor-january-2022-parents-and-kids-update/

Novavax EUA submitted

- Spike protein nanoparticle vaccine w/ adjuvant
- Phase 3 study of 29,582 volunteers
  - Median age, 47 years; 12.6% ≥65 yrs
  - 19,714 vaccine and 9868 placebo
- Follow up period: 3 months
- Symptomatic cases
  - Vaccine arm: 14 cases of COVID-19
  - Placebo arm- 63 cases
  - Vaccine efficacy, 90.4%; 95% confidence interval [CI], 82.9 to 94.6; P<0.001)
  - Efficacy of 100% against moderate to severe disease



ORIGINAL RESEARCH Annals of Internal Medicine

Measuring the COVID-19 Mortality Burden in the United States

A Microsimulation Study

Julian Reif, PhD; Hanke Heun-Johnson, PhD; Bryan Tysinger, PhD; and Darius Lakdawalla, PhD

Excess Deaths and Life Years Lost During the COVID pandemic

One million excess deaths account for a total of 13.5 million life years lost.
56% of life years lost were from people who were younger than 65 years old when they died.

	Total excess deaths	Average years of life lost	Total years of life lost
25-34 year olds	29,279	46.7	1,369,714
35-44	52,006	36.6	1,901,185
45-54	58,854	29.1	1,710,725
55-64	139,009	19	2,647,308
65-74	255,116	12.6	3,215,406
75-84	254,922	7.7	1,964,480
85+	210,817	3.4	719,334

Chart: Analysis by Reif, Heun-Johnson, Tysinger & Lakdawalla. Original data sources: CDC and CMS • Created with Datawrapper

A Tragedy Without Collective Grief

Final CDC SARS Timeline Entry

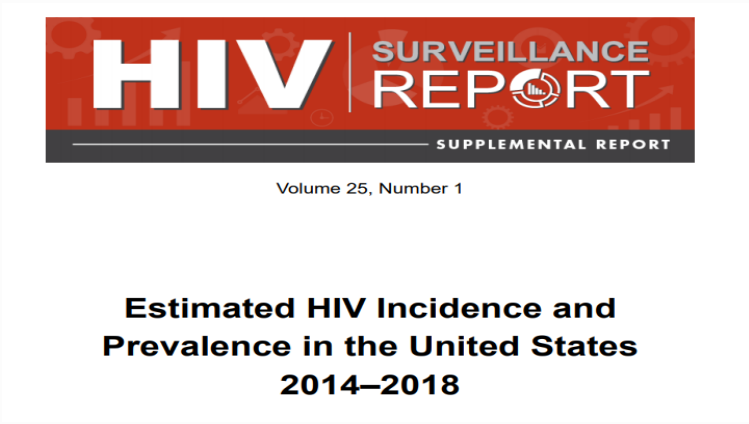
December 31: Globally, reports of SARS from 29 countries and regions; 8,096 persons with probable SARS resulting in 774 deaths. In the U.S., eight SARS infections were laboratory confirmed; and 19 probable SARS infections.

January 20, 2022: 55 reported COVID-19 deaths in South Carolina

Flags Planted On National Mall To Honor American Covid Deaths in September 2021, when the death total was 650,000 (photo credit: Kent Nishimura)

COVID Grand Rounds

- Weekly CME accredited grand rounds in Oct 2020
- 62 so far and counting……
- Many contributors and collaborators:
  - MUSC, Prisma-health, K-12 schools, SCDHEC, BCBS, College of pharmacy, and many others….
- Weekly attendance of between 250-400



- US population- 340 million
- Patients with HIV -estimated 1. million
- **Simple Math:**
- **HIV prevalence >1/350 Americans**
  - Males- 0.7% (1/150 male Americans)
  - Females-0.2%

United States Preventive Services Task Force recommendations

GRADE A for HIV

Recommendation Summary

Population	Recommendation	Grade
Pregnant persons	The USPSTF recommends that clinicians screen for HIV infection in all pregnant persons, including those who present in labor or at delivery whose HIV status is unknown.	A
Adolescents and adults aged 15 to 65 years	The USPSTF recommends that clinicians screen for HIV infection in adolescents and adults aged 15 to 65 years. Younger adolescents and older adults who are at increased risk of infection should also be screened. See the Clinical Considerations section for more information about assessment of risk, screening intervals, and rescreening in pregnancy.	A

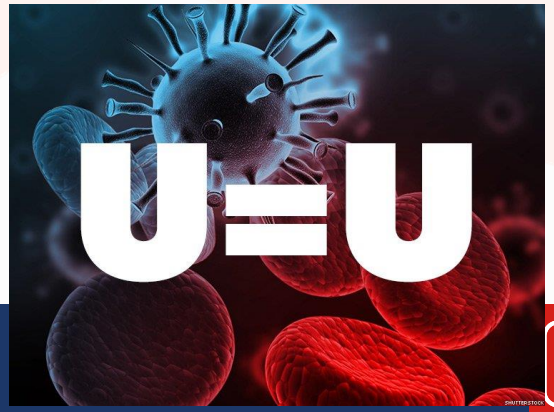
GRADE B for BREAST CANCER SCREEING

Recommendation Summary

Population	Recommendation	Grade
Women aged 50 to 74 years	The USPSTF recommends biennial screening mammography for women aged 50 to 74 years.	B
Women aged 40 to 49 years	The decision to start screening mammography in women prior to age 50 years should be an individual one. Women who place a higher value on the potential benefit than the potential harms may choose to begin biennial screening between the ages of 40 and 49 years.	C

Recommendations for Initiating ART for an HIV infected person

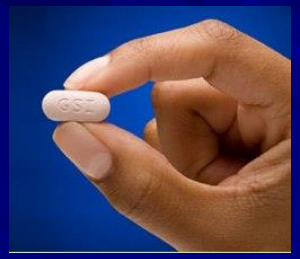
- ART (Antiretroviral therapy or HIV medications) is recommended for all HIV-infected individuals to reduce the risk of disease progression.
- Effective ART reduces transmission to almost **“0”**
- HIV is easier to treat than Diabetes, COPD, CHF
- Undetectable= Untransmissible



HIV:Single Tablet Regimens

Atripla

Genvoya



Complera

Juluca

Stribild

Odefsey

Triumeq

Biktarvy

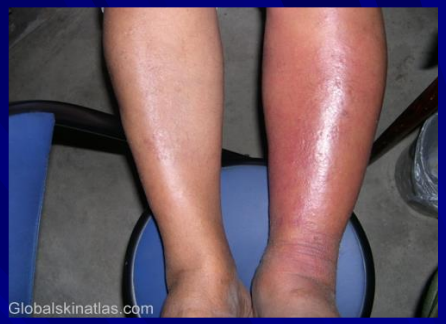
PrEP: What is HIV PrEP

- Pre-exposure prophylaxis (PrEP)
  - A method of preventing an uninfected person from acquiring the disease

  - Daily oral PrEP
  - Fixed-dose combination of
  - Tenofovir disoproxil fumarate (TDF) 300 mg and emtricitabine (FTC) 200 mg

1. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

Treatment of non-purulent cellulitis



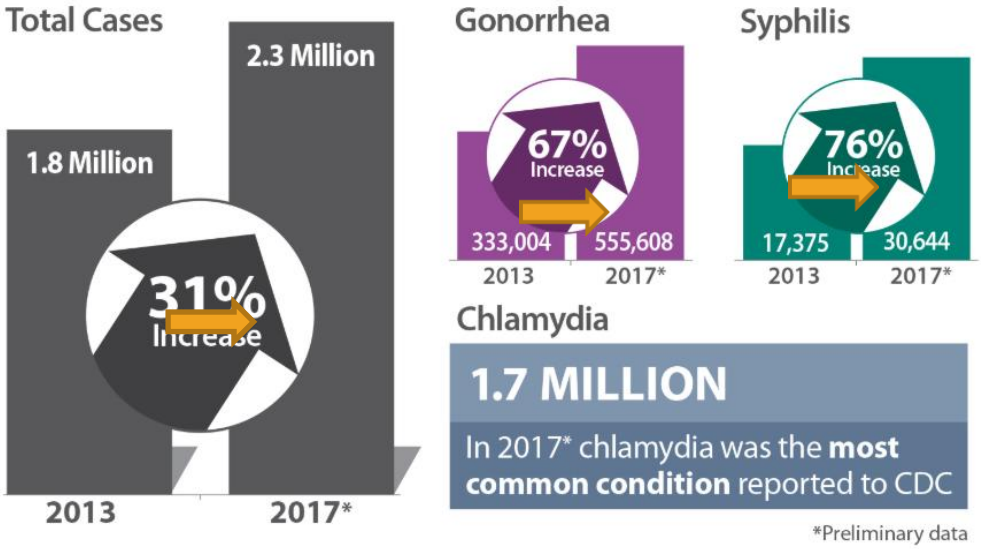
- For outpatients with nonpurulent cellulitis
- Cellulitis with no purulent drainage or exudate and no associated abscess
- Treatment:
  - Empirical therapy for infection due to β-hemolytic streptococci is recommended .
  - Empirical coverage for CA-MRSA is recommended in selected patients.
- Do not use Bactrim as monotherapy
  - S. Pyogenes can be resistant to Sulfa drugs in 30% of cases.
  - 5-7 days should be enough

Drug	Adult Dose
Cephalexin	500 QID
Dicloxacillin	500 QID
Clindamycin*	300-450 TID
Linezolid*	600 BID

*Also have activity against CA-MRSA

THE U.S. IS EXPERIENCING STEEP, SUSTAINED INCREASES IN SEXUALLY TRANSMITTED DISEASES

Combined diagnoses of chlamydia, gonorrhea, and syphilis **increased sharply over the past five years**



Chlamydia

1.7 MILLION

In 2017* chlamydia was the **most common condition** reported to CDC

*Preliminary data

UNDIAGNOSED STDS CAN LEAD TO SEVERE HEALTH PROBLEMS

Diagnosed cases of chlamydia, gonorrhea, and syphilis **represent just a small fraction** of the true disease burden

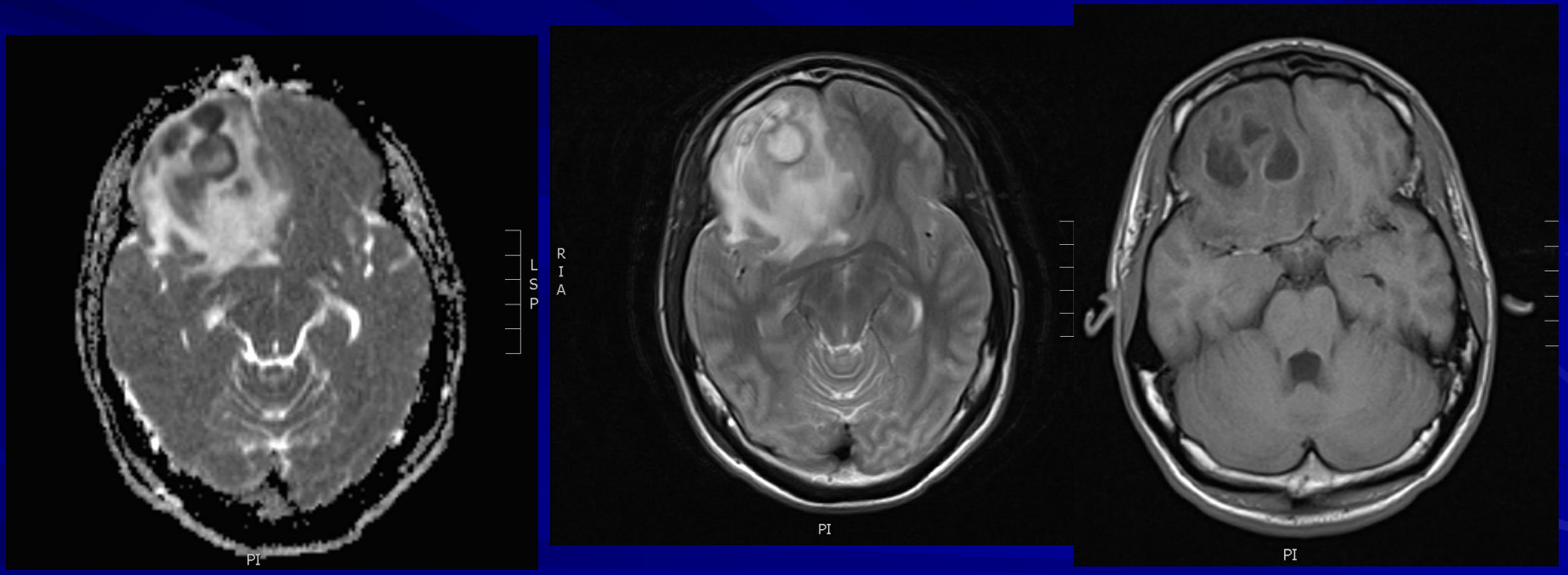
Left untreated, these STDs can produce severe, adverse effects

- infertility
- ectopic pregnancy
- increased HIV risk

Update to CDC's Treatment Guidelines for Gonococcal Infection, 2020

- *Neisseria gonorrhoeae* infections have increased 63% since 2014
  - Causes pelvic inflammatory disease, ectopic pregnancy, and infertility and facilitate transmission of HIV
- In 2007, CDC recommended not using quinolones due to increasing resistance
- In 2010, CDC recommended single 250 mg intramuscular (IM) dose of ceftriaxone AND a single 1 g oral dose of azithromycin
  - But the combination therapy approach did not stop increasing Azithromycin or Ceftriaxone MICs
- Now CDC recommends:
  - single 500 mg IM dose of ceftriaxone for treatment of uncomplicated urogenital, anorectal, and pharyngeal gonorrhea

- 26 year army captain 2 month H/O headaches



Brain Abscess

Condition	Relative frequency
Contiguous foci: otitis media, sinusitis, facial infection, dental abscess Strep, H. flu, anerobes	30-50%
Hematogenous spread : lung abscess, empyema, bronchiectasis, endocarditis Staphylococcus, strep	35%
Cryptogenic	10-35%

- MRI
  - LP contraindicated
  - Biopsy or aspiration needed especially if >2.5 cm
- Empiric antimicrobial therapy
  - Ceftriaxone + metronidazole X 4- 8 weeks
- If penetrating trauma then add Vancomycin

2021 Focused Update Guidelines on Management of Clostridioides difficile Infection in Adults

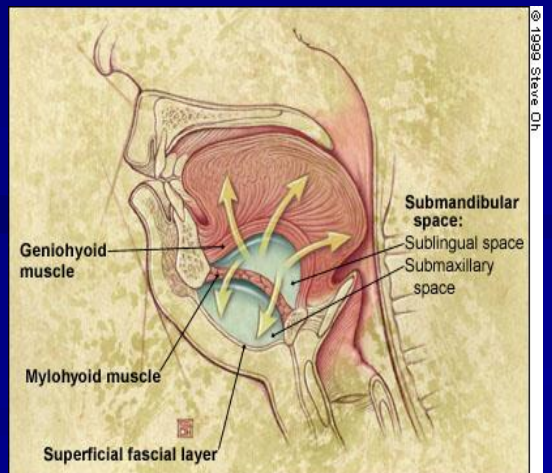
- Initial Clostridioides difficile infection (CDI) episode
  - Fidaxomicin rather than a standard course of vancomycin
- Risk factors for CDI recurrence:
  - age ≥65 years, immunocompromised host (rate 5-45%)

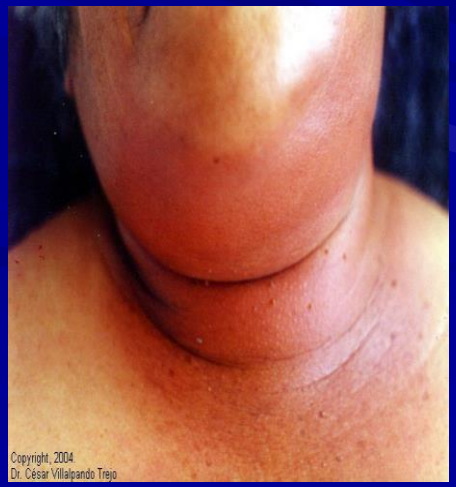
  Treatment of CDI recurrence:

  Fidaxomicin (standard or extended-pulsed regimen) rather than a standard course of vancomycin
- Recurrent CDI episode within the last 6 months
  - Add bezlotoxumab to standard-of-care (SOC) antibiotics rather than SOC antibiotics alone

Ludwig's Angina

- Soft tissue infection of the submandibular and sublingual spaces
  - Rapidly spreading
  - Brawny edema, fever, and systemically ill
  - Often originates from dental source
  - Swallowing difficulties and airway obstruction
- Treat
  - IV Unasyn or PO Augmentin,
  - Or Clindamycin and a quinolone





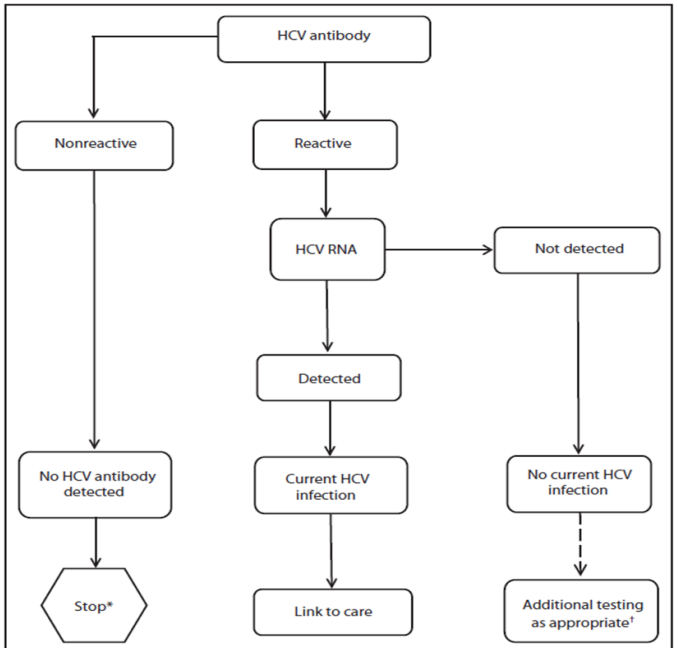
Hepatitis C Screening Recommendations

Population	Recommendation	Grade (What's This?)
Adults aged 18 to 79 years	The USPSTF recommends screening for hepatitis C virus (HCV) infection in adults aged 18 to 79 years.	B

One-Time Hepatitis C Testing

Recommendations for One-Time Hepatitis C Testing	
RECOMMENDED	RATING
One-time, routine, opt out HCV testing is recommended for all individuals aged 18 years and older.	I, B
One-time HCV testing should be performed for all persons less than 18 years old with behaviors, exposures, or conditions or circumstances associated with an increased risk of HCV infection (see below).	I, B
Periodic repeat HCV testing should be offered to all persons with behaviors, exposures, or conditions or circumstances associated with an increased risk of HCV exposure (see below).	IIa, C
Annual HCV testing is recommended for all persons who inject drugs and for HIV-infected men who have unprotected sex with men.	IIa, C

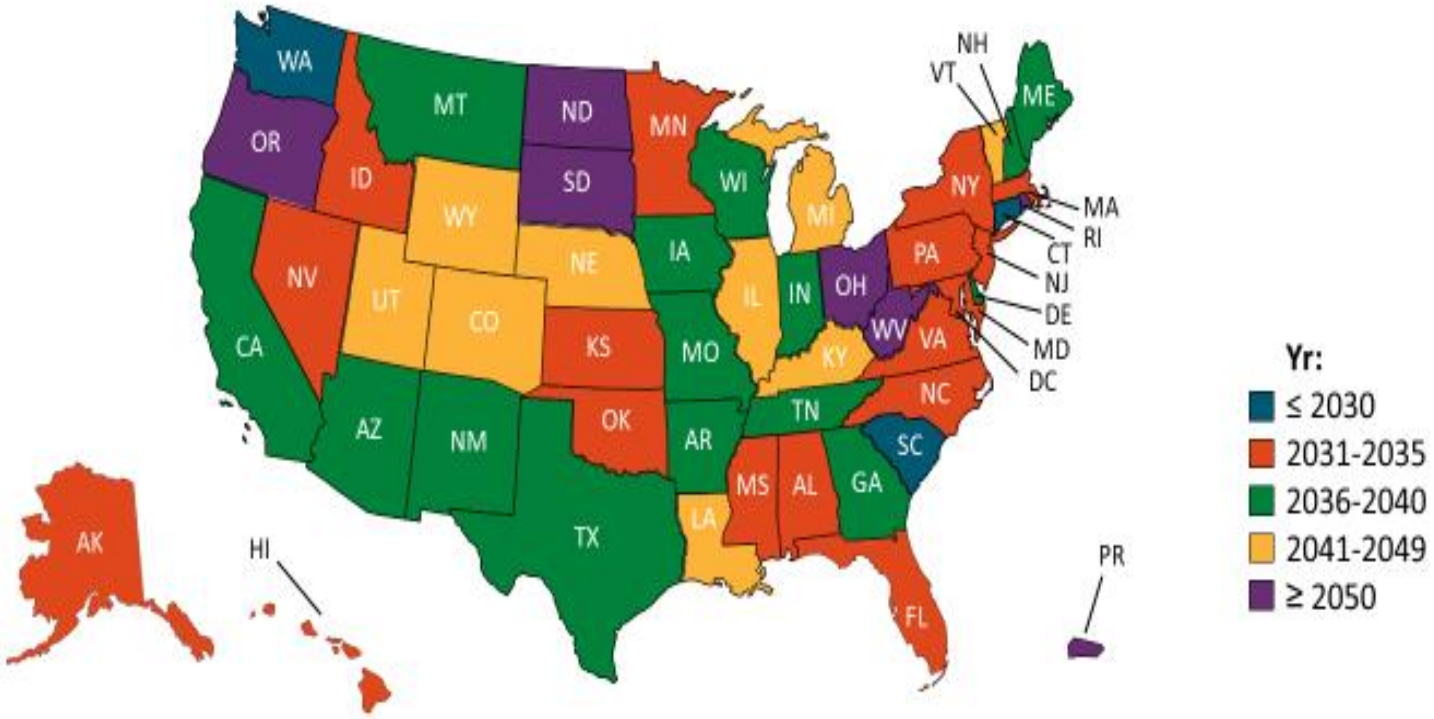
FIGURE. Recommended testing sequence for identifying current hepatitis C virus (HCV infection



Treatment of Chronic HCV

- About 2.4 million Americans with Chronic HCV
- Treatment is very easy and is recommended for ALL pts with chronic HCV
    - Exception: life expectancy likely to be < 6 months
- Goal of Treatment is - **Sustained Virological Response**
    - **SVR-** equal to cure/eradication
- SVR is associated with
    - >70% reduction in the risk of Hepatocellular carcinoma
- Current Directly acting antivirals have SVR > 98%
    - 1-3 tablets, once a day, for 8-12 weeks
    - Very well tolerated

US HCV Elimination: Estimating the Yr Each State Will Hit WHO Targets



*The estimation may be less accurate owing to the small number of patients with HCV in the area.

Sulkowski. EASL 2020. Abstr THU375.

Slide credit: clinicaloptions.com

AETC AIDS Education & Training Center Program Southeast

Monthy 1st and 3rd Wednesday and
12:00pm-1:00pm EST
11:00am-12:00pm CST
09:00am-10:00am PST

4th Wednesday
12:00pm-1:00pm CST
01:00pmpm-2:00pm EST
10:00am-11:00am PST

South East Viral Hepatitis Interactive Case Conference

Community acquired pneumonia

- 6th leading cause of death
- Average mortality 14%
- Community acquired pneumonia affects ~4 million patients and results in 10 million physician visits, 1 million hospitalizations, and >50,000 deaths annually
- Acute onset (3–5 days) of symptoms, fevers, chills, rigors, chest pain, cough productive of purulent sputum, and dyspnea.
- Incidence of invasive pneumococcal disease (including bacteremia)
  - General population
    - 3.8 / 100,000 in adults aged 18–34 years
  - 36.4 / 100,000 among those aged ≥65 years
- (*Vaccinate PCV13 and PPSV23*)

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Joshua P. Metlay*, Grant W. Waterer*, Ann C. Long, Antonio Anzueto, Jan Brozek, Kristina Crothers, Laura A. Cooley, Nathan C. Dean, Michael J. Fine, Scott A. Flanders, Marie R. Griffin, Mark L. Metersky, Daniel M. Musher, Marcos I. Restrepo, and Cynthia G. Whitney; on behalf of the American Thoracic Society and Infectious Diseases Society of America

This official clinical practice guideline was approved by the American Thoracic Society May 2019 and the Infectious Diseases Society of America August 2019

Table 1. 2007 Infectious Diseases Society of America/American Thoracic Society Criteria for Defining Severe Community-acquired Pneumonia

Validated definition includes either one major criterion or three or more minor criteria
Minor criteria
Respiratory rate ≥ 30 breaths/min
Pa_{O2}/F_{IO2} ratio ≤ 250
Multilobar infiltrates
Confusion/disorientation
Uremia (blood urea nitrogen level ≥ 20 mg/dl)
Leukopenia* (white blood cell count < 4,000 cells/μl)
Thrombocytopenia (platelet count < 100,000/μl)
Hypothermia (core temperature < 36°C)
Hypotension requiring aggressive fluid resuscitation
Major criteria
Septic shock with need for vasopressors
Respiratory failure requiring mechanical ventilation
*Due to infection alone (i.e., not chemotherapy induced).

Community-acquired pneumonia in adults: Assessing severity and determining the appropriate site of care

- CURB-65

Confusion (based upon a specific mental test or new disorientation to person, place, or time)

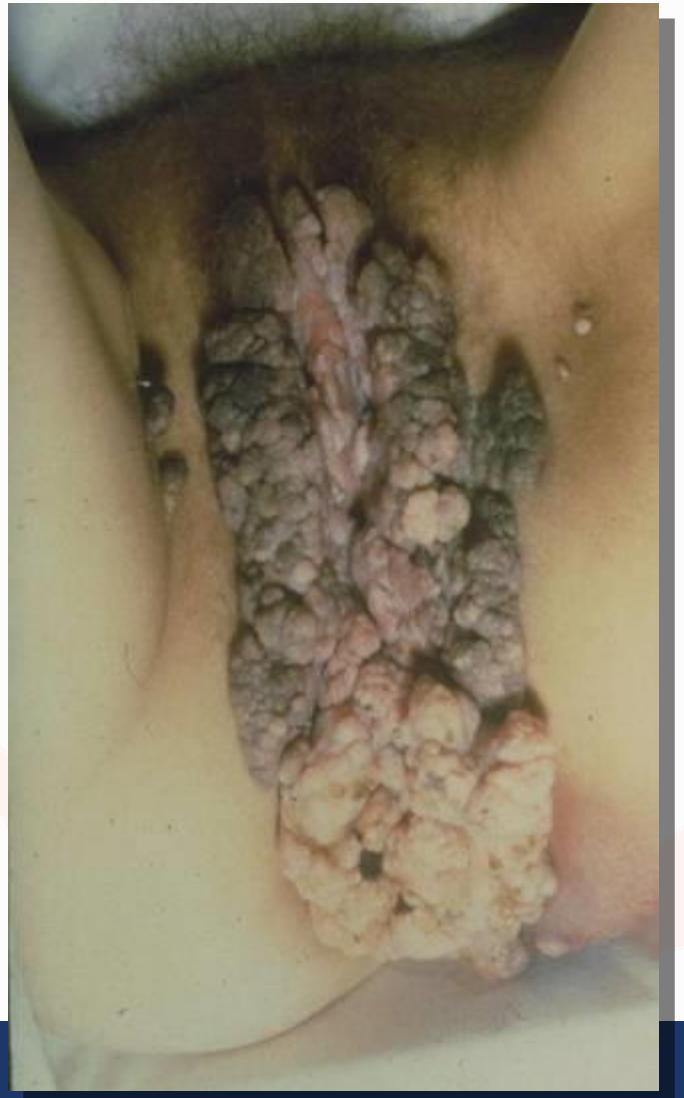
Urea (BUN > 20 mg/dL)

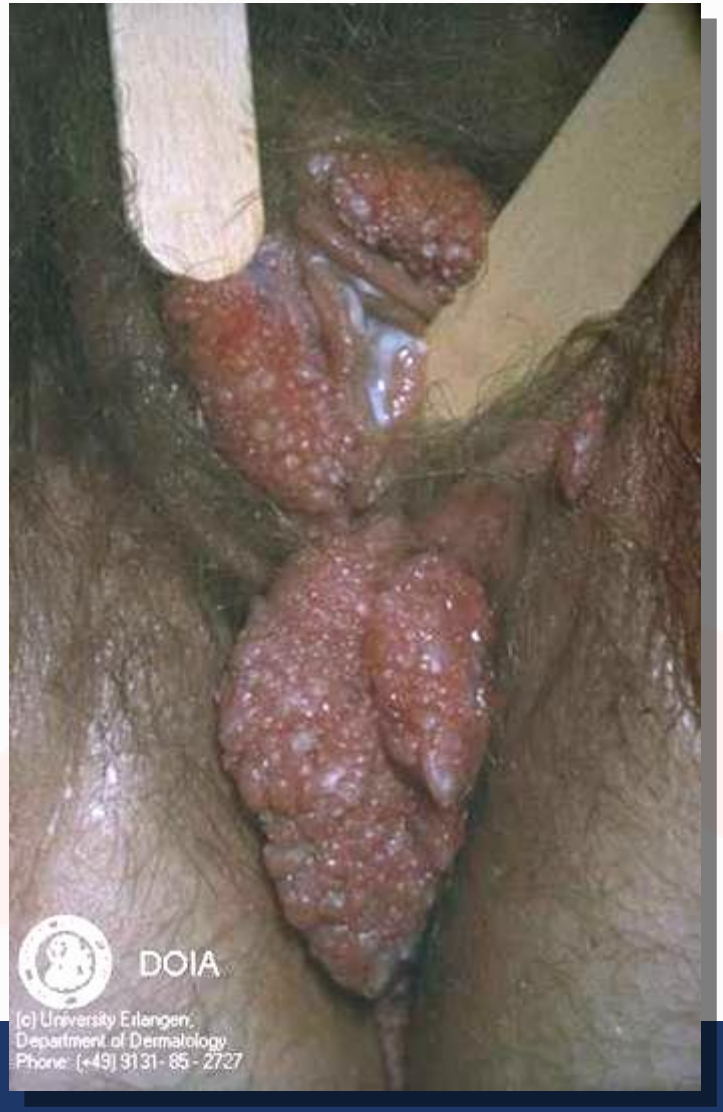
Respiratory rate ≥30 breaths/minute

Blood pressure (BP; systolic <90 mmHg or diastolic ≤60 mmHg)

Age ≥65 years

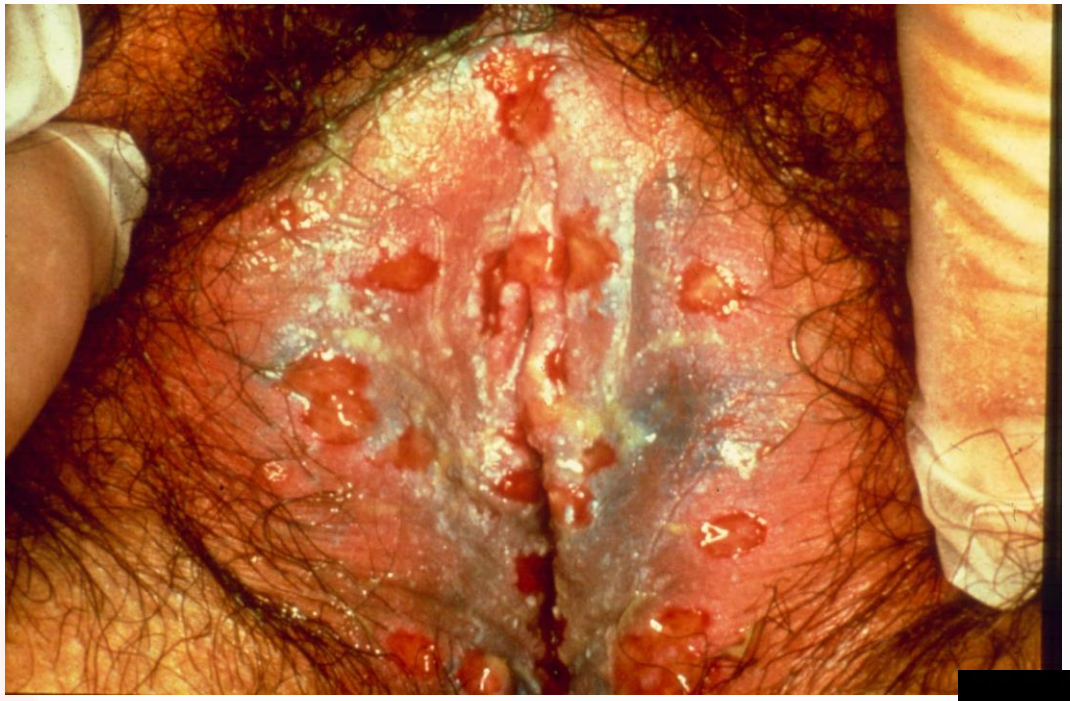
CLINICAL PRESENTATION OF GENITAL WARTS: VULVA

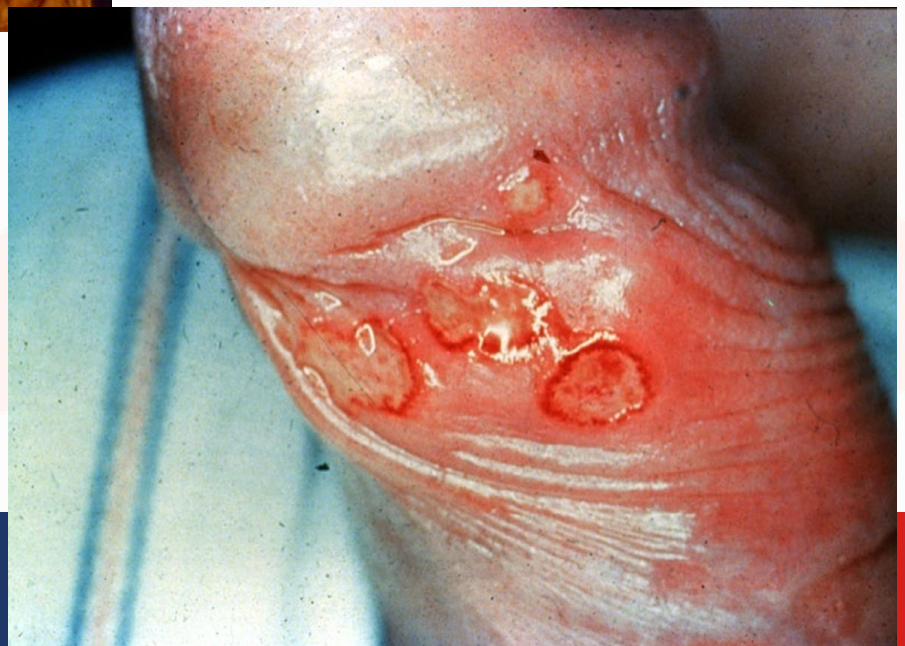




Vaccine

- Bivalent vaccine (Cervarix)
  - HPV types 16 and 18
- Quadrivalent vaccine (Gardasil)
  - Prevents infection - 6, 11, 16, and 18
- 9-valent vaccine
  - Prevents infection -6, 11, 16, 18, 31, 33, 45, 52, 58.





Genital ulcer-Does it hurt?

- Painful
  - Chancroid
  - Genital herpes simplex
- Painless
  - Syphilis
  - Lymphogranuloma venereum
  - Granuloma inguinale

Asymptomatic Bacteriuria

- 5% of sexually active young women
- 10% men and 20% women over 65 years
- Don't treat unless:
  - pregnant, preschool children or renal transplant
  - No deleterious effects of infection
  - No beneficial effects of treatment
  - Bacteruria recurs in a significant number
  - Increasing resistance to antibiotics
  - Not associated with long-term outcomes such as sepsis, pyelonephritis, or renal failure

Mody L, Juthani-Mehta M. Urinary Tract Infections in Older Women: A Clinical Review. JAMA. 014;311(8):844-854.

Antimicrobial Therapy for Acute Cystitis

- A short course of one of the following 3 antibiotics is recommended

1. **Nitrofurantoin** (Macrobid 100 mg PO BID for 5 days)
   - Avoid if CrCl <30 ml/min
2. **Trimethoprim-sulfamethoxazole** (1 DS tablet BID for 3 days)
   - Avoid if prior use within past 12 months
3. **Fosfomycin** 3 g PO once (for uncomplicated cystitis only)

Acute Cystitis

- Fluoroquinolone use is strongly discouraged!
  - Risk of AE (e.g., CDI, tendonitis, neurotoxicity, QTC prolongation, induction of resistance) exceeds potential benefit

- Oral 3rd generation cephalosporins should be avoided
  - Low urinary concentrations
  - High risk of AE such as induction of resistance (ESBL)

A 30 yo male presents to his physician's office c/o multiple lesions over face of 2 days duration. The patient reported itching and denied other symptoms