Adult vaccines and shared clinical decision making - with focus on RSV

Helmut Albrecht, MD
Heyward Gibbes Distinguished Professor of Internal Medicine
Medical Director, Center for Infectious Diseases Research & Policy
Prisma Health/USC

Adult Immunization Schedule 2024

- https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html

- By Age
  - https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html#table-age
  - Online, printable (PDF), mobile download

- By Indication
  - https://www.cdc.gov/vaccines/schedules/hcp/imz/adult-conditions.html
  - Online, printable (PDF), mobile download

Table 1 Recommended Adult Immunization Schedule by Age Group, United States, 2024

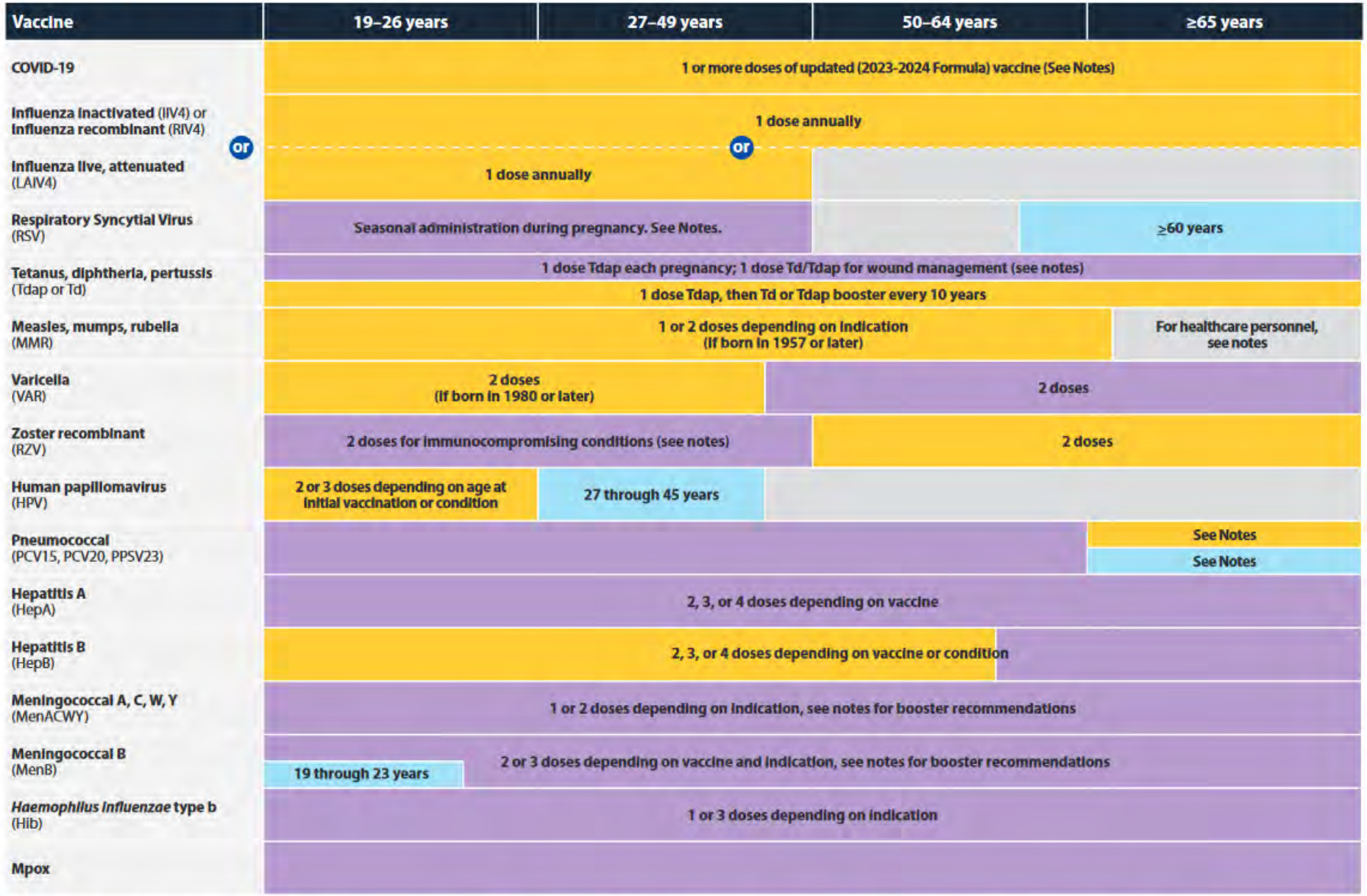


Table 2 Recommended Adult Immunization Schedule by Medical Condition or Other Indication, United States, 2024

Always use this table in conjunction with Table 1 and the Notes that follow. Medical conditions or indications are often not mutually exclusive. If multiple medical conditions or indications are present, refer to guidance in all relevant columns. See Notes for medical conditions or indications not listed.

VACCINE	Pregnancy	Immunocompromised (excluding HIV infection)	HIV infection CD4 percentage and count		Men who have sex with men	Asplenia, complement deficiency	Heart or lung disease	Kidney failure, End-stage renal disease or on dialysis	Chronic liver disease; alcoholism[a]	Diabetes	Healthcare Personnel[b]
			<15% or <200mm	≥15% and ≥200mm							
COVID-19		See Notes									
IIV4 or RIV4	1 dose annually										
LAIV4					1 dose annually if age 19 - 49 years		1 dose annually if age 19 - 49 years				
RSV	Seasonal administration. See Notes	See Notes				See Notes					
Tdap or Td	Tdap: 1 dose each pregnancy	1 dose Tdap, then Td or Tdap booster every 10 years									
MMR	*										
VAR	*		See Notes								
RZV		See Notes									
HPV	*	3 dose series if indicated									
Pneumococcal											
HepA											
Hep B	See Notes									Age ≥ 60 years	
MenACWY											
MenB											
Hib		HSCT: 3 doses[c]				Asplenia: 1 dose					
Mpox	See Notes				See Notes						See Notes

- Recommended for all adults who lack documentation of vaccination, **OR** lack evidence of immunity
- Not recommended for all adults, but recommended for some adults based on either age **OR** increased risk for or severe outcomes from disease
- Recommended based on shared clinical decision-making
- Recommended for all adults, and additional doses may be necessary based on medical condition or other indications. See Notes.
- Precaution: Might be indicated if benefit of protection outweighs risk of adverse reaction
- Contraindicated or not recommended *Vaccinate after pregnancy, if indicated
- No Guidance/ Not Applicable

a. Precaution for LAIV4 does not apply to alcoholism.

b. See notes for influenza; hepatitis B; measles, mumps, and rubella; and varicella vaccinations.

c. Hematopoietic stem cell transplant.

Shared Clinical Decision Making

- ACIP has 5 recommendations for vaccination based on SCDM
  - RSV for adults aged 60 years and older
  - Meningococcal B (MenB) for adolescents/young adults aged 16–23 years
  - Hepatitis B (HepB) for diabetics aged 60 years and older
  - HPV for adults aged 27–45 years
  - Pneumococcal conjugate vaccination (PCV20) for adults aged 65 years and older who have completed the recommended vaccine series with both PCV13 (at any age) and PPSV23 (which was administered at age ≥65 years)

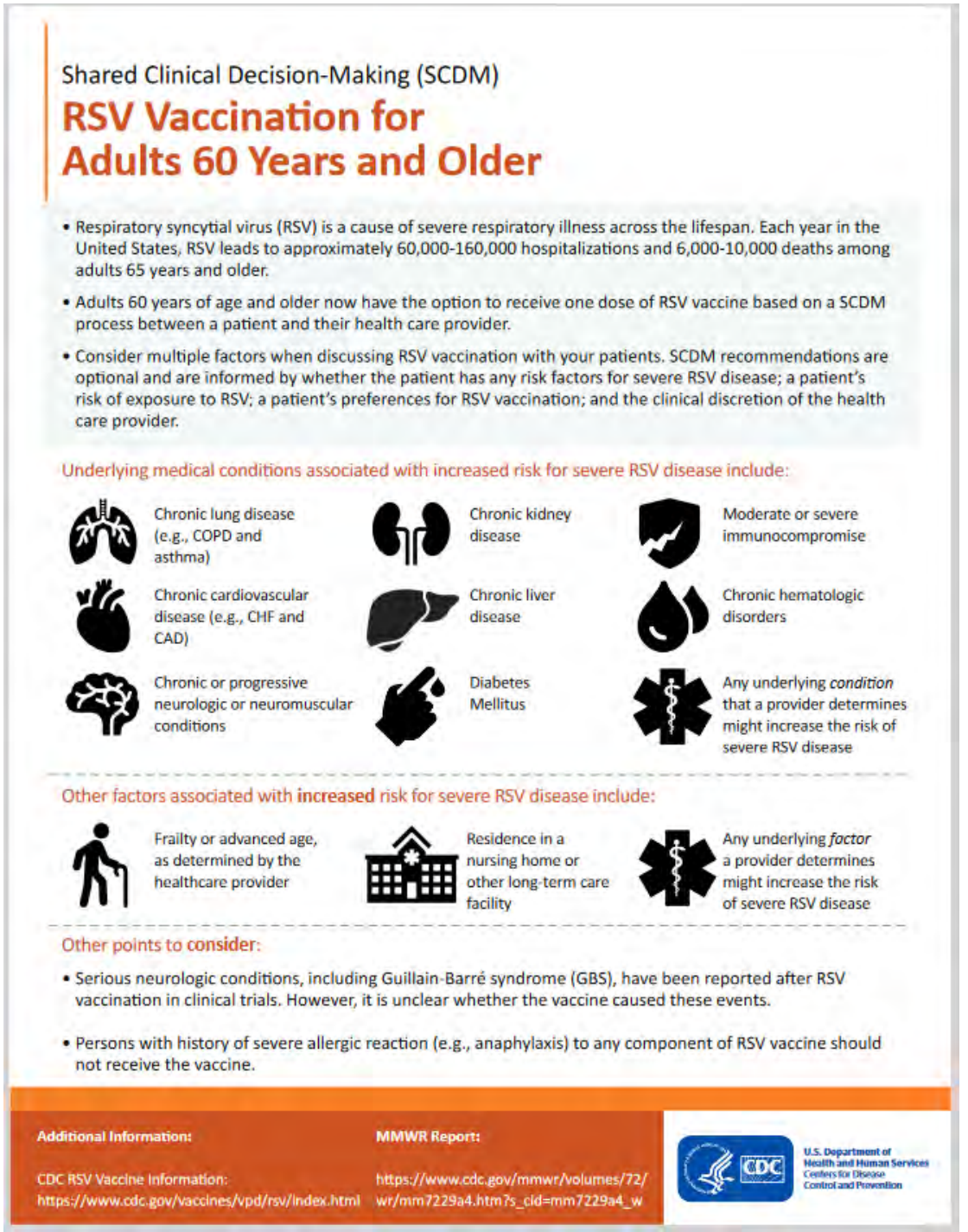
Vaccinations based on SCDM

- Individuals may benefit, but unlikely to result in population benefit
- “Unlike routine, catch-up, and risk-based recommendations, SCDM vaccinations are not recommended for everyone in a particular age group or everyone in an identifiable risk group”
- “Rather, SCDM recommendations are individually based and informed by a decision process between the health care provider and the patient or parent/guardian”
- Difference: No default decision to vaccinate unless contraindication
- Goal/outcome is discussion, not vaccination (but where is trigger?)

What the heck is Shared Clinical Decision Making?

• Is it new?	Yes (for vaccines) No (for HCPs)
• Is it a compromise??	Yes
• Is it better than not approving a vaccine?	Yes
• Is it a cop out?	Yes
• Does this work?	Yes (for lawyers) No (for HCPs & patients)
• Could this be done better?	Yes
• Should this been done better?	Yes

CDC is here to help!?



Shared Clinical Decision-Making (SCDM)

RSV Vaccination for Adults 60 Years and Older

- Respiratory syncytial virus (RSV) is a cause of severe respiratory illness across the lifespan. Each year in the United States, RSV leads to approximately 60,000-160,000 hospitalizations and 6,000-10,000 deaths among adults 65 years and older.
- Adults 60 years of age and older now have the option to receive one dose of RSV vaccine based on a SCDM process between a patient and their health care provider.
- Consider multiple factors when discussing RSV vaccination with your patients. SCDM recommendations are optional and are informed by whether the patient has any risk factors for severe RSV disease; a patient's risk of exposure to RSV; a patient's preferences for RSV vaccination; and the clinical discretion of the health care provider.

Underlying medical conditions associated with increased risk for severe RSV disease include:

- Chronic lung disease (e.g., COPD and asthma)
- Chronic kidney disease
- Moderate or severe immunocompromise
- Chronic cardiovascular disease (e.g., CHF and CAD)
- Chronic liver disease
- Chronic hematologic disorders
- Chronic or progressive neurologic or neuromuscular conditions
- Diabetes Mellitus
- Any underlying *condition* that a provider determines might increase the risk of severe RSV disease

Other factors associated with **increased** risk for severe RSV disease include:

- Frailty or advanced age, as determined by the healthcare provider
- Residence in a nursing home or other long-term care facility
- Any underlying *factor* a provider determines might increase the risk of severe RSV disease

Other points to consider:

- Serious neurologic conditions, including Guillain-Barré syndrome (GBS), have been reported after RSV vaccination in clinical trials. However, it is unclear whether the vaccine caused these events.
- Persons with history of severe allergic reaction (e.g., anaphylaxis) to any component of RSV vaccine should not receive the vaccine.

Additional Information:

CDC RSV Vaccine Information:
https://www.cdc.gov/vaccines/vpd/rsv/index.html

MMWR Report:

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm?s_cid=mm7229a4_w

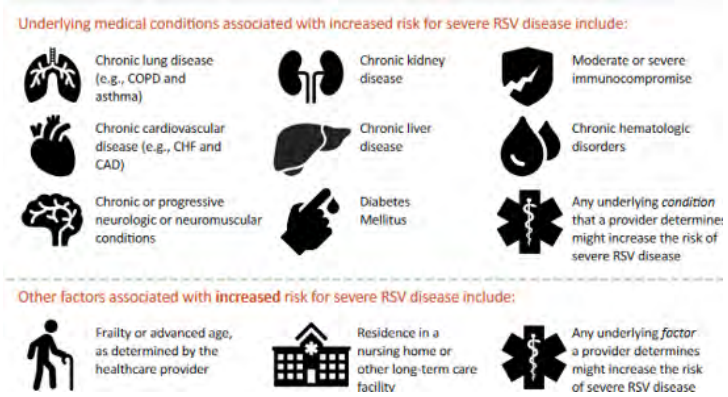
U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

So what do we do with this?

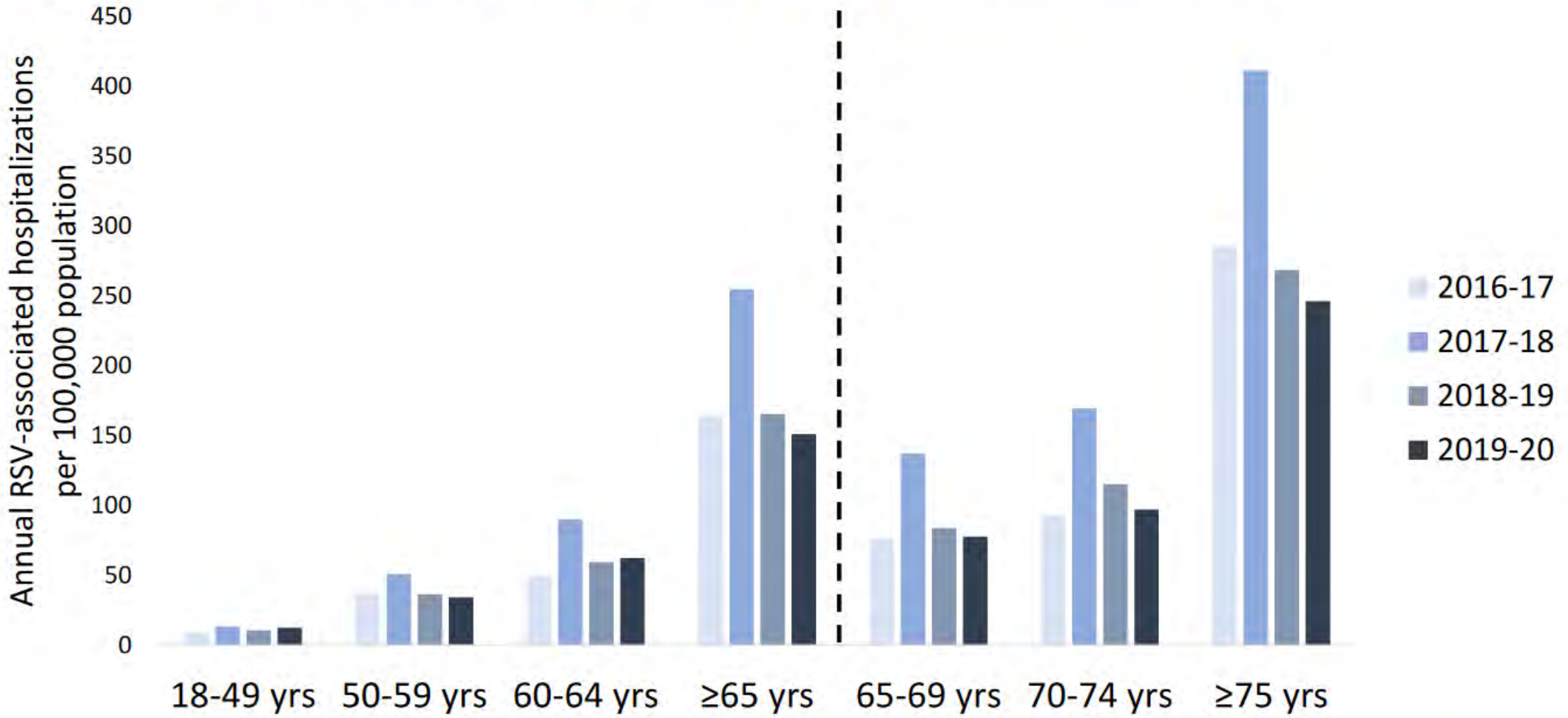
- I do not know what you do but I use

The Albrecht Index

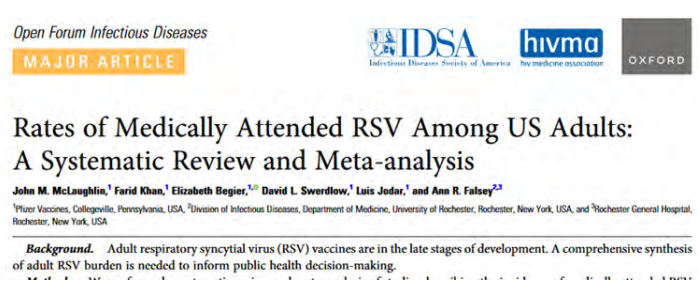
- **But first lets see some data**
- **And some background info**
- **And some sort of grading system for**



RSV-NET estimated annual hospitalizations per 100,000 adults: 2016–2017 to 2019–2020



CDC RSV-NET unpublished data. Estimates are adjusted for under-testing and incomplete test sensitivity. https://www.cdc.gov/rsv/research/rsv-net/index.html



Open Forum Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Rates of Medically Attended RSV Among US Adults: A Systematic Review and Meta-analysis

John M. McLaughlin,[1] Farid Khan,[1] Elizabeth Begier,[1,a] David L. Swerdlow,[1] Luis Jodar,[1] and Ann R. Falsey[2,3]

[1]Pfizer Vaccines, Collegeville, Pennsylvania, USA, [2]Division of Infectious Diseases, Department of Medicine, University of Rochester, Rochester, New York, USA, and [3]Rochester General Hospital, Rochester, New York, USA

Background. Adult respiratory syncytial virus (RSV) vaccines are in the late stages of development. A comprehensive synthesis of adult RSV burden is needed to inform public health decision-making.

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Incidence of Respiratory Syncytial Virus Infection Among Hospitalized Adults, 2017–2020

Angela R. Branche,[1] Lisa Saiman,[2,3] Edward E. Walsh,[1,4] Ann R. Falsey,[1,4] William D. Sieling,[2] William Greendyke,[5] Derick R. Peterson,[6] Celibell Y. Vargas,[2] Matthew Phillips,[7] and Lyn Finelli[7]

[1]Department of Medicine, Division of Infectious Diseases, University of Rochester, Rochester, New York, USA; [2]Department of Pediatrics, Columbia University Irving Medical Center, New York, New York, USA; [3]Department of Infection Prevention and Control, New York–Presbyterian Hospital, New York, New York, USA; [4]Rochester General Hospital, Rochester, New York, USA; [5]Department of

- Asthma, COPD, CHF previously described but not population based
- >10k hospitalized symptomatic patients 2017 – 2019
- 93% tested, >1k RSV pos
- Criteria, especially hospitalization, works for me (cave with vs. due to RSV)
- RRs varied by age (>85 >> 65 – 85 > 50 - 65) and diagnosis
- Significant RRs: CHF 4.0 – 33.2, CAD 3.7 – 7.0, COPD 3.2 – 13.4
- Less convincing RRs: Asthma 2.0 – 3.6, DM 2.3 – 11.4 (young)
- No RRs for ESRD, ESLD, cancer, nursing home, neurological conditions
- Least convincing RRs: Obesity 0.7 – 3.1
- Rates higher than in NZ study (2013-15, 56% of patients tested)

So what do we do with this?

- I do not know what you do but I use

The Albrecht Index

Albrecht Index

• Age > 65 years	2 points
• Age > 85 years	2 points
• Nursing home residence	2 points
• COPD on therapy/pathology	2 points
• CAD s/p event	2 points
• DM on therapy	1 point
• Asthma on therapy	1 point
• Immunocompromised (ESRD, ELD, cancer, HIV, transplant)	1 point
• Pregnant 28w – 36w gestation	4 points
• Expecting father, grandparent	2 points

• 2 points	Discuss vaccine in detail
• 4 points	Recommend vaccine

Albrecht Index

- Criteria based on data
- Weighting/index based on personal bias
- Not validated
- Low discriminatory effect
- Works for me, but may not for you (think “Gestalt” >> index/numbers)
- Race, household membership, other conditions, and smoking omitted because of lack of consistent data but probably relevant
- Will be refined once we have better data on vaccine efficacy, duration of that VE, rare vaccine side effects, better population based data for rarer conditions

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 72 / No. 14
April 7, 2023

Seasonality of Respiratory Syncytial Virus — United States, 2017–2023

Sarah Hamid, PhD[1,2]; Amber Winn, MPH[2]; Rishika Parikh, MPH[2,3]; Jefferson M. Jones, MD[2]; Meredith McMorrow, MD[2]; Mila M. Prill, MSPH[2]; Benjamin J. Silk, PhD[2]; Heather M. Scobie, PhD[2]; Aron J. Hall, DVM[2]

- COVID changed RSV
  - Different epidemic?!
  - Different definitions!
  - Different surveillance!

FIGURE 1. Percentage* of polymerase chain reaction test results positive for respiratory syncytial virus, by epidemiologic week — National Respiratory and Enteric Virus Surveillance System, United States, July 2017–February 2023

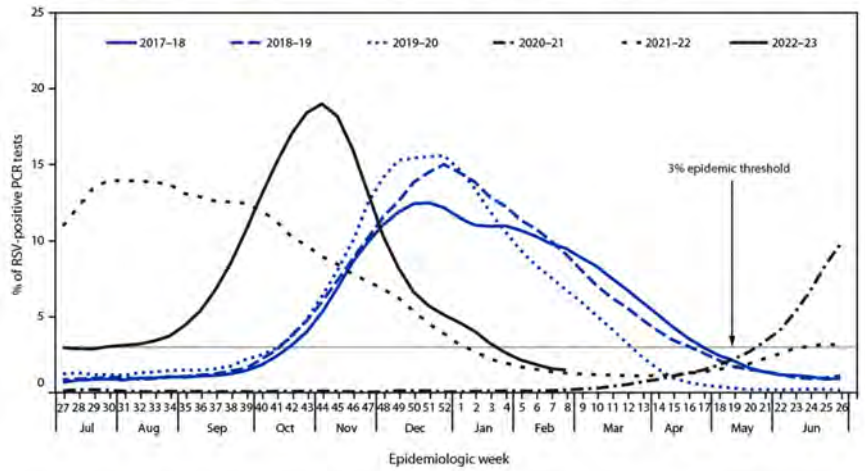
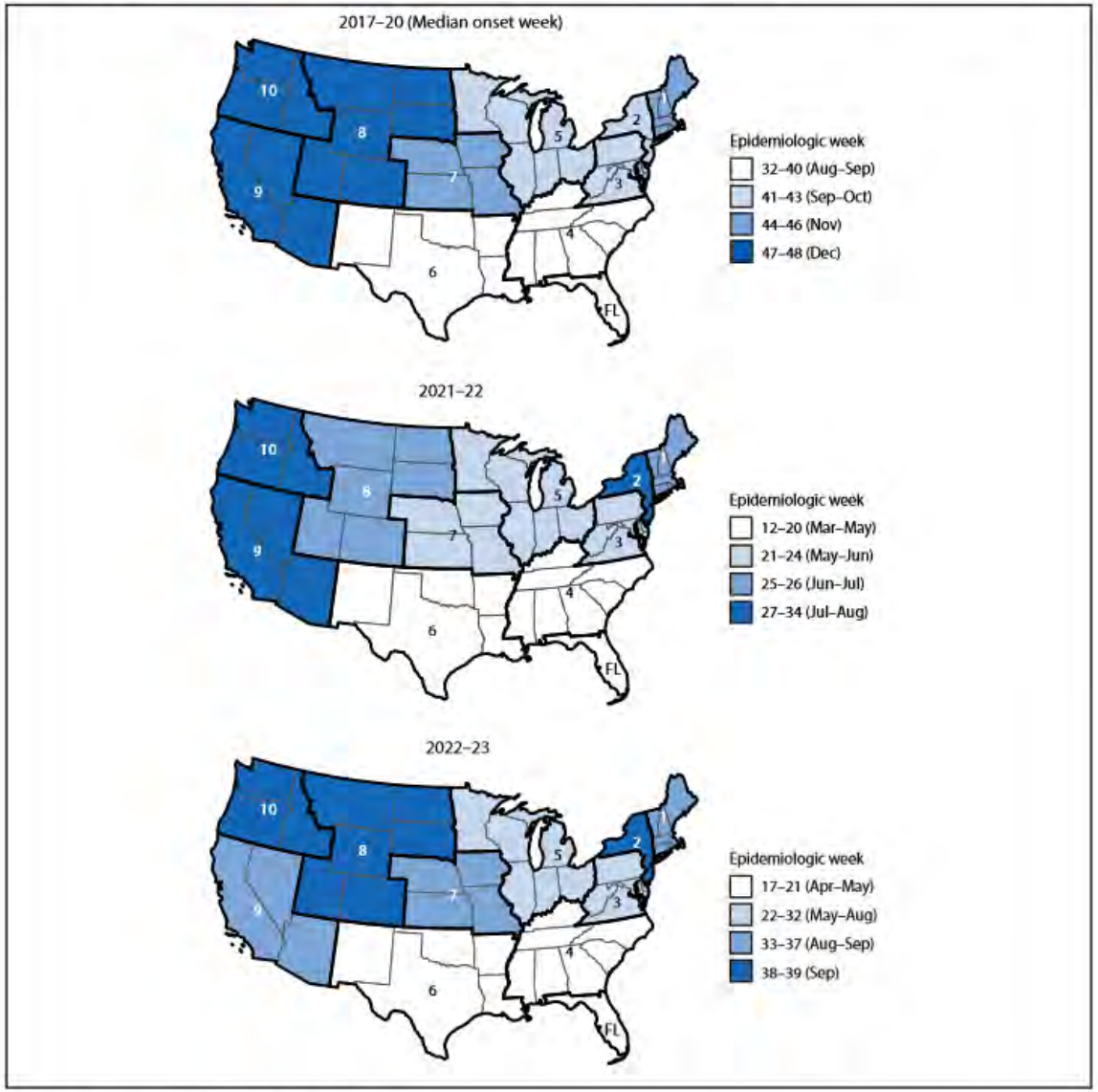


FIGURE 2. Respiratory syncytial virus epidemic onsets* in U.S. Department of Health and Human Services Regions 1–10† and in Florida — National Respiratory and Enteric Virus Surveillance System, United States, July 2017–February 2023§



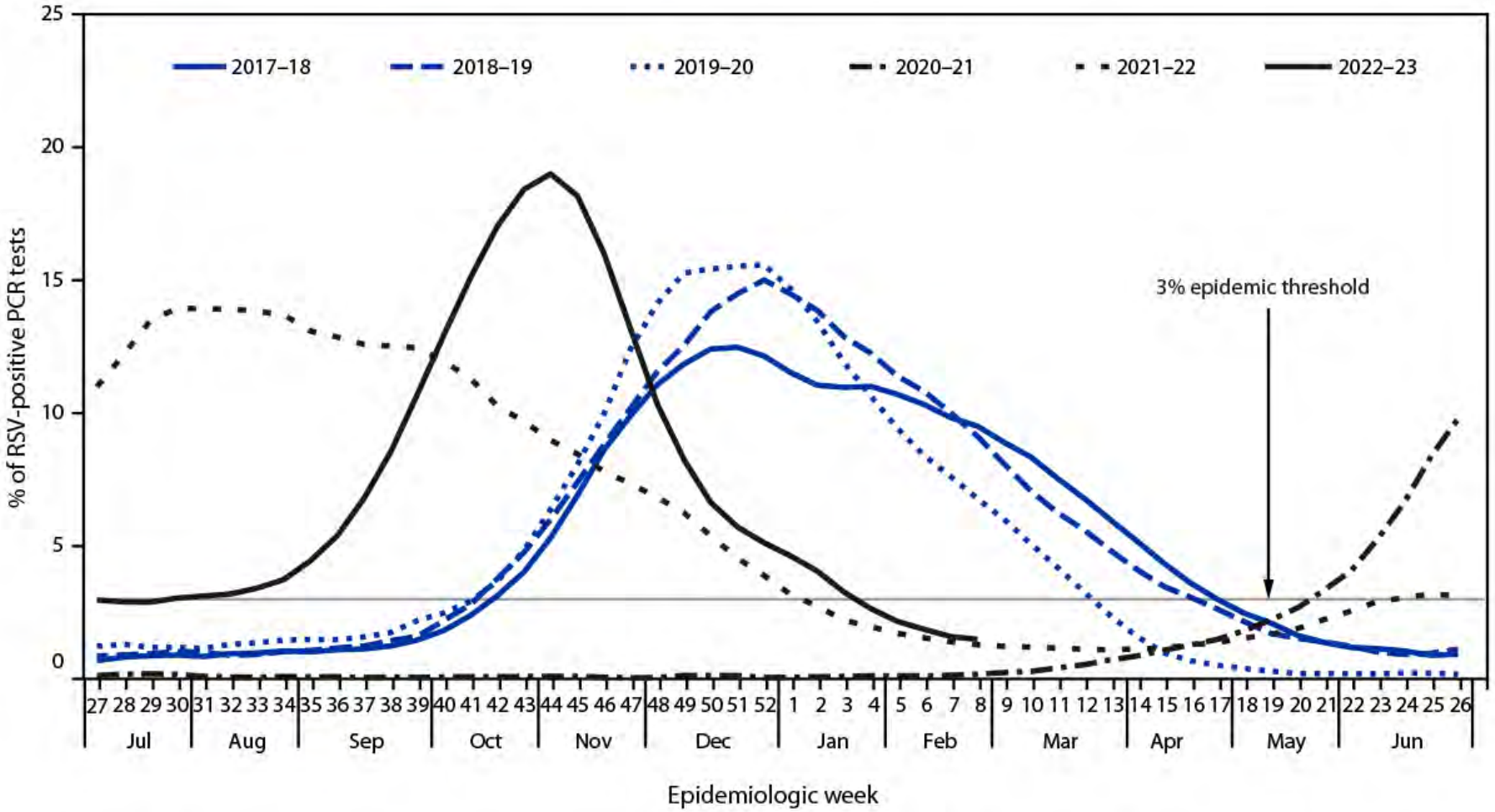
Abbreviations: FL = Florida; RSV = respiratory syncytial virus.

* The epidemic onset was defined as the first of 2 consecutive weeks of a surveillance year when the percentage of PCR tests positive for RSV was ≥3%. Median epidemic onset weeks were calculated for the three RSV epidemics that occurred before the COVID-19 pandemic (2017–18, 2018–19, and 2019–20).

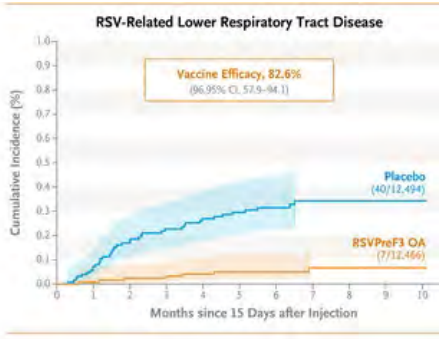
† https://www.hhs.gov/about/agencies/iea/regional-offices/index.html. Patterns of weekly RSV circulation in Alaska, Florida, and Hawaii are distinct from other states within their assigned regions; therefore, these states were excluded from regional analyses. State-level seasonality for Florida is reported; however, there are an insufficient number of laboratories consistently reporting polymerase chain reaction testing data to present state-level seasonality in Alaska and Hawaii.

§ Surveillance years were defined based on troughs in RSV circulation. During 2017–2020, surveillance years began in epidemiologic week 27 (early July) and ended the following year in epidemiologic week 26 (late June). The aberrant 2020–21 surveillance year was defined as week 27 through week 8 (late February) inclusive. During the COVID-19 pandemic (2021–22 and 2022–23), surveillance years began in epidemiologic week 9 (early March) and ended the following year in epidemiologic week 8.

FIGURE 1. Percentage* of polymerase chain reaction test results positive for respiratory syncytial virus, by epidemiologic week — National Respiratory and Enteric Virus Surveillance System, United States, July 2017–February 2023



GSK vaccine (Arexvy™) Approved May 2023



- Ongoing phase 3 study of almost 25k immunocompetent participants aged ≥60 years randomized 1:1 to receive 1 dose of 120 μg preF protein vaccine with $AS01_E$ adjuvant or saline placebo
- Published efficacy findings based on analyses of data collected during May 2021–March 2023 (2 RSV seasons in North, 1 in South). Mean follow up 15 months.
- 1 dose of the vaccine prevented symptomatic, laboratory-confirmed RSV-associated LRTD (43 vs 7 events). 82.6% efficacy for the 1st RSV season and 56.1% for the 2^{nd}.
- Hospitalization (5 vs 1), respiratory support (5 vs 1), deaths (0 vs 0), severe reactogenicity events (0.9% vs. 3.8%) for placebo vs. vaccine.
- 2,500 additional participants 60 years of age and older received Arexvy
  - 2 SA patients developed acute disseminated encephalomyelitis (ADEM) 7 & 22 days after receiving Arexvy/influenza vaccine combo (clinical diagnosis, no imaging)
  - Fatal case later reclassified by treating physician as “dementia with hypoglycemia”
  - 1 Japanese patient developed Guillain-Barré Syndrome 9 days after receiving Arexvy

GSK: Total inflammatory neurologic events reported within 42 days of vaccination across all clinical trials

Participant age	Country	Reported as	Onset	Trial	Work group case review
78 years	Japan	GBS[a], Brighton Collaboration[b] level 3	9 days post-vaccination	• Open-label phase 3 trial without a placebo control, evaluating the immunogenicity of different revaccination intervals	Likely GBS[a]
71 years	South Africa	ADEM[c], fatal* *Site investigator updated diagnoses: hypoglycemia & dementia	7 days post-vaccination	• Randomized, blinded co-administration study with standard dose seasonal influenza vaccine • Case occurred in the simultaneous administration arm of the study	ADEM[c] cannot be ruled out, however, other diagnoses appear more likely
71 years	South Africa	ADEM[c]	22 days post-vaccination	• Randomized, blinded co-administration study with standard dose seasonal influenza vaccine • Case occurred in the simultaneous administration arm of the study	ADEM[c] cannot be ruled out, however, other diagnoses appear more likely

[a] GBS = Guillain Barre syndrome

[b] https://brightoncollaboration.us/guillain-barre-and-miller-fisher-syndromes-case-definition-companion-guide/

[c] ADEM = acute disseminated encephalomyelitis

GSK: RSV lower respiratory tract disease (LRTD)

Age group in years	Case split (vaccine/placebo)[a]	Manufacturer-calculated vaccine efficacy[b], % (CI)	
		No adjustment by season	Adjusted by season
≥60 (all)	30/139	74.5 (60.0, 84.5)	67.2 (48.2, 80.0)
≥65	25/100	70.3 (53.5, 81.6)	61.2 (39.0, 76.1)
≥70	13/65	76.4 (56.7, 88.1)	69.3 (43.4, 84.6)
≥75	8/24	Not shared[c]	49.3 (-18.2, 80.6)[c]
≥80	4/10	52.6 (-64.2, 89.2)[c]	38.4 (-118, 86.1)[c]

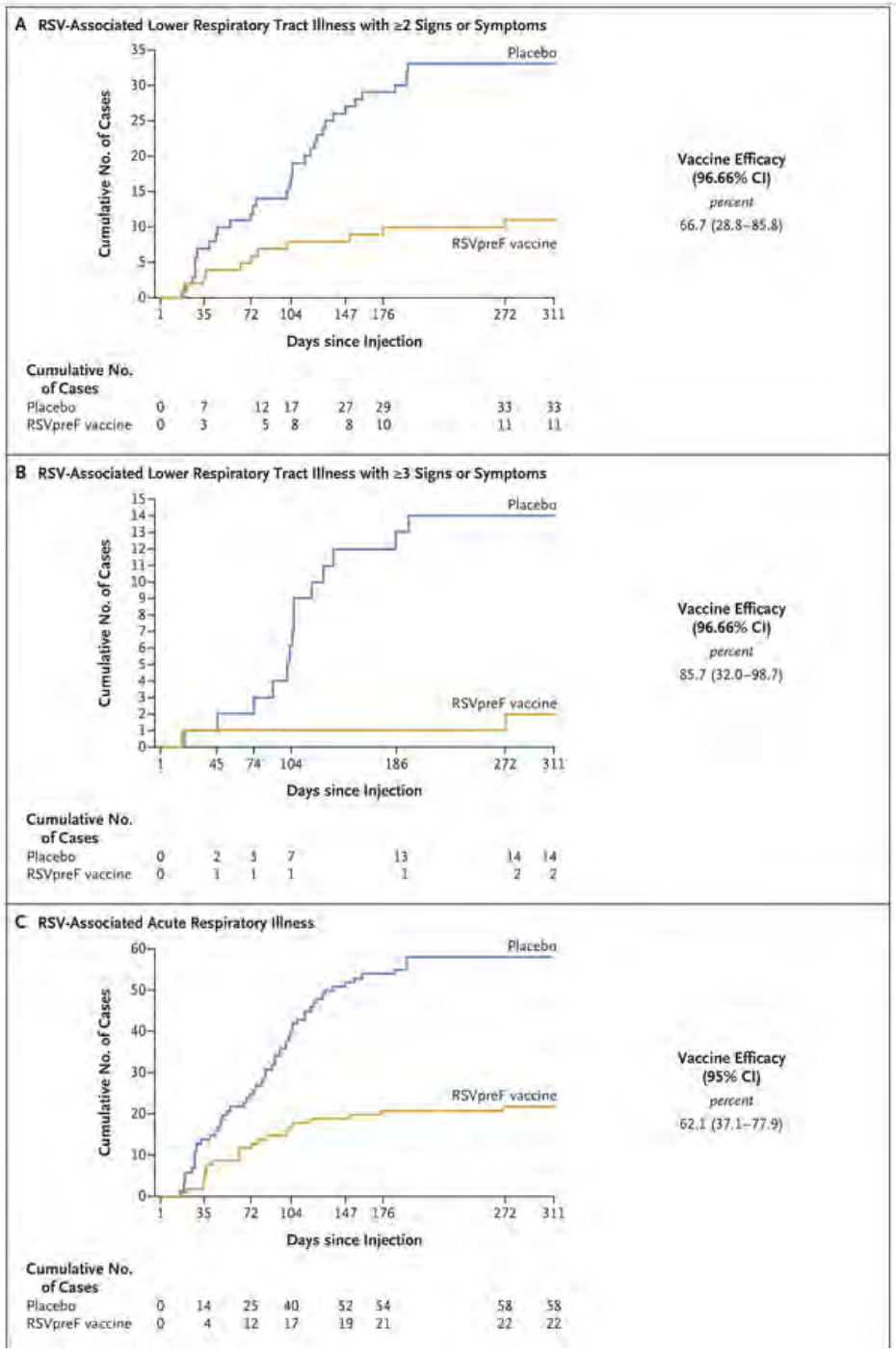
[a] GSK pivotal phase 3 trial (Papi A, et al. NEJM 2023 https://doi.org/10.1056/nejmoa2209604). Events of each outcome were included if they occurred on or after day 15 after injection. Median time, across participants, of efficacy follow up was 17.8 months, including unpublished data provided by manufacturer from season 2. Total 24,967 participants (31,932 person-years) under surveillance.

[b] Calculated using Poisson model, adjusted by season and participant age and region. Adjustment by season resulted in efficacy estimates substantially different from those estimated by CDC. Due to exclusion of follow up time after dose 2 of RSVPreF3 among participants randomized to annual re-vaccination, person-time follow up in the placebo arm exceeded that in the intervention arm.

[c] Highlighted text indicates that evidence of statistically significant efficacy is lacking.

Renior (Abrysvo™, Pfizer)

- No adjuvant, 50% A and B subtype antigen
- 34k adults >60 years
  - 11 (1.19 case per 1000y) vs. 33 (3.58 cases per 1000y) RSV LTR & 2+ symptoms for 66.7% VE
  - 2 vs 14 RSV LTR with 3+ symptoms for 85.7% VE
  - Local reactions 12% vs 7%
  - No relevant outcomes (no deaths, hospitalization 1 vs 3, O2 support 1 vs 1)
  - Systemic reactions same as for placebo
  - 1 Miller Fisher Syndrome, 1 GBS + MI, 1 GBS
- Also no immunocompromised, too young, too white, too non frail etcetera



Pfizer: RSV lower respiratory tract illness (LRTI), defined by ≥3 lower respiratory signs or symptoms

Population	Case split (vaccine/placebo)[a]	Manufacturer-calculated vaccine efficacy, % (95% CI)
All (age ≥60 years)	5/32	84.4 (59.6, 95.2)
Age ≥65 years	3/23	87.0 (56.8, 97.5)
Age ≥70 years	1/11	90.9 (37.5, 99.8)
Age ≥75 years	1/7	85.7 (-11.2, 99.7)[b]
Age ≥80 years	0/4	100.0 (-51.5, 100.0)[b]

[a] Pfizer pivotal phase 3 trial (Walsh EE, et al. NEJM 2023 https://doi.org/10.1056/nejmoa2213836). Events of each outcome were included if they occurred on or after day 15 after injection. Average time, across participants, from vaccination to end of efficacy follow up was 12 months, including unpublished data provided by manufacturer from partial season 2. Total 36,127 participants (31,986 person-years) under surveillance.

[b] Highlighted text indicates that evidence of statistically significant efficacy is lacking.

Pfizer: Total inflammatory neurologic events reported within 42 days of vaccination across all clinical trials

Participant age	Country	Reported as	Onset	Trial	Work group case review
66 years	United States	GBS[a], Brighton Collaboration[b] level 1	14 days post-vaccination	Pivotal phase 3 trial, randomized, blinded, placebo-controlled	Clinical course more consistent with CIDP[c]
66 years	Japan	GBS[a], Miller-Fisher variant, Brighton Collaboration[b] level 4	10 days post-vaccination	Pivotal phase 3 trial, randomized, blinded, placebo-controlled	Possible GBS (Miller Fisher syndrome) though other causes are also possible
68 years	Argentina	Motor-sensory axonal polyneuropathy* *Site investigator reported as not associated with vaccination	21 days post-vaccination* *Participant reported some symptoms preceded vaccination	Pivotal phase 3 trial, randomized, blinded, placebo-controlled	Undifferentiated motor-sensory axonal polyneuropathy

[a] GBS = Guillain Barre syndrome

[b] https://brightoncollaboration.us/guillain-barre-and-miller-fisher-syndromes-case-definition-companion-guide/

[c] CIDP = chronic inflammatory demyelinating polyneuropathy

Background incidence of Guillain-Barré syndrome among older adults

Meta-analysis[a], 13 studies, North America & Europe

Age group, years	Annual rate per 100,000 population (95% CI)
0–9	0.62 (0.52–0.75)
10–19	0.75 (0.60–0.92)
20–29	0.90 (0.67–1.19)
30–39	1.07 (0.74–1.56)
40–49	1.29 (0.80–2.06)
50–59	1.54 (0.87–2.74)
60–69	1.85 (0.94–3.64)
70–79	2.22 (1.01–4.86)
80–89	2.66 (1.09–6.48)

Vaccine Safety Datalink, United States, 2000–2009[b]

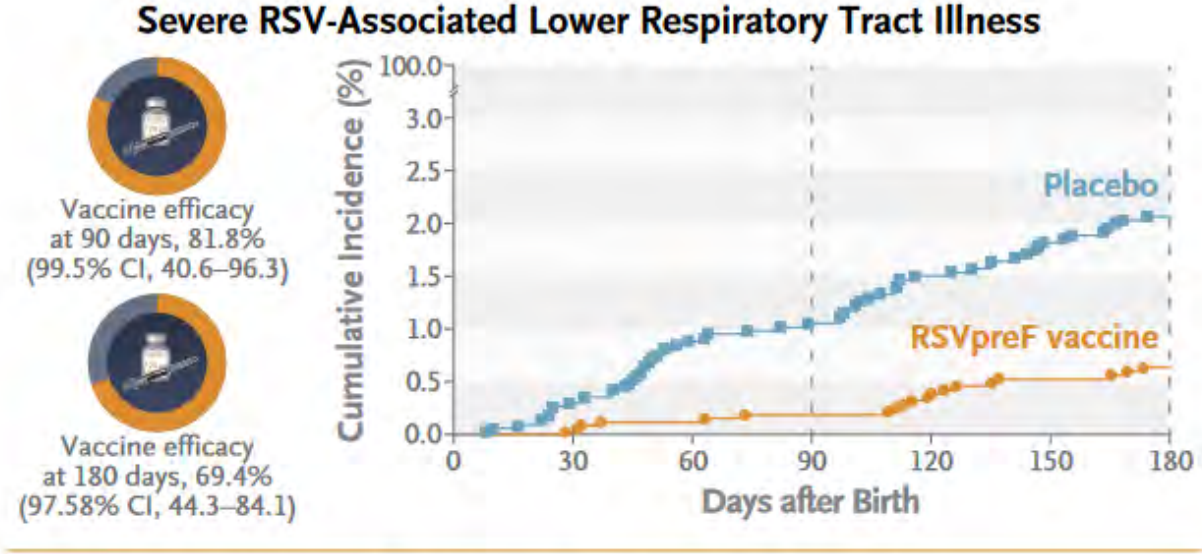
Age group, years	Annual rate per 100,000 population (95% CI)	
	Female	Male
0–4	0.51 (0.24–0.78)	0.39 (0.16–0.61)
5–17	0.43 (0.29–0.57)	0.62 (0.46–0.79)
18–24	0.64 (0.39–0.89)	0.75 (0.47–1.03)
25–49	1.00 (0.85–1.15)	1.39 (1.20–1.57)
50–64	2.19 (1.90–2.50)	2.85 (2.49–3.21)
≥65	4.68 (4.14–5.21)	7.06 (6.31–7.81)

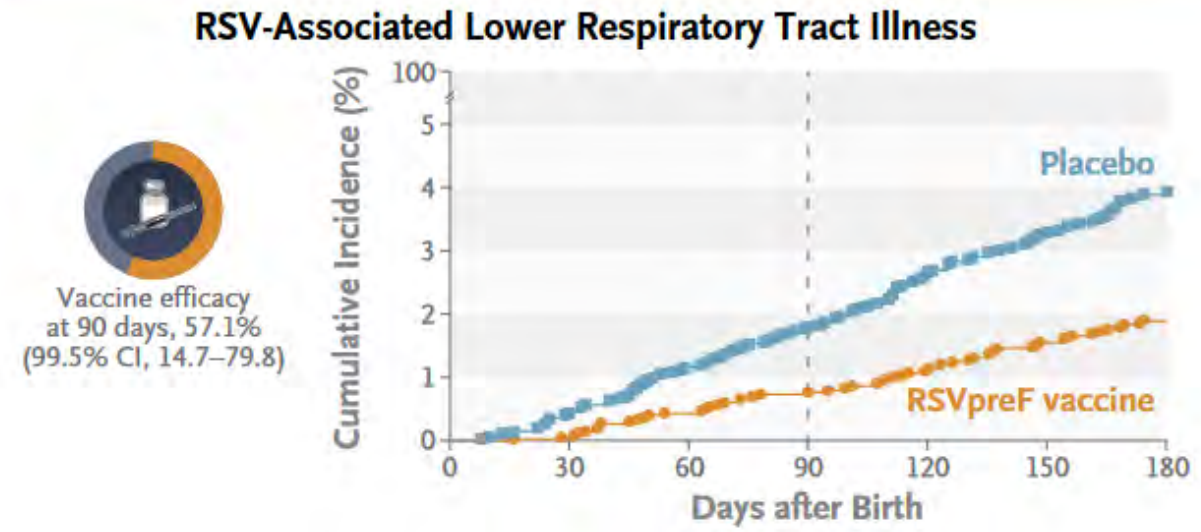
[a] Sejvar JJ, et al. Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis. Neuroepidemiology. 2011;36(2):123-33. https://doi.org/10.1159/000324710
[b] Shui IM, et al. Guillain-Barré syndrome incidence in a large United States cohort (2000-2009). Neuroepidemiology. 2012;39(2):109-15. https://doi.org/10.1159/000339248

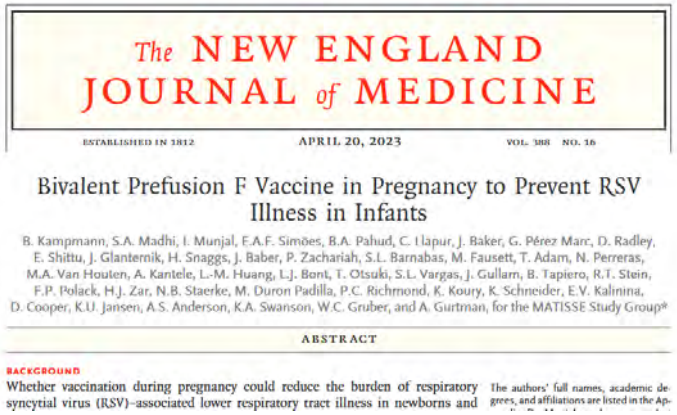
Problems

- Highly statistically significant but clinically meaningful?
- Hospitalization, deaths, transmissibility not different
- COVID interrupted typical RSV pattern (and all RSV studies)
- 100% immunocompetent (lower risk)
- “Younger” (lower risk)
- > 75% “fit” on frailty score (lower risk)
- Too white (80%, who have higher average age at hospitalization)
- RSV subtype A (more common) but protected for B
- 2 years (boostable?)
- Expensive ($295 vs 30-145 for flu and COVID vaccines)

MATISSE 7.5k pregnant patients (31.3w median gestation), Abrysvo™






The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 20, 2023 VOL. 388 NO. 16

Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants

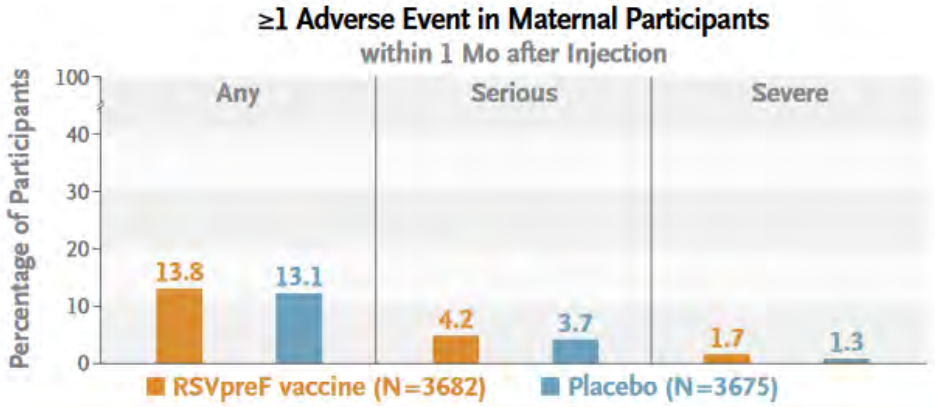
B. Kampmann, S.A. Madhi, I. Munjal, F.A.F. Simões, B.A. Pahud, C. Llapur, J. Baker, G. Pérez Marc, D. Radley, E. Shittu, J. Glanternik, H. Snaggs, J. Baber, P. Zachariah, S.L. Barnabas, M. Fausett, T. Adam, N. Perreras, M.A. Van Houten, A. Kantele, L.-M. Huang, L.J. Bont, T. Otsuki, S.L. Vargas, J. Gullam, B. Tapiero, R.T. Stein, F.P. Polack, H.J. Zar, N.B. Staerke, M. Duron Padilla, P.C. Richmond, K. Koury, K. Schneider, E.V. Kalinina, D. Cooper, K.U. Jansen, A.S. Anderson, K.A. Swanson, W.C. Gruber, and A. Gurtman, for the MATISSE Study Group*

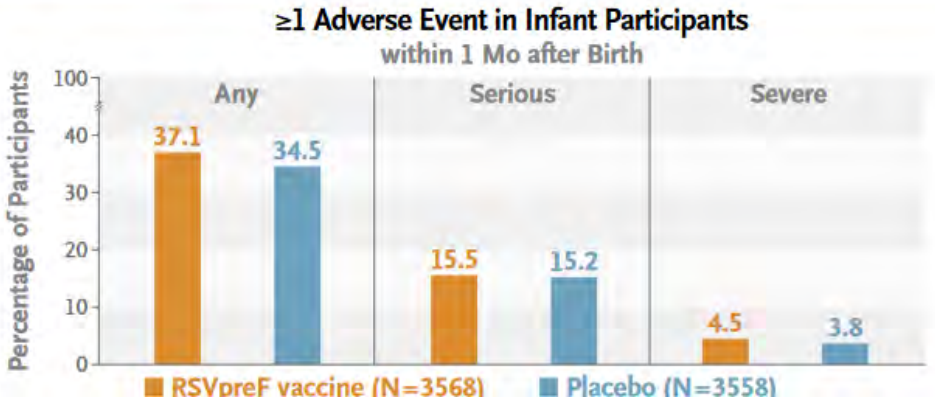
ABSTRACT

BACKGROUND

Whether vaccination during pregnancy could reduce the burden of respiratory syncytial virus (RSV)–associated lower respiratory tract illness in newborns and

The authors' full names, academic degrees, and affiliations are listed in the Ap-





Nirsevimab

- Monoclonal RSV antibody
- IM injection (thigh) vs placebo similar adverse events
- In phase 3 clinical trial nirsevimab reduced medically attended RSV-LRTI 76.4% and cut RSV hospitalizations in healthy full-term and near-full-term infants by 76.8%