Vaccine Updates 2024

Candice K. Smith, MD

AIMS AND OBJECTIVES

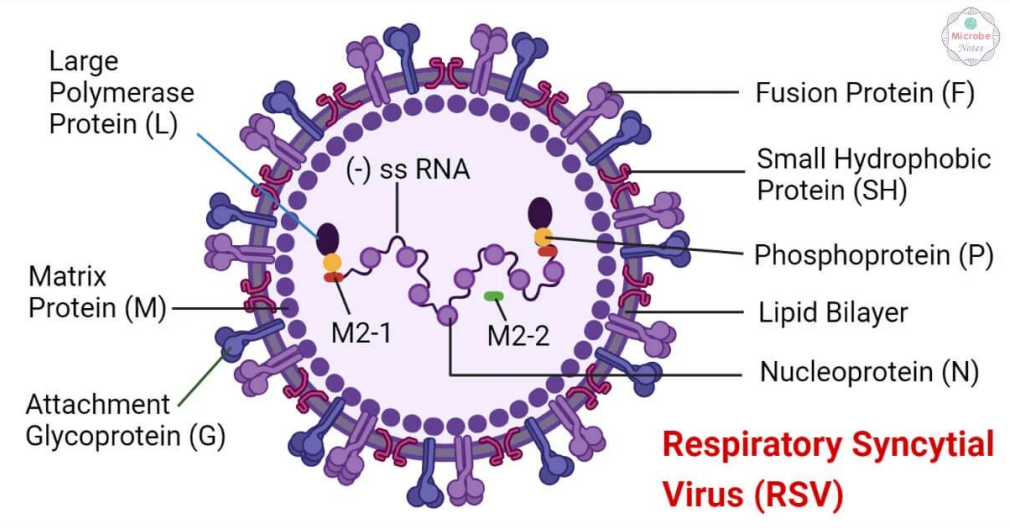
OSMS May 2024

1. Familiarize with New Vaccines
2. Familiarize with updated vaccine recommendations
3. Identify high risk populations which would benefit from new and updated vaccines

Disclosures

Nothing to disclose

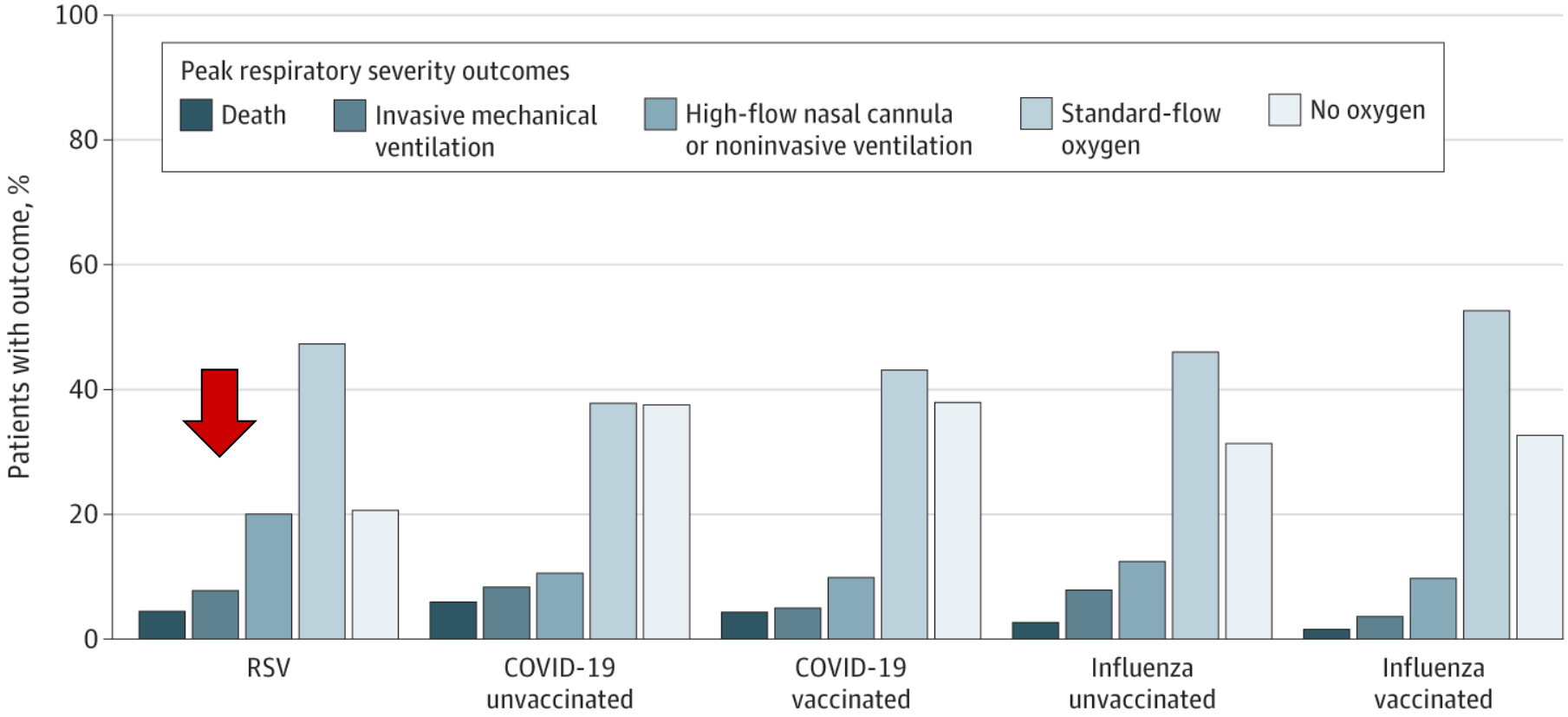
RSV Vaccines



What is the YEARLY BURDEN of RSV?

- 2.1 million outpatient (non-hospitalization) visits among children younger than 5 years old.
- 58,000-80,000 hospitalizations among children younger than 5 years old.
- 60,000-160,000 hospitalizations among adults 65 years and older.
- 6,000-10,000 deaths among adults 65 years and older.
- 100–300 deaths in children younger than 5 years old.

RSV burden Compared to Covid and Flu



NEW RSV Vaccines

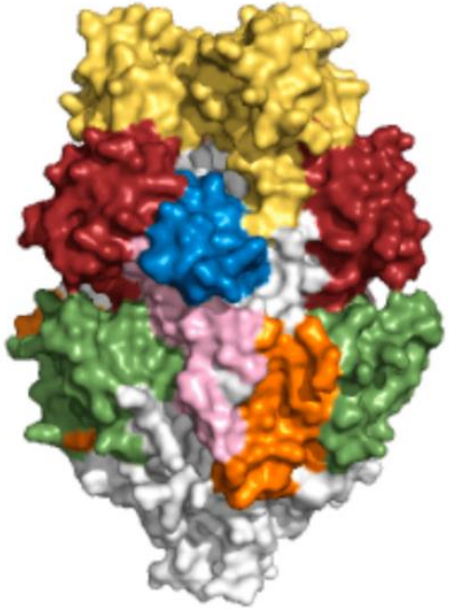
Infant Protection

- Infant monoclonal antibody (infant vaccination)
  - Nirsevimab (Beyfortus)
  - Passive immunity to the baby
  - Not a vaccine!
- Pregnant RSV vaccination
  - Pfizer (Abrysvo) which is Active immunity to the mom
  - Passive immunity to the baby

Older Adult Protection

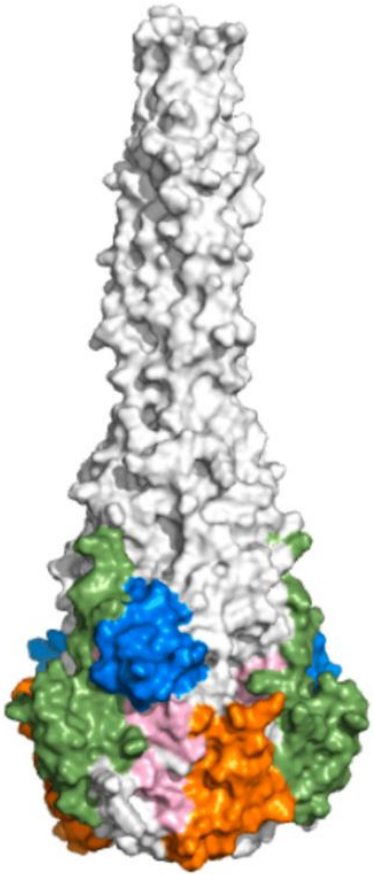
- Adult RSV vaccination (single dose) with
  - GSK’s Arexvy
  - Pfizer’s Abrysvo

NIH Studies Cracked the Code

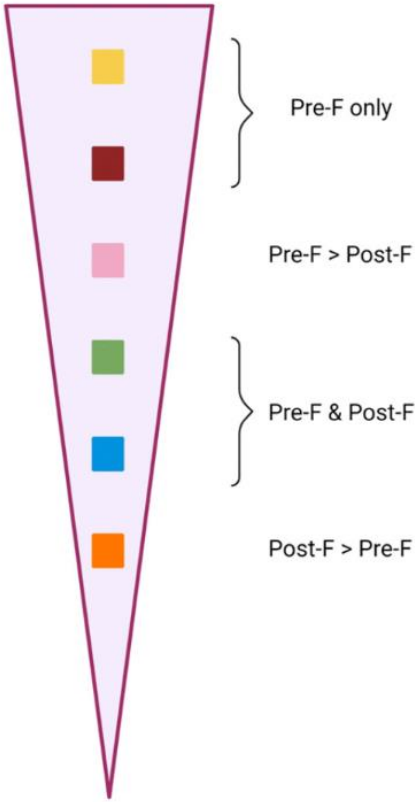


Prefusion

Site Ø
Site I
Site II
Site III
Site IV
Site V



Postfusion



Neutralizing potency

GSK's Arexvy

- vaccine includes an adjuvant AS01 (the same adjuvant used in GSK's recombinant zoster vaccine [Shingrix]), which is a component that is intended to enhance the immune response to vaccination.
- recombinant protein vaccine prefusion form of a spike protein on the surface of the RSV virus that cause the immune system to produce RSV antibodies

Pfizer's Abrysvo

- vaccine does not contain an adjuvant
- recombinant bivalent protein vaccine prefusion form of a spike protein on the surface of the RSV virus that cause the immune system to produce RSV antibodies

Vaccine ACIP Recommendations

- Recommended nirsevimab for infants aged <8 months born during or entering their first RSV season and for infants and children aged 8–19 months who are at increased risk of severe RSV disease entering their second RSV season.

- Recommended RSV vaccine for pregnant persons at 32–36 weeks' gestation using seasonal administration (meaning September–January in most of the United States) to prevent RSV-associated LRTI in infants aged <6 months.

- Recommended that persons aged ≥60 years may receive a single dose of RSV vaccine, using shared clinical decision-making.

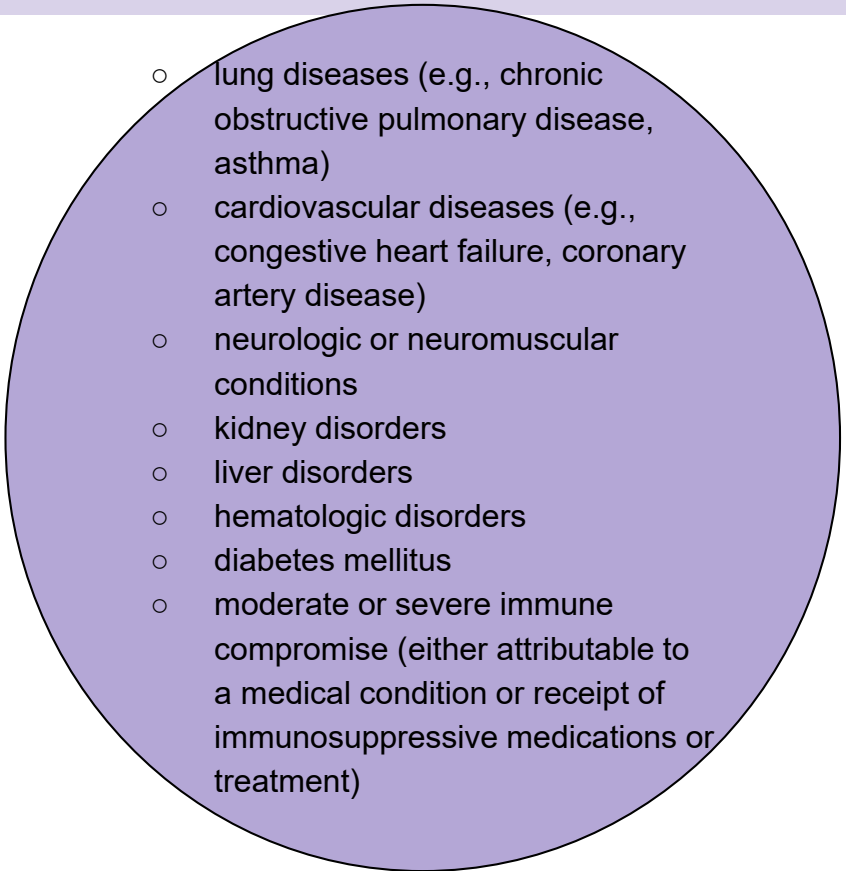
Shared Clinical Decision Making (SCDM)

Decision to vaccinate a patient is based on individual health characteristics and informed by discussions between the patient and health care provider

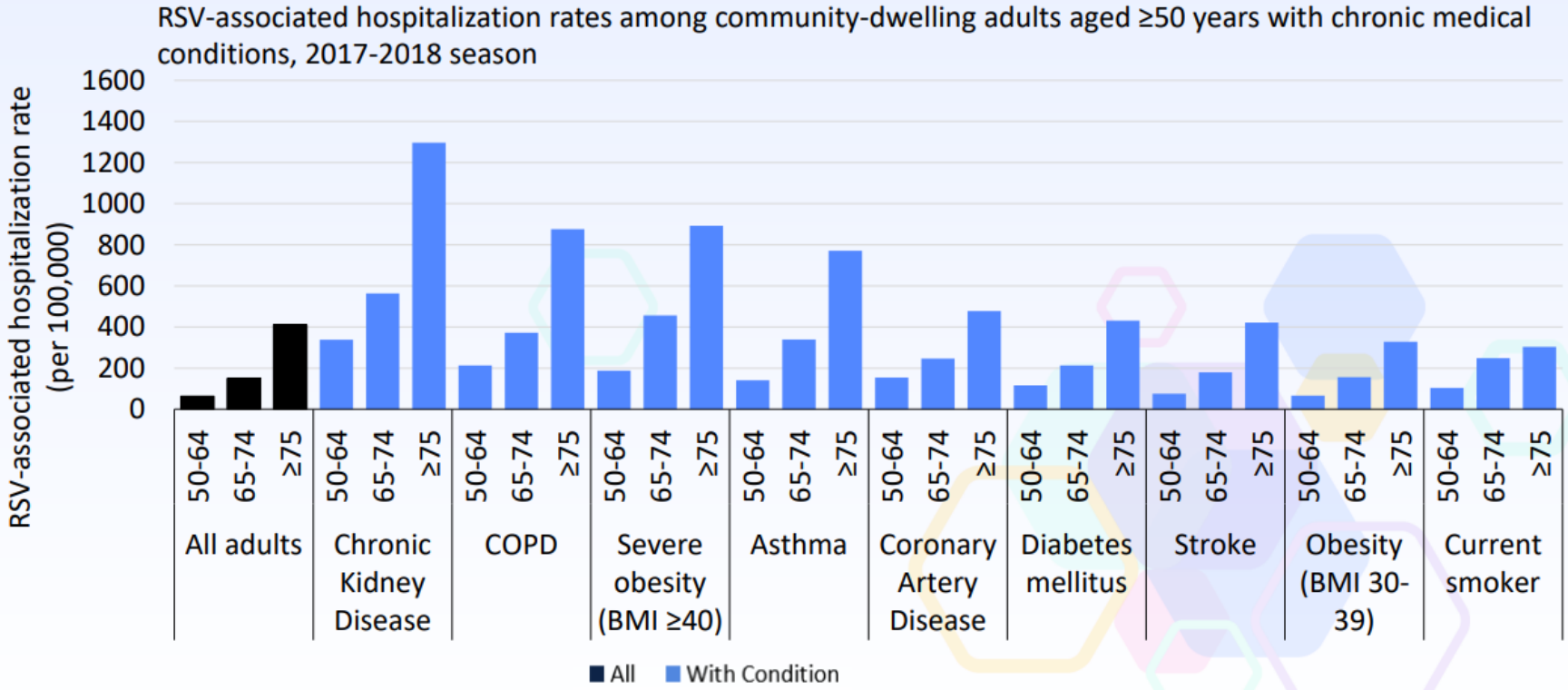
- any risk factors for severe RSV disease,
- the safety profile of the RSV vaccine
- a patient’s preferences for RSV vaccination,
- the clinical discretion of the health care provider in that patient’s case.

What are the patient risk factors?

- those with comorbid medical conditions
- those who are frail
- those of advanced age (highest risk is over 75)
- those who reside in nursing homes or other long-term care facilities

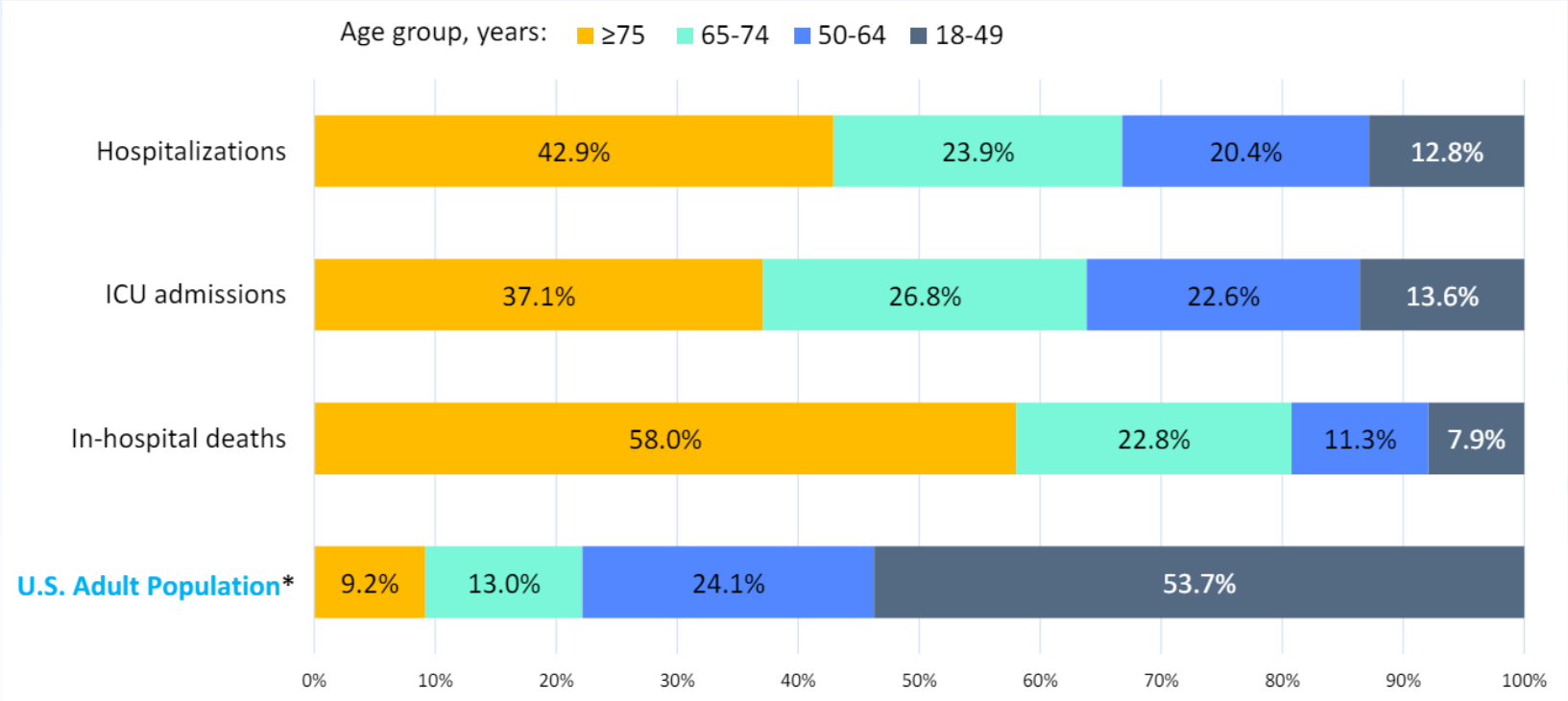


RSV-Associated Hospitalization Rates by Chronic Condition and Age Group



COPD: Chronic Obstructive Pulmonary Disease. Data are preliminary and unpublished. Rates of laboratory-confirmed RSV-associated hospitalization account for under-detection of RSV infection among hospitalized adults and sensitivity of diagnostic tests; rates exclude residents of nursing homes and long-term care facilities and are not adjusted for sex or race/ethnicity group.

Estimated age distribution of national RSV-associated hospitalizations, ICU admissions, and in-hospital deaths among adults ≥18 years, RSV-NET, 2022–2023, compared with U.S. population



Unpublished data. Underlying rates are adjusted using multipliers for the frequency of RSV testing during each season and for the sensitivity of RSV diagnostic tests. Estimates from 2022-2023 are preliminary. These estimates use the same multipliers as for 2019-2020.

*As of 2022. https://www.census.gov/popclock/

Inputs: Vaccine Efficacy (VE)

Outcome (RSV-Associated)	Arexvy, GSK[1] VE (95% CI)		Abrysvo, Pfizer[2] VE (95% CI)	
	Season 1 (months 0-7 post-injection)	Season 2 (months 13-18 post-injection)[3]	Season 1 (months 0-7 post-injection)	Season 2 (months 8-14 post-injection)[3]
Outpatient visits[4] *Trial efficacy against medically-attended RSV ARI*	**79.0%** (54.3, 91.5)	**27.8%** (0, 60.4)	**65.2%** (36.0, 82.0)	**55.0%** (0, 82.0)
Hospitalizations, ICU Admissions, and In-hospital Deaths *Trial efficacy against medically-attended RSV LRTD/LRTI*	**87.5%** (58.9, 97.6)[5]	**52.9%** (0, 81.2)[5]	**84.6%** (32.0, 98.3)[6]	**75.0%** (0, 97.4)[6]

Point estimates were used in this analysis. Uncertainty in vaccine efficacy was not incorporated into uncertainty in estimated preventable outcomes.

Ref (Slide 18): https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/05-RSV-Adults-Ortega-Sanchez-508.pdf

[1] GSK Phase 3 Trial; interim analysis 2023; CDC-calculated vaccine efficacy in participants ages ≥60 years

[2] Pfizer Phase 3 Trial; interim analysis 2023; CDC-calculated vaccine efficacy in participants ages ≥60 years

[3] Efficacy estimates are not directly comparable. Clinical trials used different outcome definitions and the follow up time in differed substantially across trials. Further, efficacy estimates are associated with substantial uncertainty.

[4] CDC-calculated VE against medically-attended RSV acute respiratory illness (ARI)

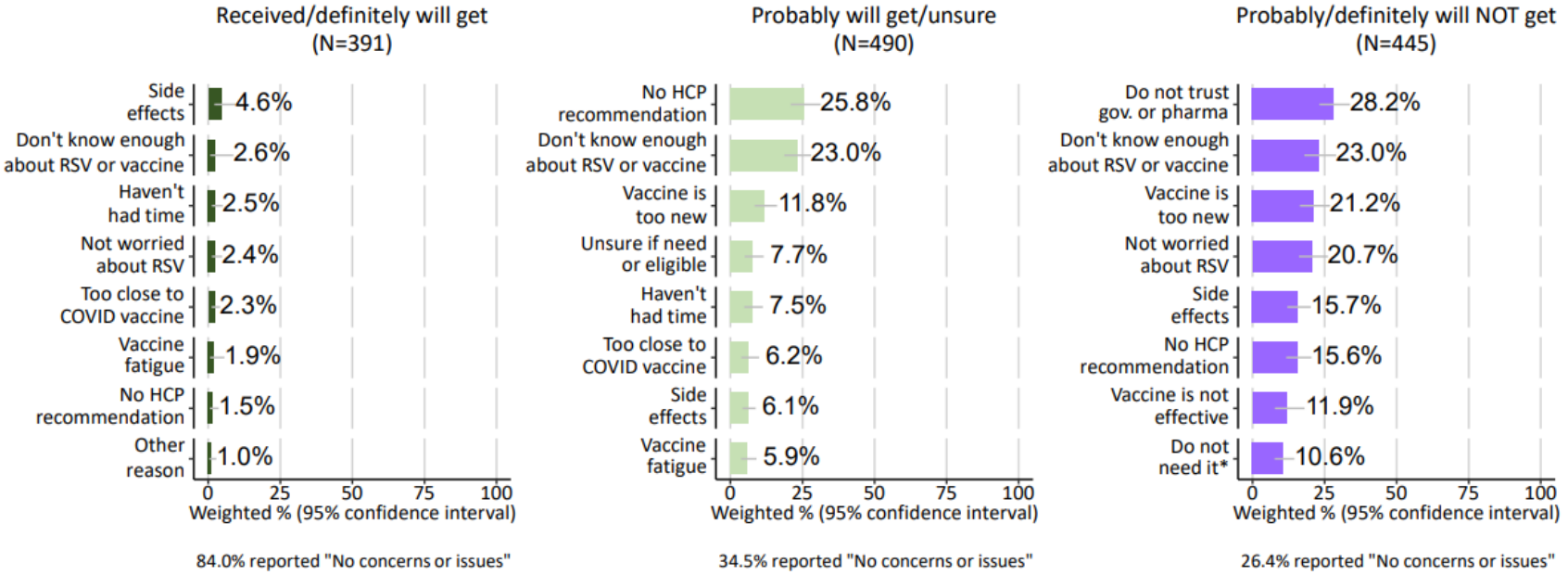
[5] CDC-calculated VE against medically-attended RSV lower respiratory tract disease (LRTD)

[6] CDC-calculated VE against medically-attended RSV lower respiratory tract illness (LRTI) with at least 3 lower respiratory symptoms

SMALL PRINT

- Few people enrolled in the clinical trials were either frail or of advanced age (80 or older), and none lived in long-term care facilities.
- People with immunocompromising conditions were excluded from clinical trials.
- For this reason, the clinical trials did not measure how well the vaccines would work in the people at highest risk of serious RSV disease.

Top RSV Vaccination Concerns and Issues Among Adults ≥60 Years of Age, by Status/Intent, Omnibus Surveys, January 5-29, 2024 (N=1,326)



Other response options included: "Cost/insurance issues," "Already had RSV*," "HCP recommended against," "Medical reasons*," "Afraid of needles," "Vaccine not available."
*Option not offered to those who already received the vaccine.

Safety Considerations- GBS

Results – PPV-adjusted Analyses

Adjusted IRR and 95% CI of GBS Following an RSV vaccination

RSV Vaccine Exposure	Eligible Vaccines	IRR	IRR* 95% Confidence Interval (CI)	GBS Rate** per 1 million doses	95% CI**
RSVPreF	**682,267**	**6.9**	**(1.9, 12.0)**	**25.1**	**(6.7, 43.4)**
RSVPreF3+AS01	1,379,335	2.8	(0.5, 5.0)	10.0	(1.7, 18.3)

Summary

- An elevated IRR was observed for GBS following RSVPreF vaccination
  - 6.9 (95% CI: 1.9, 12.0)
- A non-statistically significant elevated IRR was observed for GBS following RSVPreF3+AS01 vaccination
  - 2.8 (95% CI: 0.5, 5.0)
- Adjusted GBS rates per 1 million doses:
  - RSVPreF: 25.1 (95% CI: 6.7, 43.4)
  - RSVPreF3+AS01: 10.0 (95% CI: 1.7, 18.3)
- Multiple imputation was not successful in estimating IRR for age and sex subgroups due to the small number of cases
- Medical charts for observed cases have been requested and will be reviewed

Red font indicates statistically significant elevation in GBS risk.
**Adjusted estimate based on multiple imputation.*

What to Expect in the next year for RSV Vaccines?

- Moderna RSV Vaccine has finished Phase 1 and presented to FDA and ACIP with great vaccine efficacy and great safety data.
- JUNE ACIP 2024 will make recommendations about RSV vaccine schedule
    - Move away from SCDM??
    - Standard recommendation (75 years??)
    - Risk Based 60 +??
  - AGE RANGES WILL CHANGE
  - HOW OFTEN TO Vaccinate (Clinical trials are 3 years out)
    - Boosting after 12 months did NOT increase VE

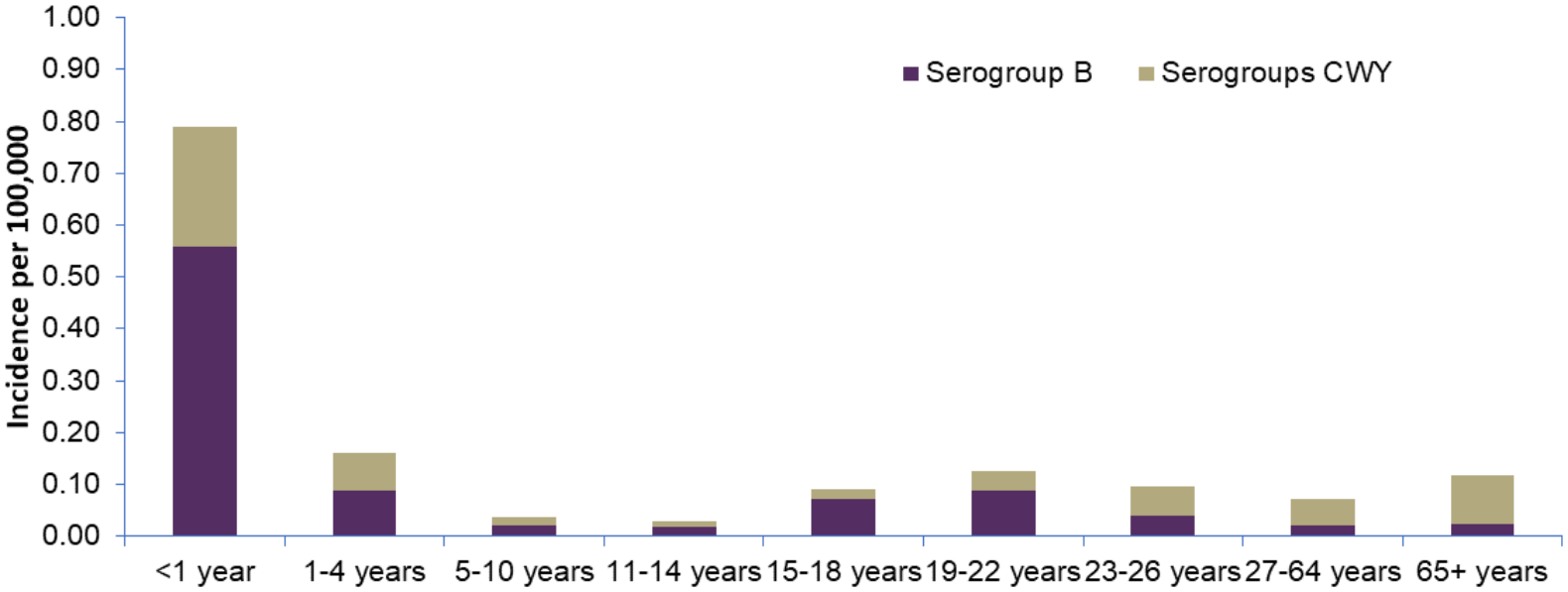
Meningococcal Vaccines

Meningococcal Disease Trends

Bacterial sepsis or bacterial meningitis

- At risk population is infants and then teens and young adults
- At risk places like colleges and dormitories
- At risk people who are baseline more susceptible (asplenic, complement deficiencies)
- Cases of meningococcal disease in the United States have increased sharply since 2021 and now exceed pre-pandemic levels
- High risk in under 1 years old

Meningococcal incidence by serogroup* and age-group, 2012–2021



* Unknown serogroup (12%) and other serogroups (9%) excluded

SOURCE: CDC; National Notifiable Diseases Surveillance System with additional serogroup data from Active Bacterial Core surveillance and state health departments

Meningococcal Vaccines

MEN-ACWY

- Scheduled dose at 11 years,
- then 16 years for the booster

MEN-B

(Bexsero® and Trumenba®)

- preferred age is 16 through 18 years
- Bexsero is 2 doses 1 month apart
- Trumenba is 2 doses 6 months apart

New Meningococcal Vaccines

PENTAVALENT (ACWY+B)

Which will now be called ABCWY

- Pfizer has FDA approval and ACIP approval, GSK is coming

Current
CDC Recommendations for Meningococcal LATE TEEN Vaccination

- should receive a single dose of meningococcal conjugate (MenACWY) vaccine.
- may also receive a MenB vaccine.
    - **Change in June 2019"ACIP recommends a MenB primary series for individuals aged 16–23 years based on shared clinical decision-making".**

Additional Factors Associated with Increased Risk among College Students

- 4-year college students had a **5.2**-fold (95% CI: 3.6-7.7) higher risk of serogroup B disease than non-undergraduates aged 18-24 years
  - Risk among 2-year college students was comparable to non-undergraduates (RR 1.0, 95% CI: 0.4-2.1)
- First-year students were at **3.8**-fold (95% CI: 2.4-6.0) higher risk of serogroup B disease than non-first-year students
- On-campus residents at **2.9**-fold (95% CI: 1.8-4.6) higher risk of serogroup B disease than off-campus residents
- Students participating in Greek life were at **9.8**-fold (95% CI: 4.6-21.2) higher risk of serogroup B disease than other students during outbreaks

Weil L, et al. OFID 2023

HOW LONG DOES THE IMMUNITY LAST?

- MenACWY
  - Protection wanes 3 to <8 years postvaccination
    - <1 year: 79%
    - 1 to <3 years: 69%
    - 3 to <8 years: 61%
- MenB
  - Protection wanes 1-2 years following primary vaccination

Mbaeyi S, et al. MMWR Recomm Rep 2020 https://www.cdc.gov/mmwr/volumes/69/rr/pdfs/rr6909a1-H.pdf; Stephens D, et al. in Plotkin's Vaccines 8th edit 2024; Dretler A, et al. Hum Vacc & Immuno 2018; Cohn A, et al. Pediatr 2018

WILL EVERYTHING GET CHANGED IN THE NEXT YEAR?

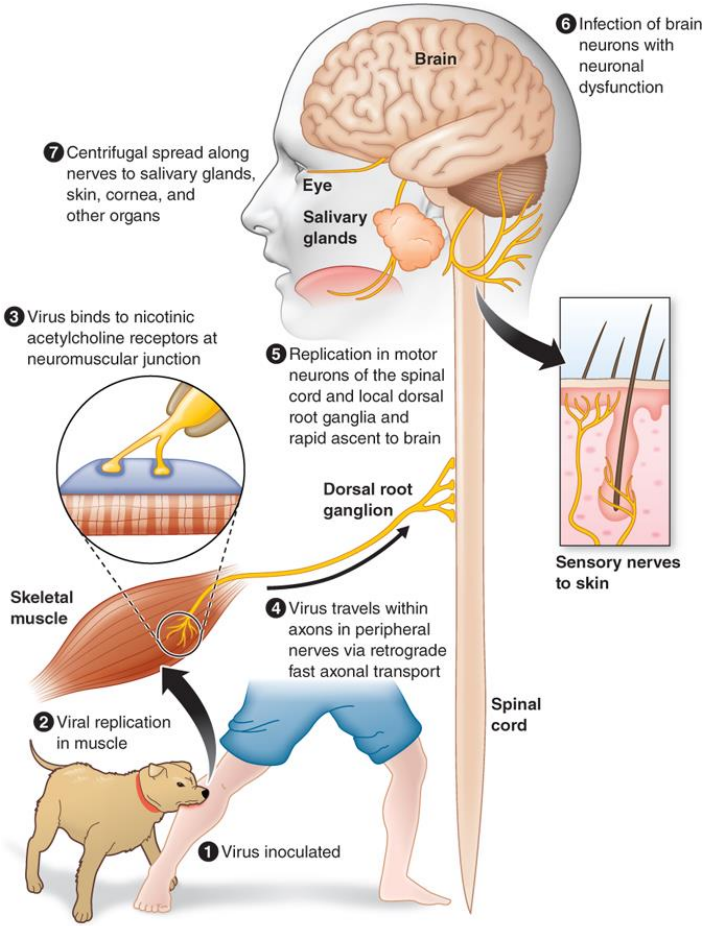
Option	ACWY Dose#1	ACWY Dose#2	B Dose#1	B Dose#2
Current recomm.	11–12 yrs	16 yrs	16 yrs – 23 years (preferred 16–18 yrs) SCDM	
1	11–12 yrs	16 yrs	16 yrs	17–18 yrs
2	11–12 yrs	16 yrs	16 yrs risk-based	17–18 yrs risk-based
3	No dose	16 yrs	16 yrs risk-based	17–18 yrs risk-based
4	15 yrs	17–18 yrs	17–18 yrs	17–18 yrs
	Proposed recommendations are for routine vaccination unless specified as "risk-based"; option numbers do not represent ordering of preference			

SCDM, shared clinical decision-making

Rabies Vaccine

Pathogenesis

- Retrograde migration slowly up peripheral nerve 50 mm a day
- Once in the dorsal root ganglion can move quickly up the spinal cord
- Initially infecting the diencephalon, hippocampus, and brainstem
- Virus spreads along somatic and autonomic nerves
- Productive viral replication and shedding occurs in highly innervated areas, such as the salivary glands



Source: J.L. Jameson, A.S. Fauci, D.L. Kasper, S.L. Hauser, D.L. Longo, J. Loscalzo: Harrison's Principles of Internal Medicine, 20th Edition

Epidemiology

Rabies is estimated to cause 59,000 human deaths annually in over 150 countries, with 95% of cases occurring in Africa and Asia

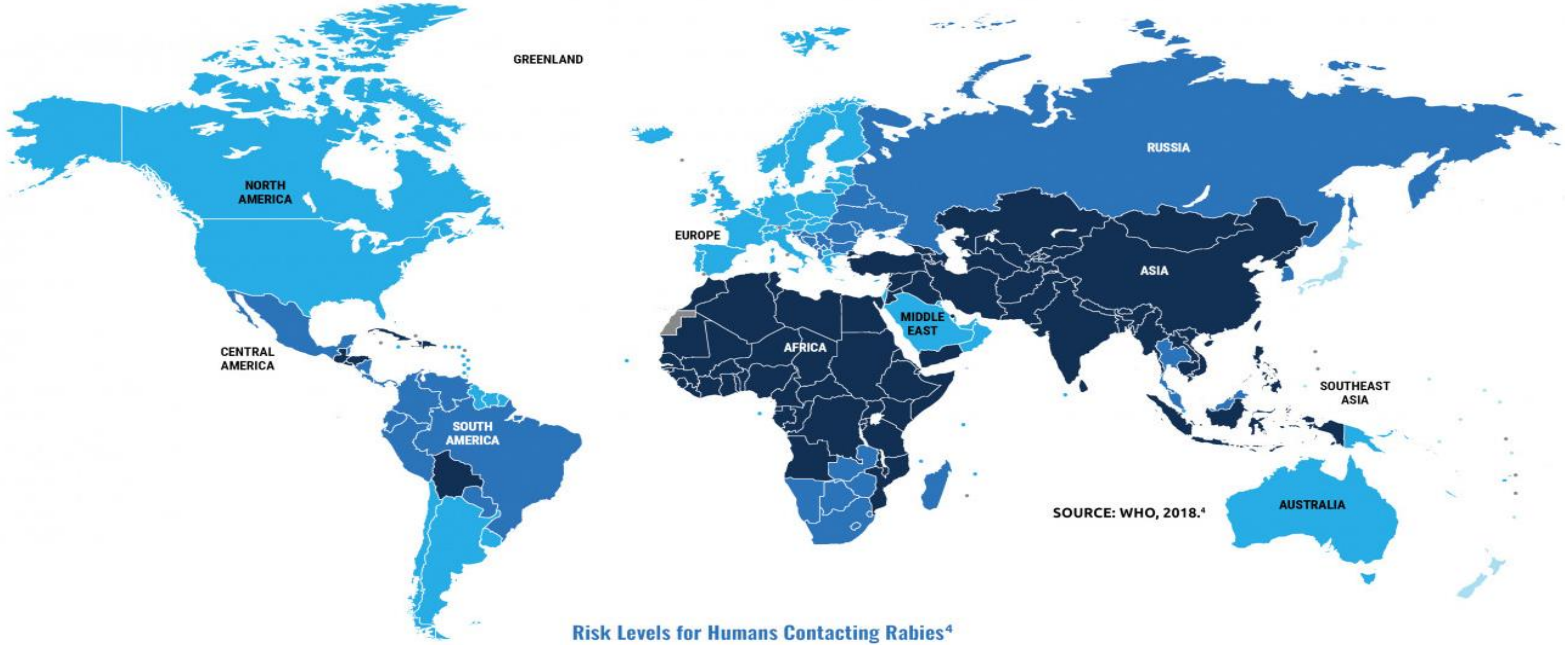
Asia,

- 35,172 human deaths per year.
- India accounts for 59.9% of rabies deaths

Africa

- 21,476 human deaths occur each year in Africa
- 1,875 human deaths in Central Asia and 229 human deaths per year in the Middle East.

High Risk Areas of the World



Where Rabies IS NOT

- Antarctica
- New Zealand
- Japan
- Sweden
- Norway
- Spain
- Hawaii
- some Caribbean Islands

International Travelers to High Risk Areas

People travelling to rural areas or involved in activities such as running, bicycling, camping or hiking should receive pre-exposure prophylaxis.

-CDC's Yellow Book states that children who travel to canine-rabies endemic regions are at a particular risk for rabies. It mentions their inquisitive nature, inability to read behavioral cues from dogs, and increased likelihood for severe bites to high-risk anatomic regions due to short stature in recommending rabies PrEP for travelers to canine rabies endemic regions, including children[3]

NO PRE-EXPOSURE PROPHYLAXIS

- Rabies vaccine started given in 4 doses
- Day 0, 3, 7, 14-28
- Immunocompromised need the 5th dose on day 28
- PLUS Rabies IG on day 0 (HAS TO BE GIVEN BEFORE DAY 7)

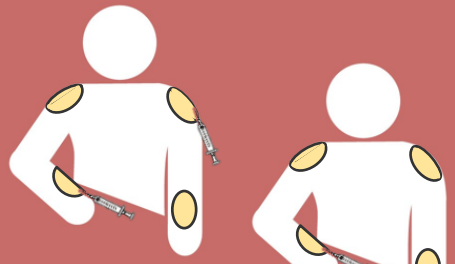
Use of a Modified Preexposure Prophylaxis Vaccination Schedule to Prevent Human Rabies: Recommendations of the Advisory Committee on Immunization Practices — United States, 2022

Agam K. Rao, MD[1]; Deborah Briggs, PhD[2]; Susan M. Moore, PhD[2]; Florence Whitehill, DVM[1,3]; Doug Campos-Outcalt, MD[4]; Rebecca L. Morgan, PhD[5]; Ryan M. Wallace, DVM[1]; José R. Romero, MD[6]; Lynn Bahta, MPH[7]; Sharon E. Frey, MD[8]; Jesse D. Blanton, DrPH[1]

Rabies Vaccine Pre- Travel Vaccine Changes MMWR 2022

Risk Category	Typical Population	Pre-Exposure prophylaxis
1.High Risk	RABIES LAB	IM Rabies Vaccine Day 0, 7
2. Elevated Risk	Frequent Bat Contact	IM Rabies Vaccine Day 0, 7
3. Elevated Risk	Veterinarians, Animal Control, Spelunkers Travelers >3 years to high risk areas	IM Rabies Vaccine Day 0, 7
4. Elevated Risk	Travelers < 3 years with high recreation exposure to dog, outdoor activities, or rural area	IM Rabies Vaccine Day 0, 7
5. Low Risk	Typical US Citizen	None

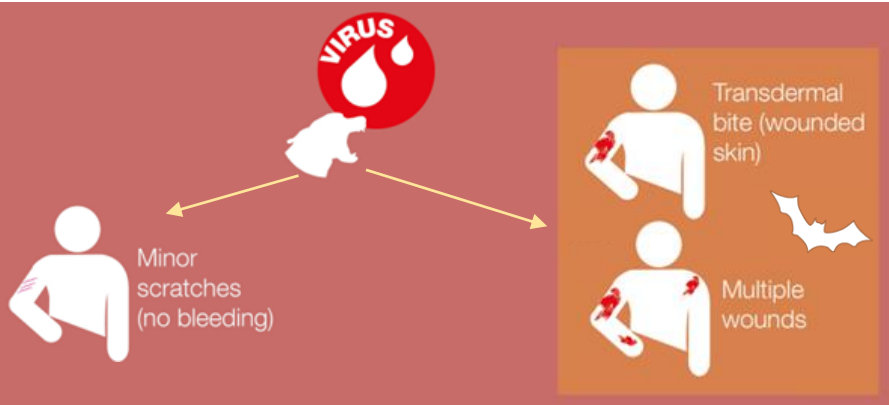
WHO SCHEDULE PRE AND POST-EXPOSURE



2 ID shots
on day 0

2 ID shots
on day 7

PRE-
EXPOSURE



Category II

\+ Vaccine
1 ID or IM
shot on day
0

Category III

\+ Vaccine
1 ID or IM
shot on
day 0

\+ Vaccine
1 ID or IM
shot on
day 3

POST-
EXPOSURE

Tick Borne Encephalitis

TBE vaccine

- TBE vaccine (TICOVAC) approved by FDA in 2021 for use in persons aged ≥1 year
- Current formulation available internationally for >20 years
- >75 million doses administered
- Marketed in ~30 countries, primarily in Europe

TBE in endemic areas

- Focally endemic in parts of Europe and Asia
- ~5,000–10,000 cases reported annually
- Incidence variable
  - Country-to-country
  - Within countries
  - Year-to-year
- Seasonal risk from April through November

Source: Dobler et al, Wien Med Wochenschr 2012

Potential severity of neuroinvasive disease

- Most persons require hospitalization
  - No antiviral treatment
- Sequelae rates of 10% to 50%
  - Can include permanent physical disabilities or cognitive impairment
- Case fatality rates of 1% to 20%

TBE Vaccine Recommendations

Laboratory workers

- TBE vaccination is recommended for laboratory workers with a potential for exposure to TBE virus.

Persons who travel abroad

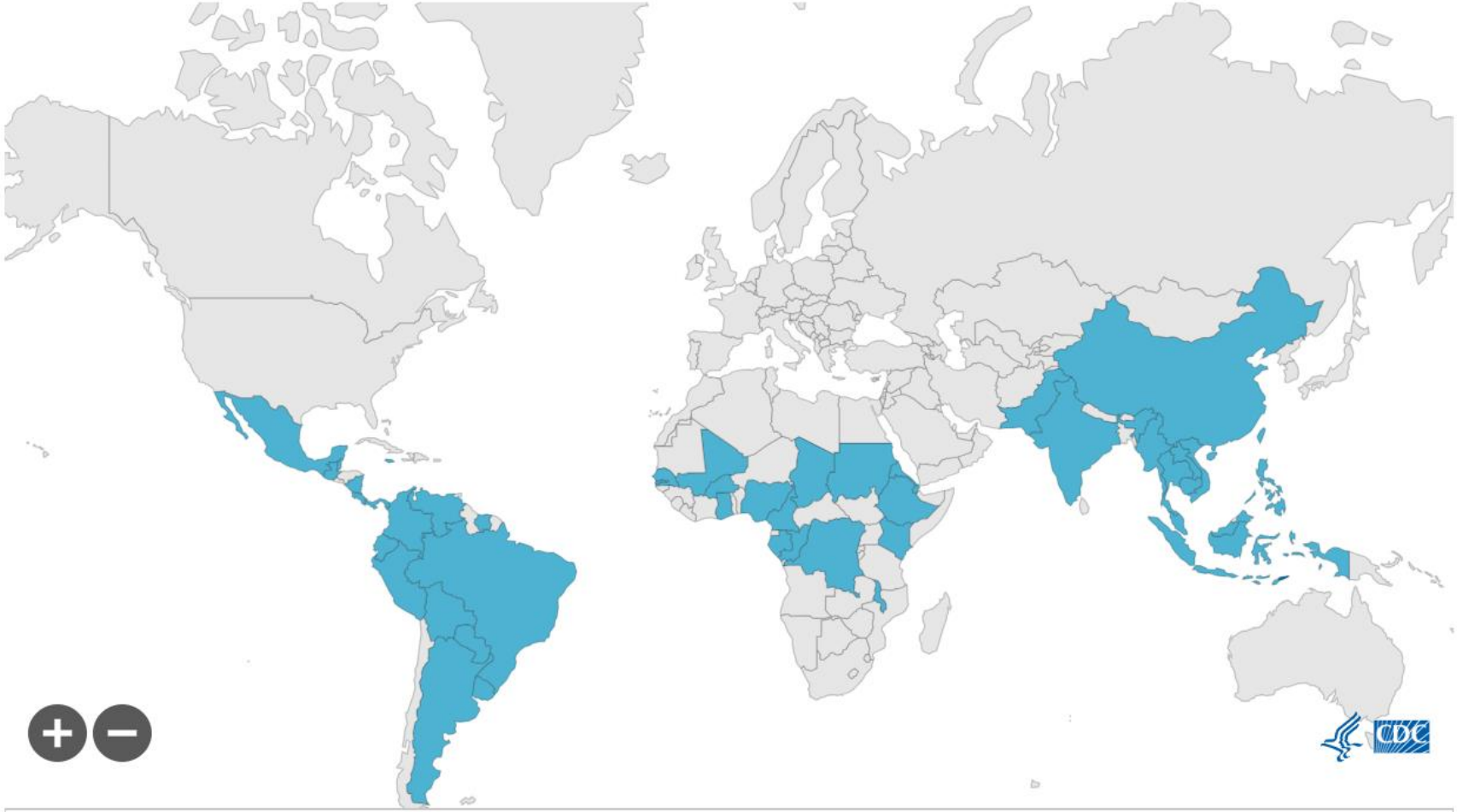
- TBE vaccine is recommended for persons who are moving abroad or traveling to a TBE-endemic area and will have extensive exposure to ticks based on their planned outdoor activities and itinerary.
- (*In addition*) TBE vaccine might be considered for persons traveling or moving to a TBE-endemic area who might engage in outdoor activities in areas ticks are likely to be found. The decision to vaccinate should be based on an assessment of their planned activities and itinerary, risk factors for a poorer medical outcome, and personal perception and tolerance of risk.

ALL UPDATED NOW IN THE YELLOW BOOK

	infants 6–11 months, according to CDC's measles vaccination recommendations for international travel.	
Rabies	Rabid dogs are commonly found in Moldova. However, if you are bitten or scratched by a dog or other mammal while in Moldova, rabies treatment is often available. Consider rabies vaccination before your trip if your activities mean you will be around dogs or wildlife. Travelers more likely to encounter rabid animals include • Campers, adventure travelers, or cave explorers (spelunkers) • Veterinarians, animal handlers, field biologists, or laboratory workers handling animal specimens • Visitors to rural areas Since children are more likely to be bitten or scratched by a dog or other animals, consider rabies vaccination for children traveling to Moldova.	Rabies - CDC Yellow Book
Tick-borne Encephalitis	For travelers moving or traveling to TBE-endemic areas TBE vaccine is recommended for persons who will have extensive exposure to ticks based on their planned outdoor activities and itinerary. TBE vaccine may be considered for persons who might engage in outdoor activities in areas ticks are likely to be found.	Tick-borne Encephalitis - CDC Yellow Book

Chikungunya Vaccine

Countries with outbreaks or evidence of chikungunya virus transmission to humans during last 5 years

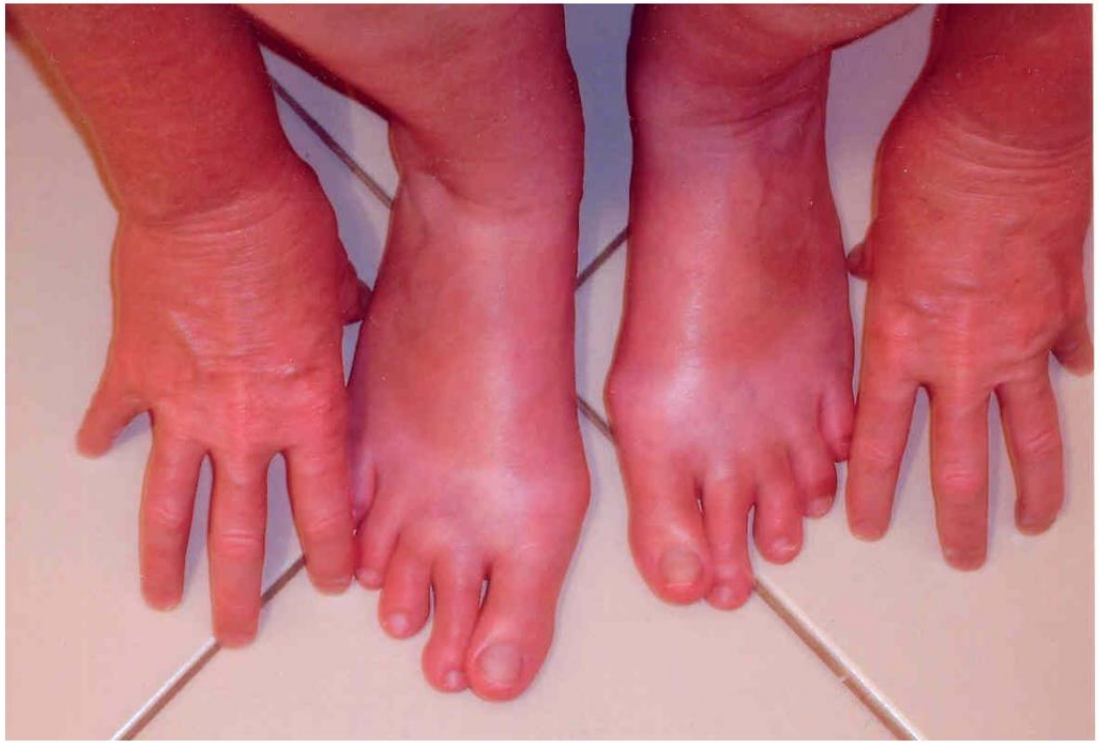


Chikungunya Swahili for “to become contorted/bent”

- Alpha virus, First found in Tanzania, 1953
- Vector: Ae. aegypti and albopictus mosquitoes
- Incubation 3-7 days
- Fever, headache, fatigue, nausea, vomiting, muscle pain, rash, joint pain
- Duration: few days to several weeks
- **Prolonged residual joint pain and/or arthritis**

Debilitating Joint Pain

- 43% of the cases will become chronic
- Difficulty walking
- Swollen joints
- Last for months to years
- Can’t wear shoes
- Need Wheelchair



Treatment Options

- There is no medicine to treat Chikungunya virus.
- Symptomatic treatment – rest, maintain hydration, acetaminophen for fever and pain
- Do not take aspirin and other non-steroidal anti-inflammatory drugs (NSAIDS until dengue can be ruled out to reduce the risk of bleeding).
- Acute Chikungunya - prevent mosquito bites for the first week of illness. During the first week of infection, Chikungunya virus can be found in the blood and passed from an infected person to a mosquito through mosquito bites. An infected mosquito can then spread the virus to other people.

Prevention

- Mosquito bite prevention
- NEW VACCINE-a live attenuated vaccine, 98% rate seropositive after 1 dose

ACIP recommends chikungunya vaccine for persons aged ≥18 years traveling to a country or territory where there is a chikungunya outbreak

In addition, chikungunya vaccine may be considered for the following persons traveling to a country or territory without an outbreak but with evidence of chikungunya virus transmission among humans within the last 5 years

- Persons aged >65 years, particularly those with underlying medical conditions, who are likely to have at least moderate exposure* to mosquitoes, OR
- Persons staying for a cumulative period of 6 months or more

ANY QUESTIONS?