Pulmonary Infections in the Older Adult

JANUARY 18TH, 2024

Supaksh Gupta, MD
Paula Carvalho, MD, FCCP

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Disclosures

None to report for
- Dr. Gupta
- Dr. Carvalho

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Bacterial pulmonary infections

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Learning Objectives

At the end of this portion of the teaching session, you will be able to:

- Identify the most common causes of bacterial pneumonia
- Describe common presenting symptoms for bacterial pneumonia and risk factors for CAP in the elderly
- Review best practices and guideline recommendations surrounding initial selection of antibiotics and vaccine recommendations in the older adult

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Epidemiology of Community-Acquired Pneumonia (CAP)

Annual incidence of CAP is 248 cases per 100,00 adults

However, it increases to…

- 634 cases per 100,000 adults 65 to 79 years of age (2.5x increase)
- 16,430 per 100,000 adults 80 years and older (66x increase)

CAP is the third most common reason for hospitalization for persons aged 65 years and over

- Nearly 50% of hospitalized patients with CAP are in this age group!

Petrosillo N, Cataldo MA, Pea F. Treatment options for community-acquired pneumonia in the elderly people. Expert Rev Anti Infect Ther. 2015;13(4):473-485

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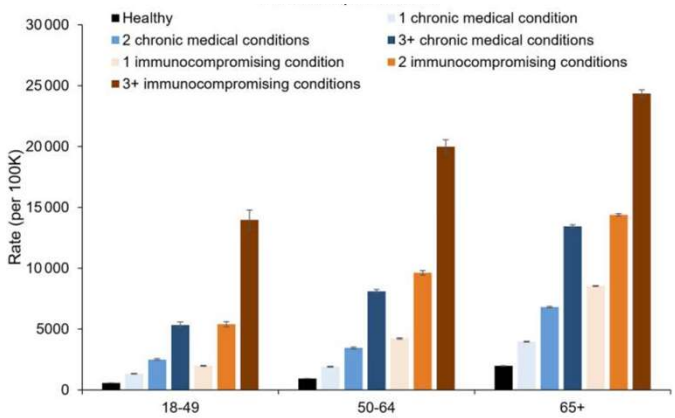
Epidemiology of Community-Acquired Pneumonia (CAP)

All-cause Pneumonia



Grant LR, Meche A, McGrath L, et al. Risk of pneumococcal disease in us adults by age and risk profile. Open Forum Infect Dis. 2023;10(5):192.

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Mortality in Community-Acquired Pneumonia (CAP)

Mortality in hospitalized CAP patients ranges between 10% and 25%

Based on a population study of individuals in Spain, 30-day mortality significantly increased with age:

- 7.2% in individuals 65-74 years old
- 13.5% in individuals 75-84 years
- 23.5% in individuals ≥ 85 years old

Petrosillo N, Cataldo MA, Pea F. Treatment options for community-acquired pneumonia in the elderly people. Expert Rev Anti Infect Ther. 2015;13(4):473-485

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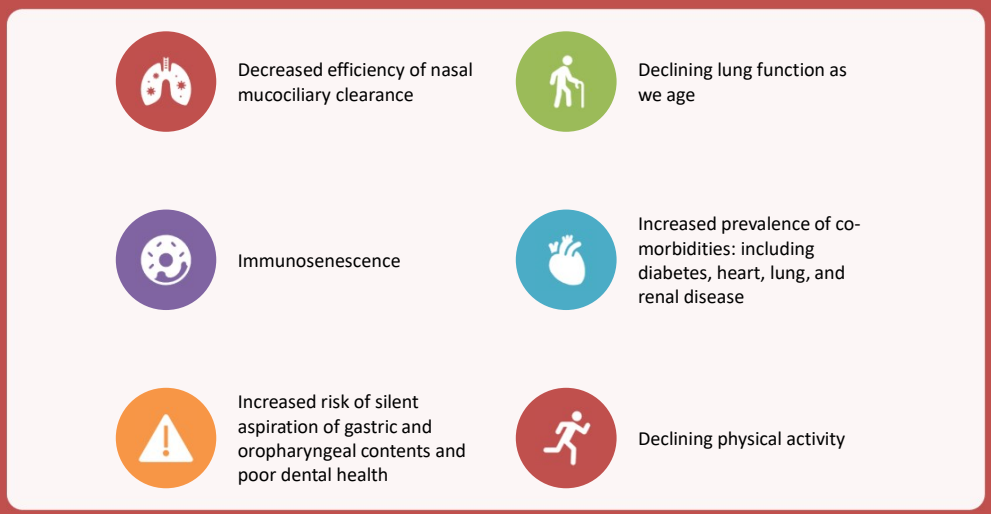
Risk Factors for CAP in the elderly



Simonetti AF, Viasus D, Garcia-Vidal C, Carratalà J. Management of community-acquired pneumonia in older adults. Ther Adv Infect Dis. 2014;2(1):3-16.

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Common Bacterial Pathogens in Adults

Etiologic agent	MacFarlane et al. (71)	Snijders et al. (73)	Lim et al. (74)	Johansson et al. (75)	Huijskens et al. (72)
Pneumococcus	30	37	48	64	34
Haemophilus	8	0	7	11	5
S. aureus	1	1	1	1	2
Gram-negative rods	1	4	1	1	4
Legionella	0	4	3	1	4
Viruses	8	5	19	29	29
Mycoplasma/Chlamydia	1	7	18	8	2
No pathogen detected	56	44	25	11	36

Gadsby NJ, Musher DM. The microbial etiology of community-acquired pneumonia in adults: from classical bacteriology to host transcriptional signatures. Clin Microbiol Rev. 2022;35(4):1522.

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Symptoms for CAP in the elderly

	Fernández-Sabé *et al.* [2003] ≥80 years hospitalized	Zalacain *et al.* [2003] ≥65 years hospitalized	Riquelme *et al.* [1996] ≥65 years hospitalized
Cough	–	81%	66%
Fever	68%	76%	63%
Dyspnea	–	70%	70%
Purulent sputum	53%	22%	–
Chills	45%	53%	23%
Pleural pain	37%	43%	34%
Altered mental state	21%	26%	45%
Arthromyalgias	8%	19%	–
Headache	7%	15%	–
Asthenia	–	39%	57%

Altered mental status or sudden decline in functional capacity were very common and may be the only symptoms in the elderly

Advanced age associated with lower symptom report and decrease in fevers

Due to potential unusual presentation, diagnosis of CAP in the elderly is often delayed!

Simonetti AF, Viasus D, Garcia-Vidal C, Carratalà J. Management of community-acquired pneumonia in older adults. Ther Adv Infect Dis. 2014;2(1):3-16.

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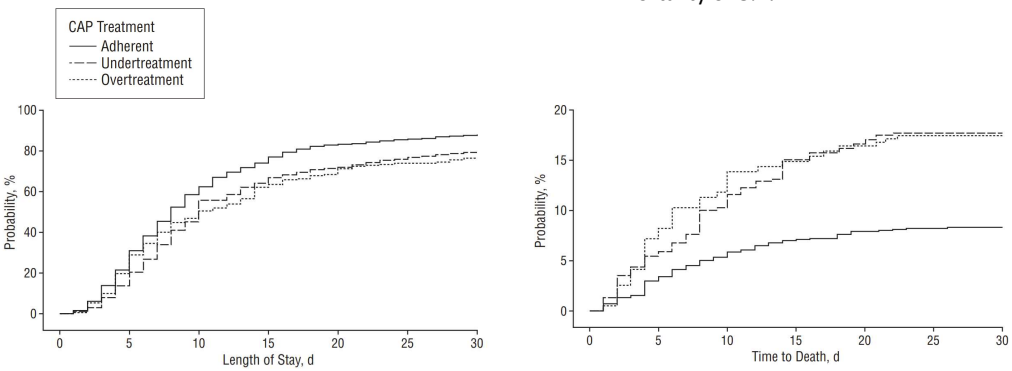
Guidelines … who needs guidelines?

- IDSA/ATS guideline adherence was associated with a shorter length of stay by 2 days (8 vs. 10) and a decreased overall in-hospital mortality of 8%!



Arnold FW, LaJoie AS, Brock GN, et al. Improving outcomes in elderly patients with community-acquired pneumonia by adhering to national guidelines: Community-Acquired Pneumonia Organization International cohort study results. Arch Intern Med. 2009;169(16):1515-1524.

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Clinical Question

An elderly 75-year-old man with a history of diabetes and hypertension presents to the ER with altered mental status and shaking chills, chest X-ray reveals a lobar infiltrate. He is afebrile, HR is 86, respiratory rate is 32, and BP is 145/93.

What do you recommend next?

A. No treatment needed
B. Outpatient treatment for CAP
C. Inpatient admission for CAP
D. I need more information!

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Risk stratification – CURB-65 Score

- Confusion
- Urea > 20 mg/dL
- Respiratory rate ≥ 30/min
- Blood pressure (SBP <90 or DBP < 60)
- Age ≥ 65

CURB-65 Score

0 or 1	2	3 or more
Mortality low (1.5%)	Mortality intermediate (9.2%)	Mortality high (22%)
Likely suitable for home treatment	Consider hospital supervised treatment	Manage in hospital as severe pneumonia

Lim WS, van der Eerden MM, Laing R, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax. 2003;58(5):377-382.

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Risk stratification – PSI / PORT Score

Demographics	Co-morbidities	Physical exam / vital signs	Laboratory / imaging
▪ Age (1 point per year) Male Yr Female Yr -10 ▪ Nursing home residency +10	▪ Neoplasia +30 ▪ Liver disease +20 ▪ CHF +10 ▪ Cerebrovascular disease +10 ▪ Renal disease +10	▪ Mental confusion +20 ▪ Respiratory rate +20 ▪ SBP +20 ▪ Temperature +15 ▪ Tachycardia +15	▪ Arterial pH +30 ▪ BUN +20 ▪ Sodium +20 ▪ Glucose +10 ▪ Hematocrit +10 ▪ Pleural effusion +10 ▪ Oxygenation +10

Risk class (Points)	Mortality (%)	Recommended site of care
I (<50)	0.1	Outpatient
II (51–70)	0.6	Outpatient
III (71–90)	2.8	Outpatient or brief inpatient
IV (91–130)	8.2	Inpatient
V (>130)	29.2	Inpatient

Rello J. Demographics, guidelines, and clinical experience in severe community-acquired pneumonia. Crit Care. 2008;12 Suppl 6(Suppl 6):S2.

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Should a Clinical Prediction Rule for Prognosis plus Clinical Judgment versus Clinical Judgment Alone Be Used to Determine Inpatient versus Outpatient Treatment Location for Adults with CAP?

In addition to clinical judgement, **we recommend that clinicians use a validated clinical prediction rule for prognosis** … to determine the need for hospitalization in adults diagnosed with CAP.

Metlay JP, Waterer GW, Long AC, et al. 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. Am J Respir Crit Care Med. 2019;200(7):e45-e67.

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Clinical Question

A 68-year-old woman with a history of chronic kidney disease presents to the ER with subjective fevers and productive cough for 3 days. Chest X-ray reveals a pulmonary infiltrate. Her temp is 98.6, HR is 65, respiratory rate is 18, and BP is 112/74.

Which of the following are recommended as part of the diagnostic work-up?

A. Urinary antigens (legionella and pneumococcal)
B. Sputum culture
C. Blood cultures
D. A and B
E. None of the above

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Diagnostic Testing Recommendations

Do not recommend obtaining sputum, blood culture, or urine antigens (pneumococcal and legionella) in the outpatient setting

Conditional recommendation to not obtain the above tests in hospitalized patients with non-severe CAP

Exceptions include …

- Unless being empirically treated for MRSA or Pseudomonas aeruginosa (or history of prior infections with these organisms)
- Received IV antibiotics in the last 90 days

Do recommend obtaining pre-treatment sputum, blood culture, and urinary antigens (pneumococcal and legionella) in hospitalized patients with severe CAP

Metlay JP, Waterer GW, Long AC, et al. 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. Am J Respir Crit Care Med. 2019;200(7):e45-e67.

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What's severe CAP anyways?

Diagnosis requires one major criteria or 3 or more minor criteria

Criteria for Severe Community-Acquired Pneumonia

Major criteria

Respiratory failure requiring mechanical ventilation

Severe shock requiring vasopressors

Minor criteria

Blood urea nitrogen ≥ 20 mg per dL (7.14 mmol per L)

Confusion or disorientation

Core temperature < 96.8°F (36°C)

Hypotension requiring aggressive fluid resuscitation

Multilobar infiltrates

Partial pressure of oxygen/fraction of inspired oxygen ratio ≤ 250

Platelet count < 100×10^3 per μL (100×10^9 per L)

Respiratory rate ≥ 30 breaths per minute

White blood cell count < 4,000 per μL (4.00×10^9 per L) due to infection alone (i.e., not chemotherapy induced)

Armstrong, Carrie. Community-Acquired Pneumonia: Updated Recommendations from the ATS and IDSA Am Fam Physician. 2020;102(2):121-124

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Clinical Question

Which of the following outpatient antibiotic regimens would be appropriate for our patient (68-year-old woman with chronic kidney disease)?

A. Amoxicillin
B. Azithromycin
C. Doxycycline
D. Cefpodoxime
E. B and D

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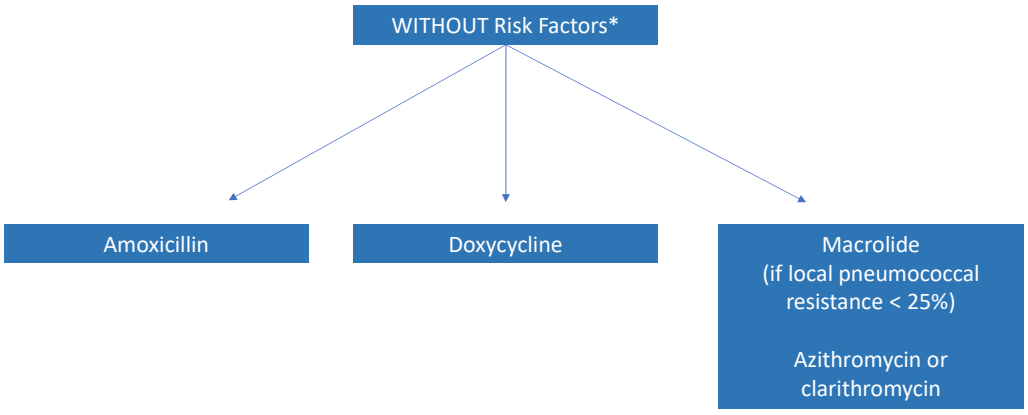
Antibiotics in the Outpatient Setting



*Risk Factors include comorbidities such as alcoholism, diabetes, cancer, or chronic heart, lung, liver or kidney disease

Armstrong, Carrie. Community-Acquired Pneumonia: Updated Recommendations from the ATS and IDSA Am Fam Physician. 2020;102(2):121-124

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Macrolide resistance in the WWAMI region

	Hospital/Region			
	Harborview (Seattle, WA)	Anchorage region, Alaska	Billings, Montana	Idaho
Macrolide Resistance to Streptococcus pneumoniae	28%	11%	39%	26%

https://hsl.uw.edu/antibiograms/2023-Antibiogram-HMC-UWML-UWNW.pdf
https://health.alaska.gov/dph/Epi/id/SiteAssets/Pages/HAI/default/AK%202020%20Antibiograms.pdf
https://dphhs.mt.gov/publichealth/cdepi/antimicrobialresistance
https://www.gethealthy.dhw.idaho.gov/antibiogram

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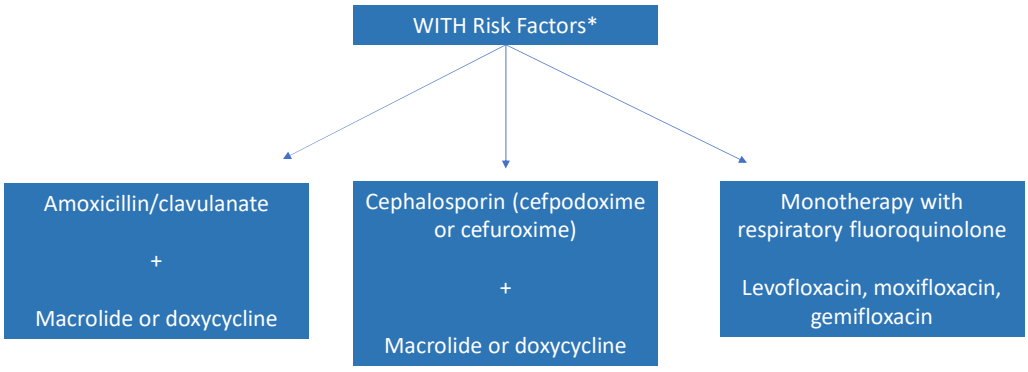
Antibiotics in the Outpatient Setting



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Armstrong, Carrie. Community-Acquired Pneumonia: Updated Recommendations from the ATS and IDSA Am Fam Physician. 2020;102(2):121-124

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Clinical Question

Our patient has been admitted to the medicine wards for CAP.

What antibiotics do you recommend starting for severe CAP? He has no risk factors for MRSA or Pseudomonas.

A. Vancomycin and Cefepime
B. Ceftriaxone and Azithromycin
C. Ceftriaxone
D. Azithromycin
E. Levofloxacin

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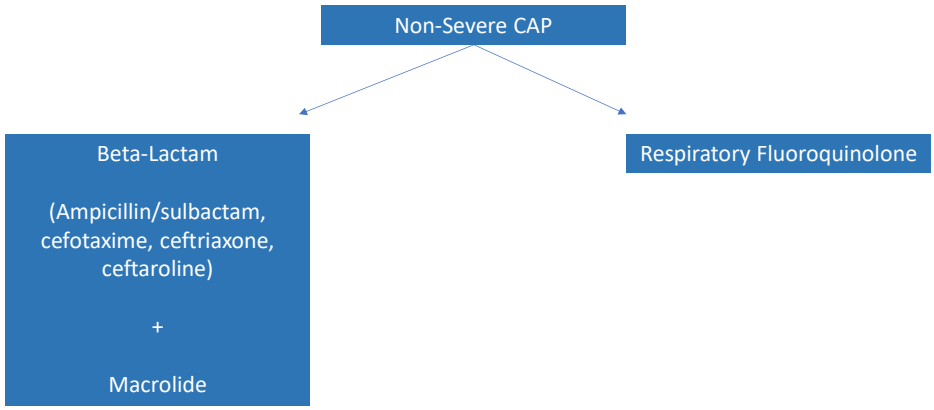
Antibiotics in the Inpatient Setting



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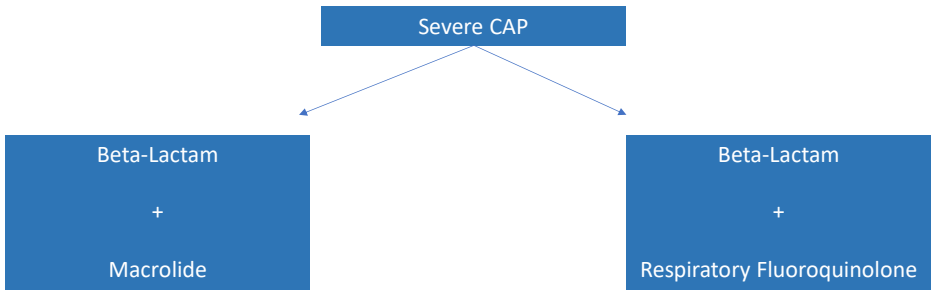
Antibiotics in the Inpatient Setting



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Clinical Question

Your patient sees you for follow-up in clinic 3 months later. She is doing great! You note that the patient had received pneumococcal conjugate vaccine (PCV20) one year ago. What additional vaccines do you recommend right now?

A. Pneumococcal polysaccharide (PPSV23)
B. PCV 13
C. PCV 15
D. PCV 20 again since it's been one year
E. No additional vaccines necessary

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Pneumococcal Vaccine Efficacy

Pneumococcal polysaccharide vaccine (PPSV23) decreases the relative risk of CAP by 28% in adults 65 years or older

Pneumococcal conjugate vaccine (PCV13) reduces the risk of community-acquired pneumonia by 45%

Pneumococcal vaccination coverage among adults who reached 65–70 years of age during the pandemic (2020–2021 combined) was 61%

https://www.cdc.gov/vaccines/vpd/pneumo/hcp/recommendations.html
Bonten MJM, Huijts SM, Bolkenbaas M, et al. Polysaccharide conjugate vaccine against pneumococcal pneumonia in adults. N Engl J Med. 2015;372(12):1114-1125.

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Current pneumococcal vaccine recommendations for adults ≥ 65 years old

- PCV20 [*Prevnar 20*] → Then you're done!
- PCV15 → PPSV23 [*Pneumovax*] one year later
- PPSV23 → PCV15 or PCV20 one year after receiving PPSV23
- PCV13 [*Prevnar 13*] is no longer recommended for routine use
- If you have received PCV13 (at any age) and PPSV23 (after age 65), then based on shared decision-making can consider receiving PCV20

https://www.cdc.gov/vaccines/vpd/pneumo/hcp/recommendations.html

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Non-pharmacologic Interventions for Risk Reduction

- Oral care is important for removing pathogenic bacteria from the oral mucosa and improving swallowing
- Regular physical activity has been shown to delay functional decline
- Make sure your patient is appropriately vaccinated
- Evaluate for and try to address any aspiration issues that may be ongoing
- Ensure patient compliance with medications, especially inhalers!
- Work on addressing substance use issues (tobacco and alcohol)
- Nutrition is important!

Simonetti AF, Viasus D, Garcia-Vidal C, Carratalà J. Management of community-acquired pneumonia in older adults. Ther Adv Infect Dis. 2014;2(1):3-16.

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Recap of Highlights

- Strep pneumoniae is still the most common cause of CAP, make sure their vaccines are up-to-date!
- CAP may present unusually in the elderly (altered mental status, functional decline), have a high index of suspicion
- Low threshold for inpatient admission, especially if vital sign abnormalities are present
- Optimize non-pharmacologic interventions!

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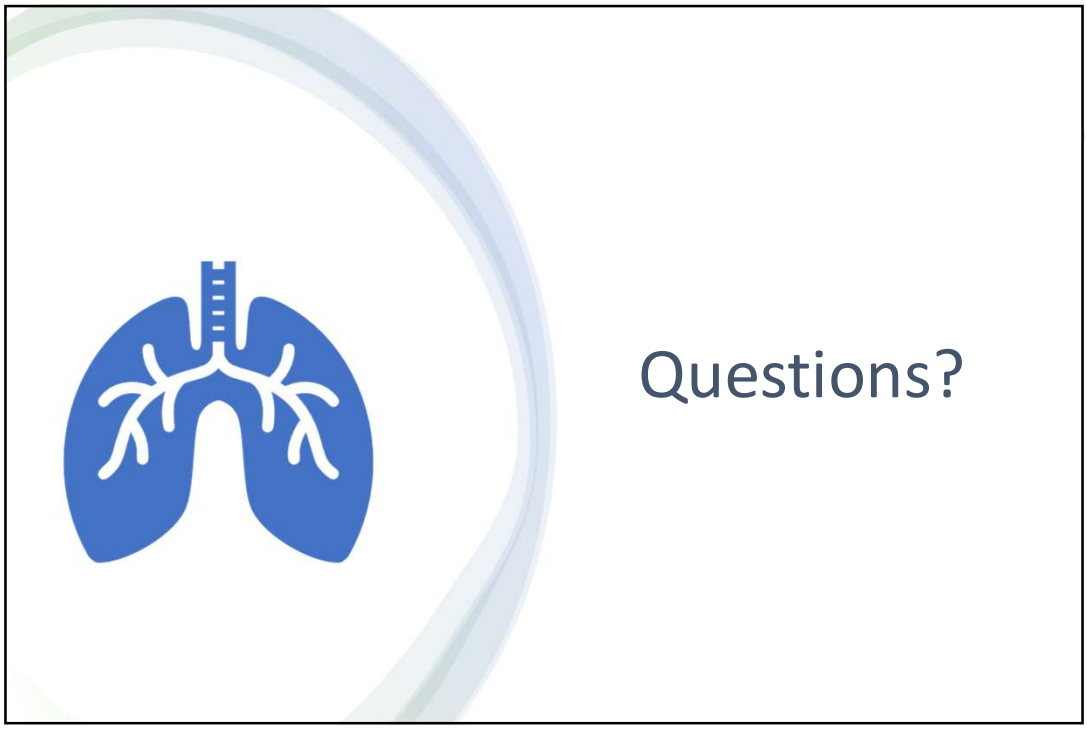

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A case:

- A 75-year-old man presents with fever, cough, and increased dyspnea for 48 hours. He lives at an assisted living facility where several residents have been hospitalized with similar symptoms and have tested positive for COVID, influenza A, or RSV.

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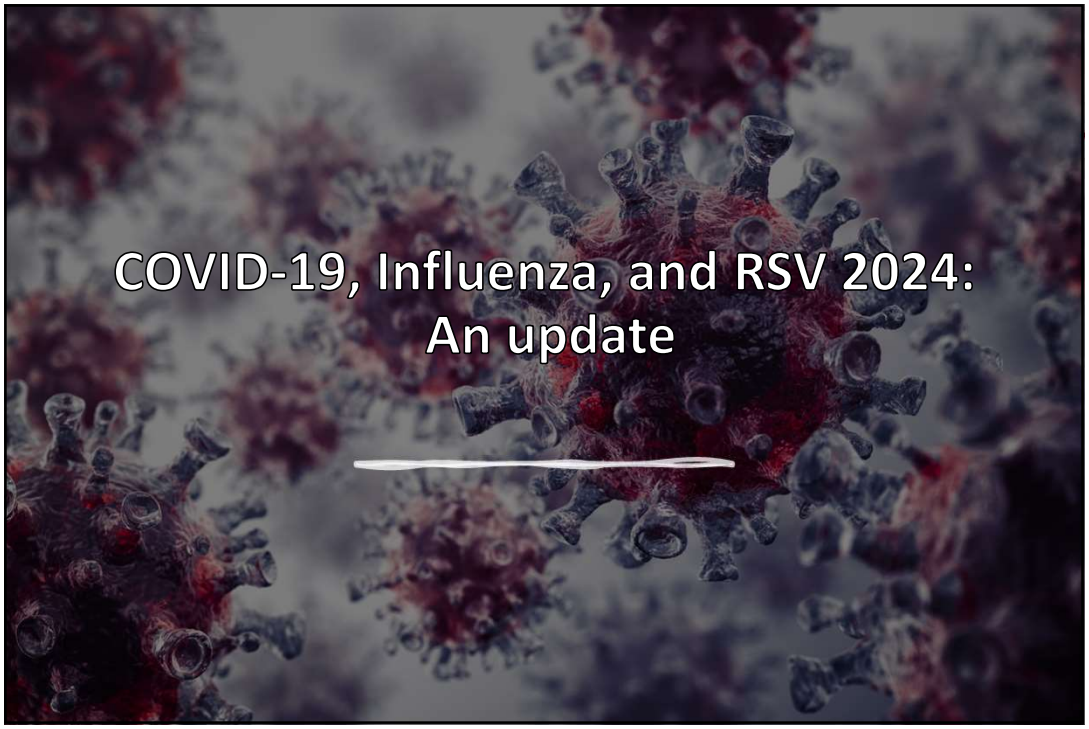

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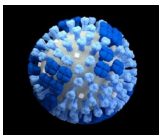
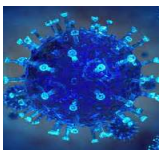
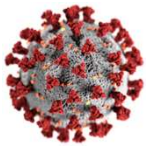
Our agenda:

1. A review of influenza, RSV, and SARS-CoV-2

2. Epidemiology and transmission

3. A review of treatments and vaccines

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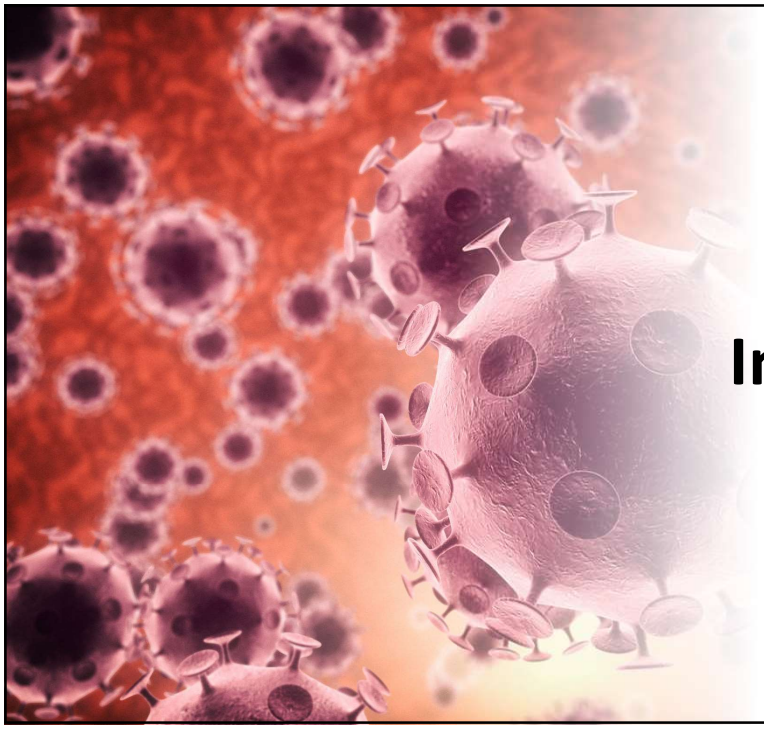

Influenza

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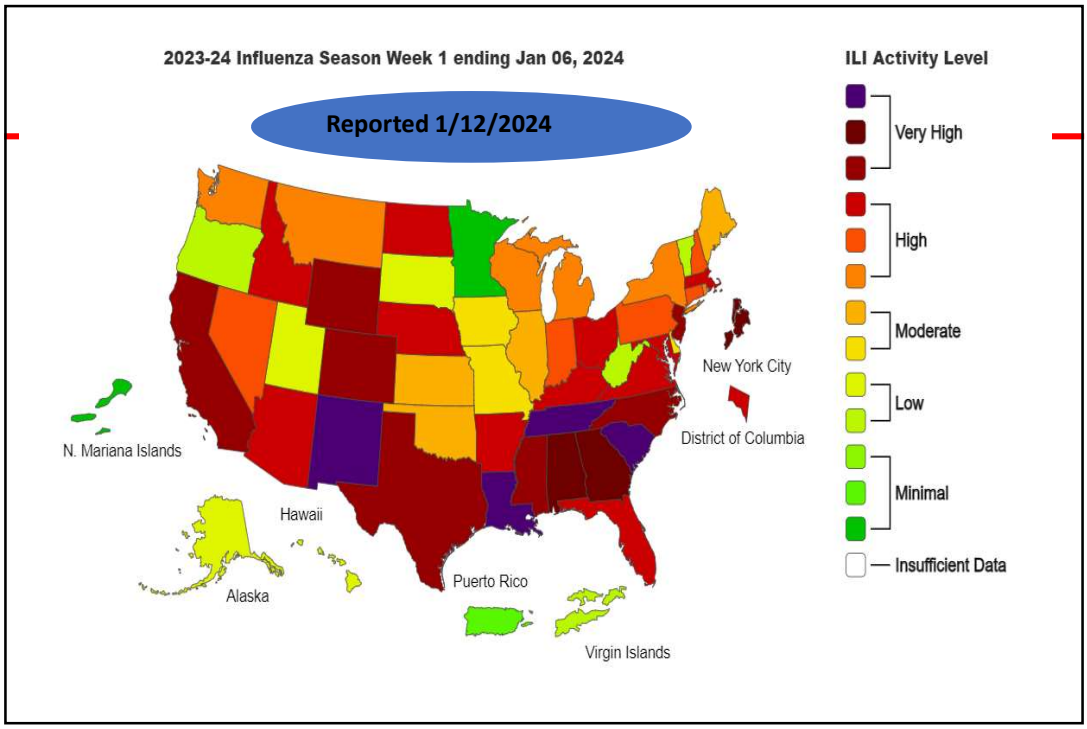
2023-24 Influenza Season Week 1 ending Jan 06, 2024
Reported 1/12/2024
ILI Activity Level
Very High
High
Moderate
Low
Minimal
Insufficient Data
New York City
District of Columbia
N. Mariana Islands
Hawaii
Alaska
Puerto Rico
Virgin Islands

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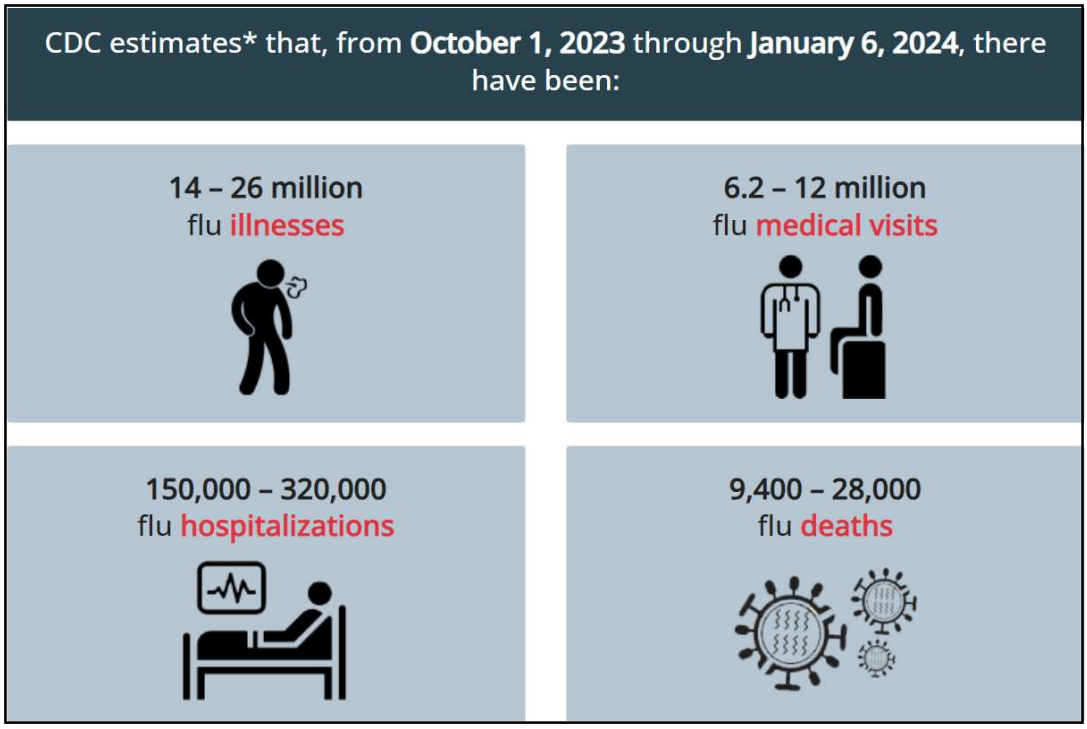
CDC estimates* that, from October 1, 2023 through January 6, 2024, there have been:
14 – 26 million
flu illnesses
6.2 – 12 million
flu medical visits
150,000 – 320,000
flu hospitalizations
9,400 – 28,000
flu deaths

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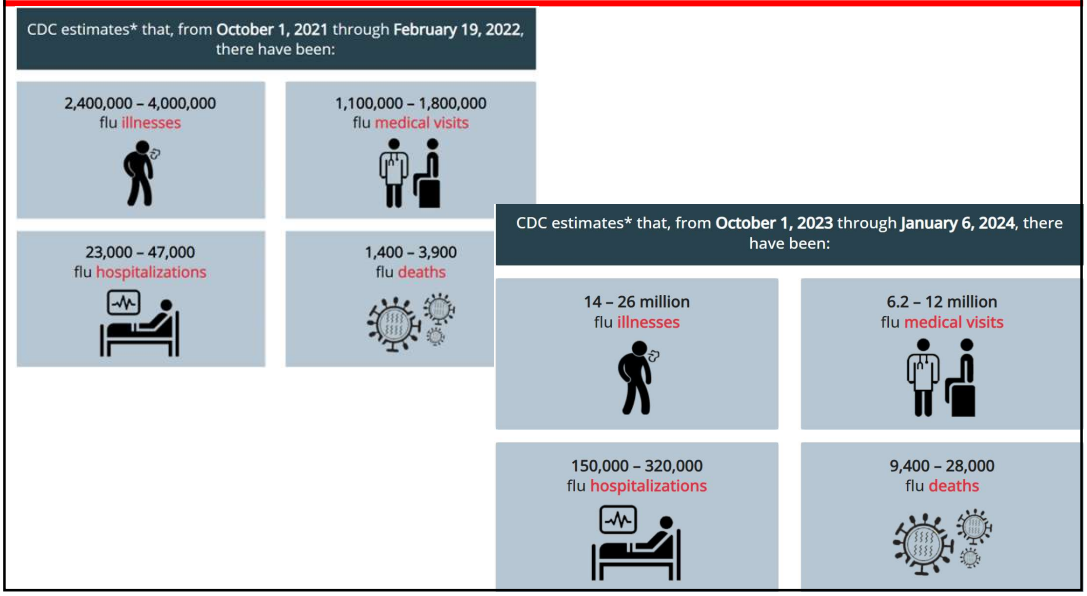
CDC.gov: 2021-2022 versus 2023-2024



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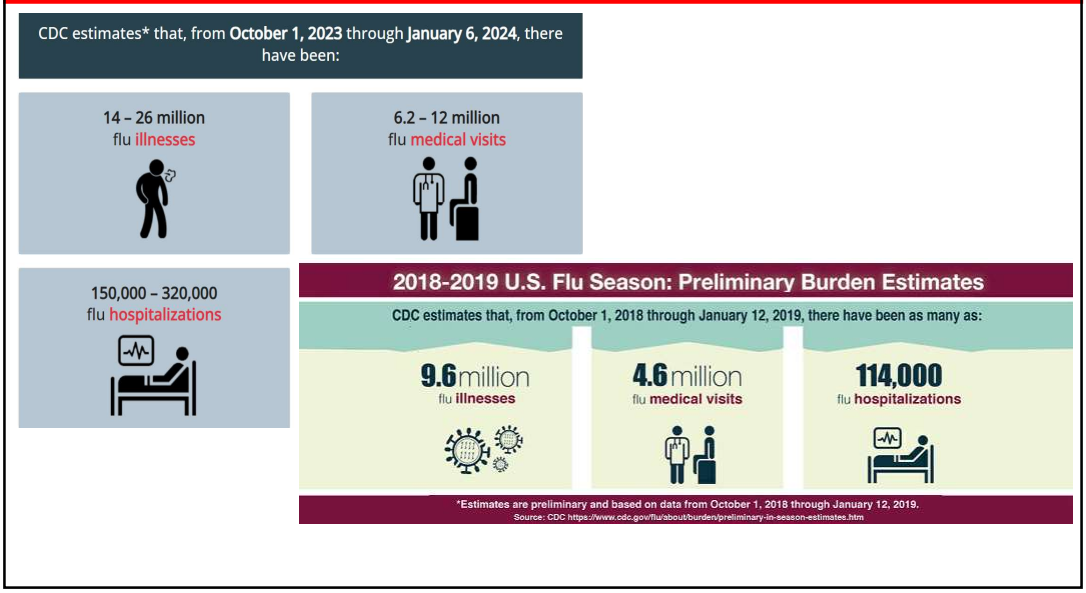
CDC.gov: 2023-2024 versus pre-COVID 2018-2019



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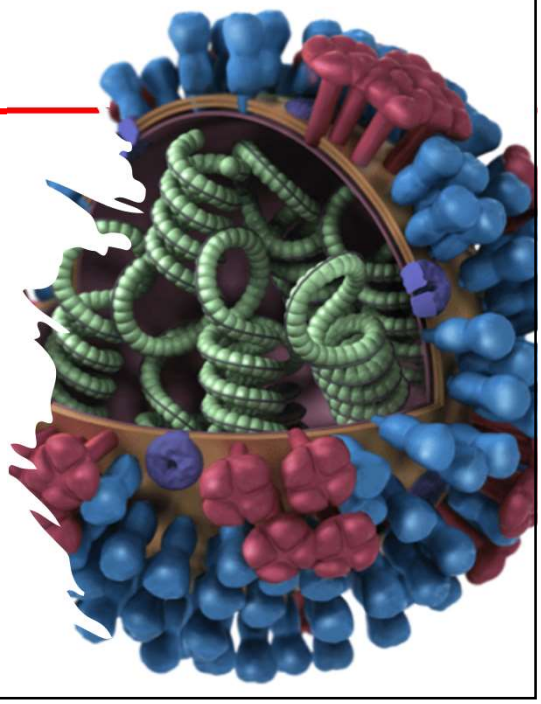
Influenza: Anatomy and epidemiology



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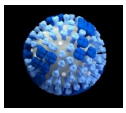
Human infection: The types of influenza



There are four types of influenza:

- **Influenza D:** Infections only in cattle, not humans
- **Influenza C:** Common, but seldom causes disease symptoms in adults (occasionally in children)
- **Influenza B:** Human infection only

  There are two lineages: B/Yamagata and B/Victoria

  Genetic and antigenic properties of influenza B viruses change more slowly than influenza A viruses

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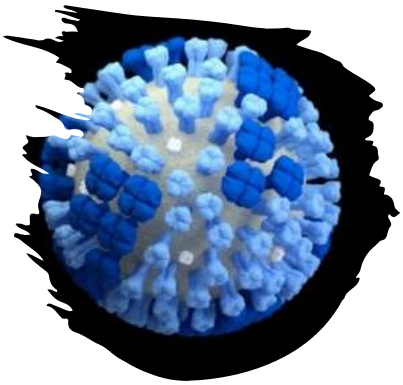
Human infection: The types of influenza

Influenza A:

Responsible for regular outbreaks, including the pandemic of 1918

Influenza A also infects domestic animals (pigs, horses, chickens, ducks) and some wild birds



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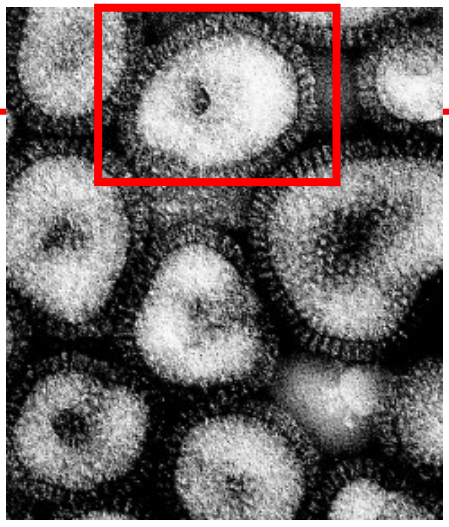

Electron micrograph (credit to Dr. K. G. Murti)
Shows several influenza virus particles at a magnification of 265,000x
The surface projections are molecules of **hemagglutinin** and **neuraminidase**

Influenza A was responsible for the Spanish Flu that swept around the world in 1918 killing 675,000 people in the U.S. and an estimated 20–50 million people worldwide

No one at the time knew what disease agent was causing the pandemic

The viral etiology of this infection was only established in 1930 (in pigs) and 1933 (in humans)

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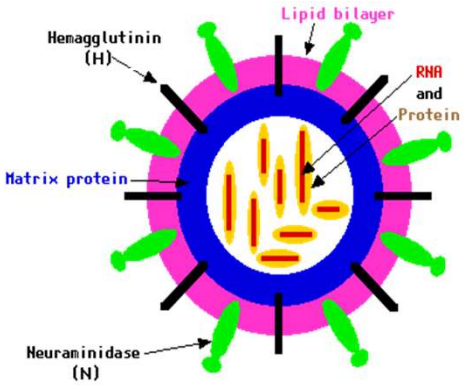
Influenza A and its parts:



- RNA virus wrapped in a lipid bilayer
- Studded in the lipid bilayer are membrane proteins
  - ~ 500 molecules of hemagglutinin (H)
  - ~ 100 molecules of neuraminidase (N)
- Encased by the lipid bilayer are
  - ~ 3000 molecules of matrix protein
  - 8 segments of RNA
- Each of the 8 RNA molecules is associated with many copies of a nucleoprotein

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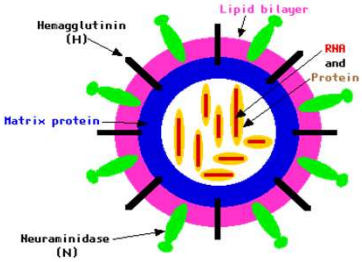
Influenza A and its parts:

- There are 3 main subtypes of hemagglutinin:
  - **H1, H2, H3 in human viruses**
  - (bind to respiratory epithelial cells)
  - 15 other subtypes in animal viruses
- There are 2 main subtypes of neuraminidase:
  - **N1 and N2 in human viruses**
  - 9 other subtypes in animal viruses



- Only influenza A viruses are known to cause global pandemics

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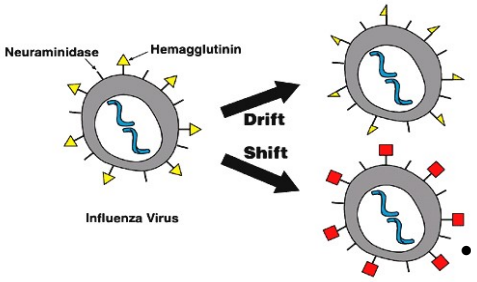
Influenza: Antigenic shift and drift



Antigenic drifts:

Minor changes in H and N

⬇

Localized outbreaks

Antigenic shifts:

Major changes in H and N

⬇

Epidemics and pandemics

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How do pandemic strains emerge?

- Influenza viruses have a segmented genome that can result in high rates of reassortment among viruses coinfecting the same sell
- Reassortment between animal and human viruses may result in pandemic strains
- Pandemics of 1957, 1968, and 2009 were due to animal/avian and human reassortments

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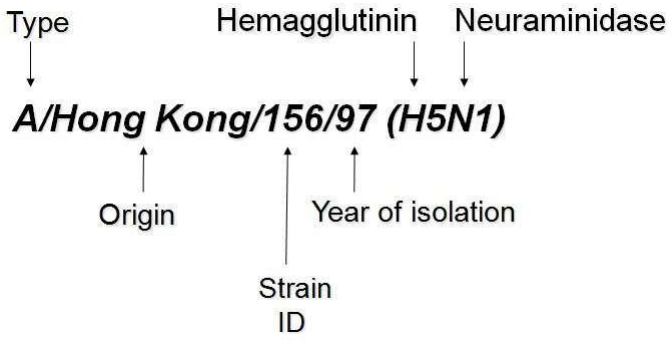
Influenza: Nomenclature



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Pandemics and antigenic shift:

Date	Strain	Subtype	Notes
1918	A/Spain/8	H1N1	Pandemic of Spanish flu 500 million infections 50 million deaths
1957	A/Singapore/57	H2N2	Pandemic of Asian flu
1962	A/Japan/62	H2N2	Epidemic
1964	A/Taiwan/64	H2N2	Epidemic
1968	A/Aichi/68	H3N2	Pandemic of Hong Kong flu
1976	A/New Jersey/76	H1N1	Swine flu in recruits
1977	A/USSR/77	H1N1	Russian flu (descendant of 1918)
2009	A/California/09	H1N1	Pandemic of Swine flu [now designated A(H1N1)pdm09]

50

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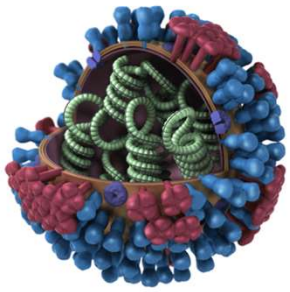
The current influenza strain: 2023-2024 (CDC.gov)

- Influenza A/H1N1pdm09 has been the predominant virus circulating in all regions in 2023-2024
- The majority of influenza viruses detected in the 2022-2023 season were A/H3N2

51

Influenza: Transmission, presentation and diagnosis



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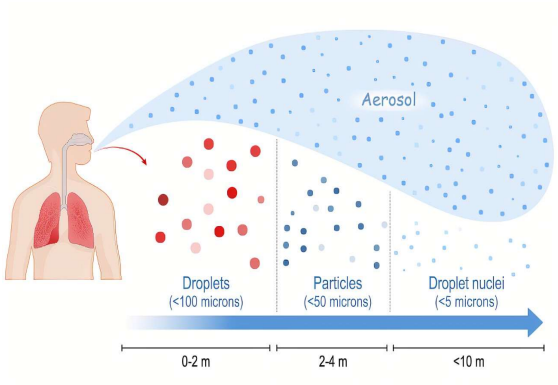
Influenza: Transmission

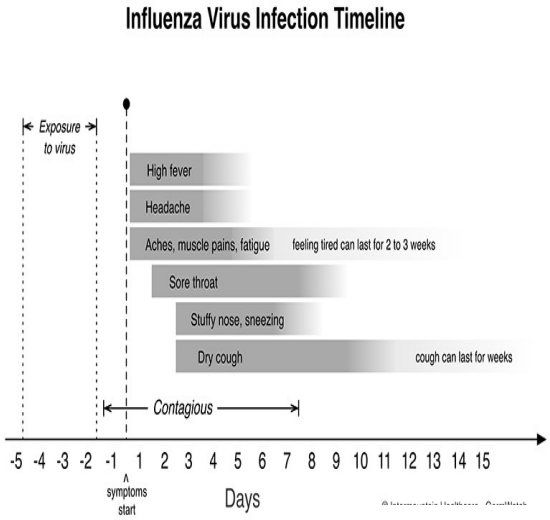


Respiratory transmission via close-range contact

Microdroplets suspended in air over time

Surface transmission from contaminated site to mucous membranes

53



Incubation period:

1 to 4 days (average 2 days)

Viral shedding :

Onset: 0-24 hours before symptoms
Peak: 24-48 hours of illness
Decline: 5-10 days
Longer periods of shedding (weeks to months) in adults >/= 65 years, those with obesity, chronic disease, and immunosuppression

Serial interval (onset of illness among household contacts) :

3 to 4 days

54

Influenza in immunocompetent adults:

Abrupt onset of intense symptoms

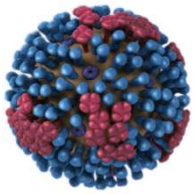
- Headache, fever, chills, dry cough, pharyngeal irritation, myalgias, malaise, eye pain, conjunctivitis, and anorexia
- "Like I got hit by a truck"

Fever

- High grade
- Average 3 days (range 2 - 8 days)

Cough

- Initially nonproductive and may persist for weeks



CDC.gov

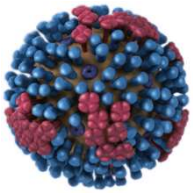
55

Influenza: Clinical course of uncomplicated disease

Fever and respiratory symptoms: 3 days

Complete recovery: 10 to 14 days
(longer in adults >/= 65 years)

Less common: Fatigue for several weeks



CDC.gov

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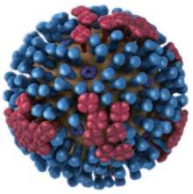
Influenza:
Elderly and immunocompromised adults

Immunocompromise due to age and chronic immunosuppression

Symptoms:

Nasal congestion/sore throat (may be the only symptoms)
Lethargy
Altered mental status
Anorexia
Cough



Fever may be absent

CDC.gov

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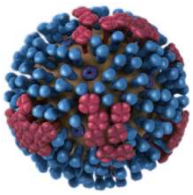
Groups at high risk for complications:

- Adults ≥ 65 years old
- Morbidly obese (BMI ≥ 40 for adults)
- Immunosuppressed/immunocompromised
- Pregnant or within 2 weeks post delivery
- Native Americans and Alaskan Natives
- Long term/chronic care setting residents



Uyeki et al. Ann Intern Med 2017; 167:ITC33-ITC48

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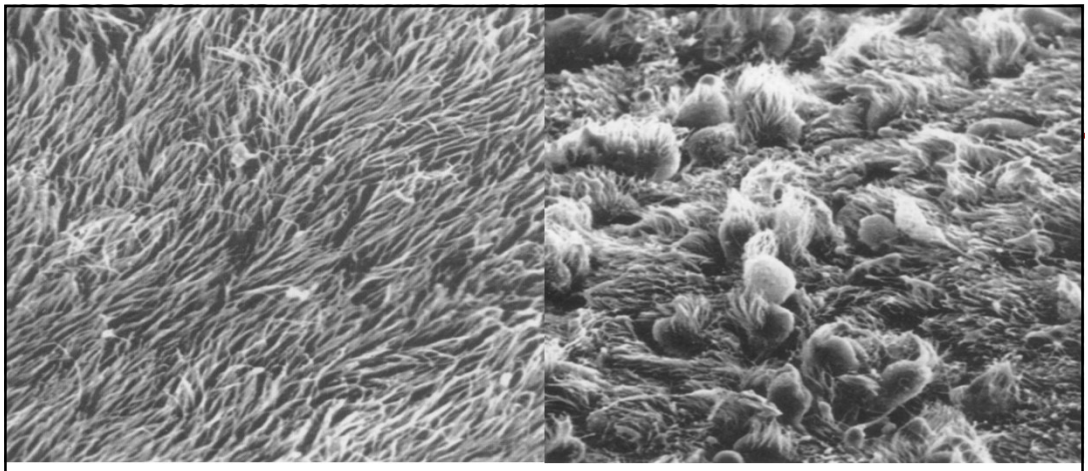


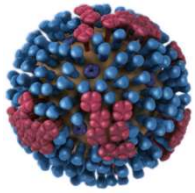
Respiratory viruses denude ciliated epithelium increasing risk of bacterial pneumonia

Reed and Boyde (1972) Infection and Immunity 6(1):68-76

59

Influenza: Cardiac complications

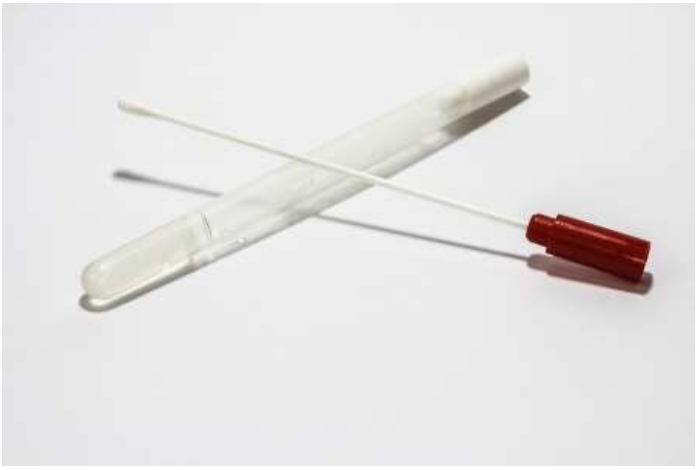
- Congestive heart failure
- Myocarditis
- Pericarditis
- Acute myocardial infarction
  Incidence is ~ 12%, but lower when patients are vaccinated (risk ratio = 0.86)



Chow et al., Ann Intern Med 2020;173:605
CDC.gov

60

Influenza: Diagnostic tests



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Diagnostic tests *CDC.gov/IDSA 2024*

Method	Test time
Rapid influenza diagnostic test (screening antigen detection) Low to moderate sensitivity, high specificity	< 15 minutes
Rapid molecular assay (viral RNA or nucleic acid detection) High sensitivity and specificity	15 – 30 minutes
Direct immunofluorescence or indirect flluorescent antibody staining (antigen detection) Moderate sensitivity, high specificity	1 - 4 hours
RT-PCR and other molecular assays (viral RNA or nucleic acid detection) High sensitivity and specificity	1 – 8 hours
Rapid cell culture (shell vials; cell mixtures; yields live virus) Moderately high sensitivity, highest specificity	1 – 3 days
Viral tissue cell culture (conventional, yields live virus)	3 – 10 days

62

Diagnostic tests *CDC.gov/IDSA 2024*

Method	Test time
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63

Vaccines:

64

64

Vaccine 2023-2024:
Advisory Committee on Immunization Practices

New recommendations:

- The antigenic composition has been updated
- Egg allergy alone no longer requires additional safety measures for influenza vaccination regardless of severity of previous reaction to egg protein

United States: Quadrivalent vaccines

- Several inactivated influenza vaccines (IIVs)
- One live attenuated influenza vaccine (LAIV)
- One recombinant vaccine

65

Influenza vaccine: 2023-2024

For the 2023-2024 northern hemisphere influenza season, egg-based influenza vaccines contain hemagglutinin (H) derived from :

- An influenza A/Victoria/4897/2022 (H1N1)pdm09-like virus
- An influenza A/Darwin/9/2021 (H3N2)-like virus
- An influenza B/Austria/1359417/2021-like virus (B/Victoria lineage)
- An influenza B/Phuket/3073/2013-like virus (B/Yamagata lineage)

For the 2023 to 2024 northern hemisphere influenza season, cell culture based inactivated (ccIIV4) and recombinant (RIV4) influenza vaccines contain HA derived from:

- An influenza A/Wisconsin/67/2022 (H1N1)pdm09-like virus
- An influenza A/Darwin/6/2021 (H3N2)-like virus
- An influenza B/Austria/1359417/2021-like virus (B/Victoria lineage)
- An influenza B/Phuket/3073/2013-like virus (B/Yamagata lineage)

66

66

Influenza vaccines 2023-2024:

Vaccine	Approved Ages	Dose volume
Afluria Quadrivalent	6 through 35 months ≥3 years	0.25 mL 0.5 mL
Fluarix Quadrivalent	≥6 months	0.5 mL
FluLaval Quadrivalent	≥6 months	0.5 mL
Fluzone Quadrivalent	6 through 35 months ≥3 years	0.5 mL (see below) 0.5 mL
Flucelvax Quadrivalent	≥6 months	0.5 mL
Flublok Quadrivalent	≥18 years	0.5 mL
Fluzone High-Dose Quadrivalent	≥65 years	0.7 mL
Fluad Quadrivalent	≥65 years	0.5 mL

67

Influenza vaccines 2023-2024:

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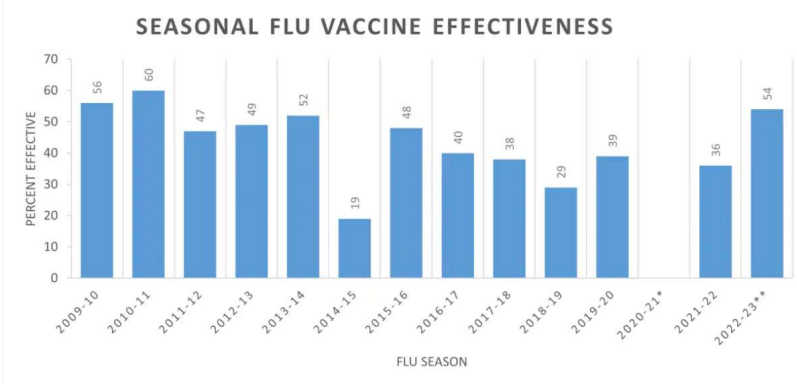
Fluad Quadrivalent	≥65 years	0.5 mL

68

Influenza incidence and vaccine effectiveness (2023-2024): (CDC.gov)

(January 2024)

Recombinant influenza vaccine = more effective than the inactivated vaccine in preventing influenza in adults >/= 65 years of age



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Influenza: Antivirals

70

What antiviral drugs are recommended this flu season?

Timing of treatment:

Preferably within < 48 hours of symptom onset

BUT:

Treat patients at high risk of complications even if symptoms > 48 hours

Oseltamivir phosphate (neuraminidase inhibitor, efficacy = - 24 hours):

- FDA approved for early treatment in all people (CDC) or 14 days and older (American Academy of Pediatrics)
- May be used in pregnancy
- Oseltamivir side effect = Nausea and vomiting
- Better efficacy against influenza A than influenza B

71

What antiviral drugs are recommended this flu season?

Peramivir

(Neuraminidase inhibitor, efficacy = -24 hours of symptoms, IV only)

- Peramivir side effect = Diarrhea, neuropsychiatric symptoms, erythema multiforme, Stevens-Johnson

Zanamivir (only in UK and EU)

Baloxavir (insufficient data)

72

What antiviral drugs are recommended this flu season?

Peramivir

(Neuraminidase inhibitor, efficacy = -24 hours of symptoms, IV only)

- Peramivir side effect = Diarrhea, neuropsychiatric symptoms, erythema multiforme, Stevens-Johnson

Zanamivir (only in UK and EU)

Baloxavir (insufficient data)

73

Influenza: Who should receive antiviral treatment?

Patients with documented or suspected flu, irrespective of vaccination history and meeting any of the following criteria:

1. Patients requiring hospitalization
2. Confirmed or suspected influenza with severe, complicated, or progressive illness
3. Outpatients at higher risk for complications
4. Adults ≥ 65 years old
5. Pregnant women and those within 2 weeks postpartum

CDC.gov

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Influenza:
Who should receive antiviral treatment?

- Lower risk outpatients presenting ≤ 2 days of onset
- Symptomatic outpatients living in households with high-risk persons (immunocompromised)
- Symptomatic healthcare providers whose patients are at high risk

CDC.gov

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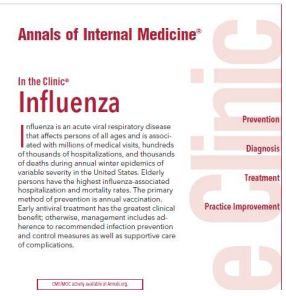
Important Resources



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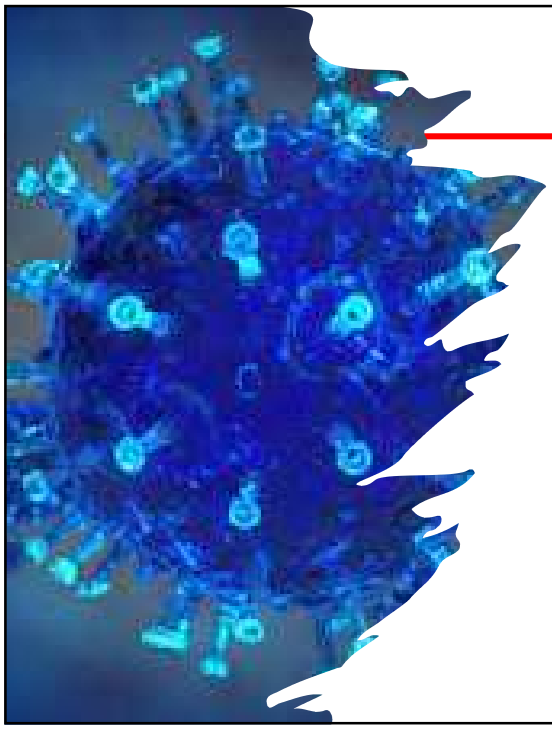

Respiratory Syncytial Virus (RSV)

77

RSV: What is it?

- Causes a highly contagious seasonal lung infection
- Northern hemisphere: October to May (peak January and February)
- Southern hemisphere: May to September
- Tropics: During rainy season

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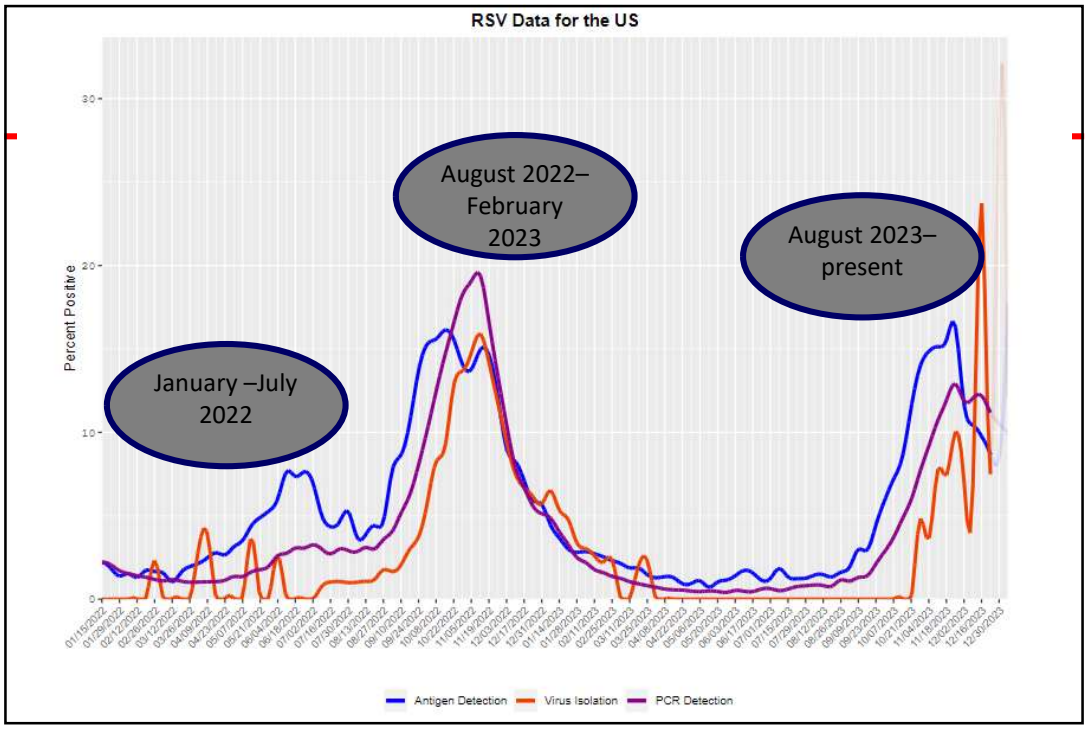

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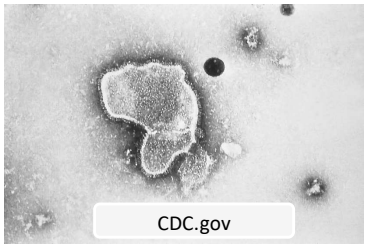
RSV: Morbidity and mortality

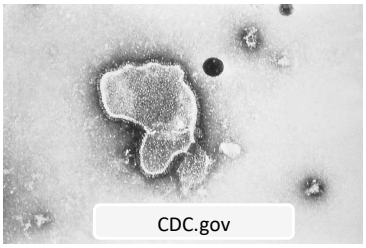
- Most common cause of lower respiratory infection in children less than 1 year of age
- Second highest cause of death from infection in infants
- Almost all children are infected by age 2
- Overall mortality in children = 6.7%



80

RSV: Morbidity and mortality

- Common in adults, but minimal to no symptoms
- Now: Increasing symptomatic disease in adults
- Diagnosis is often missed
- Possible genetic component for severe disease
- **Overall mortality in adults > 50 years = 8%**



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RSV: More bad news (December 22, 2023)

The Journal of Infectious Diseases

MAJOR ARTICLE

Respiratory syncytial virus infects peripheral and spinal nerves and induces chemokine-mediated neuropathy

Kevin J. Pollard[1], Vicki Traina-Dorge[2,3], Stephen M. Medearis[4,5,6], Alexander Bosak[1], Gregory J. Bix[7,8,9,10], Michael J. Moore[1,10,11], Giovanni Piedimonte[4,5,6]*

RSV can infect nerve cells and enter spinal cord…

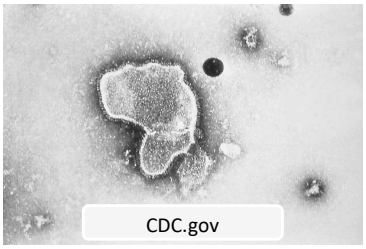
82

RSV: Diagnosis

- Via nasal swab or via bronchoscopy if intubated

- Rapid antigen tests:
  May have false negatives, results in less than 30 minutes

- Polymerase chain reaction:
  Highest sensitivity, results in
  < 3 hours to days



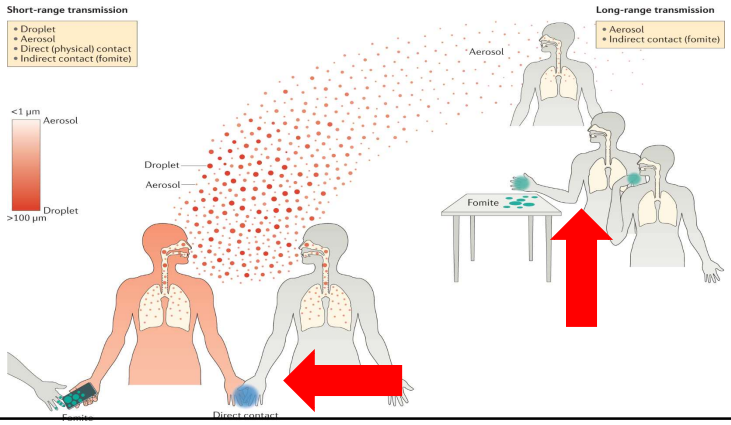
83

RSV: Transmission and Incubation

Most common: Direct and indirect contact

Lives several hours on hands and surfaces

Other: Large droplet aerosol

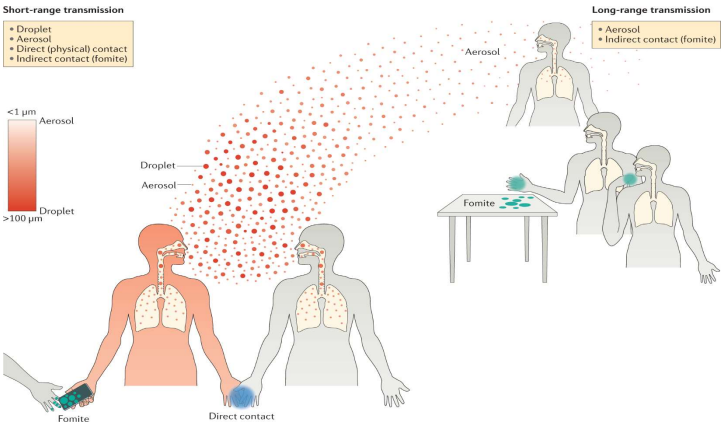


84

RSV: Transmission and Incubation

Incubation: 4 to 6 days

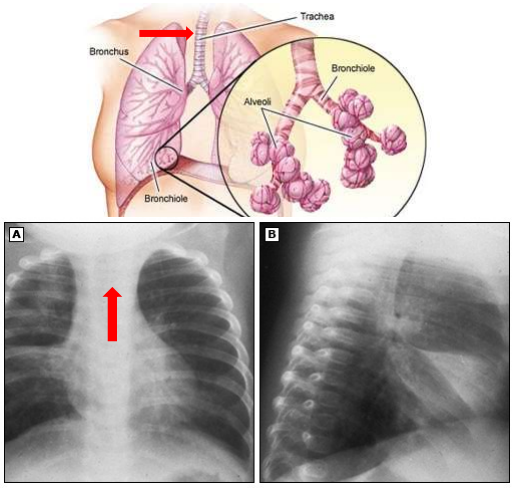
Viral shedding: 3 to 8 days, longer in HIV and neonates



85

RSV: Clinical presentation

Lower respiratory tract infection



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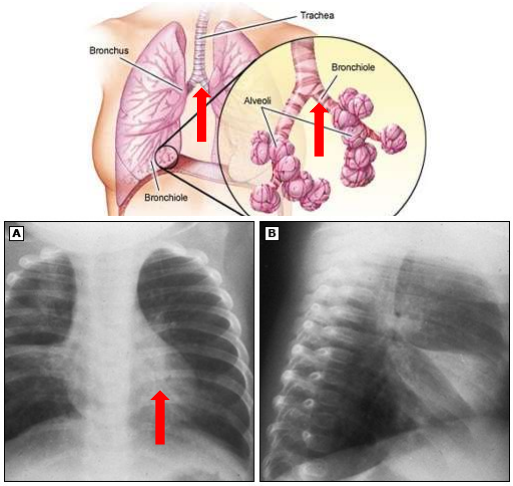
RSV: Clinical presentation

Lower respiratory tract infection



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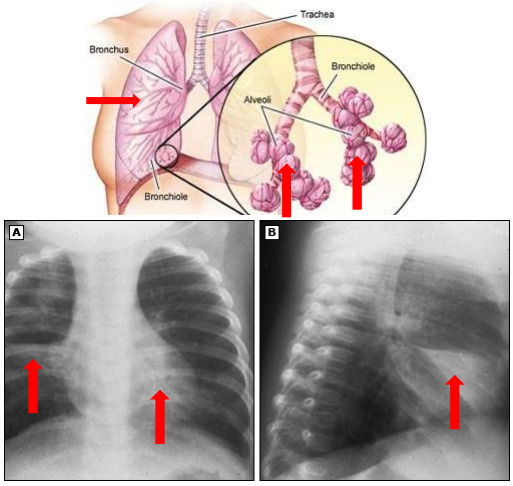
RSV: Clinical presentation

Lower respiratory tract infection



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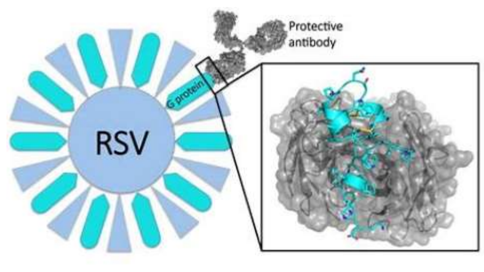
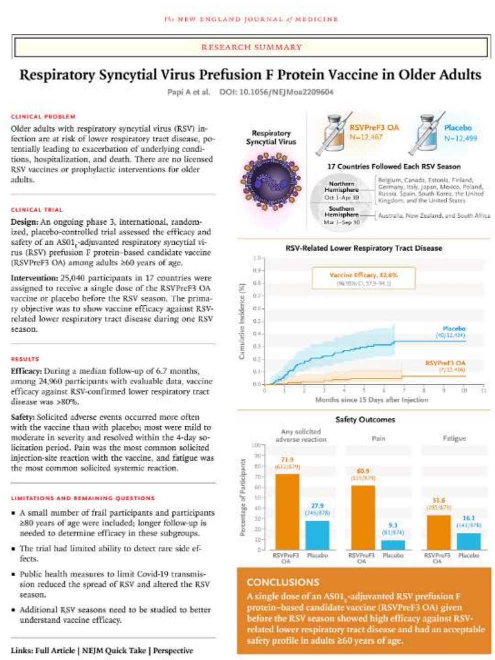
RSV vaccine: What do we know?

- In the United States, two vaccines were approved by the US Food and Drug Administration (FDA) in 2023 for persons >/= 60 years and for pregnant women
- The vaccines affects the viral fusion protein (protein F) that RSV uses to enter human cells
- Antibodies specific to the viral fusion protein are highly effective at blocking infection



RSV Vaccine:

Vaccine efficacy in older adults was similar against the RSV A and B subtypes (for RSV-related lower respiratory tract infection):
RSV A 84.6%
RSV B 80.9%



The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults

Papi A et al. DOI: 10.1056/NEJMoa2209604

CLINICAL PROBLEM

Older adults with respiratory syncytial virus (RSV) infection are at risk of lower respiratory tract disease, potentially leading to exacerbation of underlying conditions, hospitalization, and death. There are no licensed RSV vaccines or prophylactic interventions for older adults.

CLINICAL TRIAL

Design: An ongoing phase 3, international, randomized, placebo-controlled trial assessed the efficacy and safety of an $AS01_E$-adjuvanted respiratory syncytial virus (RSV) prefusion F protein–based candidate vaccine (RSVPreF3 OA) among adults ≥60 years of age.

Intervention: 25,040 participants in 17 countries were assigned to receive a single dose of the RSVPreF3 OA vaccine or placebo before the RSV season. The primary objective was to show vaccine efficacy against RSV-related lower respiratory tract disease during one RSV season.

RESULTS

Efficacy: During a median follow-up of 6.7 months, among 24,960 participants with evaluable data, vaccine efficacy against RSV-confirmed lower respiratory tract disease was >80%.

Safety: Solicited adverse events occurred more often with the vaccine than with placebo; most were mild to moderate in severity and resolved within the 4-day solicitation period. Pain was the most common solicited injection-site reaction with the vaccine, and fatigue was the most common solicited systemic reaction.

LIMITATIONS AND REMAINING QUESTIONS

- A small number of frail participants and participants ≥80 years of age were included; longer follow-up is needed to determine efficacy in these subgroups.
- The trial had limited ability to detect rare side effects.
- Public health measures to limit Covid-19 transmission reduced the spread of RSV and altered the RSV season.
- Additional RSV seasons need to be studied to better understand vaccine efficacy.

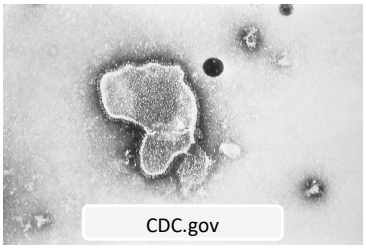
Links: Full Article | NEJM Quick Take | Perspective

CONCLUSIONS

A single dose of an $AS01_E$-adjuvanted RSV prefusion F protein–based candidate vaccine (RSVPreF3 OA) given before the RSV season showed high efficacy against RSV-related lower respiratory tract disease and had an acceptable safety profile in adults ≥60 years of age.

RSV: Treatment in adults

- **Immunocompetent adults:** Supportive only
- **Immune globulin + ribavirin:**
  Reserved for immunocompromised patients



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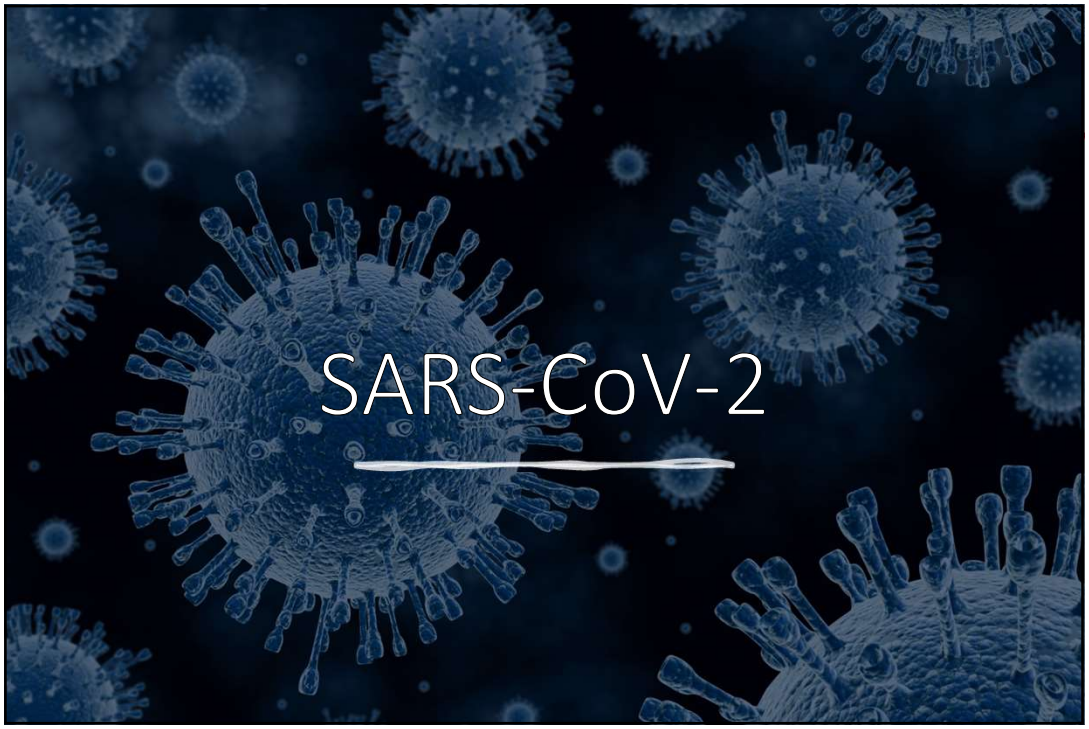
Back to our patient:

- Rapid testing for COVID was positive.
- Testing for RSV and Influenza A/B was negative.
- The patient developed worsening hypoxemic respiratory failure and is now in the ICU. His hospital course has been complicated by a DVT with pulmonary embolism and NSTEMI.

92



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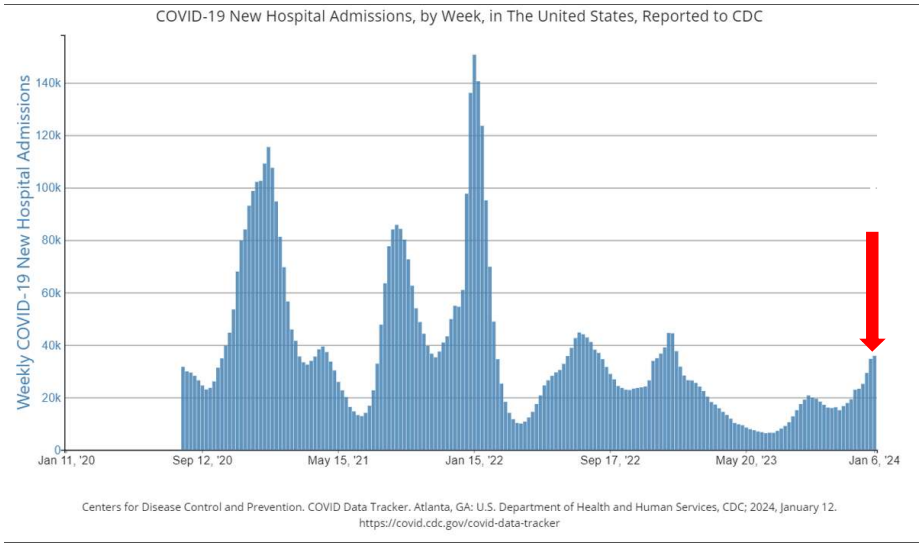
COVID-19: How are we doing?



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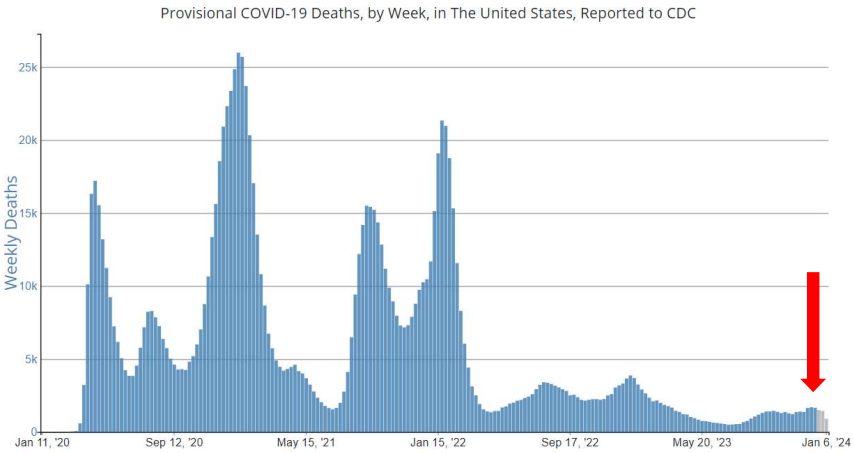
COVID-19: How are we doing?



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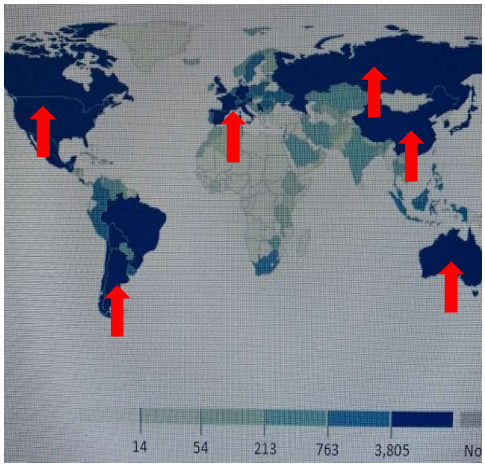
COVID-19: How are we doing?

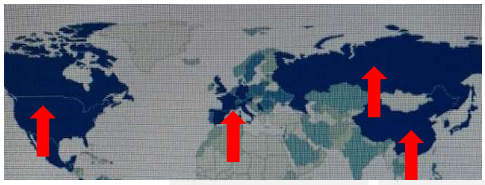


- World Health Organization
- 7-day data, 2023

US: 102,171,644 total cases
42,163 7-day average

96

COVID-19: How are we doing?



- World Health Organization
- 7-day data, 2023

Coronavirus World Map: Tracking the Global Outbreak

Updated March 10, 2023

This page was archived on March 10 as global data on cases and deaths is no longer reported by our data source for all countries except the United States.

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A quick review of variants:

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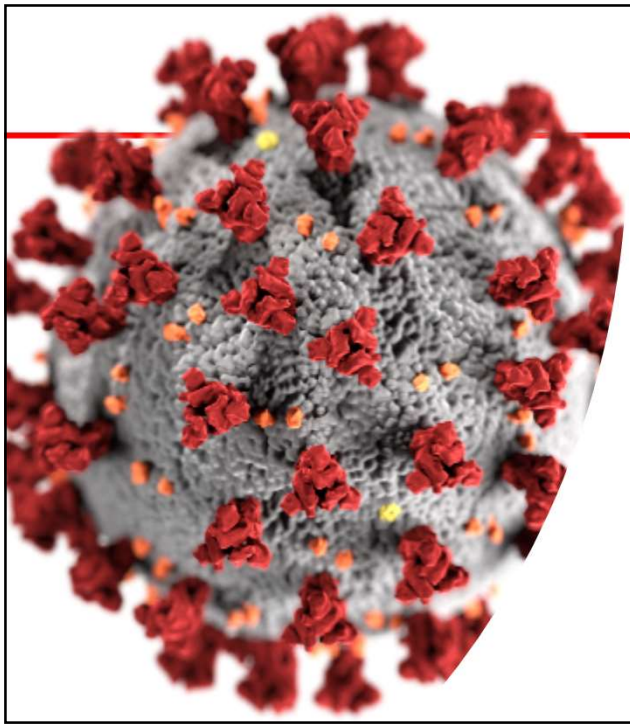
A word on variants: www.CDC.org

	Original virus China 2019	Beta B.1.351 S. Africa 2020	Alpha B.1.1.7 UK 2020	Delta B.1.617.2 India 2020	Omicron B.1.1.529 S. Africa 2021
Transmission	1	1.5	1.5	3	9-12

99



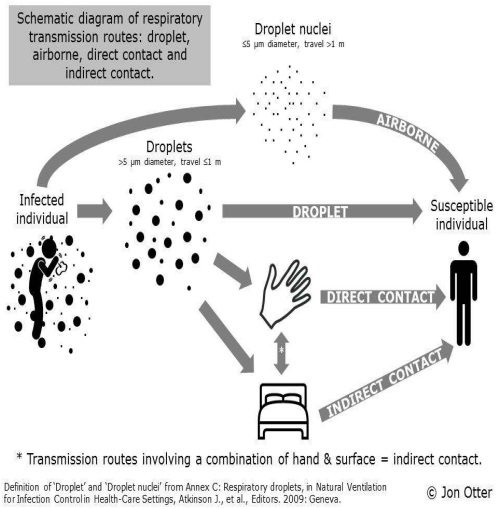
What is out there now?

COVID subvariant JN.1 accounts for about 62% of cases in the U.S. as of January 5, 2024 (<5% of cases in November 2023)

JN.1 is also the dominant variant in Europe and is rising sharply in Asia

100

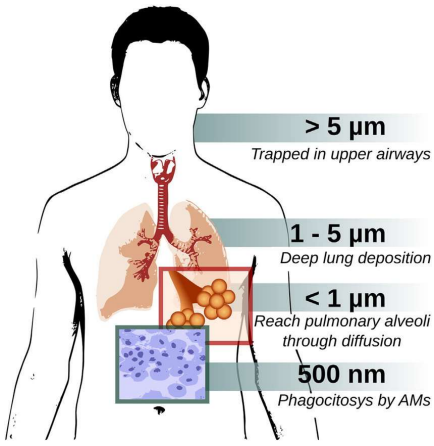
How does COVID-19 spread?



- Respiratory droplets = > 5.0 microns
- Biological aerosols ("droplet nuclei") =
  0.5-3.0 microns
- Coronavirus ~ **60-140 nm**

101

How does COVID-19 spread?



- Respiratory droplets =
  > 5.0 microns
- Biological aerosols ("droplet nuclei") =
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- Coronavirus ~ **60-140 nm**

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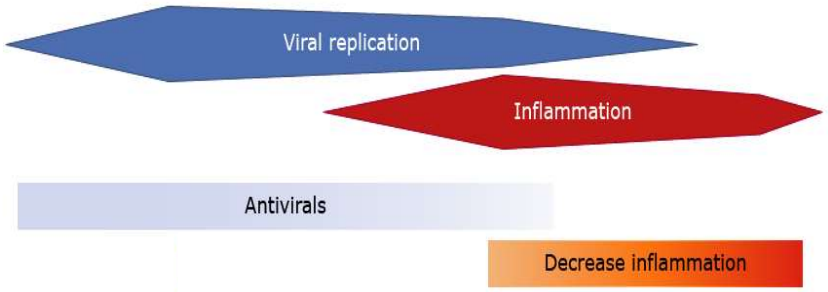
COVID-19 stages of infection:
Potential targets

Stage/severity:	Asymptomatic/ presymptomatic	Mild illness	Moderate illness	Severe illness	Critical illness
	+ SARS-CoV-2 test but no symptoms	Mild symptoms (eg, fever, cough, taste/smell changes); no dyspnea	O_2 saturation ≥94%, lower respiratory tract disease	O_2 saturation <94%, respiratory rate >30/min; lung infiltrates >50%	Respiratory failure, shock, multi-organ dysfunction/failure



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Complications of COVID-19:

- Respiratory
- Neurological/Psychiatric
- Cardiovascular
- Renal
- Hematologic
- Gastrointestinal
- Endocrine

AdobeStock image

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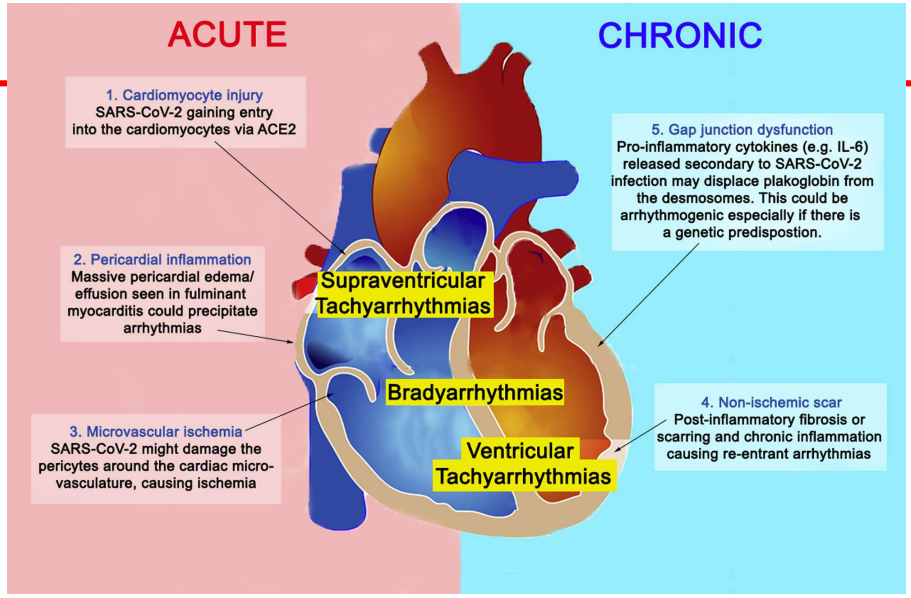

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COVID and lung destruction

106

Post-acute COVID-19 syndrome: Pulmonary complications

Pulmonary vascular thrombosis have been observed in 20–30% of patients with COVID-19 which is higher than in other critically ill patient populations (1–10%)

*Huang, C. et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet **397**, 220–232 (2021)*

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Post-acute COVID-19 syndrome: An evolving definition

"Persistence of symptoms or development of sequelae beyond 3-4 weeks from the onset of acute symptoms of COVID-19, as replication-competent SARS-CoV-2 has not been isolated after 3 weeks"

*Datta et al. A proposed framework and timeline of the spectrum of disease due to SARS-CoV-2 infection: illness beyond acute infection and public health implications. J. Am. Med. Assoc. **324**, 2251–2252 (2020)*

*Greenhalgh et al. Management of post-acute COVID-19 in primary care. Brit. Med. J. **370**, m3026 (2020)*

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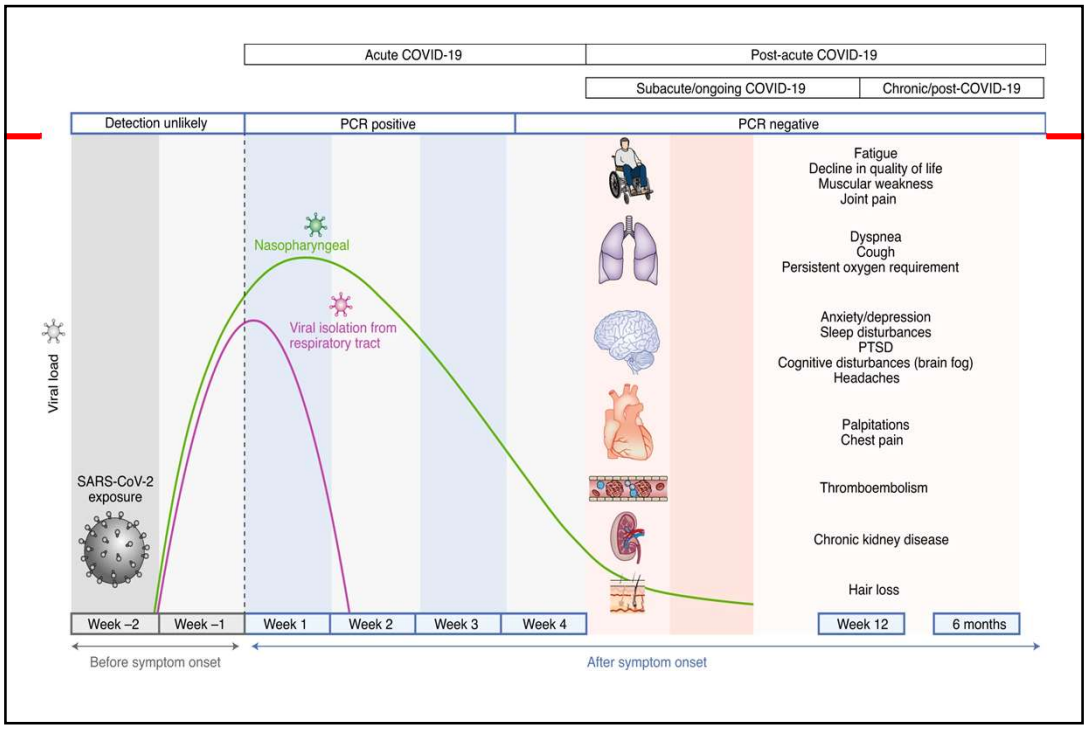
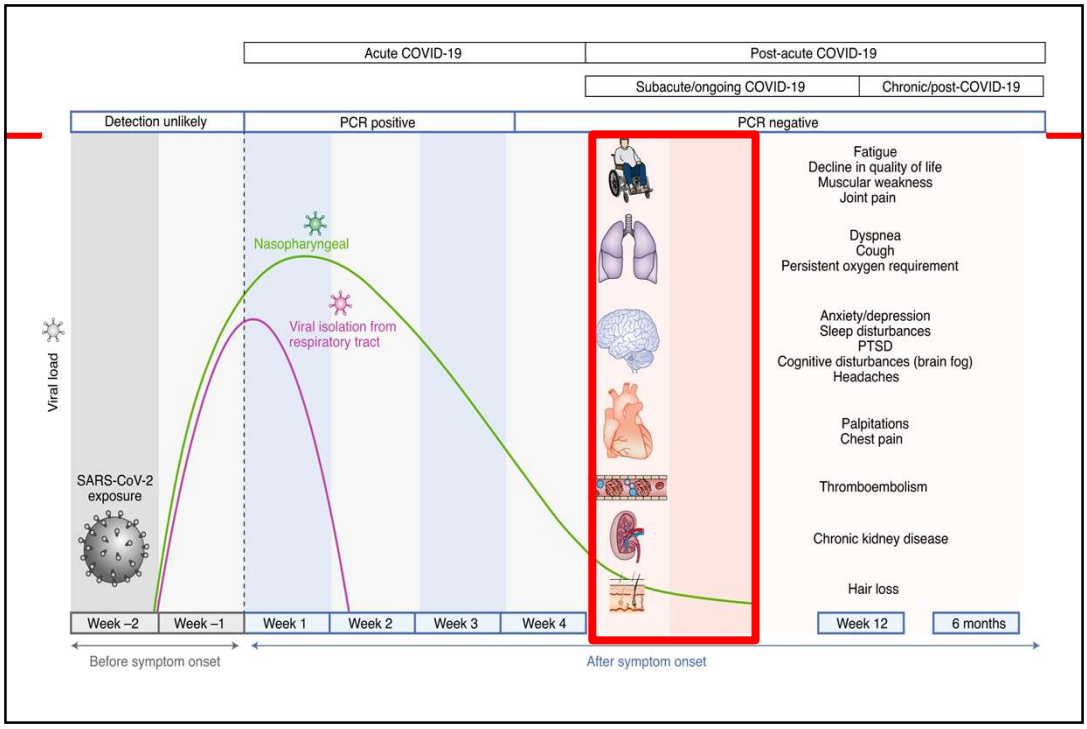

Acute COVID-19
Post-acute COVID-19
Subacute/ongoing COVID-19
Chronic/post-COVID-19
Detection unlikely
PCR positive
PCR negative
Viral load
Nasopharyngeal
Viral isolation from respiratory tract
SARS-CoV-2 exposure
Fatigue
Decline in quality of life
Muscular weakness
Joint pain
Dyspnea
Cough
Persistent oxygen requirement
Anxiety/depression
Sleep disturbances
PTSD
Cognitive disturbances (brain fog)
Headaches
Palpitations
Chest pain
Thromboembolism
Chronic kidney disease
Hair loss
Week –2
Week –1
Week 1
Week 2
Week 3
Week 4
Week 12
6 months
Before symptom onset
After symptom onset

109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Headaches
Palpitations
Chest pain
Thromboembolism
Chronic kidney disease
Hair loss
Week –2
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Week 1
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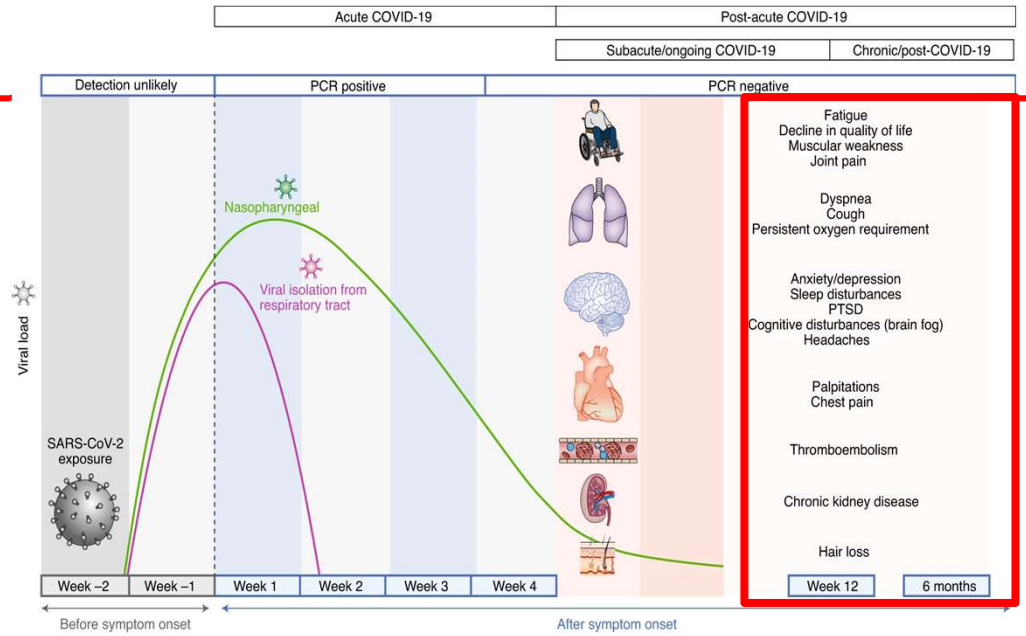
Week 4
Week 12
6 months
Before symptom onset
After symptom onset

110



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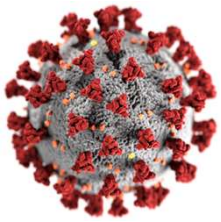
Post-acute COVID-19 syndrome: Cardiovascular complications



- Persistent symptoms:

  Palpitations, dyspnea and chest pain

- Long-term sequelae:

  Myocardial fibrosis or scarring (detectable via cardiac MRI), arrhythmias, tachycardia and autonomic dysfunction (POTS, IST, syncope)

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Post-acute COVID-19 syndrome: Neuropsychiatric complications

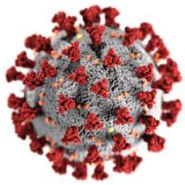
ICU Survivors: Acute brain dysfunction

"There is an epidemic within the pandemic of disastrous brain dysfunction" *Wes Ely, MD*

Delirium in the ICU:

1990s: Monitoring started with CAM-ICU Incidence ~ 70%

2015 to pre-COVID: Incidence 40% *



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Post-acute COVID-19 syndrome: Neuropsychiatric complications

Delirium in the ICU with COVID:

The COVID-D study (Ely et al.):

2100 patients in 70 ICUs around the world

The average number of delirium-free days = 5/21 (24%)

Factors:

Inability to communicate, inability to pay attention, increased depression, increased mortality

Highest predictors of COVID-induced delirium:

- Increased benzodiazepine use
- Decreased family presence

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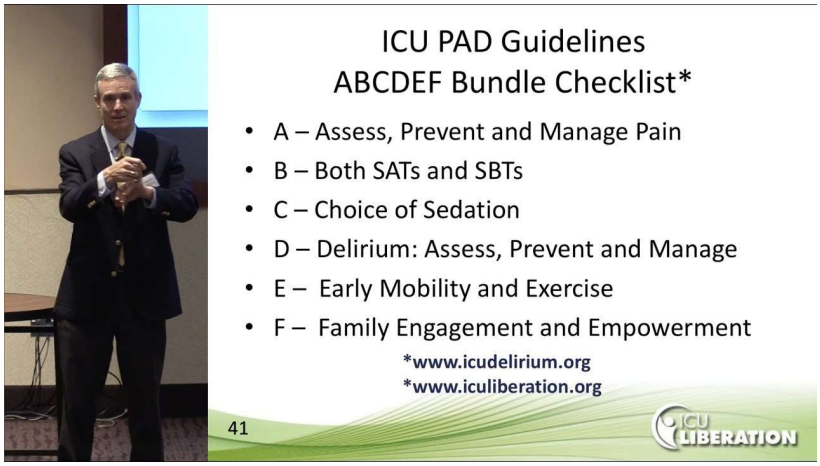
Measures to avoid ICU delirium:



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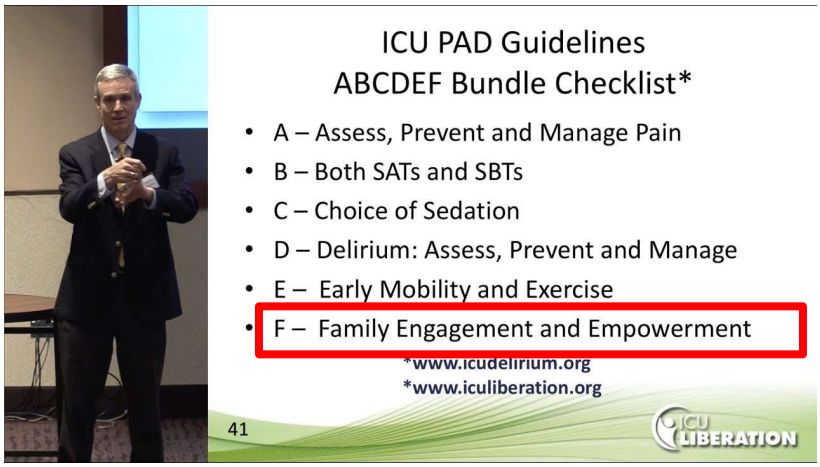
Measures to avoid ICU delirium:



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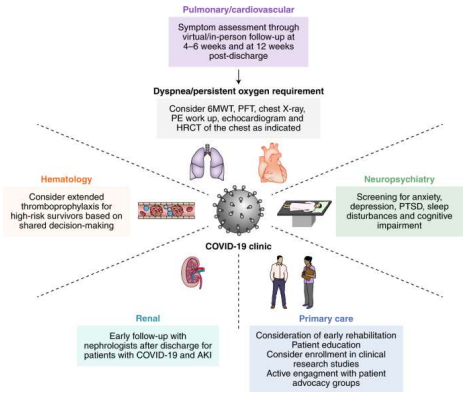
Post-acute COVID-19 syndrome: What can we do?



Cardiopulmonary rehabilitation

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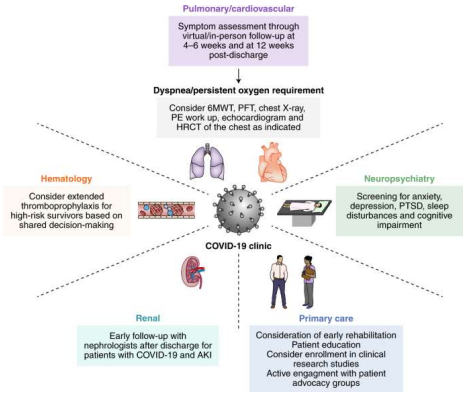
Post-acute COVID-19 syndrome: What can we do?



Cardiopulmonary rehabilitation

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New information: January 4, 2024
Chronic fatigue and impaired oxygen extraction in muscles after COVID…it's real

nature communications

Article

https://doi.org/10.1038/s41467-023-44432-3

Muscle abnormalities worsen after post-exertional malaise in long COVID

Received: 21 March 2023

Accepted: 13 December 2023

Published online: 04 January 2024

Check for updates

Brent Appelman[1,2,15], Braeden T. Charlton[3,4,15], Richie P. Goulding[3,4], Tom J. Kerkhoff[3,4,5,6], Ellen A. Breedveld[3,4], Wendy Noort[3,4], Carla Offringa[3,4], Frank W. Bloemers[4,7], Michel van Weeghel[8], Bauke V. Schomakers[8], Pedro Coelho[9,10,11], Jelle J. Posthuma[7,12], Eleonora Aronica[11], W. Joost Wiersinga[1,2,13], Michèle van Vugt[2,14,15] & Rob C. I. Wüst[3,4,15]

A subgroup of patients infected with SARS-CoV-2 remain symptomatic over three months after infection. A distinctive symptom of patients with long COVID is post-exertional malaise, which is associated with a worsening of fatigue- and pain-related symptoms after acute mental or physical exercise, but its underlying pathophysiology is unclear. With this longitudinal case-control study (NCT05225688), we provide new insights into the pathophysiology of post-exertional malaise in patients with long COVID. We show that skeletal muscle structure is associated with a lower exercise capacity in patients, and local and systemic metabolic disturbances, severe exercise-induced myopathy and tissue infiltration of amyloid-containing deposits in skeletal muscles of patients with long COVID worsen after induction of post-exertional malaise. This study highlights novel pathways that help to understand the pathophysiology of post-exertional malaise in patients suffering from long COVID and other post-infectious diseases.

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Post-acute COVID-19 syndrome: Lung transplant

- Patients with COVID-19-associated ARDS underwent bilateral lung transplantation
- Transplant centers in US, Europe, India
- All patients had severe lung damage that did not improve despite prolonged mechanical ventilation and extracorporeal membrane oxygenation

Song W et al., Confronting COVID-19-associated cough and the post-COVID syndrome: role of viral neurotropism, neuroinflammation, and neuroimmune responses. Lancet 9:533 (2021)

Tasoudis et al., Outcomes following lung transplant for COVID-19-related complications in the US. JAMA Surgery 158:1159 (2023)

120

Post-acute COVID-19 syndrome: Lung transplant

General findings:

The lung transplant procedure was technically challenging with severe pleural adhesions, hilar lymphadenopathy, and increased intraoperative transfusion requirements

Pathology of the explanted lungs showed extensive, ongoing acute lung injury with features of lung fibrosis

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Post-acute COVID-19 syndrome: Lung transplant

There was no recurrence of SARS-CoV-2 in the allografts

All patients with COVID-19 were weaned off extracorporeal support and showed short-term survival similar to that of transplant recipients without COVID-19

122

Post-acute COVID-19 syndrome: Lung transplant

Bharat A et al., Early outcomes after lung transplantation for severe COVID-19: a series of the first consecutive cases from four countries

Published:March 31 2021,Lancet DOI:https://doi.org/10.1016/S2213-2600(21)00077-1

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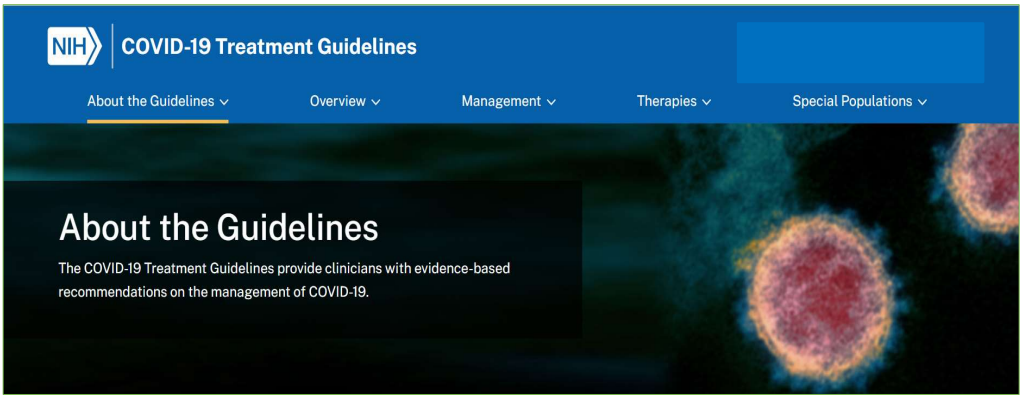
www.covid19treatmentguidelines.nih.gov



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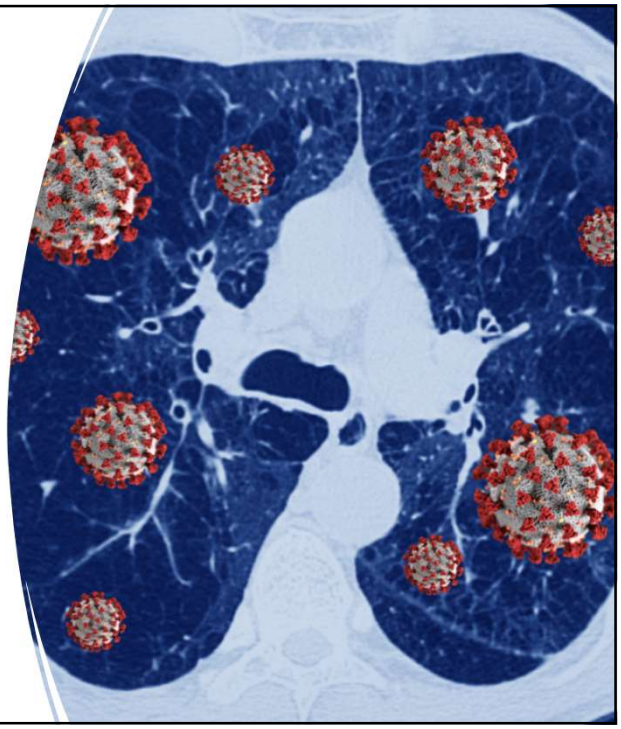
Questions?



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