Individuals using assistive technology may not be able to fully access the information contained in this file. For assistance, please call 800-835-4709 or 240-402-8010, extension 1. CBER Consumer Affairs Branch or send an e-mail to: ocod@fda.hhs.gov and include 508 Accommodation and the title of the document in the subject line of your e-mail.

RSV Epidemiology and Disease Burden in Infants from Birth through 6 Months of Age

Katherine Fleming-Dutra, MD
Coronavirus and Other Respiratory Viruses Division
National Center for Immunization and Respiratory Diseases
May 18, 2023

Outline

- Burden of RSV in U.S. children
- Burden of RSV in pregnant people
- RSV Seasonality in the United States

Burden of RSV in U.S. children

RSV is the leading cause of hospitalization in U.S. infants[1]

- Most (68%) infants are infected in the first year of life and nearly all (97%) by age 2 years[2]
- 2-3% of young infants will be hospitalized for RSV[3,4,5]
- RSV is a common cause of lower respiratory tract infection in infants
- Infants with RSV can have difficulty breathing and eating and sometimes need oxygen/respiratory support and hydration

Image: Goncalves et al. Critical Care Research and Practice 2012

[1]Suh et al. JID 2022. [2]Glezen et al, Arch Dis Child, 1986; [3]Hall et al, Pediatrics, 2013; [4]Langley & Anderson, PIDJ, 2011; [5]CDC NVSN data

All young infants are at risk of having severe disease with RSV

- Premature infants born at <30 weeks gestation had hospitalization rates ~3x higher than term infants[1]
- Children with chronic lung disease of prematurity and congenital heart disease are also at increased risk of severe RSV disease[2]
- 79% of children hospitalized with RSV aged <2 years had no underlying medical conditions[1]

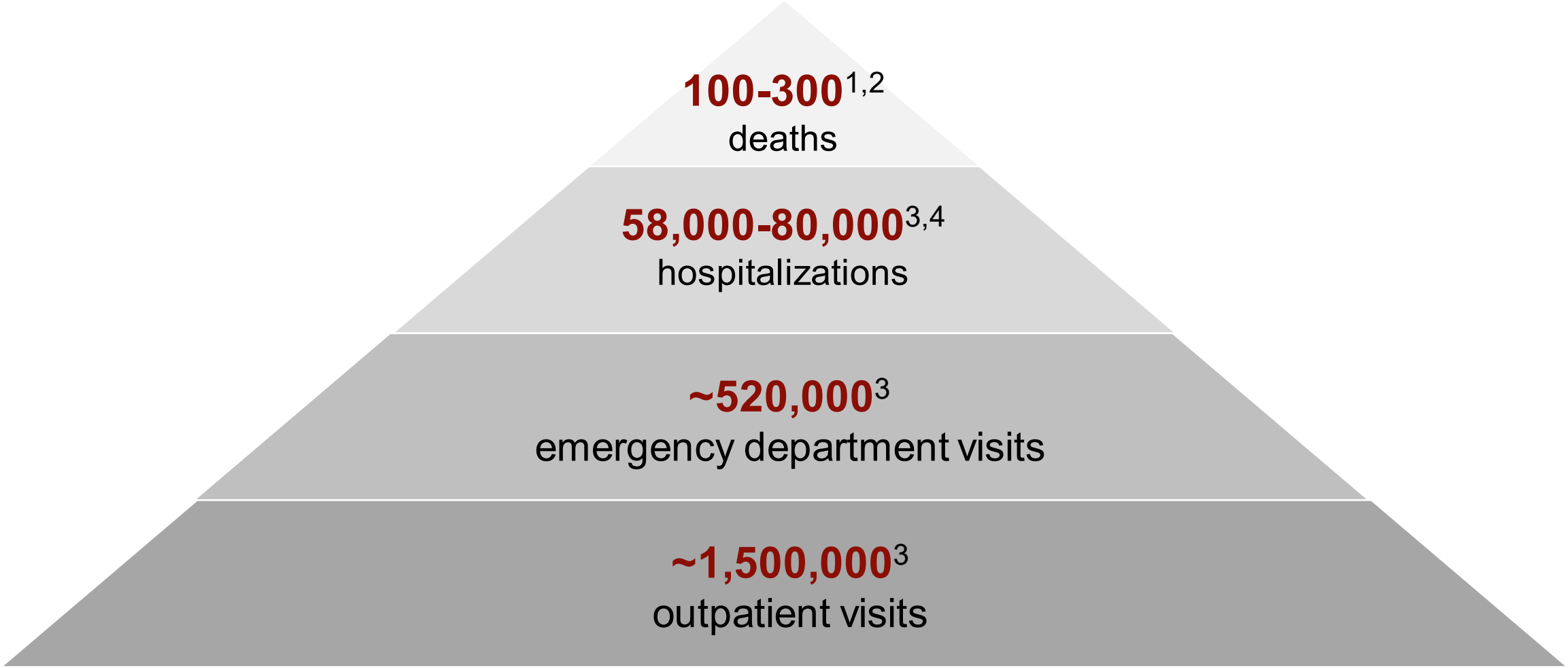
[1]Hall et al, Pediatrics, 2013; [2]Langley & Anderson, PIDJ, 2011

Prevention - Palivizumab (Synagis®)

- Humanized monoclonal IgG directed against F glycoprotein
- Monthly administration due to short half-life (28 days)
- American Academy of Pediatrics recommends use for prevention of RSV disease in infants at high risk of severe disease including[1]
  - Infants born at <29 weeks gestation during first year of life
  - Preterm infants with chronic lung disease
  - Infants with hemodynamically significant congenital heart disease
  - Infants with profound immunocompromise
- 5% of U.S. infants eligible, ~2% of U.S. infants receive one or more doses[2]

[1]American Academy of Pediatrics, Red Book, 2021; [2]Ambrose et al, Human Vaccines Immuno, 2014

Each year in U.S. children aged less than 5 years, RSV is associated with…

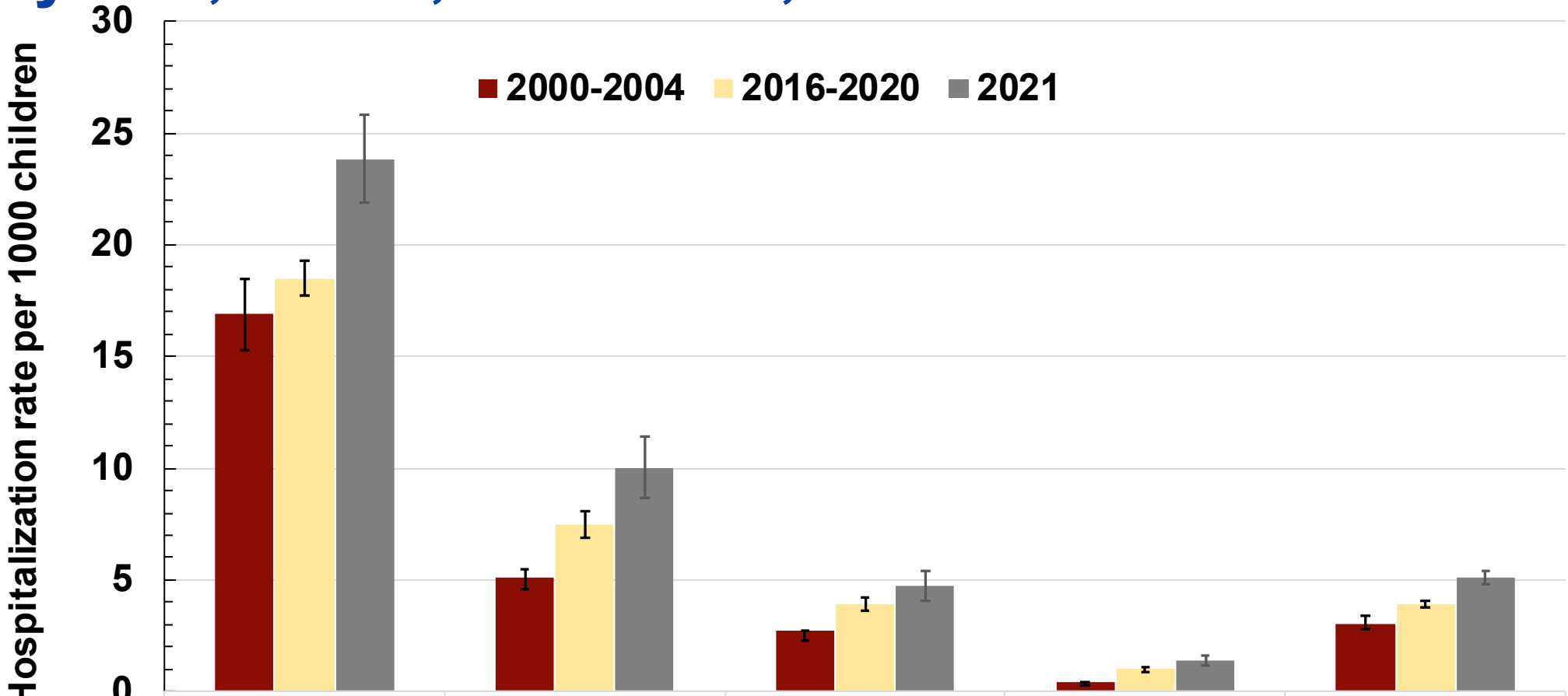


[1]Thompson et al, JAMA, 2003; [2]Hansen et al, JAMA Network Open, 2022; [3]Hall et al, NEJM, 2009; [4]McLaughlin et al, J Infect Dis, 2022 (*estimate 80,000 hospitalizations in infants <1y)

RSV-associated disease burden estimates from the New Vaccine Surveillance Network (NVSN)

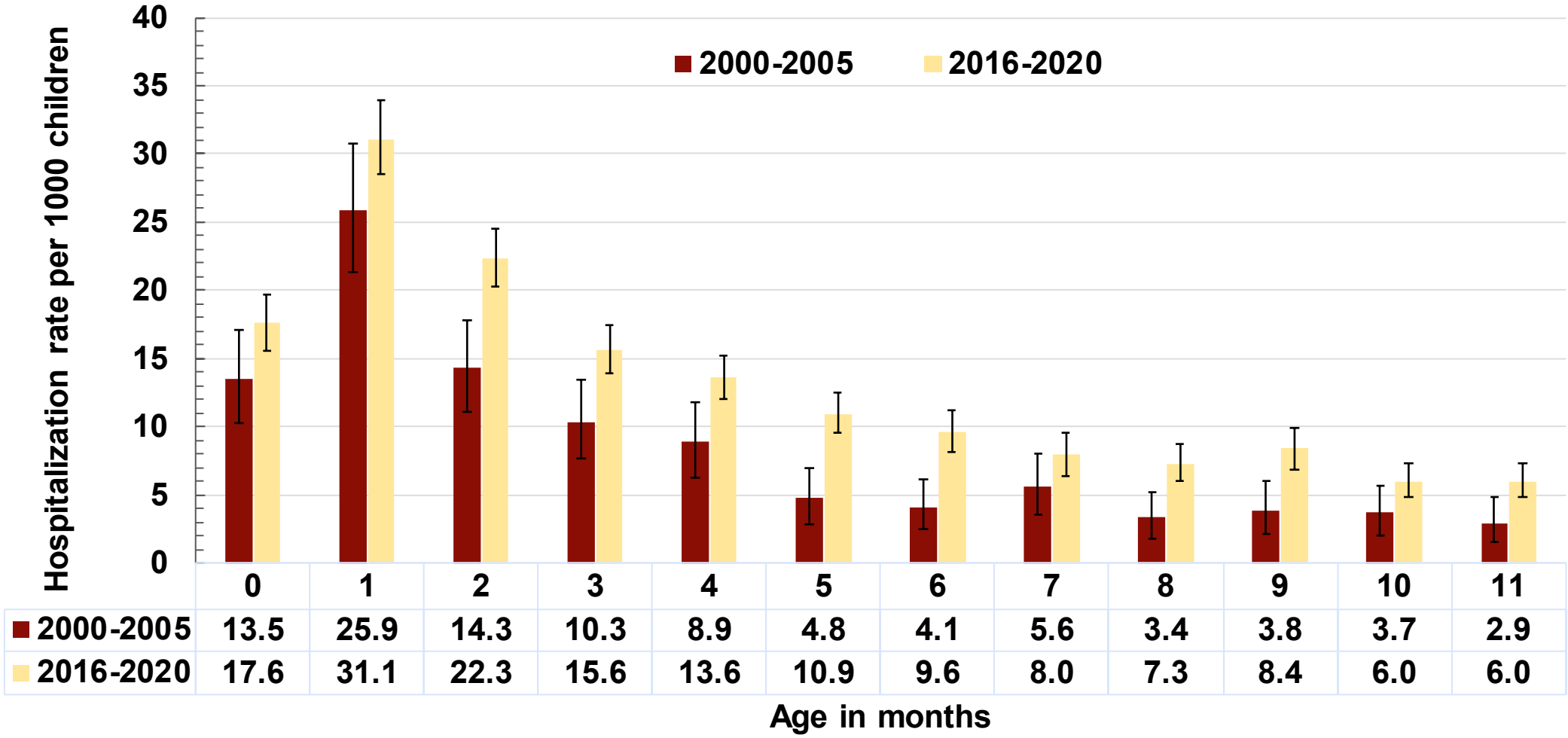
- Acute respiratory illness (ARI) surveillance at 3 sites during 2000-2009
- Expanded to 7 sites in 2016
- Prospective surveillance in inpatient, ED, outpatient clinics
- PCR testing for multiple respiratory viruses, including RSV
- Population denominators and market share used to estimate disease burden

RSV-associated hospitalization rates in children aged <5 years, NVSN, 2000-2004, 2016-2021



	0-5 months	6-11 months	12-23 months	24-59 months	0-59 months
2000-2004	16.9	5.1	2.7	0.4	3
2016-2020	18.5	7.5	3.9	1.0	3.9
2021	23.8	10.0	4.7	1.4	5.1

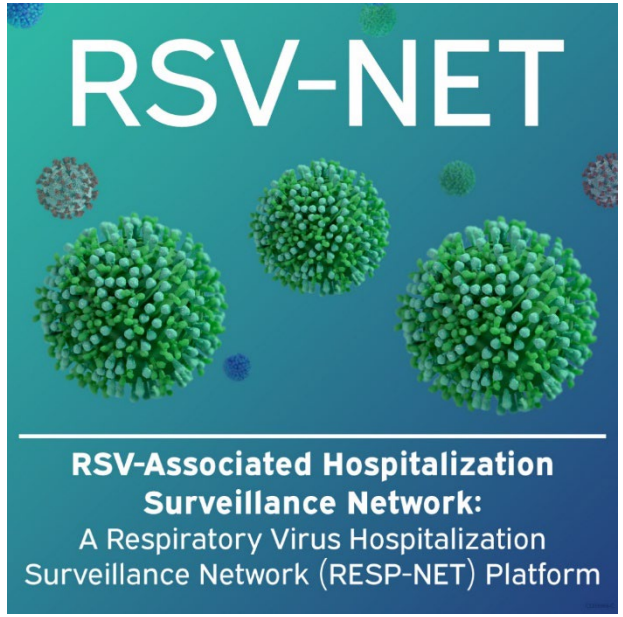
RSV-associated hospitalization rates in children aged 0–11 months, NVSN, 2000–2005 and 2016–2020



	0	1	2	3	4	5	6	7	8	9	10	11
2000-2005	13.5	25.9	14.3	10.3	8.9	4.8	4.1	5.6	3.4	3.8	3.7	2.9
2016-2020	17.6	31.1	22.3	15.6	13.6	10.9	9.6	8.0	7.3	8.4	6.0	6.0

2000–2005: Adapted from Hall et al, Pediatrics 2013,
2016–2020: CDC unpublished data

Respiratory Syncytial Virus Associated Hospitalization Surveillance Network (RSV-NET)

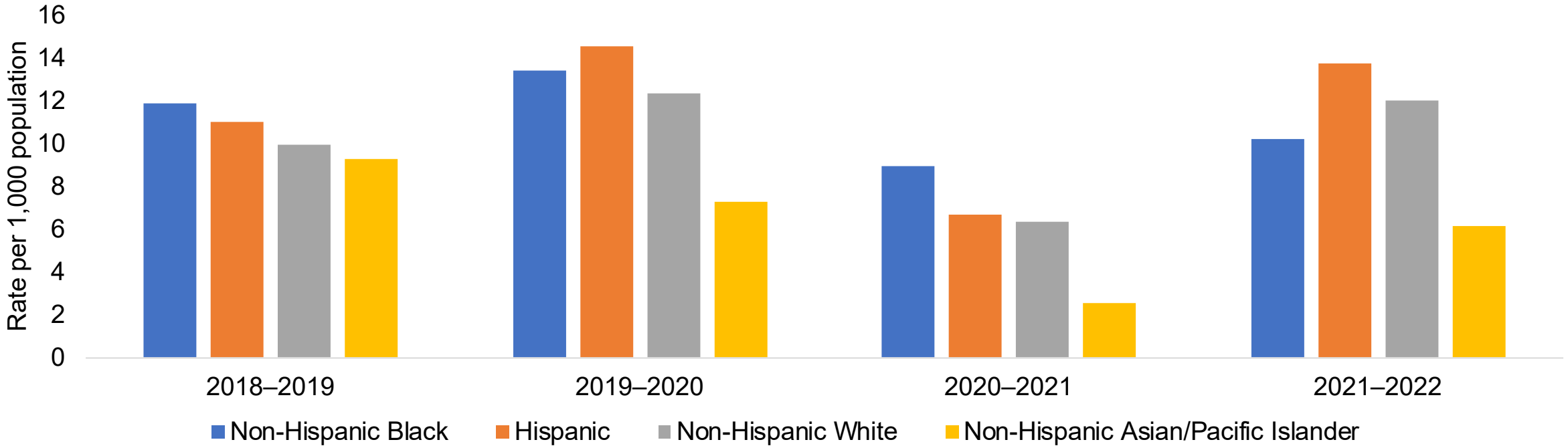


- Population-based
- Current catchment area:
  - 12 states
  - ~8% of US population

https://www.cdc.gov/rsv/research/rsv-net/overview-methods.html

https://www.cdc.gov/rsv/research/rsv-net/dashboard.html

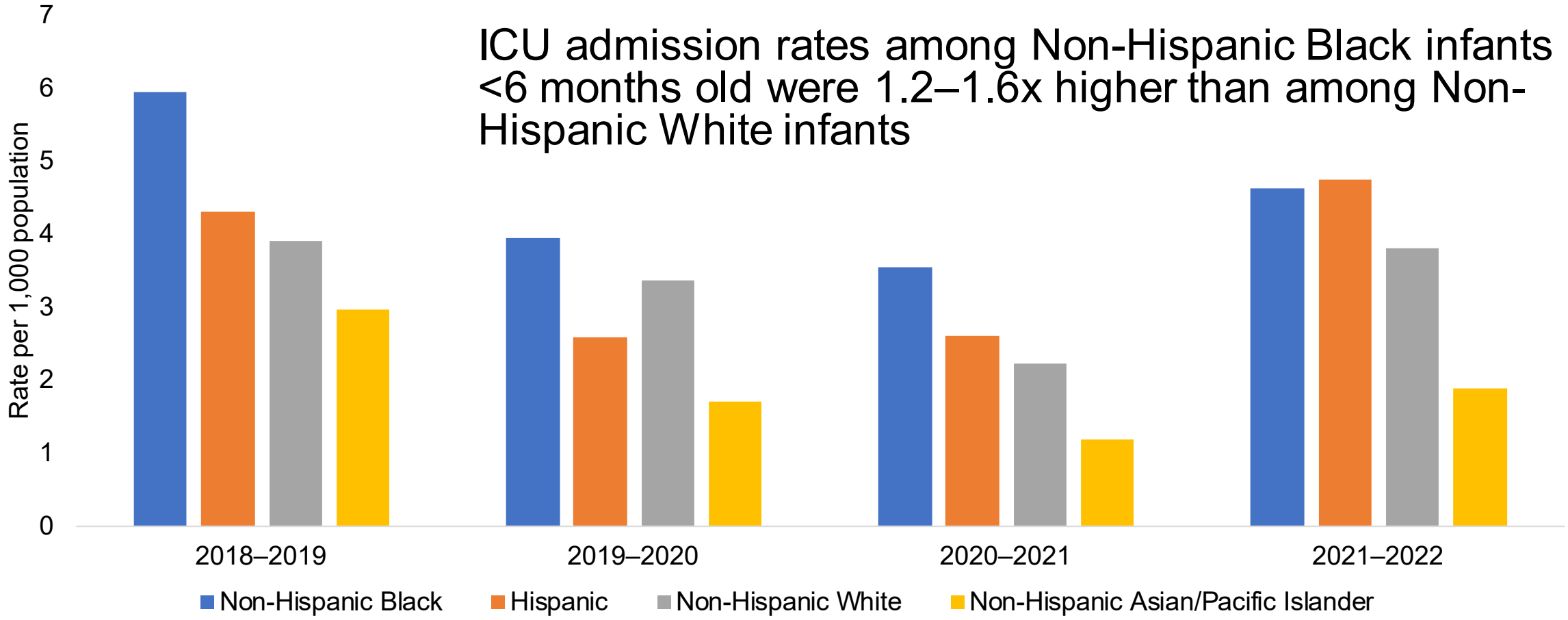
Population-based *hospitalization* rates among infants <6 months old with laboratory-confirmed RSV by race and ethnicity, RSV-NET, 2018–2019 to 2021–2022



- Hospitalization rates among infants <6 months old differ by race and ethnicity but vary by season
- Rates were not adjusted for RSV testing practices and thus may under-represent RSV hospitalization rates but should not affect distributions by race and ethnicity

RSV-NET: unpublished data. Surveillance was conducted from October–April for the 2018–19 and 2019–20 seasons, October–September for the 2020–21 season, and October–September excluding May–June for the 2021–22 season. Rates were not adjusted for RSV testing practices; testing practices may differ by racial and ethnic groups and may have changed over time. Black, White, Asian/Pacific Islander children were categorized as non-Hispanic; Hispanic children could be of any race.

Population-based *ICU admission* rates among infants <6 months old with laboratory-confirmed RSV by race and ethnicity, RSV-NET, 2018–2019 to 2021–2022



RSV-NET: unpublished data. Surveillance was conducted from October–April for the 2018–19 and 2019–20 seasons, October–September for the 2020–21 season, and October–September excluding May–June for the 2021–22 season. Rates were not adjusted for RSV testing practices; testing practices may differ by racial and ethnic groups and may have changed over time. Black, White, and Asian/Pacific Islander children were categorized as non-Hispanic; Hispanic children could be of any race.

Seasonal rate of RSV-associated hospitalizations per 1,000 children among American Indian and Alaska Native children <5 years of age, Nov 2019- May 2020 (SuNA)*

Age	Chinle, Arizona	Whiteriver, Arizona	Anchorage, Alaska	Yukon-Kuskokwim Delta, Alaska	NVSN** for comparison
0-5 Months	83.0 (52.0, 132.5)	70.4 (36.3, 136.6)	35.7 (20.4, 62.6)	132.3 (98.2, 178.1)	21.6 (20.0, 23.3)
6-11 Months	61.6 (35.9, 105.8)	90.1 (50.0, 162.3)	0.0 (0.0, 10.8)	91.6 (64.0, 131.0)	8.2 (7.1, 9.3)
0-11 Months	**71.8 (50.4, 102.4)**	**80.6 (51.9, 125.2)**	**19.2 (11.2, 33.0)**	**112.2 (89.3, 141.0)**	**14.9 (13.9, 16.0)**
12-23 Months	**42.1 (27.2, 65.3)**	**38.7 (22.0, 68.1)**	**15.6 (8.7, 27.7)**	**26.4 (16.6, 41.8)**	**4.5 (3.9, 5.2)**
24-59 Months	10.9 (6.8, 17.4)	8.2 (4.2, 16.0)	1.1 (0.3, 3.8)	5.9 (3.2, 10.9)	1.2 (1.2, 1.5)
0-59 Months	27.2 (21.4, 34.4)	25.4 (18.7, 34.5)	7.7 (5.3, 11.1)	32.7 (26.9, 39.7)	4.6 (4.3, 4.8)

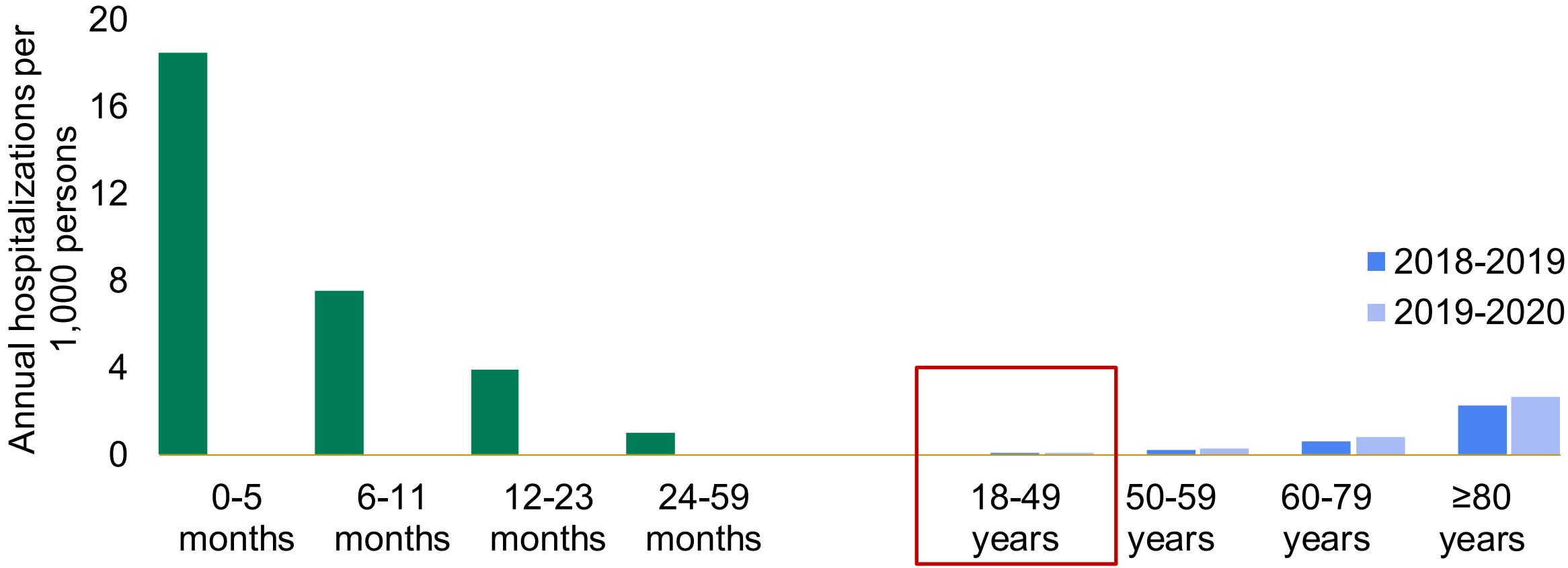
*Hartman et al, RSV2022 12th International Symposium, Belfast 9/29/2022-10/2/2022; Atwell et al. RSV among American Indian and Alaska Native children: 2019-20 (manuscript in press) SuNA = RSV Surveillance among Native American Persons

**Incidence of RSV-associated hospitalization in 2019-2020 included for comparison. NVSN = New Vaccine Surveillance Network.

Burden of RSV in pregnant people

Data on RSV in pregnant people are limited

Estimated annual rate of RSV hospitalizations among children aged <5 and adults aged ≥18 years, United States



New Vaccine Surveillance Network, 2016–2020

RSV-NET, 2018–2020

Presented at 12th International RSV Symposium; Havers FP; 2022 Sep 29 – Oct 2; Belfast, United Kingdom.

RSV severity appears to be similar in pregnant and non-pregnant people

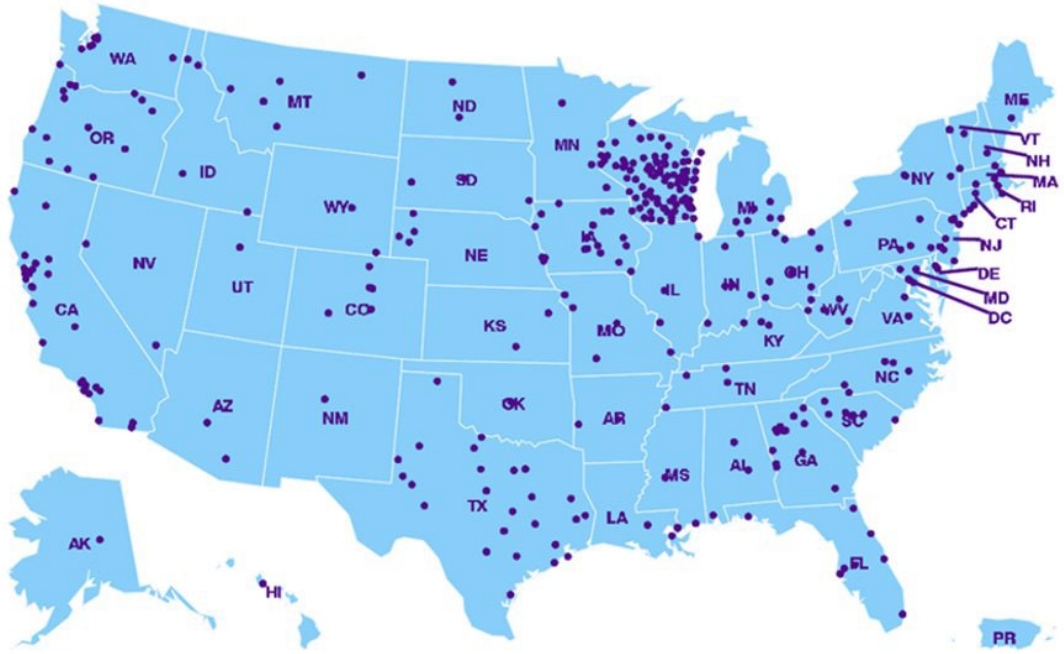
- Among 387 women aged 18-49 years were hospitalized with RSV in RSV-NET during October-April 2014-2018
  - 41 (12%) were pregnant
- Severe outcomes among pregnant women hospitalized with RSV were uncommon
  - 5 (12%) pregnant women vs. 82 (24%) non-pregnant women aged 18-49 years had severe outcomes (ICU admission/in-hospital death)
- Being pregnant was not a risk factor for a severe outcome with RSV hospitalization in multivariable analysis

Milucky et al. Outcomes of pregnant women hospitalized with RSV infection, RSV-NET, 2014-2018. ReSViNet, 2023

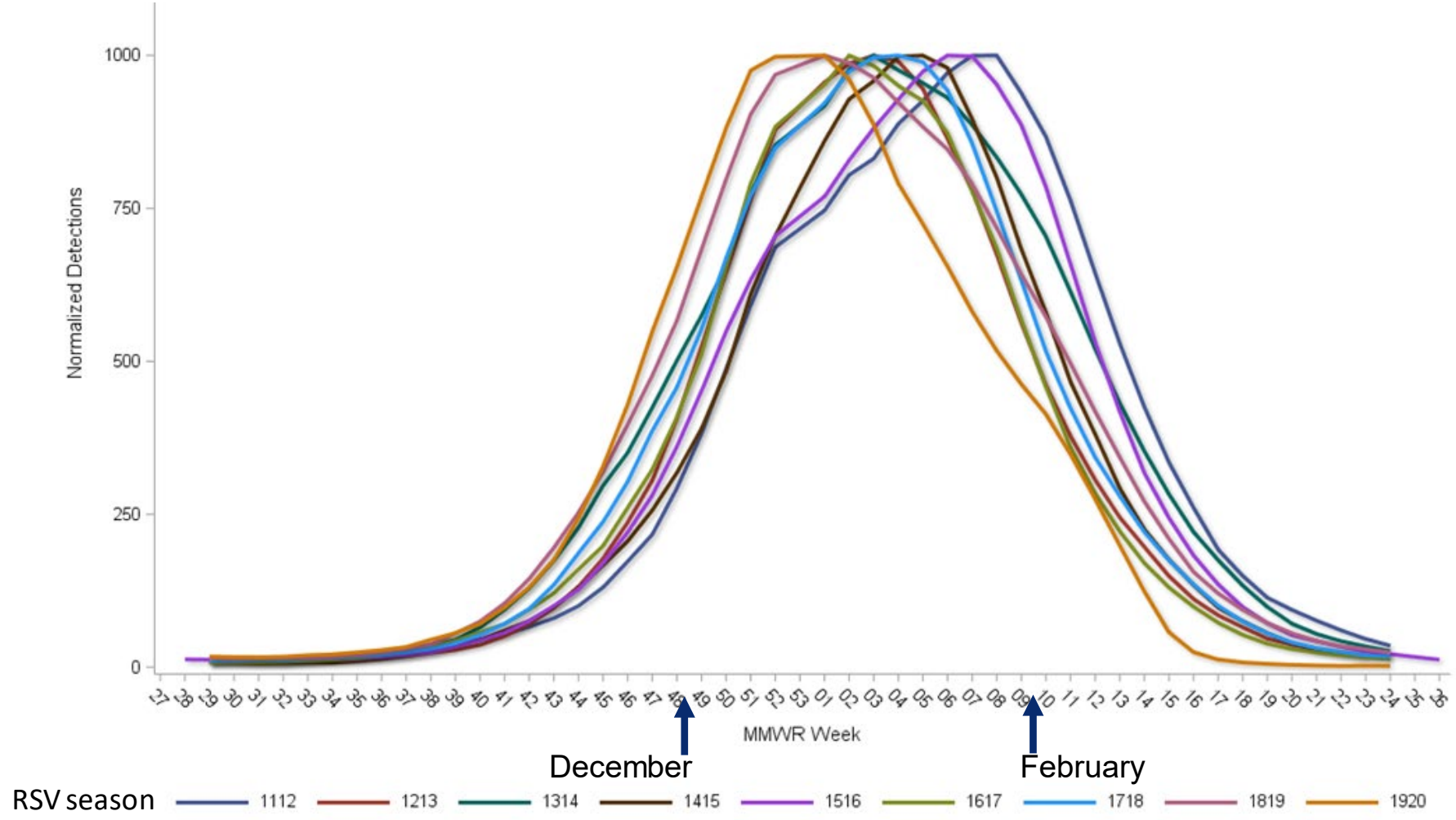
RSV Seasonality in the United States

National Respiratory and Enteric Virus Surveillance System (NREVSS) for monitoring RSV seasonality

- Passive, laboratory-based surveillance
  - Commercial, hospital, and state/local public health laboratories
  - ~300 laboratories report RSV results
  - Weekly reporting of total tests performed and RSV positive tests
- All test types (majority PCR assays)
- Testing is clinician-directed
- All ages

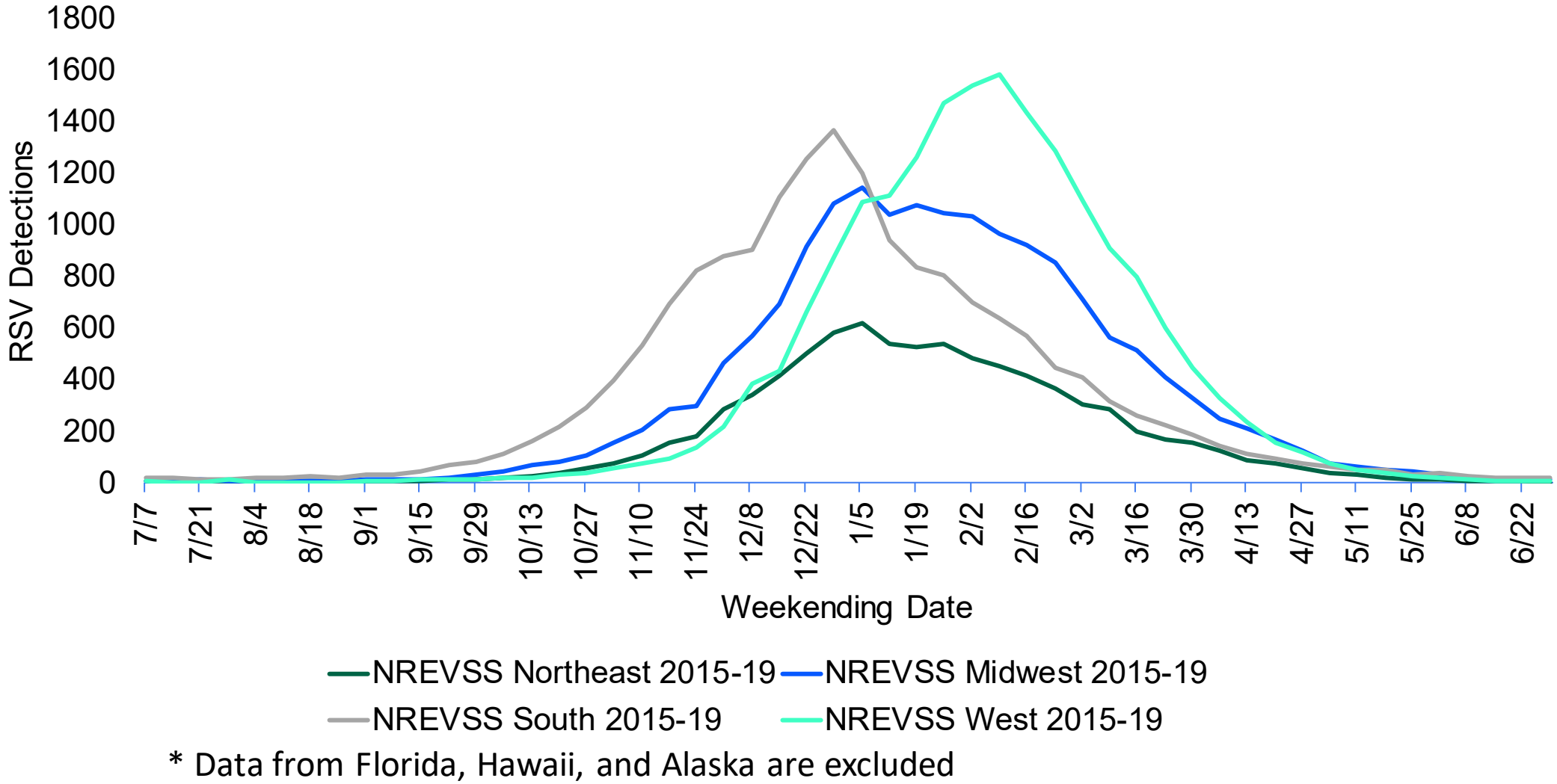


During 2011-2020, RSV circulation was highly seasonal in the U.S. with predictable peak activity during December – February annually



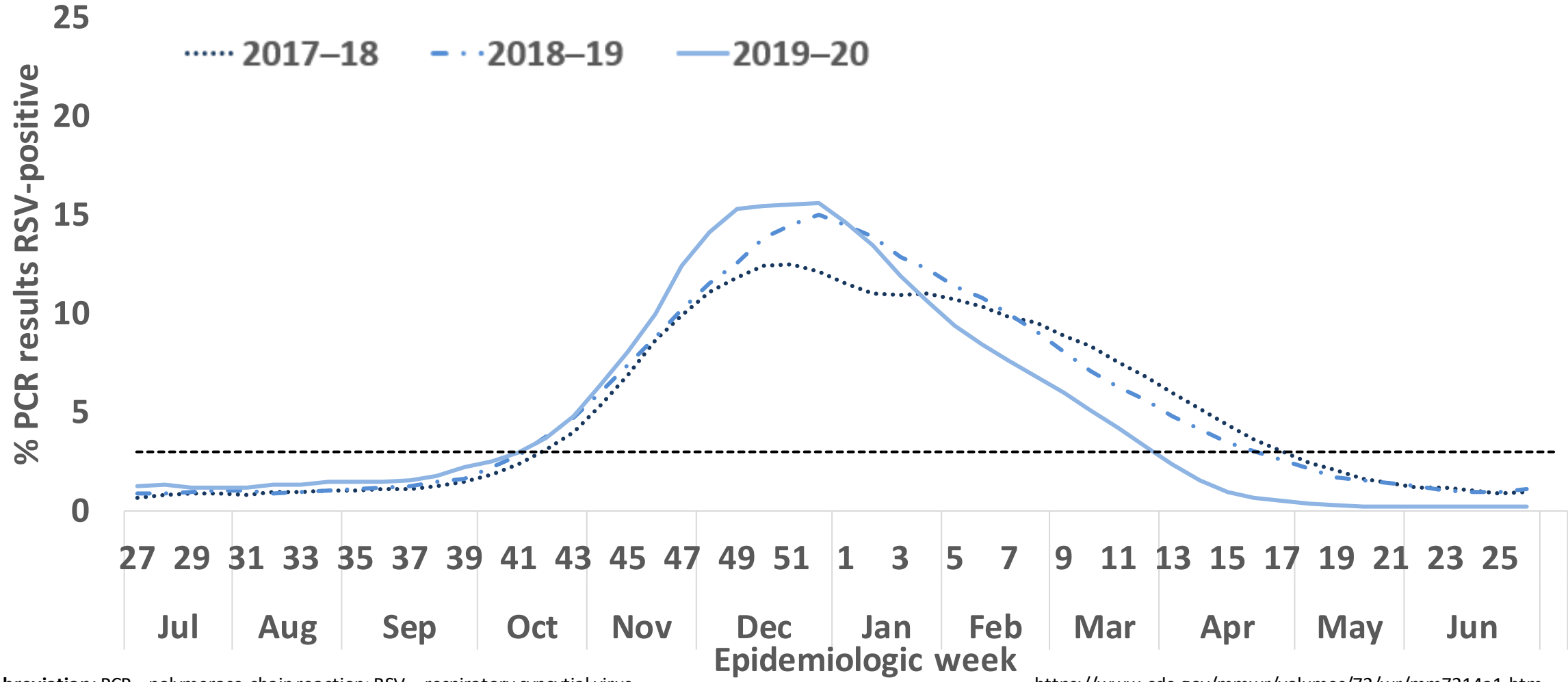
RSV Surveillance DataNREVSS | CDC

Peak RSV transmission during December – February, average weekly detections from NREVSS 2015-2019*



* Data from Florida, Hawaii, and Alaska are excluded

Changes in seasonality of RSV transmission following SARS-CoV2 introduction— NREVSS[1], 2017–2020

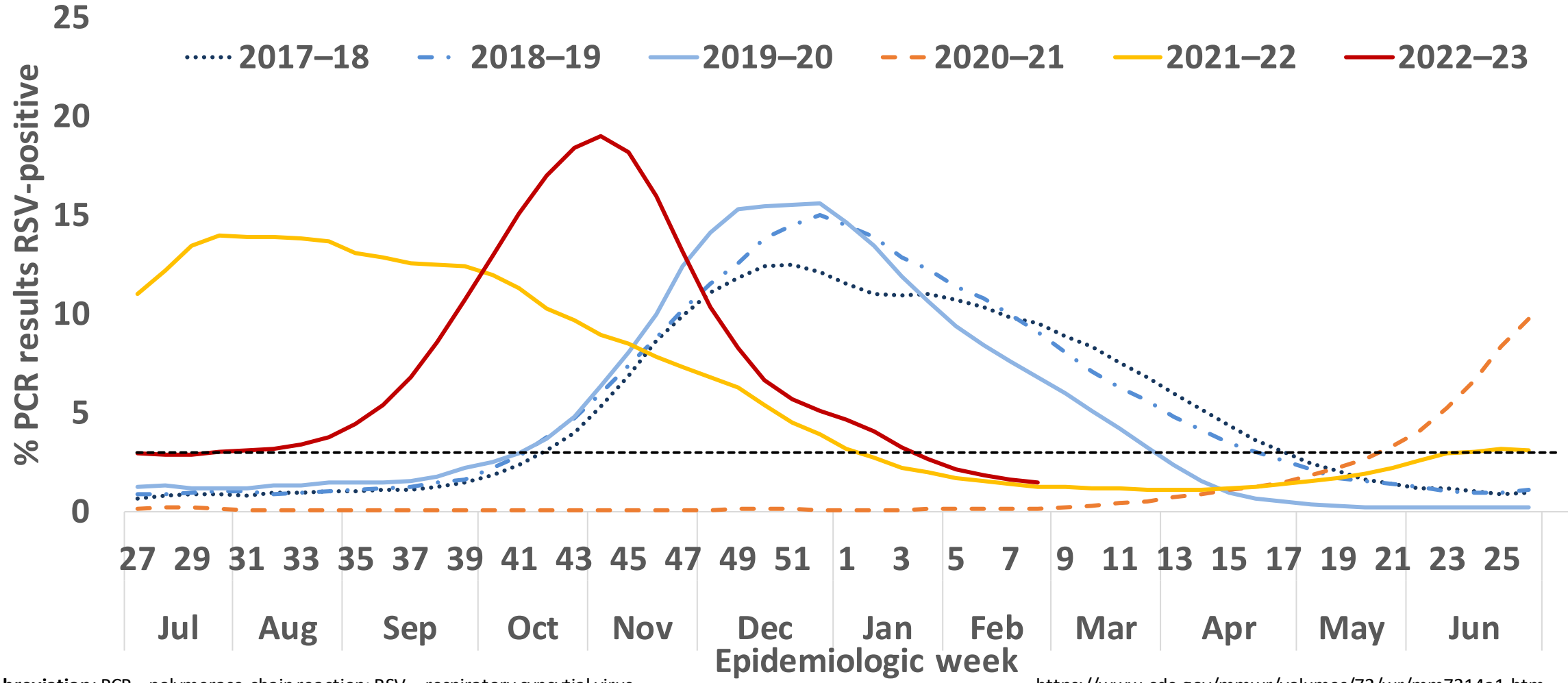


Abbreviation: PCR = polymerase chain reaction; RSV = respiratory syncytial virus.

https://www.cdc.gov/mmwr/volumes/72/wr/mm7214a1.htm

* 3-week centered moving averages of percentage of RSV-positive PCR results nationwide. The black dotted line represents the threshold for a seasonal epidemic (3% RSV-positive laboratory PCR results).

Changes in seasonality of RSV transmission following SARS-CoV2 introduction— NREVSS[1], 2017–2023



Abbreviation: PCR = polymerase chain reaction; RSV = respiratory syncytial virus.

https://www.cdc.gov/mmwr/volumes/72/wr/mm7214a1.htm

* 3-week centered moving averages of percentage of RSV-positive PCR results nationwide. The black dotted line represents the threshold for a seasonal epidemic (3% RSV-positive laboratory PCR results).

Potential considerations for timing of RSV vaccine dosing during the year

- RSV vaccine dosing could be implemented for pregnant people as a seasonal campaign or year-round
- Cost-effectiveness may vary by timing of administration due to RSV seasonality and decay of maternal antibody
  - CDC will plan to examine cost-effectiveness of seasonal RSV vaccine dosing compared to year-round dosing
- Year-round dosing would
  - Simplify implementation and potentially increase vaccine uptake
  - Protect infants in the event of atypical RSV seasonality

Potential considerations for timing of RSV vaccine dosing during the year (cont.)

- Some U.S. jurisdictions have different or less predictable RSV seasonality, and recommendations for RSV vaccine dosing in those jurisdictions would need to account for that
  - Tropical climates: parts of Florida, Puerto Rico, U.S. Virgin Islands, Hawaii, Guam, and U.S.-affiliated Pacific Islands
  - In Alaska, RSV seasonality is less predictable, and the duration of RSV activity is often longer than the national average

Summary

Conclusions

- RSV is the most common cause of hospitalization in U.S. infants
  - Highest hospitalization rates in first months of life
  - Risk declines with increasing age in early childhood
- Prematurity and other chronic diseases increase risk of RSV-associated hospitalization
- Most hospitalizations are in healthy, term infants

Conclusions (cont.)

- RSV hospitalizations are not common among reproductive-age women and being pregnant is likely not a risk factor for severe outcomes with RSV hospitalization
- Pre-pandemic RSV seasonality is well defined with limited geographic variability in most of the United States
- The COVID-19 pandemic disrupted RSV seasonality, and the most recent season suggests that RSV may be returning to typical pre-pandemic seasonality

Acknowledgements

- NCIRD/CORVD
  - Jefferson Jones
  - Mila Prill
  - Meredith McMorrow
  - Michael Melgar
  - Amadea Britton
  - Fiona Havers
  - Jenny Milucky
  - Monica Patton
  - Amber Winn
  - Heidi Moline
  - Lauren Roper
  - Aron Hall
  - Barbara Mahon
- ACIP Maternal/Pediatric RSV Working Group

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.