Summary and Work Group Considerations

Lisa Grohskopf, MD, MPH

Influenza Division, NCIRD, CDC

Advisory Committee on Immunization Practices

October 23, 2019

Acknowledgments

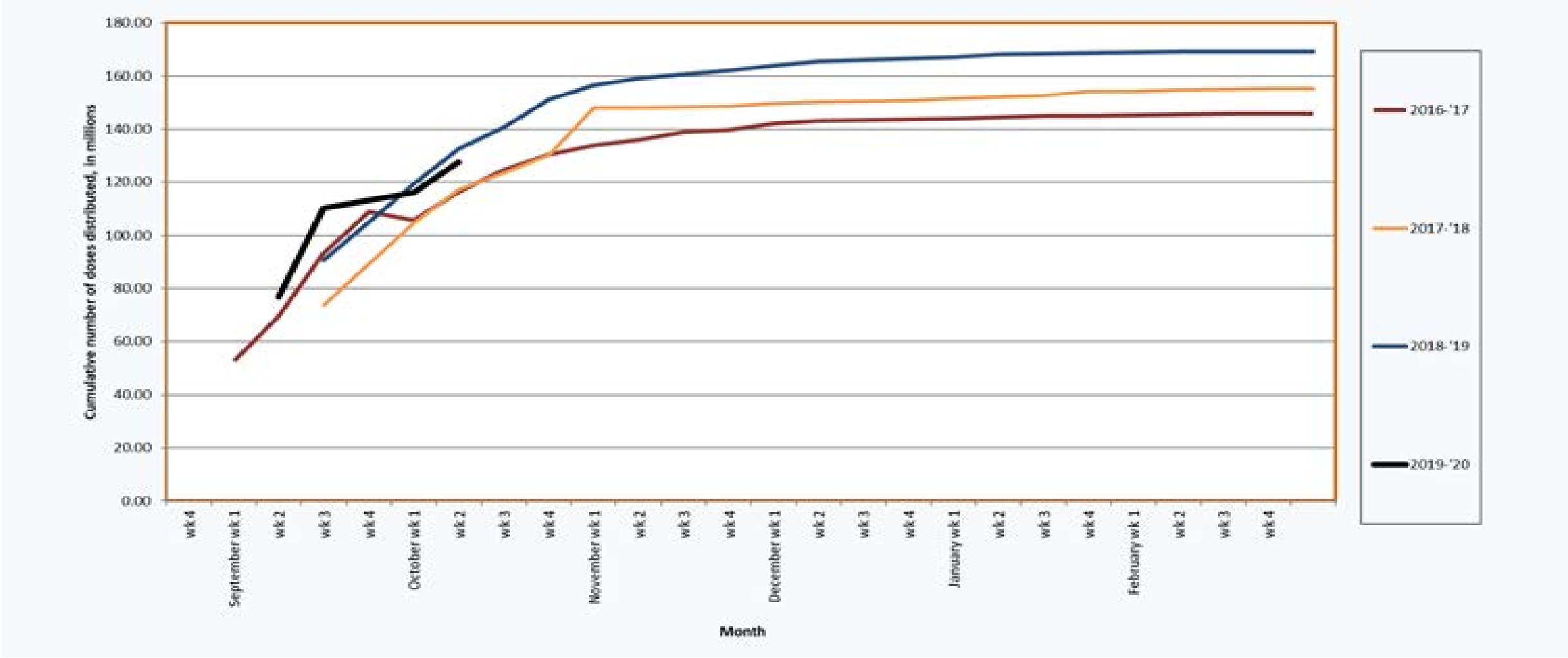
Influenza Division
Elif Alyanak
Noreen Alabi
Lenee Blanton
Lynnette Brammer
Joe Bresee
Alicia Budd
Jessie Chung
Scott Epperson
Jill Ferdinands
Brendan Flannery
Alicia Fry
Dan Jernigan
Krista Kniss
Natalie Kramer
Manish Patel
Melissa Rolfes
Jerry Tokars
Tim Uyeki

Immunization Safety Office
Karen Broder
Frank Destefano
Penina Haber
Tom Shimabukuro

Immunization Services Division
Sam Graitcer
Andrew Kroger
Amy Parker Fiebelkorn
Jeanne Santoli

Influenza Vaccine Distribution Update

Influenza Vaccine Supply Update: Cumulative Doses of Influenza Vaccine Distributed by Month, by Season—United States, 2016-17 through 2019-20 Seasons



Influenza Vaccines for Older Adults—WG Considerations

Abbreviations

IIV	Inactivated Influenza Vaccine
ccIIV	Cell culture based Inactivated Influenza Vaccine
aIIV	Adjuvanted Inactivated Influenza Vaccine
HD-IIV	High-Dose Inactivated Influenza Vaccine
RIV	Recombinant Influenza Vaccine
LAIV	Live Attenuated Influenza Vaccine

Numbers indicate the number of influenza virus antigens:

3 for trivalent: an A(H1N1), an A(H3N2), and one B (from one lineage)

4 for quadrivalent: an A(H1N1), an A(H3N2), and two Bs (one from each lineage)

Surgeon General's Statement on Influenza Immunization, 1960

Burney LE.
Public Health Rep. 1960 Oct;75(10):944

STATEMENT

By Leroy E. Burney, Surgeon General, Public Health Service

Influenza Immunization

Two outbreaks of influenza swept the United States in the fall of 1957 and the winter of 1958, resulting in 60,000 more deaths than would be expected under normal conditions. There were, in addition, more than 26,000 excess deaths during the first 3 months of 1960 which also were considered to be the result of influenza.

These departures from the usually predictable norms prompted the Surgeon General's Advisory Committee on Influenza Research to analyze the cause and to seek measures to prevent such an occurrence in the future.

The committee found that a new antigenic variant, the Asian strain, because of its widespread introduction and the general lack of resistance to it, was the direct cause of the excess number of deaths, not only in the total population but most markedly among the chronically ill, the aged, and pregnant women. As a result of these findings, the Public Health Service is urging a continuing program to protect these high-risk groups in order to prevent a recurrence of this excess mortality.

The high-risk groups who contribute most to the excess deaths and who the Public Health Service believes should be routinely immunized each year are:

1. Persons of all ages who suffer from chronic debilitating disease, in particular: (*a*) rheumatic heart disease, especially mitral stenosis; (*b*) other cardiovascular diseases, such as arteriosclerotic heart disease or hypertension—especially patients with evidence of frank or incipient insufficiency; (*c*) chronic bronchopulmonary disease, for example, chronic asthma, chronic bronchitis, bronchiectasis, pulmonary fibrosis, pulmonary emphysema, or pulmonary tuberculosis; (*d*) diabetes mellitus; (*e*) Addison's disease.
2. Pregnant women.
3. All persons 65 years or older.

The adult dosage recommended by the advisory committee for initial immunization is 1.0 cc. (500 cca units) of polyvalent vaccine, administered subcutaneously on two occasions separated by two or more months. Preferably, the first dose would be given no later than September 1 and the second no later than November 1. Persons previously immunized with polyvalent vaccine should be reinoculated with a single booster dose of 1.0 cc. subcutaneously each fall, prior to November 1. The only contraindication to vaccination would be a history of food allergy to eggs or chicken or a prior history of allergic reaction to an egg-produced vaccine, such as the commercial influenza product.

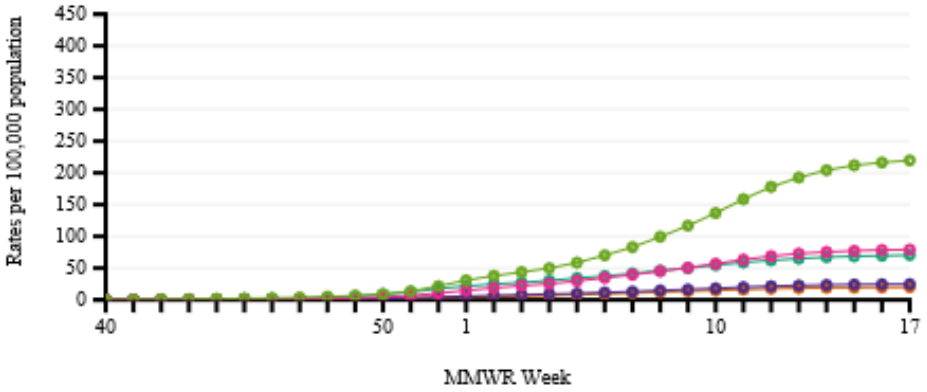
The time to start such a program is before the onset of the influenza season this fall. In the past, influenza vaccination has been sparse and sporadic, and primarily in response to an epidemic or the threat of an epidemic. The unpredictability of recurrence of influenza and its continued endemic occurrence are well known. Therefore, the Public Health Service strongly recommends that immunization of these high-risk groups be started now and continued annually, regardless of the predicted incidence of influenza for specific years.

The members of the Surgeon General's Advisory Committee on Influenza Research are: Colin M. MacLeod, M.D., chairman, University of Pennsylvania, Fred M. Davenport, M.D., University of Michigan, Morris Schaeffer, M.D., bureau of laboratories of the City of New York Health Department, George Burch, M.D., Tulane University, Dorland J. Davis, M.D., National Institute of Allergy and Infectious Diseases, Public Health Service, Thomas F. Sellers, M.D., Georgia State Department of Health, and Glenn S. Usher, M.D., Communicable Disease Center, Public Health Service.

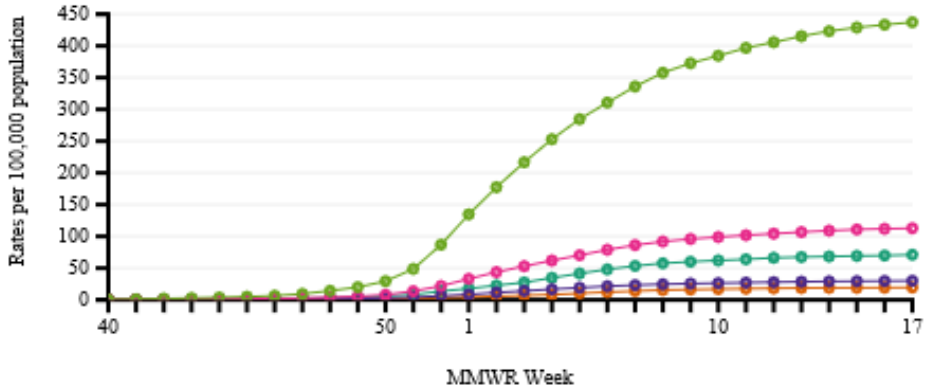
Laboratory-Confirmed Influenza Hospitalizations

Preliminary cumulative rates as of Oct 12, 2019

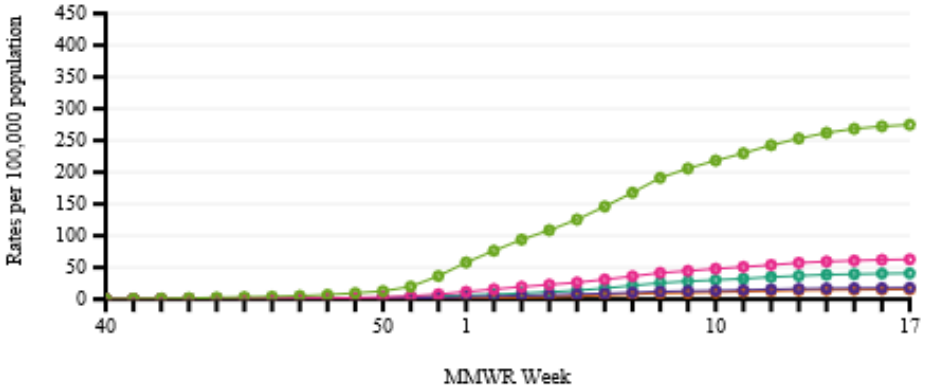
FluSurv-NET :: Entire Network :: 2018-19 Season :: Cumulative Rate



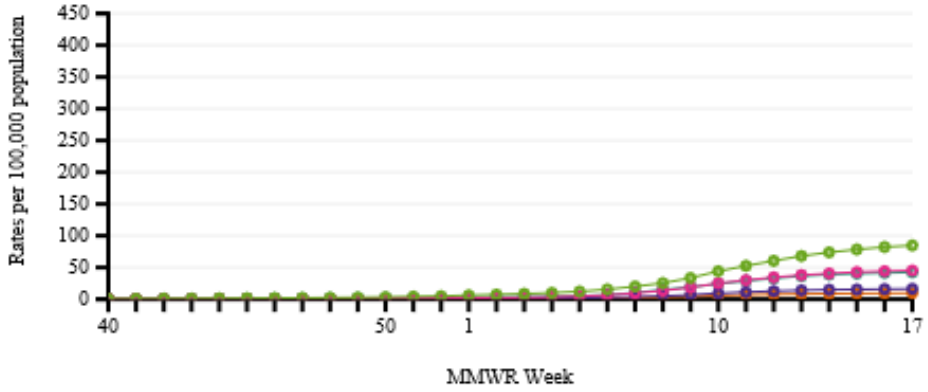
FluSurv-NET :: Entire Network :: 2017-18 Season :: Cumulative Rate



FluSurv-NET :: Entire Network :: 2016-17 Season :: Cumulative Rate



FluSurv-NET :: Entire Network :: 2015-16 Season :: Cumulative Rate

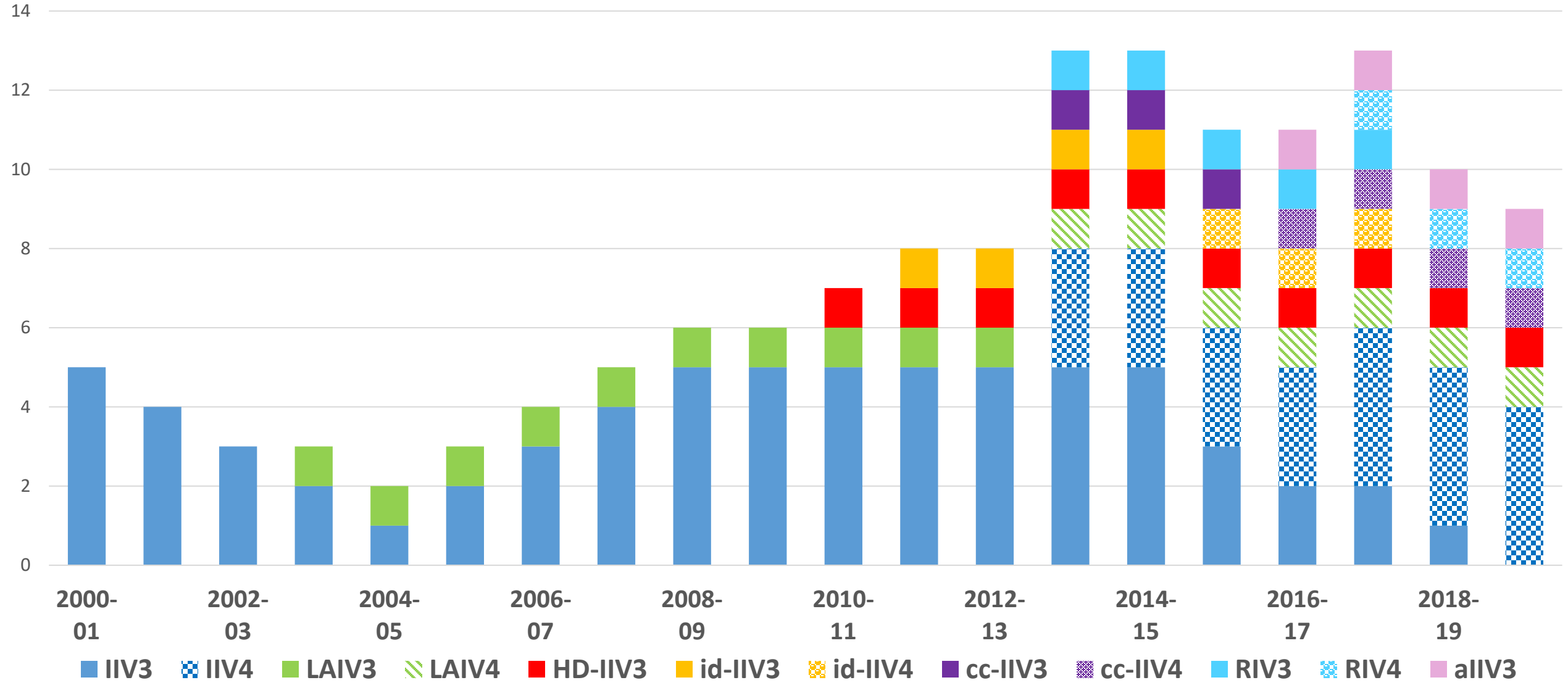


Age Selection

- ☑ 0-4 yr
- ☑ 5-17 yr
- ☑ 18-49 yr
- ☑ 50-64 yr
- ☑ 65+ yr

U.S. Seasonal Influenza Vaccines Since 2000-01

Number of unique products available by season



U.S.-Licensed Influenza Vaccines, 2019-20

Available vaccines by FDA-licensed age indication:

Vaccine type	6 through 23 mos	2 through 3 yrs	4 through 17 yrs	18 through 49 yrs	50 through 64 yrs	≥65 yrs
IIV4s (egg-based)	Afluria Quadrivalent Fluarix Quadrivalent FluLaval Quadrivalent Fluzone Quadrivalent					
IIV4 (cell-based)			Flucelvax Quadrivalent			
RIV4 (recombinant)				Flublok Quadrivalent		
Adjuvant IIV3 (egg-based)						Fluad
High-dose IIV3 (egg-based)						Fluzone High-dose
LAIV4 (egg-based)		FluMist Quadrivalent				

- ACIP recommends that a licensed, age-appropriate influenza vaccine should be used.
- No preferential recommendations are made for any specific influenza vaccine for any age group, where there is more than one that is appropriate.

Challenges in Assessing Relative Benefits of Specific Vaccines for Older Adults

- Large variety of available influenza vaccines
  - 8 are appropriate for this age group by licensed indications
- Growing canon of studies comparing individual vaccine types, but data limited for some relevant comparisons
- Vaccine effectiveness (and relative effectiveness of different vaccines) varies from season to season
  - Cannot be certain that results from one or a few high-quality studies will generalize across all or most influenza seasons

HD-IIV3, aIIV3 and RIV4 for Older Adults

Summary of studies examining laboratory-confirmed influenza outcomes:

Study Year published Ages	Season(s)	Comparison	Design	N	Relative Efficacy/effectiveness
DiazGranados 2013[1] ≥65 years	1 2009-10	HD-IIV3 vs SD-IIV3	RCT	~9,100	Not evaluable because of pandemic
DiazGranados 2014[2] ≥65 years	2 2011-12, 2012-13	HD-IIV3 vs SD-IIV3	RCT	~32,000	24.2% (95% CI = 9.7–36.5)
Dunkle 2017[3] ≥50 years	1 2014-15	RIV4 vs SD-IIV4	RCT	~8,600	30% (95% CI = 10–47)
Van Buynder 2013[4] ≥65 years	1 2011-12	aIIV3 vs SD-IIV3	observational	227	63% (95% CI = 4–86)

[1] DiazGranados CA et al, Vaccine 2013;31:861-866
[2] DiazGranados CA et al, N Engl J Med 2014;371:635-645
[3] Dunkle LM et al, N Engl J Med 2017;376:2427-2436
[4] VanBuynder PG et al, Vaccine 2013; 31:6122-6128

Planned Systematic Review/Meta-analysis--Question

Do the relative benefits and harms of HD-IIV, aIIV, and RIV as compared with one another and with other influenza vaccines favor the use of these vaccines over others for persons aged 65 years and older?

Planned Systematic Review/Meta-analysis--Summary

Population: Adults aged ≥65 years

Interventions: Trivalent/quadrivalent high dose IIV, adjuvanted IIV, or RIV
(U.S.-licensed, or similar in formulation/manufacture to U.S.-licensed)

Comparators: Other trivalent or quadrivalent influenza vaccine
(U.S.-licensed, or similar in formulation/manufacture to U.S.-licensed)
Non-influenza control vaccine
Placebo
No vaccine

Planned Systematic Review/Meta-analysis--Summary

Outcomes: (To be finalized early November)

Efficacy/Effectiveness

- All influenza -- A and B
  (sub-analysis stratified by virus type and subtype as feasible)
- Influenza-associated outpatient/emergency visits
- Influenza-associated hospitalizations
- Influenza-associated deaths

Safety

- Systemic and injection site adverse events
- Serious adverse events
- Guillain-Barre syndrome
- Severe hypersensitivity or anaphylaxis

Inclusion/Exclusion Criteria

- **Peer-reviewed literature; no language restriction**
- **Publication dates from 1990 forward**
- **Include:**
  - Randomized studies (including cluster-randomized)
  - Retrospective case-control and cohort studies
  - Prospective cohort studies
- **Exclude:**
  - Case series, case reports, registry reports without comparator information.
  - Studies/data on vaccines not licensed in the United States
  - Animal studies
  - Studies/data for which entire population falls outside of designated age range
  - Duplicate reports
  - Interim reports superseded by final reports

Thank you