COVID-19 Update
December 7, 2020

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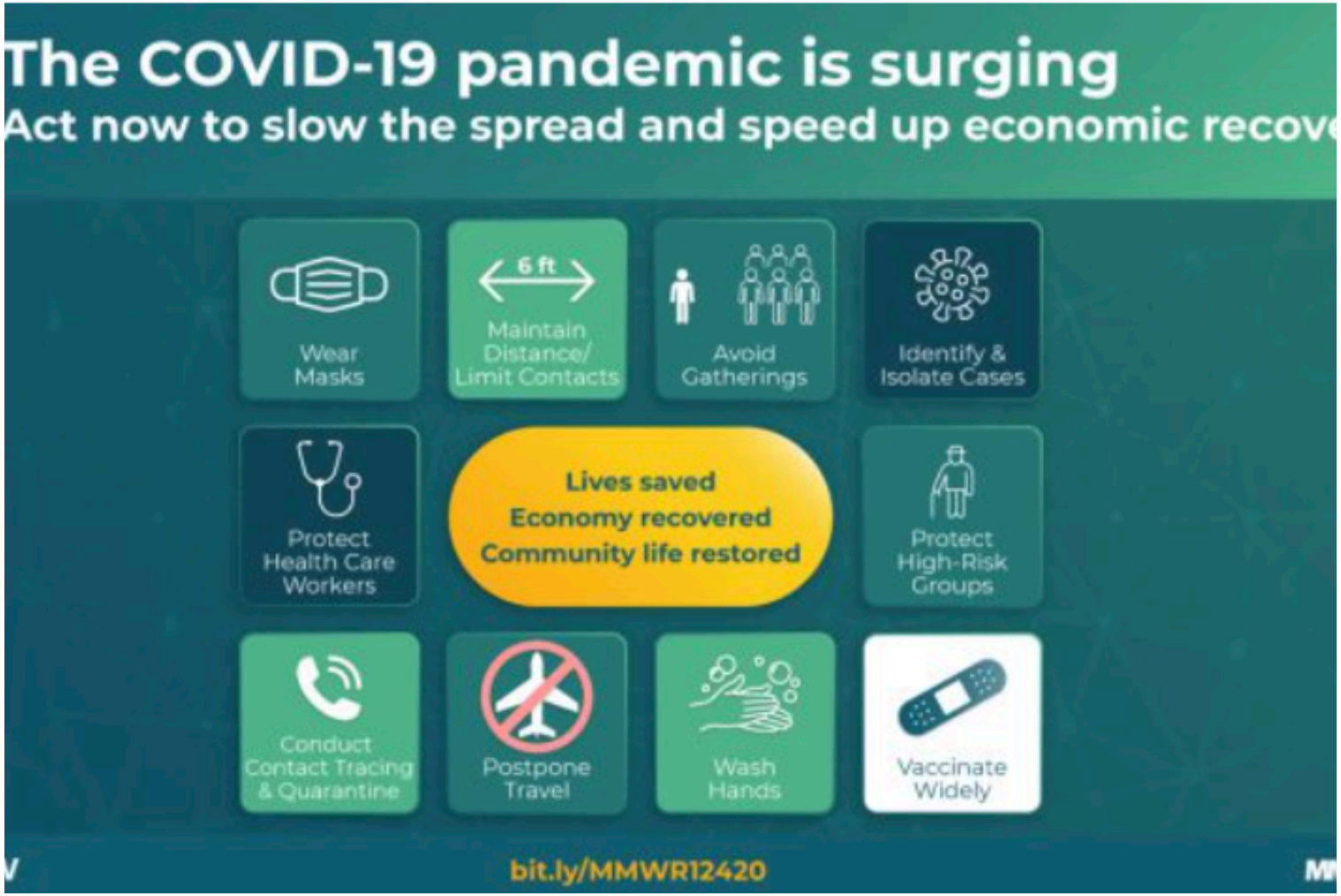

CDC Summary of Guidance for Public Health Strategies to Address High Levels of Community Transmission of SARS-CoV-2 and Related Deaths,

MMWR December,4 2020

COVID-19 Treatment Guidelines

- **All three guidelines** advise against the use of chloroquine, hydroxychloroquine, lopinavir/ritonavir, or azithromycin for the treatment of COVID-19 patients.
- **The IDSA and NIH guidelines** recommend 5 days of remdesivir for patients on supplemental oxygen, but not for those on mechanical ventilation or extracorporeal membrane oxygenation.
- **The NIH guideline** suggests coadministration of remdesivir and dexamethasone for patients with severe disease as well as for those on noninvasive ventilation and those who were recently intubated.

Rochwerg B et al. A living WHO guideline on drugs for covid-19. *BMJ* 2020 Sep 4; 370:m3379.
COVID-19 Treatment Guidelines Panel. Coronavirus disease 2019 (COVID-19) treatment guidelines. National Institutes of Health; 2020 Dec 3.
Bhimraj A et al. Infectious Diseases Society of America guidelines on the treatment and management of patients with COVID-19 Infectious Diseases Society of America; 2020 Dec 2.

COVID-19 Treatment Guidelines

- **The WHO guideline** recommends against the use of remdesivir in any situation.
- **All three guidelines** agree that dexamethasone at a dose of 6 mg once daily (or an equivalent corticosteroid) should be administered to patients with moderate-to-severe COVID-19, and all advise against its use in those with mild disease.
- **The IDSA and NIH** guidelines do not recommend routine use of tocilizumab, bamlanivimab, or convalescent plasma.

Rochwerg B et al. A living WHO guideline on drugs for covid-19. *BMJ* 2020 Sep 4; 370:m3379.
COVID-19 Treatment Guidelines Panel. Coronavirus disease 2019 (COVID-19) treatment guidelines. National Institutes of Health; 2020 Dec 3.
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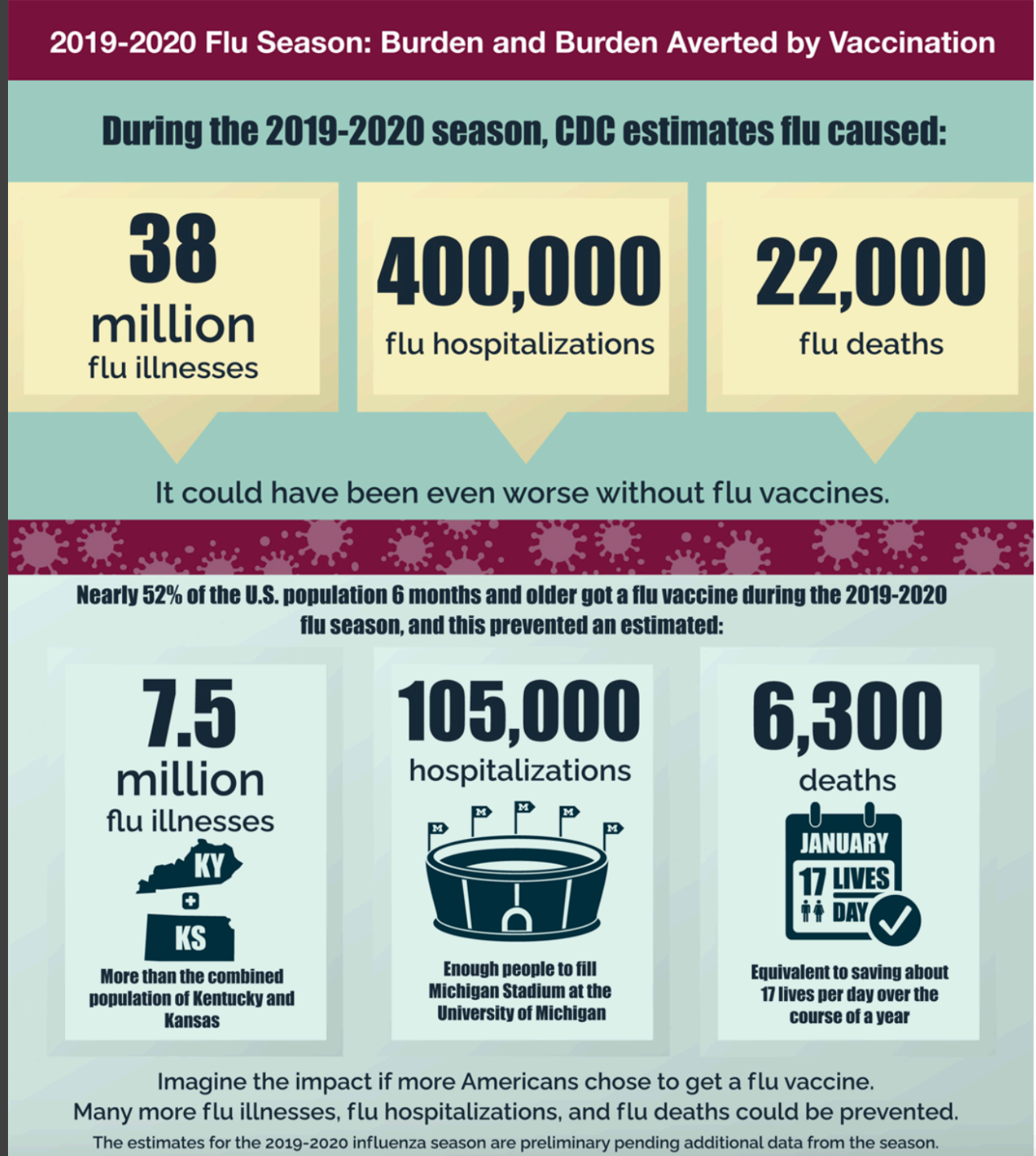
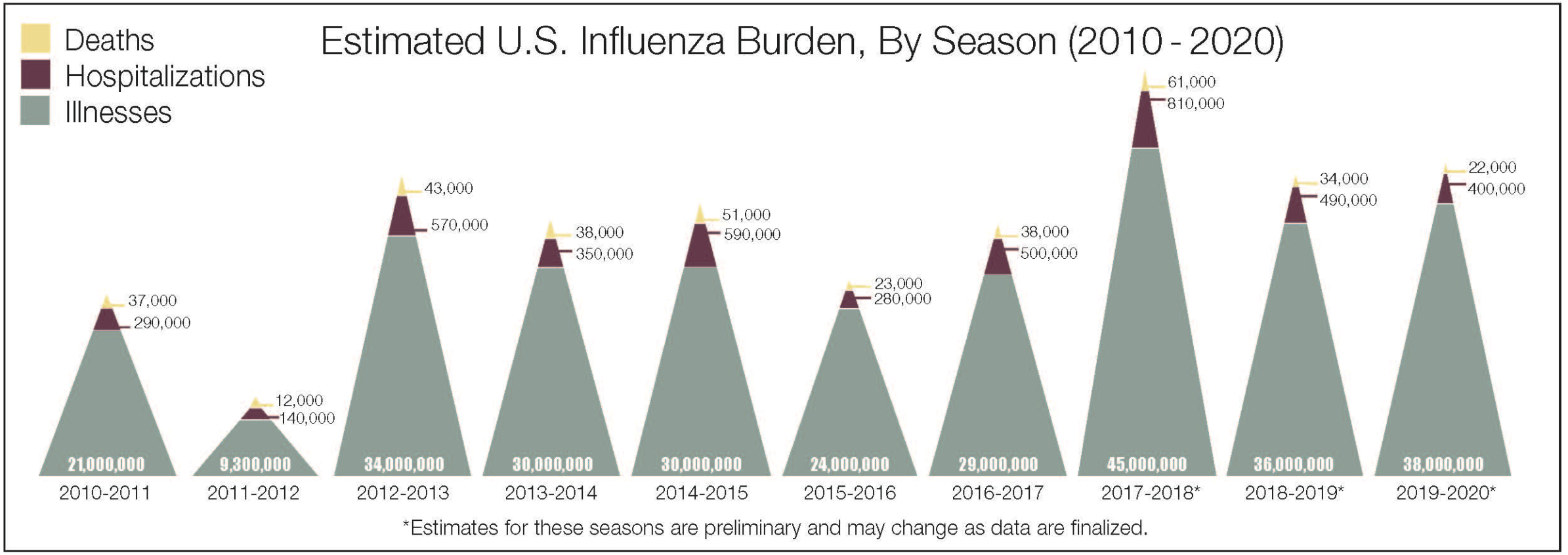
The Burden of Influenza in the USA

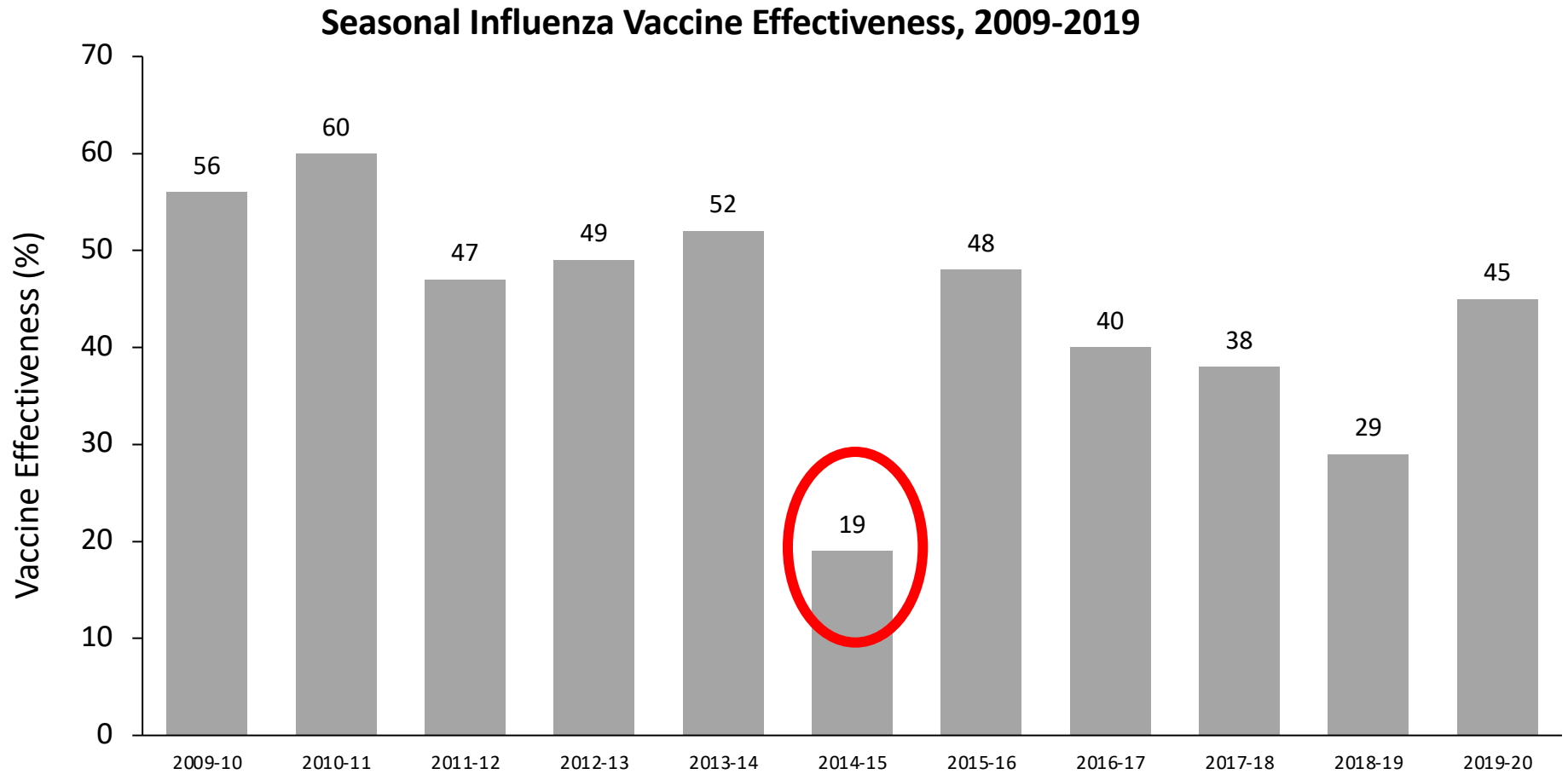
www.cdc.gov/flu/resource-center/ freeresources/graphics/flu-vaccine-protected-infographic.htm



Estimated Influenza Disease Burden, by Season
United States, 2010-11 through 2019-20 Influenza Seasons



Influenza Vaccination: 2009-2020

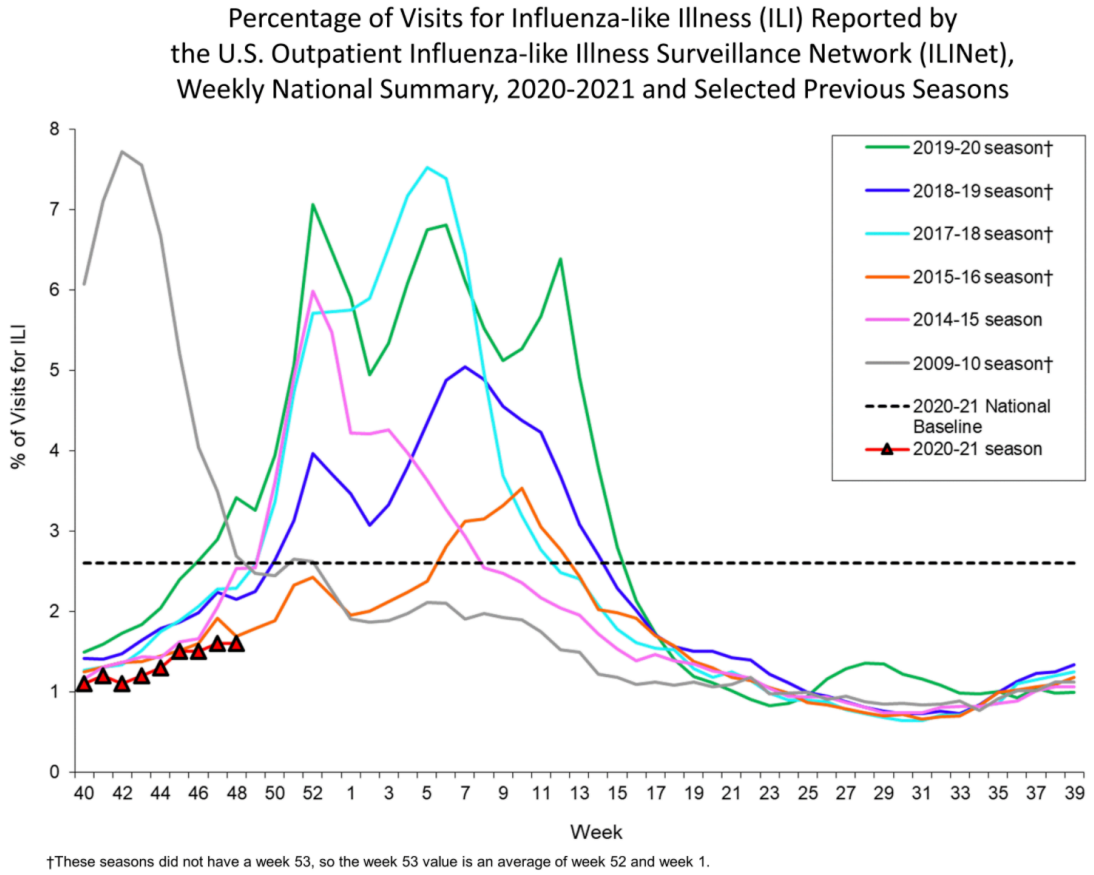


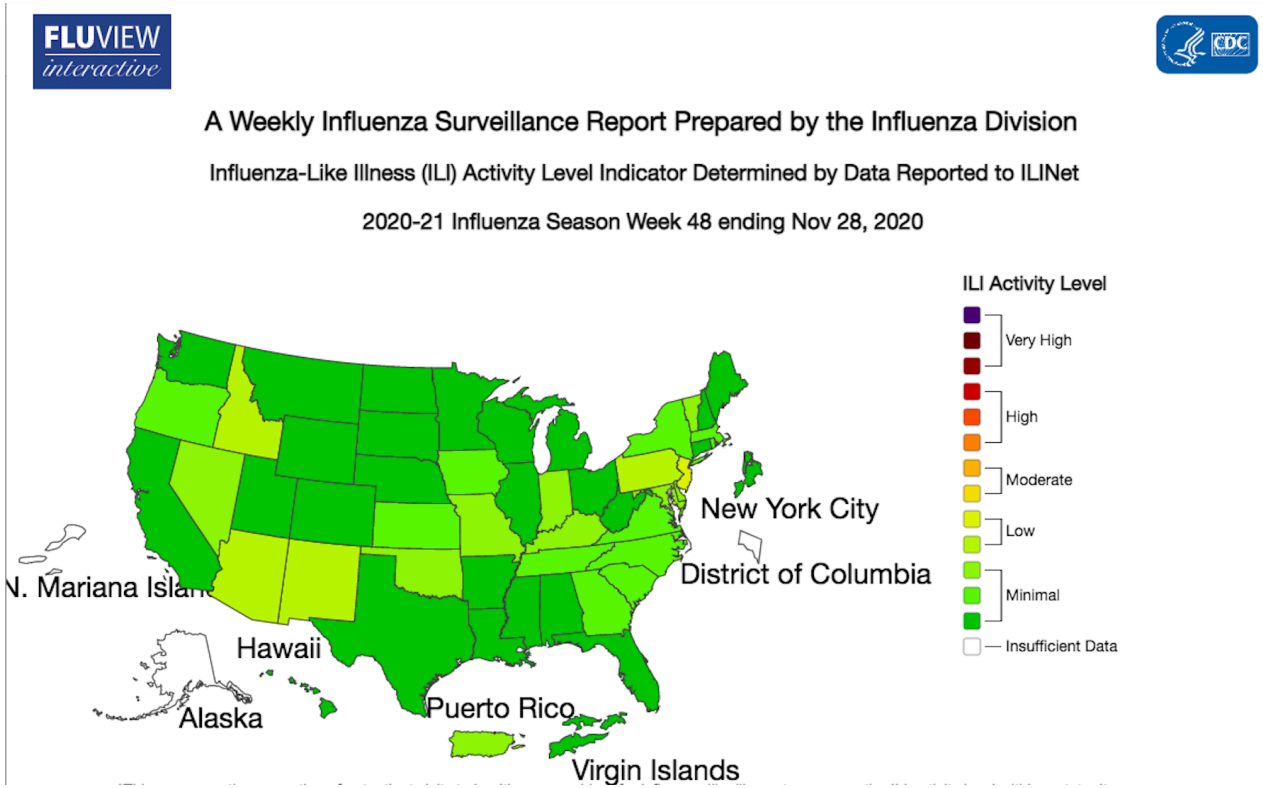
CDC. Frequently Asked Influenza (Flu) Questions: 2020-2021 Season. Available at: https://www.cdc.gov/flu/season/faq-flu-season-2020-2021.htm. Accessed 6/29/2020; CDC. Past Seasons Vaccine Effectiveness

What are CDC's Sources to Generate Influenza Epidemiologic Estimates

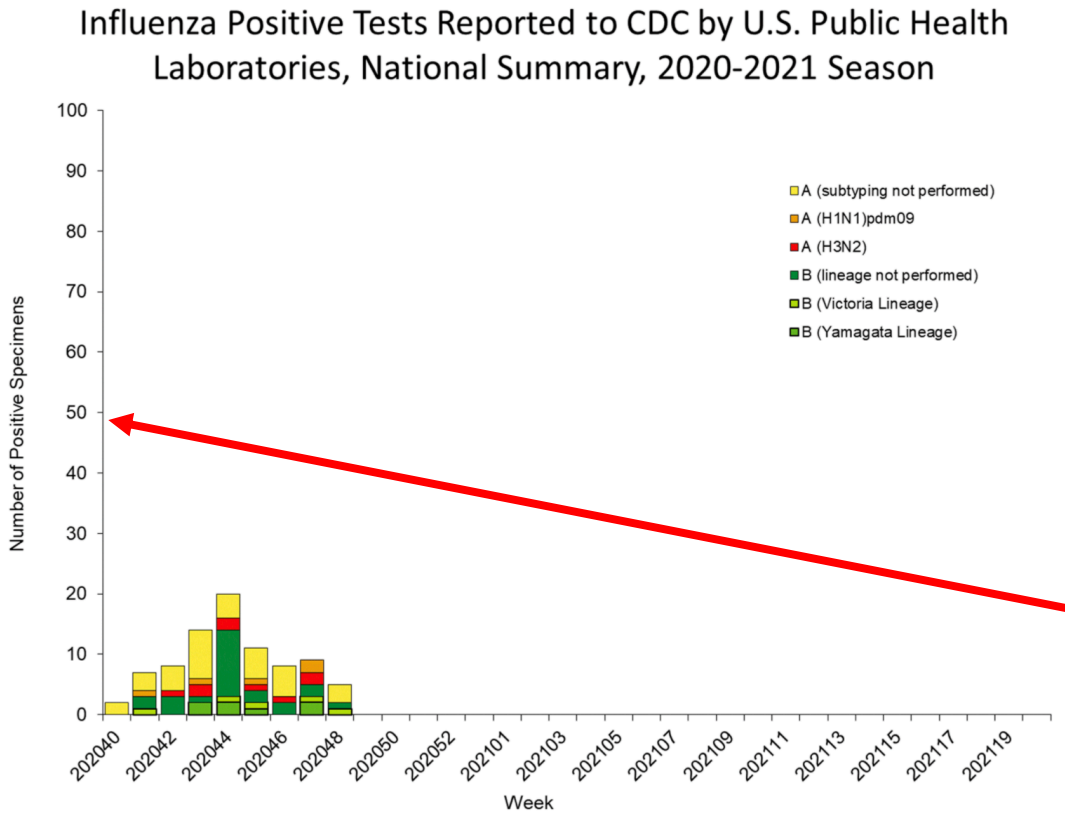
- Influenza like illness (ILI)reports
- Influenza positive tests
- Influenza public health labs positive tests
- Influenza pediatric mortality
- Other sources
  - Hospitalization due to Influenza
  - Death due to Influenza
  - Hospitalized Pneumonia due to influenza

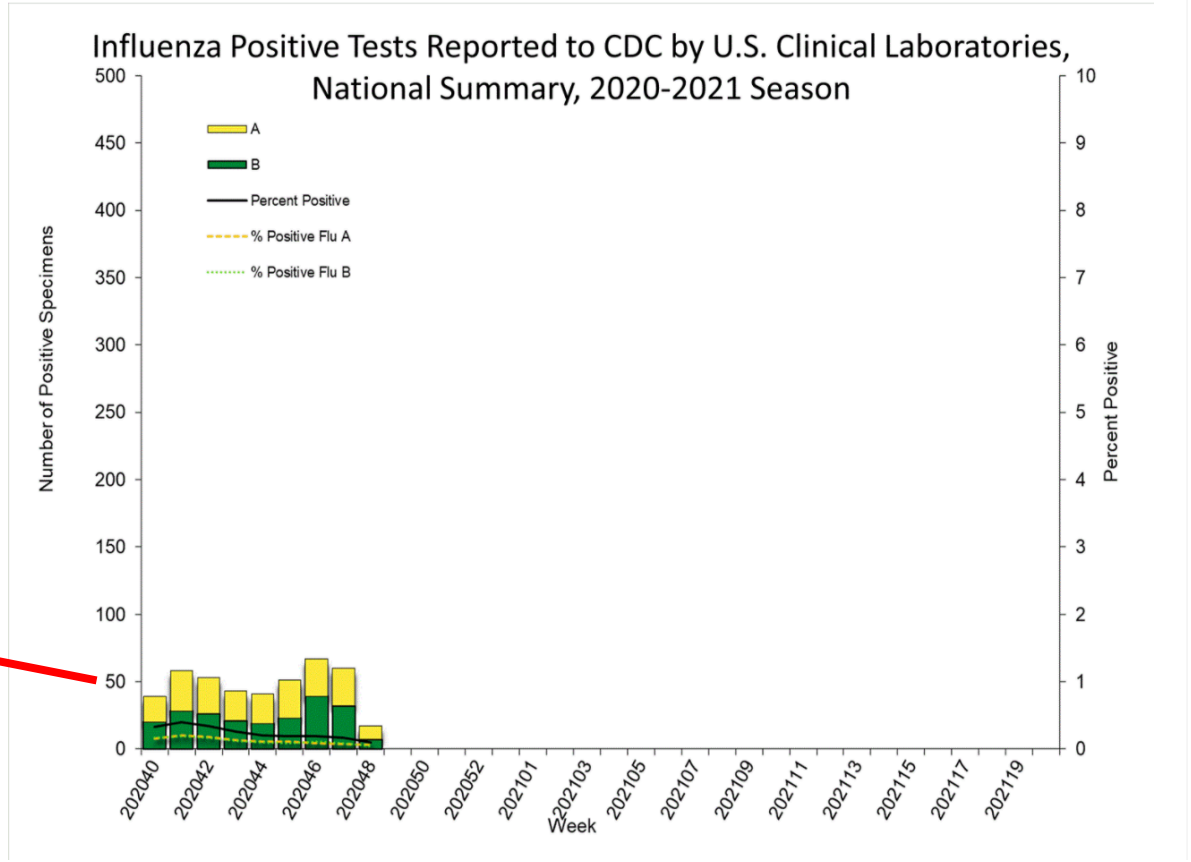
Influenza Like Illness (ILI) Reports in the US



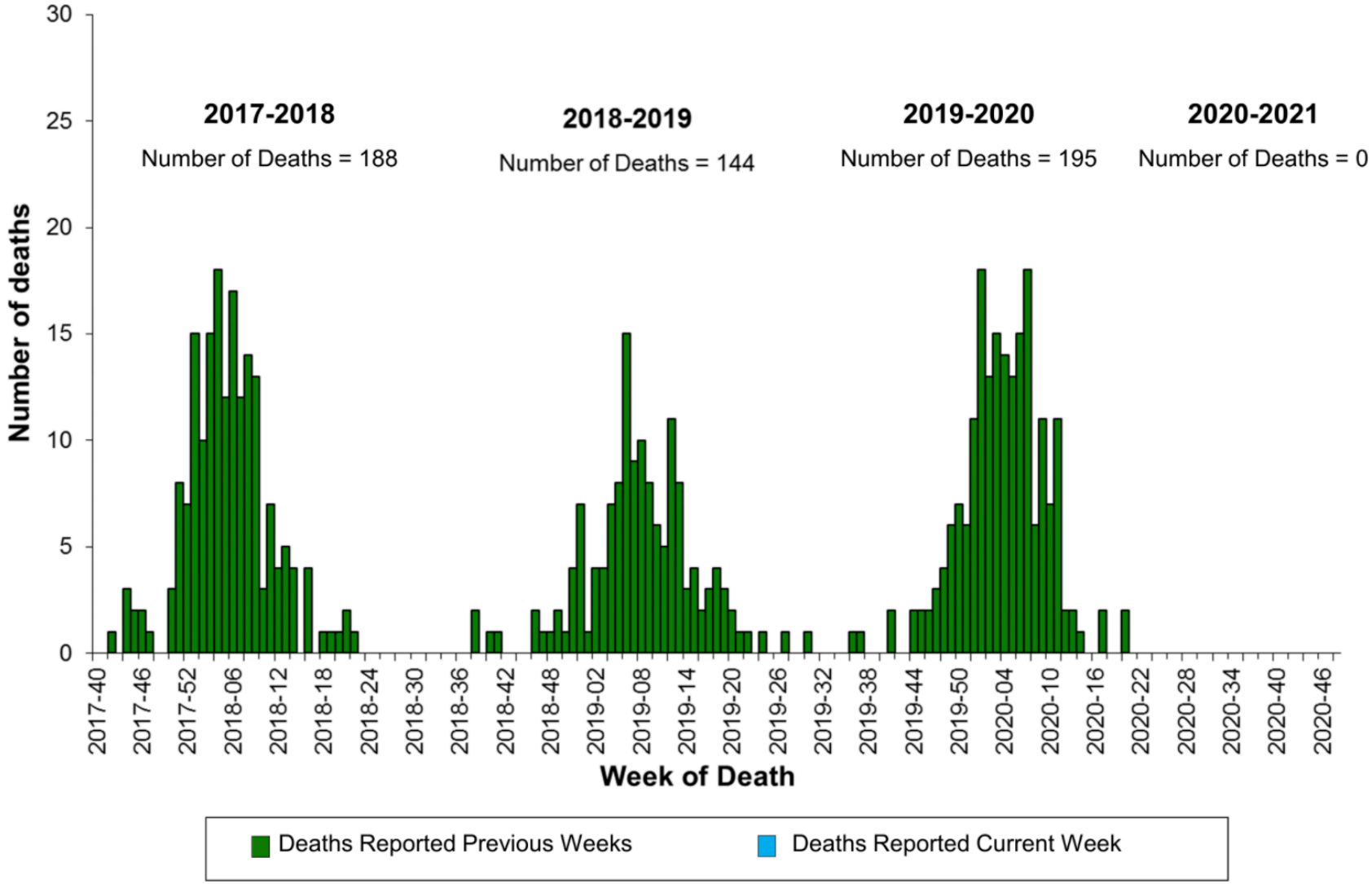


Influenza Positive Tests Results





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



Influenza Vaccines: 2020-2021 Season

Standard dose

- For all individuals > 6 months of Age
  - Trivalent (2 A and 1 B strains)
  - Quadrivalent (2 A strains and 2 B strains)

High Dose and Adjuvant

- **For patients aged ≥ 65 years**

Cell-based and Recombinant Quadrivalent

History of egg allergy with severe reactions.

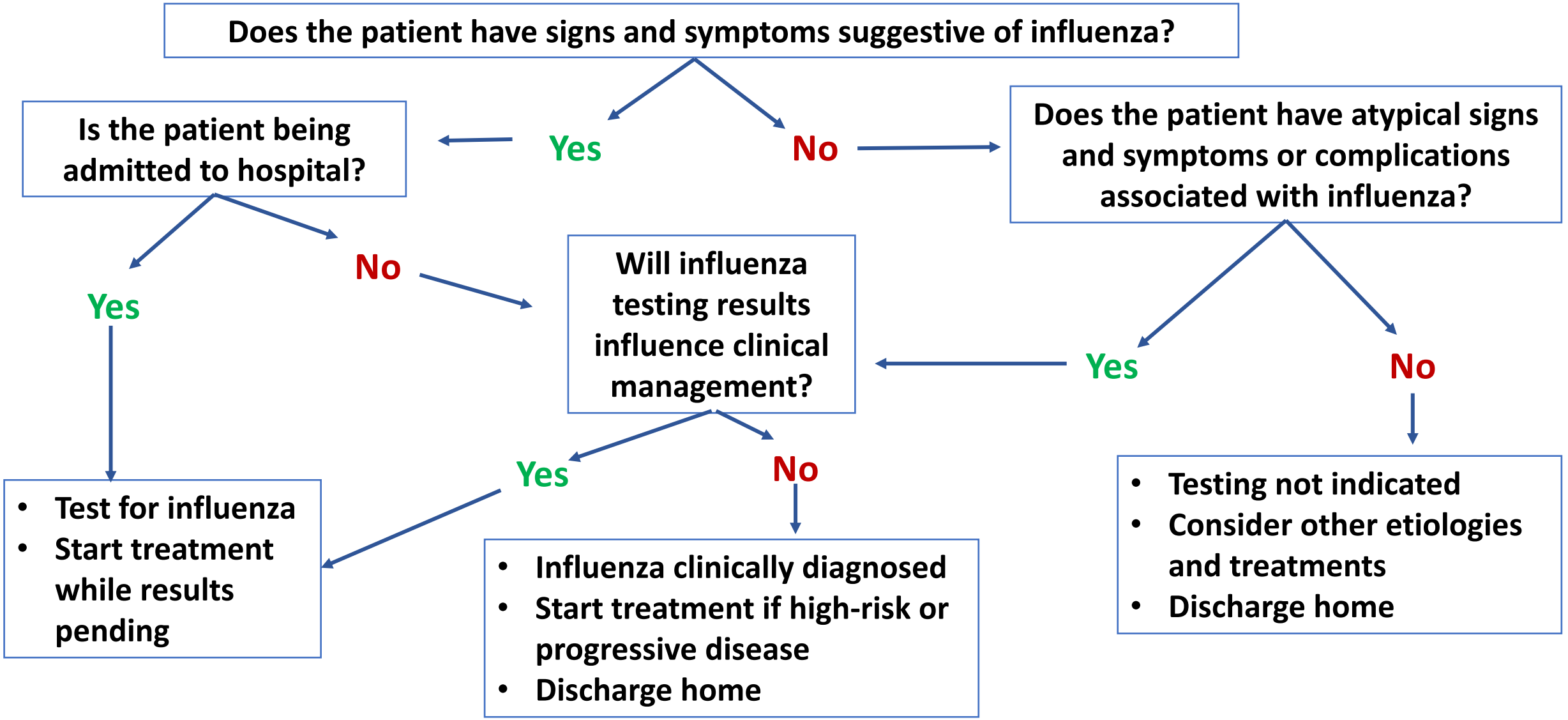
Live quadrivalent attenuated nasal spray

- For ages 2 to 49 years
- Contraindications: Children aged 2-4 years with asthma, immunocompromised individuals, pregnancy, asplenia, cochlear implant, CSF leak, recent receipt of antiviral medications

ACIP = Advisory Committee on Immunization Practices; C/I = Contraindications

CDC. Seasonal Flu Shot. https://www.cdc.gov/flu/prevent/flushot.htm. Accessed 8/10/2020; Grohskopf LA, et al. *MMWR Recomm Rep*. 2020; 69(No. RR-8):1-24; ACIP Influenza Work Group: Updates, Considerations, and Proposed Recommendations for the 2020-21 Season. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2020-06/flu-02-Grohskopf-508.pdf. Accessed 124/2020.

IDSA Decision Tree for Testing and Treatment of Influenza



IDSA = Infectious Diseases Society of America; COPD = Chronic Obstructive Pulmonary Disease; HF = Heart Failure; Uyeki T, et al. *Clin Infect Dis*. 2019;68(6):895-902.

Influenza Diagnostic Tests

Method	Testing Category	Detects	Distinguishes Influenza A Subtypes	Time to Results	Sensitivity	Specificity
Antigen Detection Assays	Rapid influenza diagnostic test	Influenza virus antigens	**No**	10-15 min	**Low to moderate** (↑ with analyzer)	**High**
Molecular Assays	Rapid molecular assay	Influenza viral RNA	**No**	15-30 min	**High**	**High**
	Conventional RT-PCR	Influenza viral RNA	**Yes**	1-8 h	**High**	**High**
	Multiplex molecular assays	Influenza and other viral/bacterial targets	**Yes**	1-2 h	**High**	**High**
Viral Culture	Rapid cell culture (shell vial and cell mixtures)	Influenza virus	**Yes**	1-3 days	**High**	**High**

RT-PCR = Reverse Transcription Polymerase Chain Reaction;

Adapted from Uyeki T, et al. *Clin Infect Dis.* 2019;68(6):895-902; CDC. CDC's diagnostic multiplex assay for flu and COVID-19 and supplies. https://www.cdc.gov/coronavirus/2019-ncov/lab/multiplex.html.

Indications for Treatment

Treatment should be provided:

- Hospitalization for influenza
- Severe or progressive illness
- High risk of complications
- Children < 2 years old
- Adults > 65 years old
- Pregnant women and those within 2 weeks post-partum

- **Treatment can be considered:**
- Illness onset ≤ 2 days before presentation
- Household contacts or healthcare providers for high-risk persons, particularly immunocompromised

Treatment should ideally start within 48 hours of symptom onset but there are exceptions

Ideally treatment should start within 6 hours

Treatment should not depend on laboratory confirmation

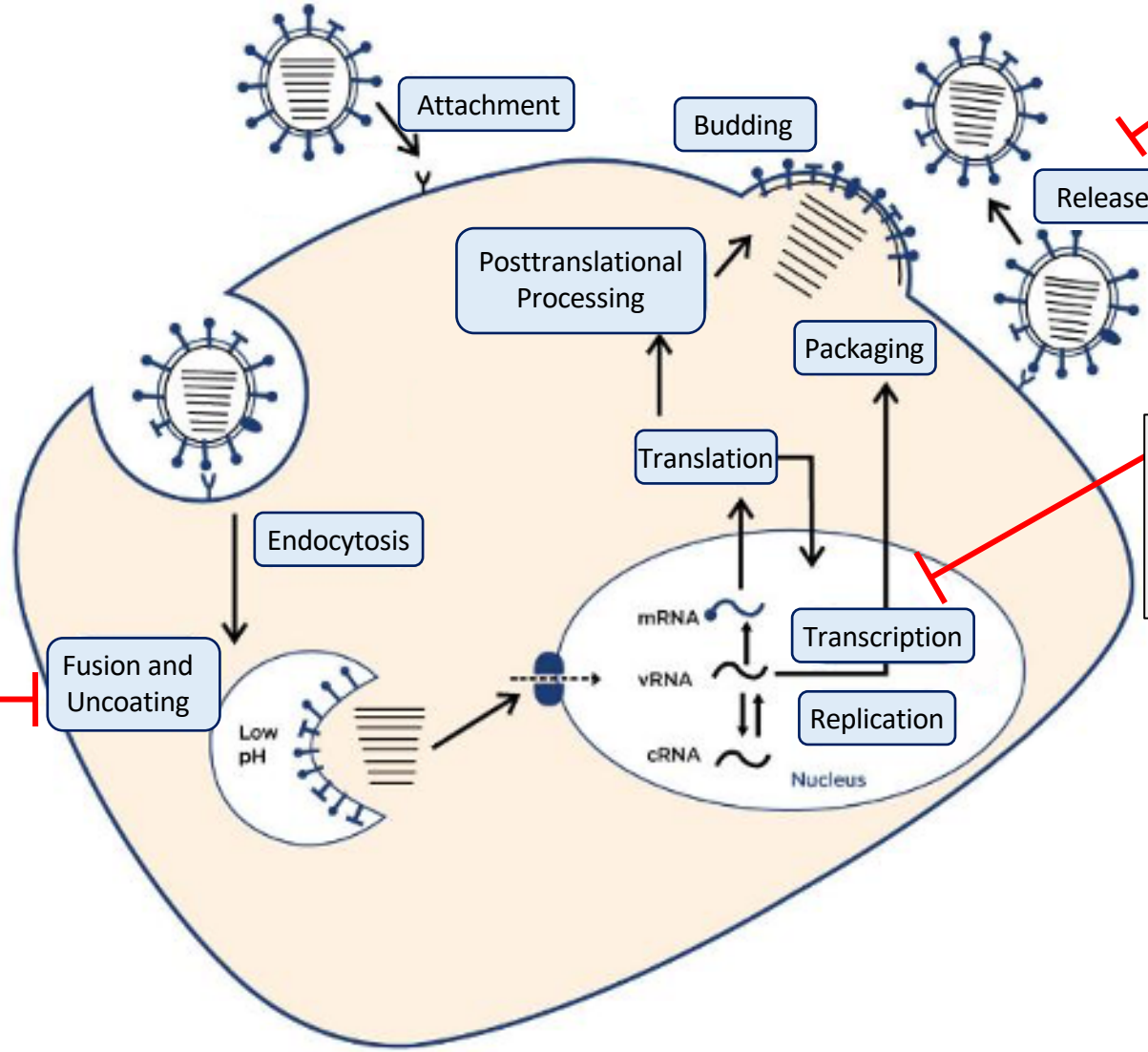
CDC. Influenza antiviral medications: summary for clinicians. Available at: https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm. Accessed 12/03/2020.

Individuals at High Risk of Complications from Influenza

- Children aged < 5 years, especially < 2 years
- Adults aged ≥ 65 years
- Immunosuppression
- Pregnancy & within 2 weeks postpartum
- Children and adolescents taking aspirin or other salicylates
- American Indian/Alaskan Native people
- Extreme obesity (BMI ≥ 40kg/m^2)
- Long-term care/nursing home residents
- **Chronic conditions:**
  - Pulmonary (including asthma)
  - Cardiovascular (excluding isolated hypertension)
  - Renal disorders
  - Hepatic disorders
  - Hematological (including sickle cell disease)
  - Intellectual disability/developmental delay
  - Metabolic disorders (including diabetes mellitus)
  - Neurological/neurodevelopmental conditions

Uyeki T, et al. *Clin Infect Dis*. 2019;68(6):895-902.

Antivirals for Influenza



Neuraminidase inhibitors
- Oseltamivir
- Zanamivir
- Peramivir

Cap-dependent endonuclease inhibitor
- Baloxavir

M2 ion channel inhibitors
- Amantadine
- Rimantadine
  - No clinical role due to widespread resistance

Shaw ML. *ACS Infect Dis.* 2017;3:691-694.

Antivirals for the Treatment of Acute Uncomplicated Influenza

Antiviral	Administration	Approved age for pediatric use	Use in patients at high risk for complications		Prophylaxis
			FDA approved	CDC recommended	
Baloxavir marboxil	Oral Single dose	≥ 12 years*	Yes	No	Yes
Oseltamivir	Oral BID x 5 days	≥ 2 weeks	No	Yes	Yes (once daily)
Peramivir	Intravenous Single dose	≥ 2 years	No	No	No
Zanamivir	Inhaled BID x 5 days	≥ 7 years	No	No	Yes ≥ 5 years (once Daily)

*NDA submitted for 1-12 years

UpToDate. Accessed 12/04/2020

Factors Influencing Treatment Selection

- **Comorbidities and risk of complications**
- **Disease severity**
- **Drug susceptibility of circulating virus**
- **Pregnancy**
- **Adherence issues**
- **Convenience of regimen**

Influenza Complications

More Frequent in Pediatrics

- *Ear Nose and Throat*
  - Otitis
  - Sinusitis
- *Muscular*
  - Myositis
  - Rhabdomyolysis

More Frequent in Adults

- *Cardiac*
  - Myocarditis/Pericarditis
  - Acute Coronary Syndrome
- *Pulmonary*
  - Viral Pneumonia
  - Bacterial Pneumonia
  - ARDS
- *Neurologic*
  - Aseptic Meningitis/Encephalitis
  - Transverse myelitis
  - Guillain Barre Syndrome

https://www.cdc.gov/flu/symptoms/symptoms.htm