



# Cijepljenje trudnica protiv RSV



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**Zavod za infektivne bolesti djece u Klinici za infektivne bolesti**

**„Dr. Fran Mihaljević” u Zagrebu**

**4. Dani vakcinacije, Novi Sad, 6. 11. 2024.**

# Kratki pregled predavanja

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- **Važne činjenice o biologiji i epidemiologiji RSV-a (promjene koje su se dogodile tijekom pandemije Covid-19 i u ranom post-pandemijskom razdoblju)**
- **Kako liječimo RSV bolest u djece**
- **Novosti u prevenciji (cijepljenje trudnica)**

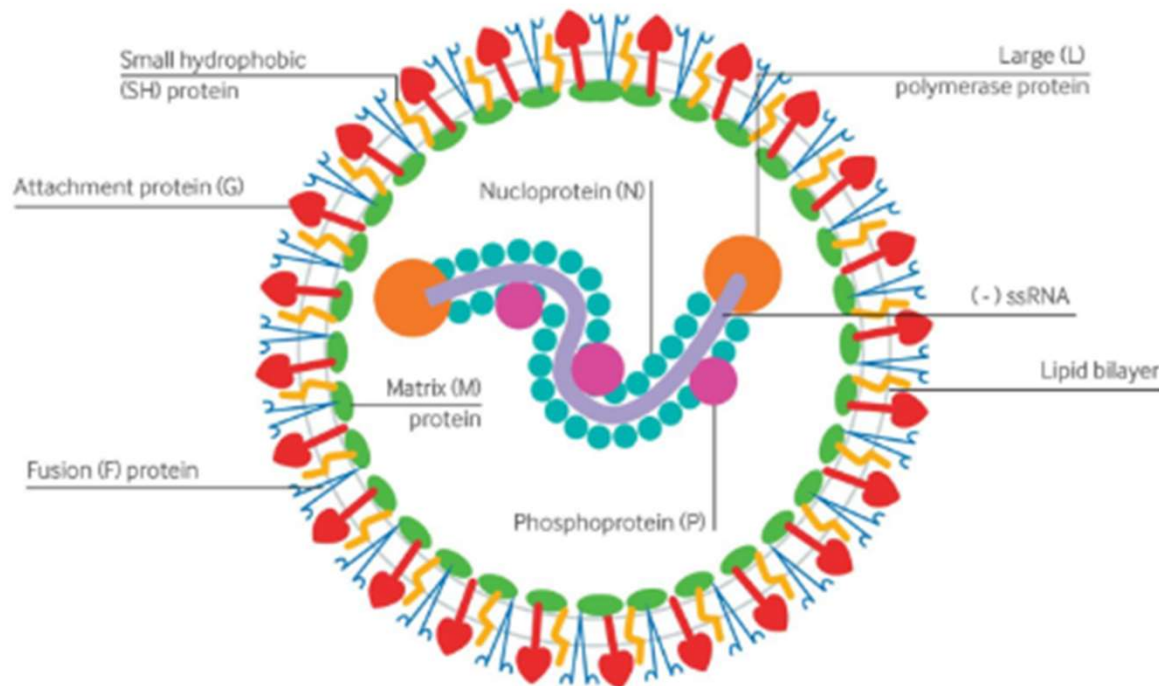
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# RSV – nekoliko riječi o patogenu...

RSV VIRION STRUCTURE



Non-structural proteins: NS1, NS2

Nucleocapsid and regulatory proteins: N (nucleoprotein), P (phosphoprotein), M2.1, M2.2, L (large polymerase)

Envelope proteins: SH (small hydrophobic), G (attachment), F (fusion)

Inner envelope protein: M (matrix)

From: <https://www.bmj.com/content/366/bmj.l5021>

# RSV – ponešto o patogenu i patogenezi infekcije/bolesti

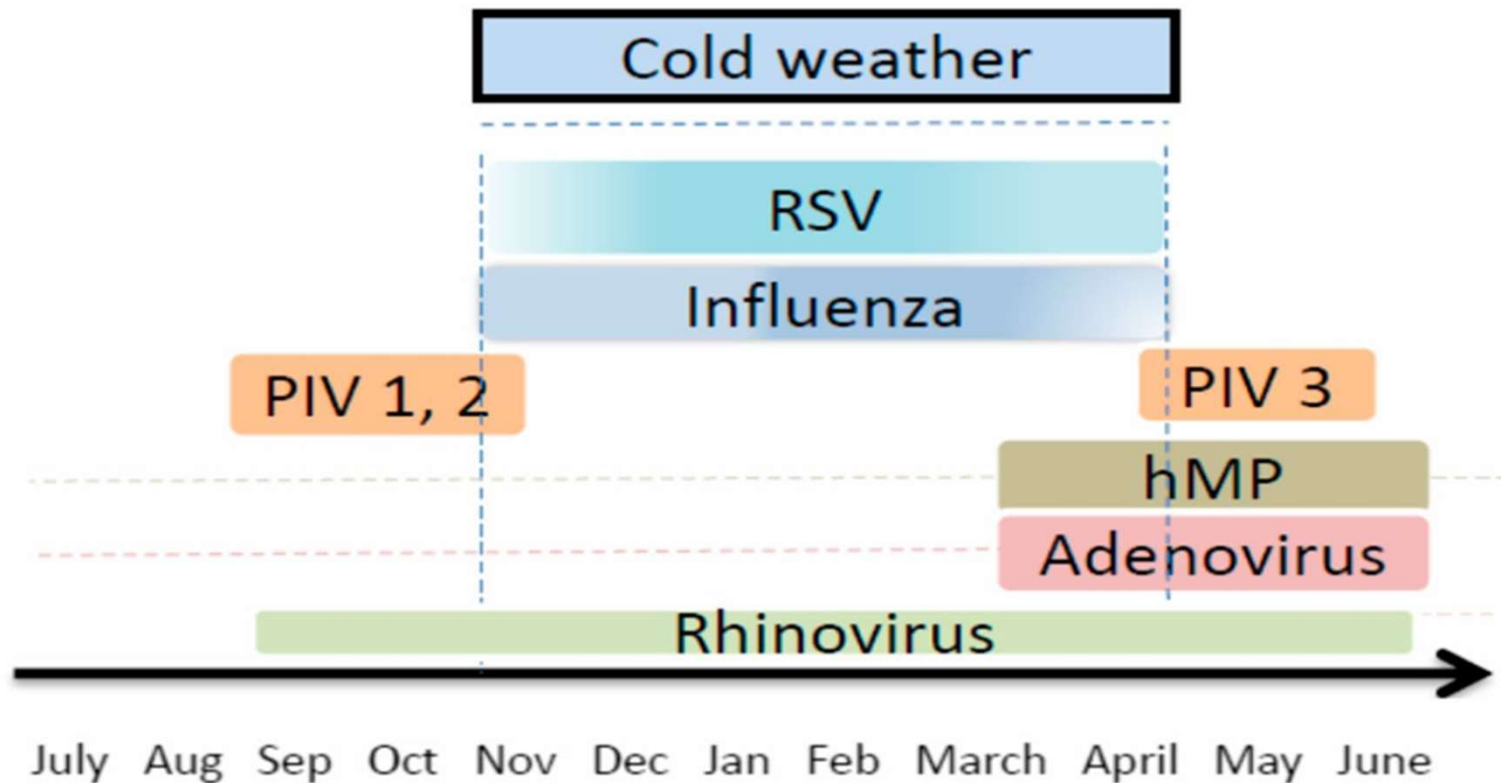
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- RSV se prenosi s osobe na osobu putem respiratornih kapljica. Virus se izlučuje 3 do 8 dana (kod dojenčadi i male djece, a kod imunokompromitiranih 3 do 4 tjedna).
- Razdoblje inkubacije nakon infekcije s RSV-om iznosi 2 do 8 dana (najčešće 4 do 6 dana).
- Nakon inokulacije u sluznicu nazofarinksa ili konjunktive, virus se brzo širi u respiratorni sustav. Ciljne su mu stanice apikalne cilijarne stanice epitela. Tamo se veže na stanične receptore pomoću glikoproteina RSV-G, zatim koristi fuzijski glikoprotein RSV-F za spajanje s membranom stanice domaćina i umetanje svoje nukleokapside u stanicu domaćina kako bi započeo unutarstaničnu replikaciju.
- Infekcija pokreće upalni imunološki odgovor domaćina, uključujući humoralnu imunost aktivaciju citotoksičnih T-stanica, a kombinacija virusne citotoksičnosti i citotoksičnog odgovora domaćina uzrokuje nekrozu respiratornih epitelnih stanica, što dovodi do opstrukcije malih dišnih putova staničnim i sluzi.
- Teži slučajevi također mogu uključivati alveolarnu infiltraciju. Infekcija/upalna reakcija uzrokuje i cilijarnu disfunkciju, poremećeno lučenje sluzi, edem dišnih putova i smanjenu plućnu popustljivost.

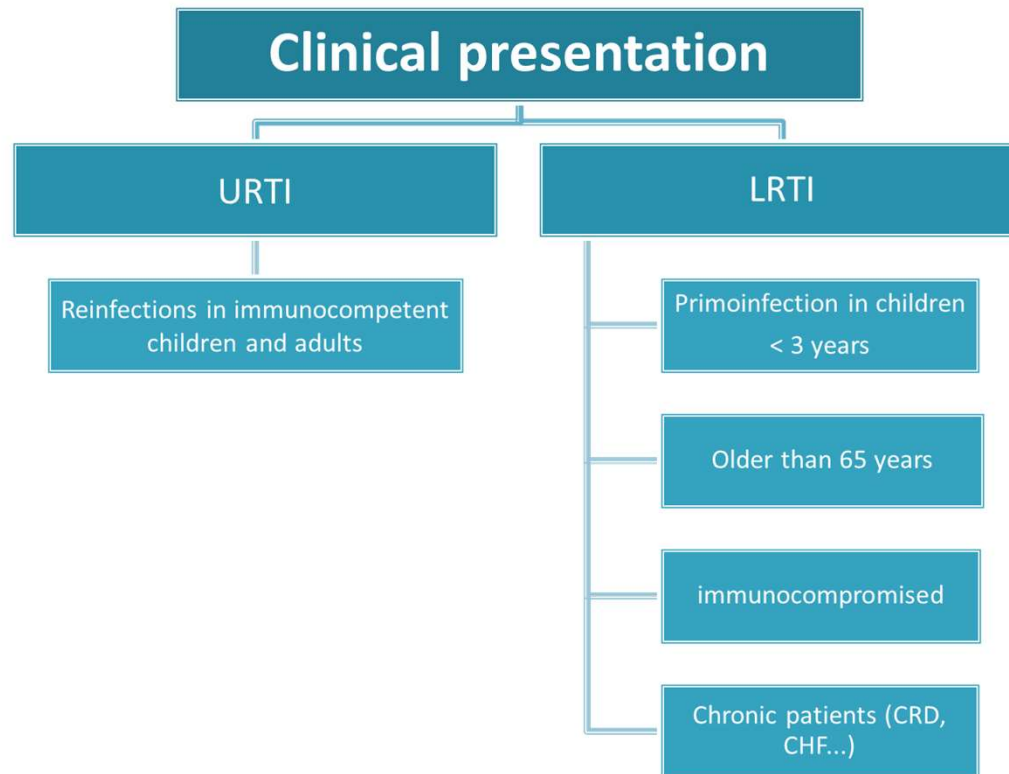
Schmidt ME, Varga SM. Cytokines and CD8 T cell immunity during respiratory syncytial virus infection. Cytokine. 2020;133:154481.



# RSV – važne činjenice



# Epidemiologija RSV – tko i kako obolijeva?



Hanish J, Schweitzer JW, Justice NA. Respiratory syncytial virus infection. Dostupno na: <https://www.ncbi.nlm.nih.gov/books/NBK459215/> Pristupljeno listopad, 2024.



# Epidemiologija RSV – tko i kako obolijeva?

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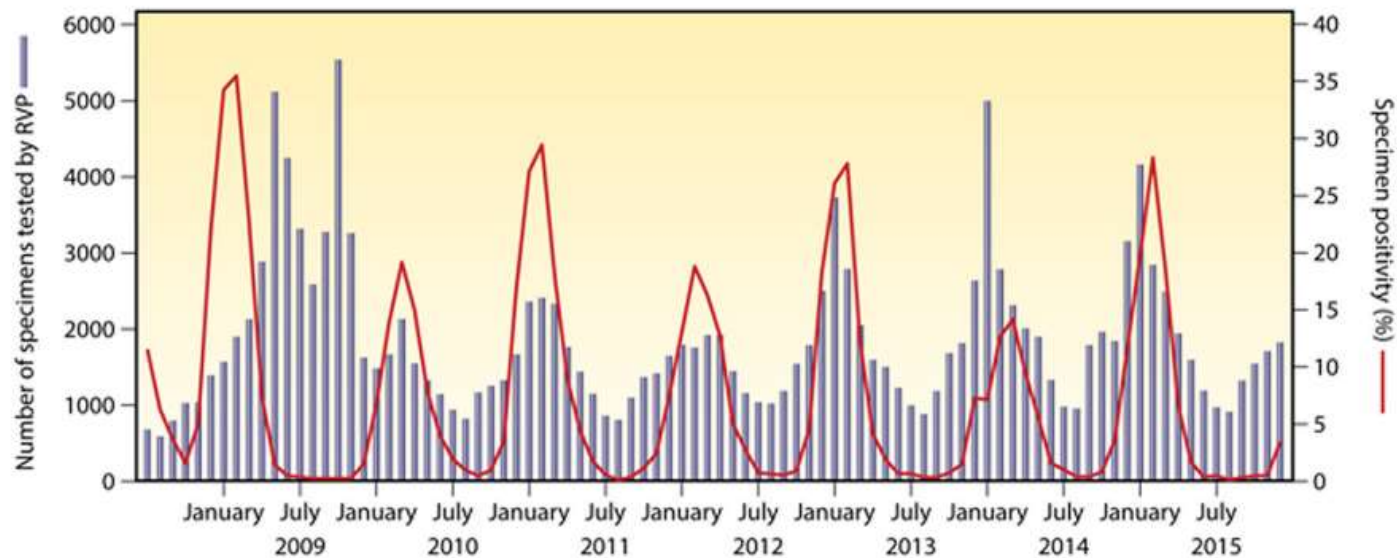
- ~ 33.1 M infekcija DDS
- ~ 3.2 M hospitaliziranih
- ~ 1.4 M hospitaliziranih su djeca mlađa od 6 mjeseci
- ~ 118 000 umrlih
  - ~ 45% su djeca mlađa od 6 mjeseci

Shi T. et al: Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. Lancet 2017;2;390(10098):946-958.





# Epidemiologija RSV infekcije (prepandemijska)

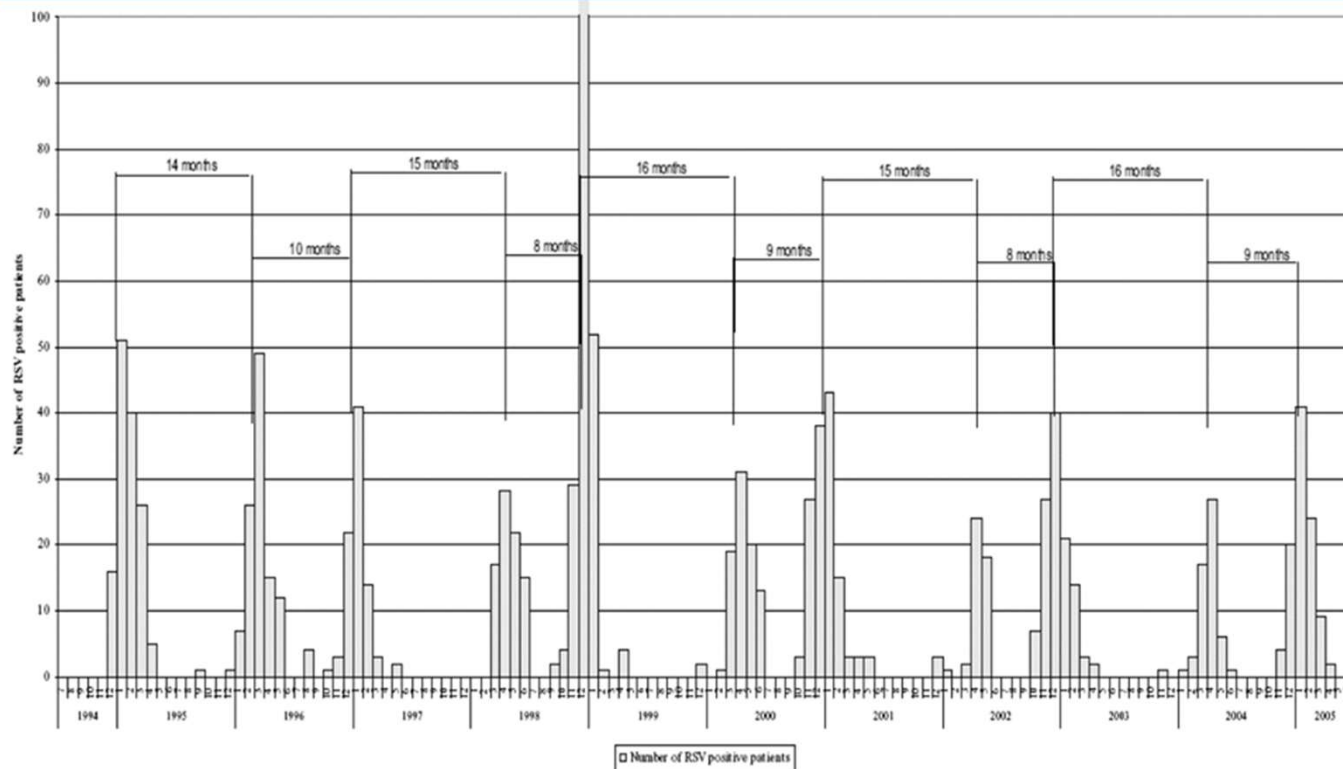


**FIG 5** Seasonality and positivity rate of RSV in Alberta, Canada, 2008 to 2015. The graph indicates RSV test-positive specimens and overall respiratory virus test volumes by Luminex RVP classic assay. Data show specimens that were influenza virus negative and do not account for mixed infections by RSV and other pathogens. Peak periods occur in winter and early spring, with positivity for RSV ranging from 15 to 35% of all specimens tested by RVP.

Griffiths C, Drews SJ, Marchant DJ. Respiratory syncytial virus: infection, detection, and new options for prevention and treatment. *Clin Microbiol Rev* 2017;30:277–319.



# Epidemiologija RSV infekcije (prepandemijska)

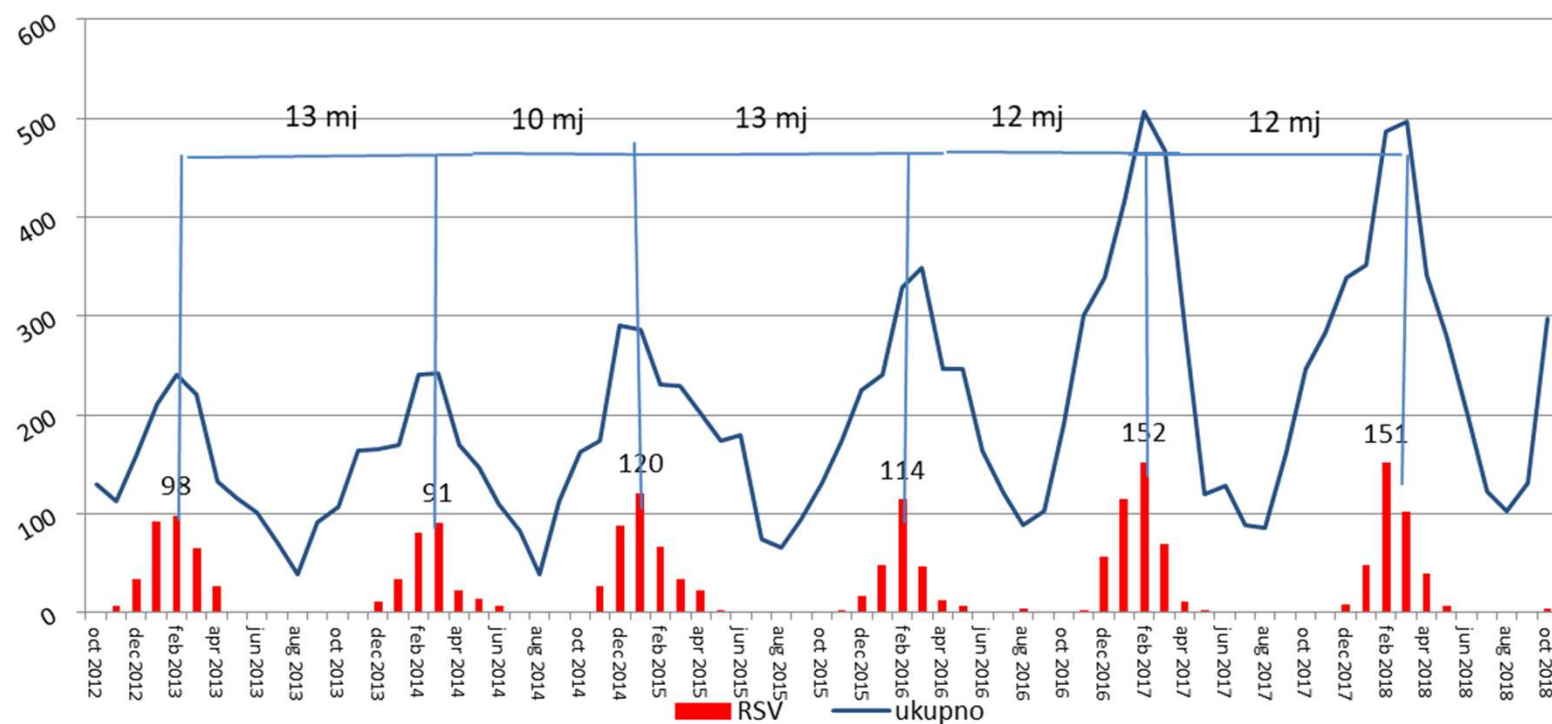


Seasonal occurrence of respiratory syncytial virus infections (number of cases) in Croatia (1994–2005).

Mlinaric-Galinovic G, Welliver RC, Vilibic-Cavlek T et al. The biennial cycle of respiratory syncytial virus outbreaks in Croatia. Virol J. 2008 Jan 28;5:18.



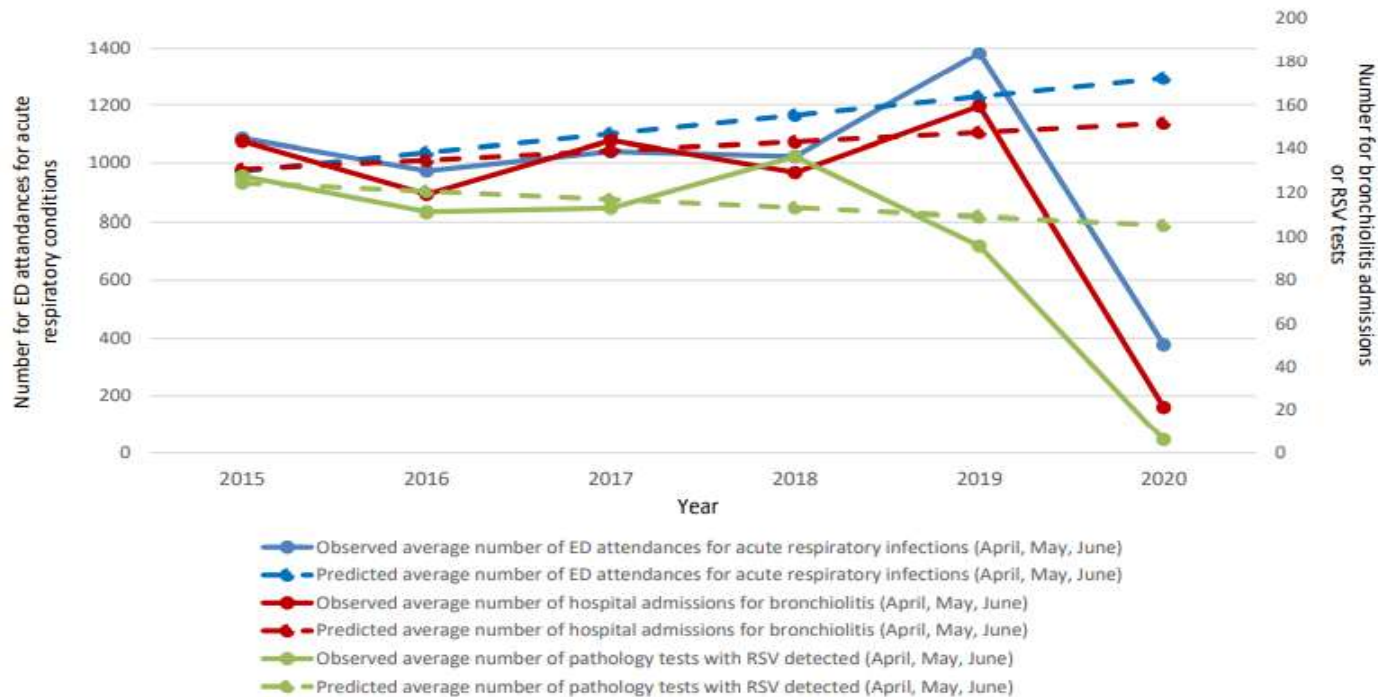
# Epidemiologija RSV infekcije (prepandemijska)



Slajd priredila Doc. Irena Tabain – HZJZ – Neobjavljeni podaci



# Kako je Covid-19 promijenio epidemiologiju RSV-a



Britton PN, Hu N, Saravanos V, et al. COVID-19 public health measures and respiratory syncytial virus. *Lancet Child Adolesc Health* 2020; published online September 18, 2020. Dostupno na: [https://doi.org/10.1016/S2352-4642\(20\)30307-2](https://doi.org/10.1016/S2352-4642(20)30307-2). Pristupljeno listopad, 2024.



# Kako je Covid-19 promijenio epidemiologiju RSV-a

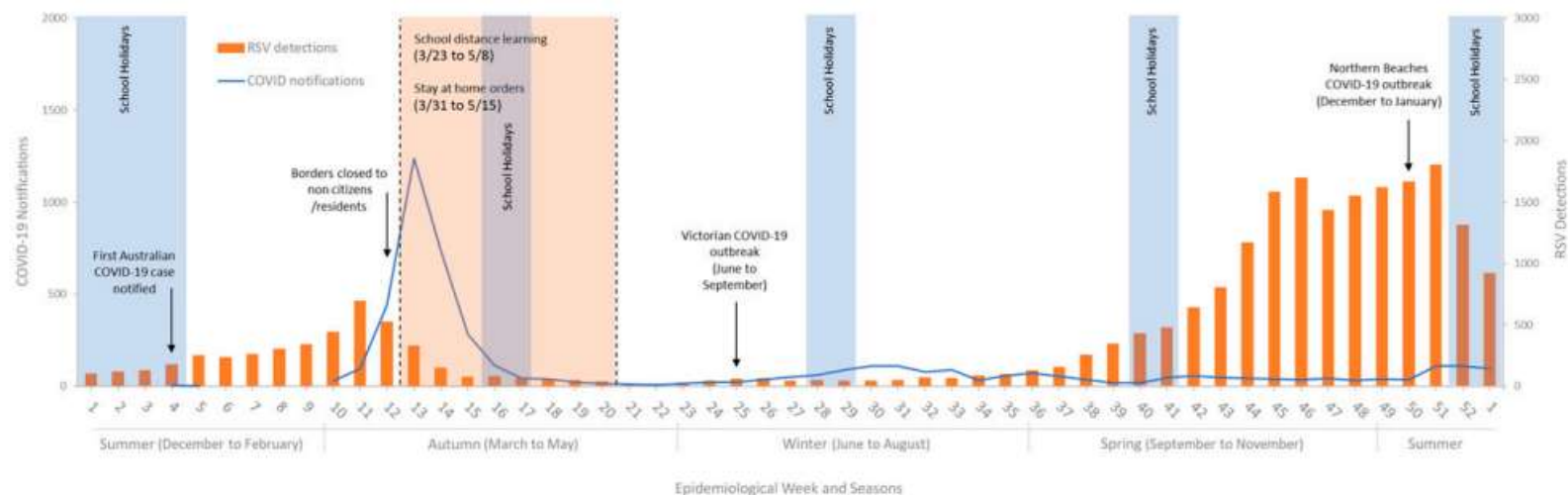
	Mean per day (95% CI*)			Mean difference, mean per day (95% CI)		Percent change 2020 with respect to 2018 and 2019 (95% CI)
	2018	2019	2020	2020 to 2018	2020 to 2019	
Infectious diseases						
Acute gastroenteritis	12.1 (9.3-15.7)	17 (13.1-22.1)	2.8 (1.9-4.2)	-9.2 (-12.6 to -5.9)	-16.6 (-18.8 to -9.6)	-89.2 (-92.5 to -84.3)
Upper respiratory tract infections	40.1 (31-51.8)	48.2 (37.3-62.2)	16.2 (12.5-21)	-23.9 (-35 to -12.8)	-32 (-45 to -18.9)	-63.9 (-73.7 to -50.5)
Lower respiratory tract infections	13.5 (10.4-17.6)	16.5 (12.7-21.3)	7.2 (5.4-9.7)	-6.3 (-10.4 to -2.2)	-9.2 (-14 to -4.4)	-58 (-69.7 to -41.7)
Lower respiratory tract infections requiring hospitalization	3.2 (2.4-4.2)	3.4 (2.5-4.5)	1.4 (1-2)	-1.7 (-2.8 to -0.7)	-1.9 (-3 to -0.8)	-55.7 (-69.9 to -34.9)
Sepsis and bacteremia	1.7 (1.1-2.6)	2.4 (1.8-3.3)	1.3 (0.6-2.5)	-0.4 (-1.5 to 0.6)	-1.1 (-2.3 to 0.01)	-81.2 (-89.3 to -67)
Varicella	1.6 (1.1-2.2)	1.8 (1.3-2.4)	0.2 (0.1-0.3)	-1.4 (-1.9 to -0.9)	-1.6 (-2.1 to -1)	-89.1 (-94.5 to -78.5)
Varicella requiring hospitalization	1.2 (0.4-3.9)	1.0 (0.3-4.0)	1.0 (0.1-15.9)	-0.2 (-3.3 to 2.9)	0 (-3.1 to 3.1)	-10 (-95.1 to 156)
Infectious mononucleosis	2.4 (1.8-3.4)	2.9 (2.1-3.9)	1.3 (0.6-2.8)	-1.0 (-2.4 to 0.2)	-1.5 (-2.8 to -0.2)	-49.9 (-77 to 9.2)
Exanthema subitum	1.3 (0.7-2.5)	1.5 (0.8-2.9)	1.0 (0.2-5.0)	-0.3 (-2.1 to 1.5)	-0.5 (-2.4 to 1.4)	-29.8 (-86.7 to 269.7)
Influenza	4.9 (3.7-6.5)	4.6 (3.5-6.1)	2.7 (2-3.6)	-2.3 (-3.9 to -0.7)	-1.9 (-3.4 to -0.4)	-44.3 (-60.9 to -20.6)
Influenza requiring hospitalization	0.2 (0.1-0.3)	0.2 (0.1-0.4)	0.1 (0.1-0.3)	-0.1 (-0.2 to 0.1)	-0.1 (-0.3 to 0.1)	-42.6 (-76.6 to 40)
Urinary tract infection	3.2 (2.4-4.4)	3.9 (2.9-5.1)	1.6 (1.2-2.2)	-1.7 (-2.7 to -0.6)	-2.3 (-3.5 to -1.1)	-55.3 (-69.4 to -34.6)
Urinary tract infection requiring hospitalization	0.8 (0.6-1.2)	0.8 (0.6-1.2)	0.4 (0.2-0.6)	-0.4 (-0.8 to -0.1)	-0.4 (-0.8 to -0.1)	-52.3 (-72.3 to -18)

Šokota A, et al. Croat Med J 2021;62:580-9.





# Što se dogodilo na kraju pandemije? (Nakon popuštanja epidemioloških mjera)



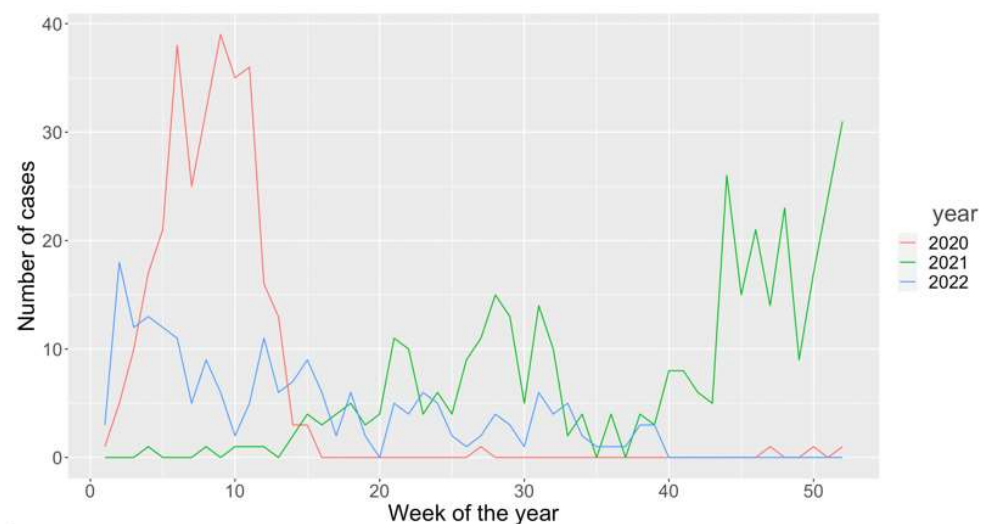
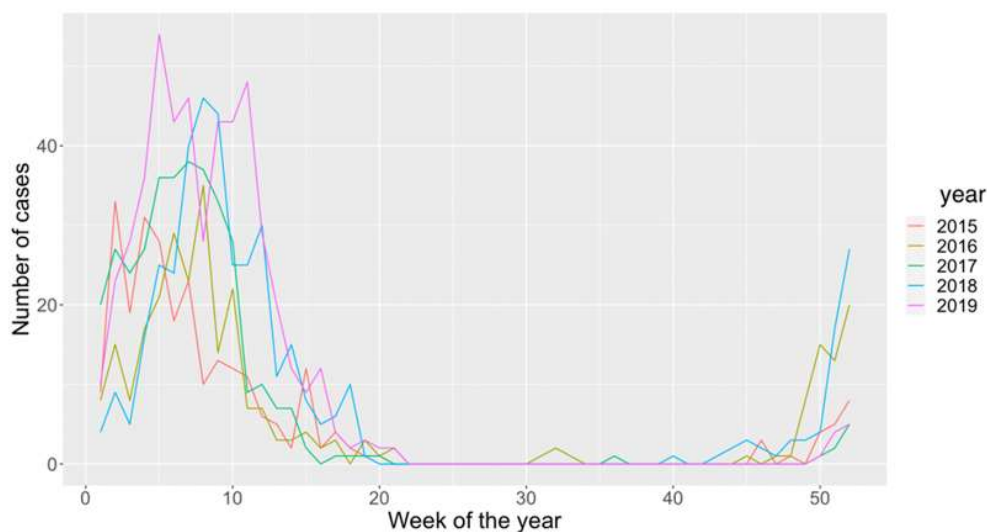
**FIGURE 1**

Timeline of COVID-19 notifications, RSV detections, and key events in NSW, 2020. Epidemiological weeks end on Saturday for COVID-19 notifications or Sunday for RSV detections. NSW Health–reported RSV detections include data from 14 NSW laboratories (public and private) and detections from one of the study site hospitals (Sydney Children’s Hospital at Randwick). RSV detection data were not reported from all laboratories for all weeks. Key events related to COVID-19 epidemiology, public health interventions, and NSW school holidays were derived from publicly available sources.<sup>14,15,17</sup>

Saravanos GL, Hu N, Homaira N, et al. RSV Epidemiology in Australia before and during COVID-19. *Pediatrics*. 2022;149(2):e2021053537



# Što se dogodilo na kraju pandemije? (Nakon popuštanja epidemioloških mjera)



Slajd pripremila Doc. Irena Tabain - HZJZ  
Neobjavljeni podaci, 2023.



# Kratki pregled predavanja

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- **Kako liječimo RSV bolest u djece**
- **Novosti u prevenciji (cijepljenje trudnica)**



	American Academy of Pediatrics (AAP) guidelines	The National Institute for Health and Care Excellence (NICE) guidelines
Albuterol or salbutamol (bronchodilator medication)	Strongly not recommended. Multiple trials have failed to show consistent benefit from $\alpha$ - or $\beta$ -agonist administration in pediatric patients with bronchiolitis. (2,22)	Not recommended. (21)
Epinephrine	Strongly not recommended. (2)	Not recommended. (21)
Systemic or inhaled corticosteroids	Strongly not recommended. No real effect was proven. (2)	Not recommended. (21)
Antibiotics	Not recommended. In the absence of specific evidence for concurrent bacterial infection, giving standard antibiotics to RSV infection patients is not recommended. (2,3)	Not recommended. (21)
Hypertonic saline	Not recommended in emergency settings. (2) Weakly recommends administration to patients with a hospital stay of longer than 3 days. However, 4 trials published after the publication of this guideline found no real benefit of using such therapy. (2,4)	Not recommended. (21)
Oxygen supplementation	Not recommended <u>when SpO<sub>2</sub> &gt; 90%. (2)</u>	<u>Recommended</u> <u>when SpO<sub>2</sub> &lt; 92%. (21)</u>
Nutrition and hydration	<u>Recommended</u> <u>for infants with bronchiolitis who cannot maintain hydration orally. (2)</u>	<u>Recommended</u> <u>for infants with bronchiolitis who cannot maintain hydration orally. (21)</u>

SpO<sub>2</sub>, peripheral capillary oxygen saturation

Xing Y, Proesmans M. New therapies for acute RSV infections: Where are we? Eur J Pediatr 2017;178:131-8.



# Kratki pregled predavanja

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- Epidemiologija RSV-a (promjene koje su se dogodile tijekom pandemije Covid-19 i u ranom post-pandemijskom razdoblju)
- Kako liječimo RSV bolest u djece
- **Novosti u prevenciji (cijepljenje trudnica)**

# Kod koga danas preveniramo RSV infekciju (PreP RSV infekcije u RH)

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1. nedonoščad
2. prirođene srčane greške
3. Sy. Down
4. kronična plućna bolest/cistična fibroza
5. (kronične) neurološke bolesti/stanja
6. imunodeficijencije

Nacionalni program seroprofilakse 2022.-2024.

Izvort: [https://zdravlje.gov.hr/UserDocsImages/2021Objave/Trogodi%C5%A1nji%20program\\_imunizacija%202022.-2024](https://zdravlje.gov.hr/UserDocsImages/2021Objave/Trogodi%C5%A1nji%20program_imunizacija%202022.-2024)



# Budućnost prevencije RSV u dojenčadi i male djece

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- **PreP za svu dojenčad (nova mAbs)**
- **Aktivna imunizacija trudnica**



**AAP Recommendations for the Prevention of RSV  
Disease in Infants and Children**

February 21, 2024



# Cjepiva protiv RSV

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AMERICAN JOURNAL OF EPIDEMIOLOGY  
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Vol. 89, No. 4  
*Printed in U.S.A.*

## FIELD EVALUATION OF A RESPIRATORY SYNCYTIAL VIRUS VACCINE AND A TRIVALENT PARAINFLUENZA VIRUS VACCINE IN A PEDIATRIC POPULATION<sup>1</sup>

JAMES CHIN, ROBERT L. MAGOFFIN, LOIS ANN SHEARER,  
JACK H. SCHIEBLE, AND EDWIN H. LENNETTE

(Received for publication August 8, 1968)



# Cjepiva protiv RSV

**TABLE 1** | RSV proteins in live attenuated or subunit vaccines.

Protein	Size aa	Functions related to vaccine design	Role in a live virus vaccine	Role in a subunit vaccine
NS1	139 aa	Inhibits type 1 interferon production to block host response to control infection	Attenuation when deleted or codon de-optimized	None
NS2	124 aa	Inhibits type 1 interferon production to block host response to control infection	Attenuation when deleted or codon de-optimized	None
Nucleoprotein (N)	391 aa	Nucleocapsid formation and T cell epitopes	Attenuation or temperature sensitivity when mutated	Induce T cell immunity
Phosphoprotein (P)	241 aa	Nucleocapsid formation, replication	Attenuation when codon pair de-optimized	Platform for RSV VLPs
Matrix protein (M)	256 aa	Envelop, virion assembly	Attenuation and temperature sensitivity when the gene start signal mutated	Induce T cell immunity and platform for RSV VLPs
Small hydrophobic (SH)	64 aa	Ion channel	Attenuation when deleted or codon pair de-optimized	Induce ADCC antibodies to decrease virus replication
G protein	292-319 aa	Attachment and immune modulation	Attenuation when deleted and improved safety and immunogenicity when mutated	Induce antibodies to inhibit virus replication by blocking binding to the cell surface receptors CX3CR1 and glycosaminoglycans and/or ADCC and to block virus-induced inflammation
F protein	574 aa	Attachment, entry, fusion	Attenuation when mutated or codon pair de-optimized and improved protective immunity and virus stability when mutated	Induce antibodies to inhibit virus replication by blocking fusion and possibly by ADCC
M2-1 protein	194 aa	Anti-termination factor during transcription	Attenuation when mutated	Induce T cell immunity, platform for RSV VLPs
M2-2 protein	90 aa	Switch from transcription to replication	Attenuation and enhanced immunity when deleted	None
L protein	2,165 aa	Viral polymerase	Attenuation when mutated or codon pair de-optimized	None

*Adapted with permission from Anderson (29).*

Boyoglu-Barnum S, Chirkova T and Anderson LJ. Biology of infection and disease pathogenesis to guide RSV vaccine development. *Front. Immunol.* 10:1675. doi: 10.3389/fimmu.2019.01675



# Cjepiva protiv RSV

The NEW ENGLAND JOURNAL of MEDICINE

## ORIGINAL ARTICLE

### RSV Prefusion F Protein–Based Maternal Vaccine — Preterm Birth and Other Outcomes

Ilse Dieussaert, I.R., Joon Hyung Kim, M.D., Sabine Luik, M.D.,  
Claudia Seidl, M.Sc., Wenji Pu, Ph.D., Jens-Ulrich Stegmann, M.D.,  
Geeta K. Swamy, M.D., Peggy Webster, M.D., and  
Philip R. Dormitzer, M.D., Ph.D.

N Engl J Med 2024;390:1009-21.  
DOI: 10.1056/NEJMoa2305478

## 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, E.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\*

N Engl J Med 2023;388:1451-64.  
DOI: 10.1056/NEJMoa2216480



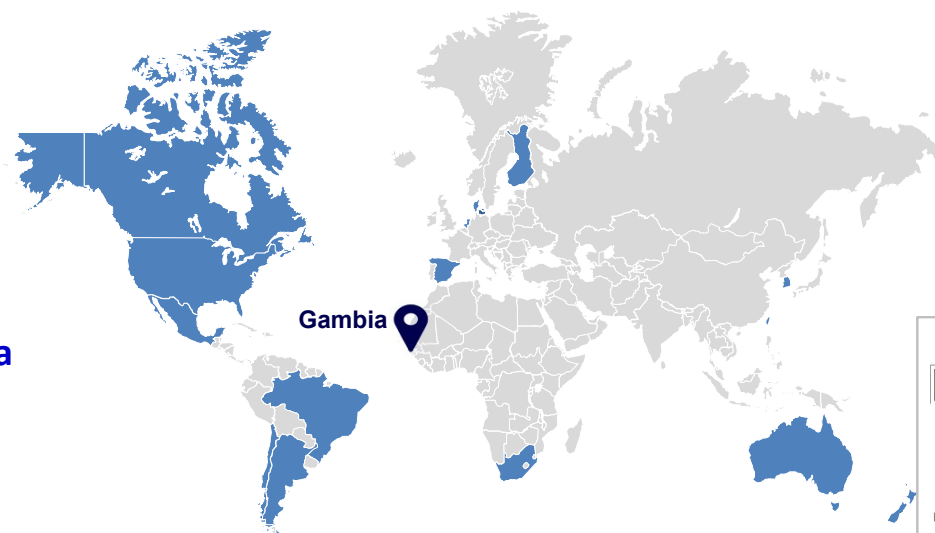
# MATISSE – faza 3 RSVpreF cjepivo u trudnoći<sup>1,2</sup>

## Faza 3, dvostruko slijepo RCT: RSVpreF 120 µg ili placebo

- Trudnice između 24 i 36 tjedana gestacije

## Primarni ishodi praćeni do 180 dana nakon poroda:

- **Teški oblici** MA RSV-LRTIs u novorođenčadi
- MA RSV-LRTIs u novorođenčadi



**18 zemalja**

**2 godine, 4 sezone**

**7420 trudnica**

**7307 novorođenčadi**

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

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

B. Kampmann, S.A. Madhi, I. Munjal, E.A.F. Simões, B.A. Pahud, C. Ulapur, 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\*

LRTI, lower respiratory tract infection; MA, medically attended; preF, prefusion F; RCT, randomized controlled trial; RSV, respiratory syncytial virus

1. Kampmann B et al. N Engl J Med 2023;388:1451-1464; 2. Munjal I. Oral presentation at RSVVW'24, February 15, 2024, Mumbai, India. Dostupno na: <https://drive.google.com/drive/folders/1I5jugJOvg2tqItokMNHdPhKGEHYSQnwX>; CC-7



# MATISSE faza 3 cijepljenje u trudnoći: konačni podaci

## Total



## Trudnice:

## Sigurnost 6 mjeseci nakon poroda

7386

(+29 više nego u prim. analizi)



## Novorođenčad:

## Sigurnost i respiratorno praćenje do 2. godine

7307

(+181 više nego u prim. analizi)

Jun  
2020

Sep  
2022

Oct  
2023

## Primarna analiza:

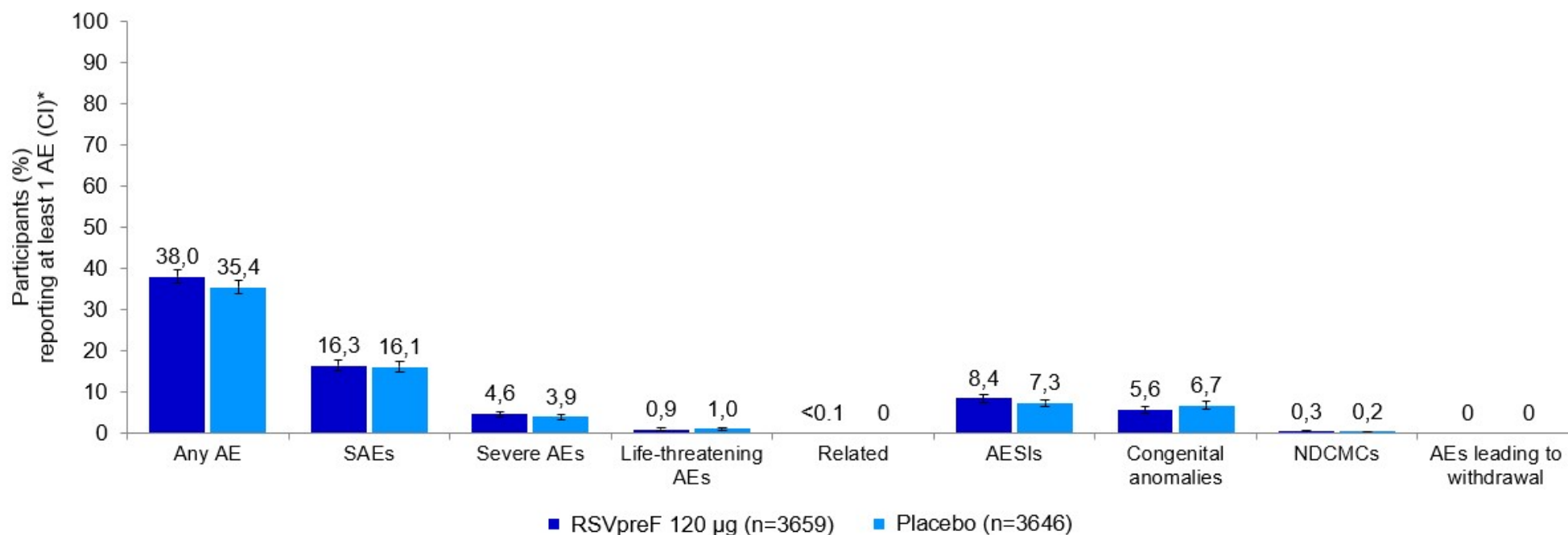
## June 2020 – September 2022

## Završna analiza:

## June 2020 – October 2023

# AEs u novorođenčadi bile su usporedive između RSVpreF i placebo grupe

Novorođenčad: AEs unutar 1 mjesec nakon rođenja



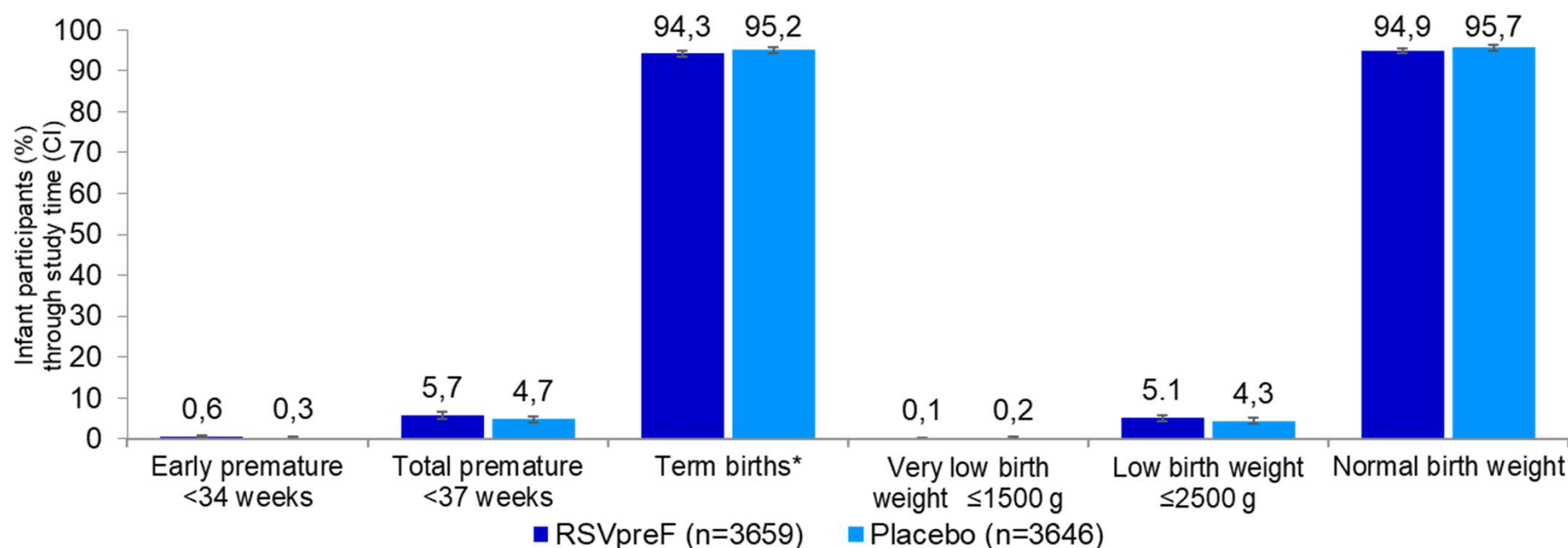
The severity of the event is determined by the investigator

\*Exact 2-sided CI calculated using the Clopper–Pearson method

AE, adverse event; AESI, adverse event of special interest; CI, confidence interval; NDCMC, newly diagnosed chronic medical condition; preF, prefusion F; RSV, respiratory syncytial virus; SAE, serious adverse event  
Munjali I. Oral presentation at RSVVW'24, February 15, 2024, Mumbai, India. Dostupno na: <https://drive.google.com/drive/folders/1I5jugIOyg2qItokMNHdPhKGEHYSQnwx>; CC-13

# Ishodi trudnoća bili su usporedivi između RSVpreF i placebo grupe

Novorođenčad: unutar 1 mjesec nakon rođenja






\*Term births: infants born ≥37 weeks

CI, confidence interval; preF, perfusion F; RSV, respiratory syncytial virus

Munjali I. Oral presentation at RSVVW'24, February 15, 2024, Mumbai, India. Dostupno na: <https://drive.google.com/drive/folders/1I5jugIOyg2tqItokMNHDPkGEHYSQnwx>; CC-14

# Ukupne smrti novorođenčadi i po kategoriji

Događaj	RSVpreF 120 µg (n=3659) n	Placebo (n=3646) n	Relativni rizik (CI)
Ukupno smrti novorođenčadi, svi uzroci (n=22)	8	14	0.57 (0.24, 1.36)
 <b>Uzrokovane RSV-om</b>	0	1	-
 <b>Smrti prematurusa</b> (<37 tjedana pri rođenju)	1*	2	0.50 (0.05, 5.49)
 <b>Neonatalne smrti</b> (<30 dana nakon rođenja)	3*	5	0.60 (0.14, 2.50)

\*A single pre-term infant died in the neonatal (<30 days) period. The infant was in the RSVpreF group and from South Africa. The infant is represented in both subcategories: pre-term and neonatal  
 CI, confidence interval; preF, prefusion F; RSV, respiratory syncytial virus  
 Munjal I. Oral presentation at RSVVW'24, February 15, 2024, Mumbai, India. Dostupno na: <https://drive.google.com/drive/folders/1I5jugIOyg2tqItokMNHDPkHkGEHYSQnwX>; CC-18

# Visoka učinkovitost protiv MA RSV-LRTIs

Podaci u skladu s podacima iz primarne analize<sup>1</sup>

Trudnice iz RSVpreF grupe

Primarna analiza <sup>1</sup>	Vremenski interval	90 dana nakon rođenja	120 dana nakon rođenja	150 dana nakon rođenja	180 dana nakon rođenja
	RSVpreF 120 µg (n=3495), n	6	12	16	19
	Placebo (n=3480), n	33	46	55	62
	Učinkovitost (CI*)	81.8% (40.6, 96.3)	73.9% (45.6, 88.8)	70.9% (44.5, 85.9)	69.4% (44.3, 84.1)

Krajnja točka primarne učinkovitosti ispunila je kriterije licenciranja donje granice >20%

Završna analiza <sup>2</sup>	Vremenski interval	0–90 dana nakon rođenja	0–180 dana nakon rođenja
	RSVpreF 120 µg (n=3585), n (%)	6 (0.2)	21 (0.6)
	Placebo (n=3563), n (%)	34 (1.0)	70 (2.0)
	Učinkovitost (95% CI)	82.4% (57.5, 93.9)	70.0% (50.6, 82.5)

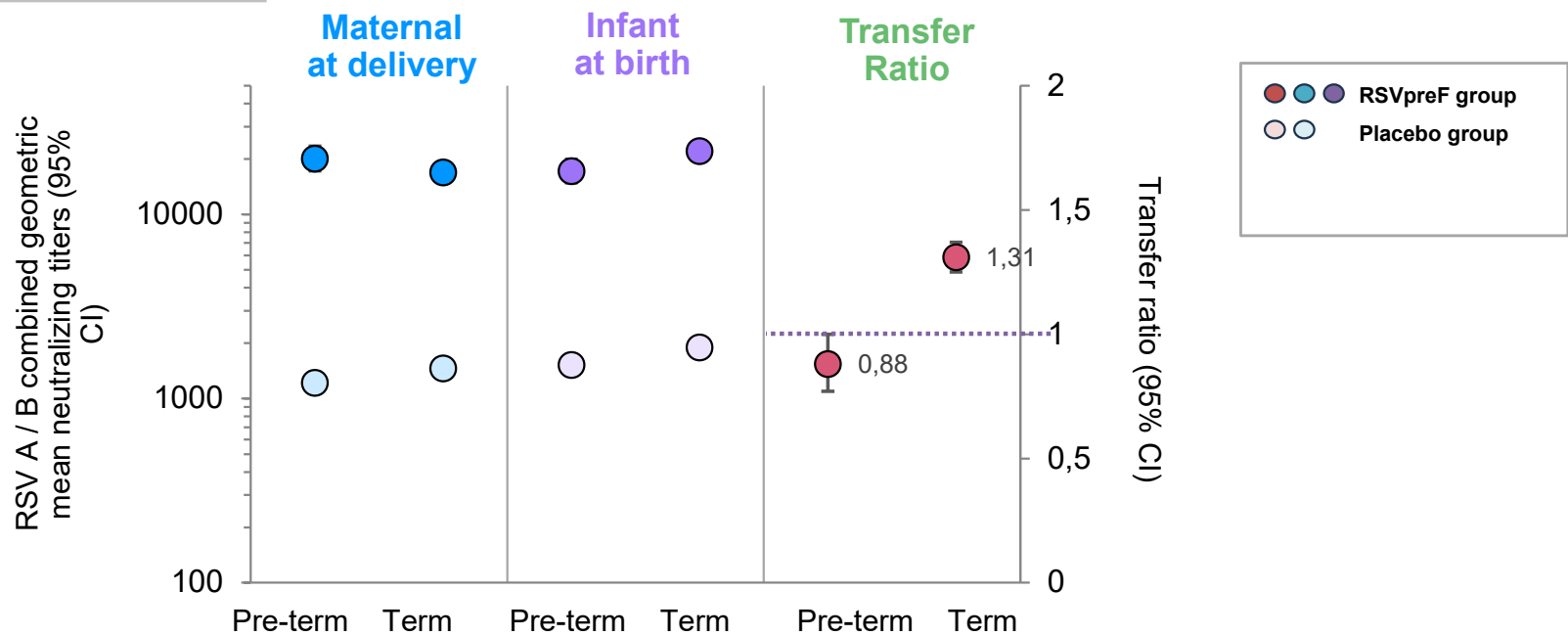
\*99.5% CI for 90 days, 97.58% CI for 120, 150, and 180 days. CI lower bound >20% for all time points. Bonferroni procedure and accounting for the primary endpoint results  
CI, confidence interval; LRTI, lower respiratory tract infection; MA, medically attended; preF, prefusion F; RSV, respiratory syncytial virus

1. Kampmann B et al. N Engl J Med 2023;388:1451-1464; 2. Munjal I. Oral presentation at RSVVW'24, February 15, 2024, Mumbai, India. Dostupno na: <https://drive.google.com/drive/folders/1I5jugJOvg2tqItokMNHdPhkGEHYSQnwx>; CC-23

# Visoki RSV neutralizirajući titar u prijevremeno rođene djece unatoč skraćenom transplacentarnom prijenosu

Subgrupe (prematurusi) prema gestacijskoj dobi pri porodu (N=379)\*

24–<28 weeks	N=2
28–<34 weeks	N=32
34–<37 weeks	N=345



\*331 evaluable available for immunogenicity analysis

CI, confidence interval; preF, prefusion F; RSV, respiratory syncytial virus

1. Kampmann B et al. Safety and immunogenicity of bivalent prefusion vaccines administered during pregnancy to prevent infant RSV. Oral presentation at INMIS Conference, March 12, 2024. Dostupno na: <https://www.inmis.org/index.php?p=program>

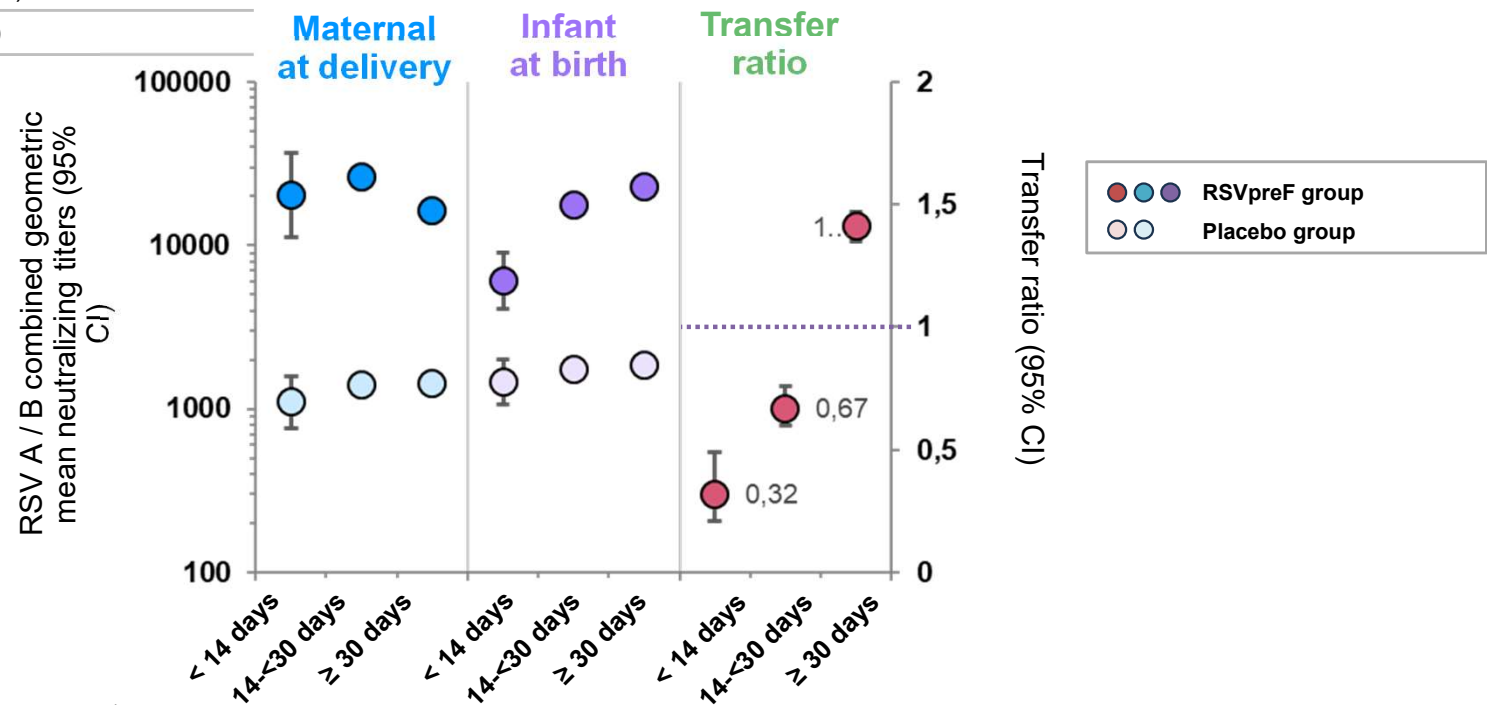
# Cijepljenje trudnice >14 dana prije poroda podržava optimalan RSV neutralizirajući titar u novorođenčeta

Podgrupe prema vremenu od cijepljenja do poroda\*

<14 days (N=32)

14–<30 days (N=147)

≥30 days (N=931)



\*From convenience sample

CI, confidence interval; preF, prefusion F; RSV, respiratory syncytial virus

1. Kampmann B et al. Safety and immunogenicity of bivalent prefusion vaccines administered during pregnancy to prevent infant RSV. Oral presentation at INMIS Conference, March 12, 2024. Dostupno na:

<https://www.inmis.org/index.php?p=program>

# MATISSE rezultati završne analize

Podaci tijekom razdoblja s duljim trajanjem praćenja dojenčadi su u velikoj mjeri u skladu s primarnom analizom



## Pozadina

- Primarna analiza (listopad 2022.) bila je osnova za registraciju cjepiva u SAD-u i EU i uključivala je 97% sudionika
- Studija je zaključena u listopadu 2023. s uključanjem podataka o dojenčadi iz druge godine praćenja te potpunim podacima o maternalnim ishodima



## Top-line rezultati

- Završna analiza učinkovitosti u skladu je s primarnom analizom
  - RSVpreF je **82.4%** učinkovit za **teške** MA RSV-LRTI unutar **90 dana** nakon rođenja; učinkovitost od **70.0%** uočena je tijekom **180 dana** nakon poroda
  - RSVpreF je **57.6%** učinkovit u smanjenju učestalosti MA RSV-LRTI u dojenčadi u roku od **90 dana** nakon rođenja; učinkovitost od **49,2%** uočena je tijekom **180 dana** nakon rođenja
- RSVpreF je bio siguran i dobro podnošljiv od strane majki, a kod dojenčadi tijekom praćenja 24 mjeseca nakon rođenja nisu otkriveni sigurnosni signali
  - Dodatnih 9 prijevremenih poroda (6 RSVpreF, 3 placebo) uključeno je u završnu analizu, pri čemu je ukupni relativni rizik (1,2 [95% CI 0,98, 1,46]) nepromijenjen u odnosu na privremenu (interim) analizu; dojenčad je ukupno imala dobre ishode unutar 2 godine praćenja

CI, confidence interval; LRTI, lower respiratory tract infection; MA, medically attended; preF, prefusion F; RSV, respiratory syncytial virus

Munjal I. Oral presentation at RSVVW'24, February 15, 2024, Mumbai, India. Dostupno na: <https://drive.google.com/drive/folders/1I5jugJOyg2tqItokMNhDpHkGEHYSQnwx>



**Use of the Pfizer Respiratory Syncytial Virus Vaccine During Pregnancy for the Prevention of Respiratory Syncytial Virus–Associated Lower Respiratory Tract Disease in Infants: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023**

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## Summary

### What is already known about this topic?

Nirsevimab is recommended in infants to prevent respiratory syncytial virus (RSV)-associated lower respiratory tract infection (LRTI). In August 2023, the Food and Drug Administration approved Pfizer RSV vaccine for pregnant persons at 32–36 weeks' gestation to prevent RSV-associated LRTI in infants aged <6 months.

### What is added by this report?

On September 22, 2023, CDC's Advisory Committee on Immunization Practices 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.

### What are the implications for public health practice?

CDC recommends protecting all infants against RSV-associated LRTI through use of either the maternal RSV vaccine or infant receipt of nirsevimab.



**TABLE 1. Effect estimates for the Pfizer maternal RSVpreF vaccine for the trial dosing interval and the approved dosing interval**

Outcome	VE or RR (CI)*	
	Trial dosing interval (24–36 weeks' gestation) <sup>†</sup>	Approved dosing interval (32–36 weeks' gestation) <sup>§</sup>
<b>Benefits (efficacy against outcome), (VE) assessed at age 0–180 days</b>		
Medically attended RSV-associated LRTI in infants	51.3 (29.4 to 66.8) <sup>¶</sup>	57.3 (29.8 to 74.7)
Severe medically attended RSV-associated LRTI in infants**	69.4 (44.3 to 84.1) <sup>¶</sup>	76.5 (41.3 to 92.1)
Hospitalization for RSV-associated LRTI	56.8 (10.1 to 80.7) <sup>††</sup>	48.2 (–22.9 to 79.6)
Intensive care unit admission from RSV hospitalization in infants	42.9 (–124.8 to 87.7)	One event in the vaccine group Two events in the placebo group
Mechanical ventilation from RSV hospitalization in infants	100 (–9.1 to 100)	Zero events in the vaccine group Two events in the placebo group
All-cause medically attended LRTI in infants	2.5 (–17.9 to 19.4) <sup>††</sup>	7.3 (–15.7 to 25.7)
All-cause hospitalization for LRTI in infants	28.9 (–2.0 to 50.8)	34.7 (–18.8 to 64.9)
<b>Harms (RR)<sup>§§</sup></b>		
Serious adverse events in pregnant persons <sup>¶¶</sup>	1.06 (0.95 to 1.17)	1.02 (0.87 to 1.20)
Reactogenicity (grade 3 or higher systemic reactions) in pregnant persons***	0.97 (0.72 to 1.31)	0.98 (0.62 to 1.54)
Serious adverse events in infants <sup>†††</sup>	1.01 (0.91 to 1.11)	1.04 (0.90 to 1.20)
Preterm birth (<37 weeks' gestational age)	1.20 (0.99 to 1.46)	1.15 (0.82 to 1.61)

**Abbreviations:** GRADE = Grading of Recommendations, Assessments, Development, and Evaluations; LRTI = lower respiratory tract infection; RR = relative risk; RSV = respiratory syncytial virus; VE = vaccine efficacy.

\* 95% CI unless otherwise noted. When 95% CI not used, the CI was adjusted using the Bonferroni procedure, accounting for the primary endpoints' results.

<sup>†</sup> Vaccine efficacy was calculated as  $(1 - [P / (1 - P)]) \times 100\%$ , where P is the number of cases in the RSVpreF group divided by the total number of cases.

<sup>§</sup> Vaccine efficacy was calculated as  $(1 - [hP / (1 - P)]) \times 100\%$ , where P is the number of cases in the RSVpreF group divided by the total number of cases and h is the ratio of number of participants at risk in the placebo group to the number of participants at risk in the RSVpreF group.

<sup>¶</sup> 97.58% CI.

\*\* Severe medically attended RSV-associated LRTI was a co-primary endpoint of the phase 3 clinical trial. This outcome was not included by CDC's Advisory Committee on Immunization Practices RSV Vaccines Pediatric/Maternal Work Group as an a priori GRADE outcome critical or important to vaccine policy decision making.

<sup>††</sup> 99.17% CI.

<sup>§§</sup> Pooled RR estimates were independently calculated using counts of events and participants in the phase 3 trial interim analysis and phase 2b trial among those who received the phase 3 vaccine formulation.

<sup>¶¶</sup> Serious adverse events in pregnant persons were collected through 6 months after delivery.

\*\*\* Up to 7 days after injection. When selecting the a priori harm outcomes, CDC's Advisory Committee on Immunization Practices RSV Vaccines Pediatric/Maternal Work Group defined reactogenicity as both local and systemic reactions. These data only reflect systemic reactions.

<sup>†††</sup> Serious adverse events in infants were collected through 6 months after delivery.



# Zaključci

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- RSV infekcija i dalje predstavlja značajan javnozdravstveni problem
- Pandemija Covid-19 (privremeno) je promijenila sezonalnost RSV infekcija
- Trenutačne terapijske opcije su skromne
- Trenutačna PreP mogla bi se osuvremeniti novim pripravcima i novim preventivnim opcijama (cjepivima)



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# Knowledge and attitudes of pregnant women on maternal immunization against COVID-19 in Croatia

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published online August 22, 2022

**Results:** A total of 430 women participated in the study. Only 16% of women expressed their willingness to be vaccinated against COVID-19 if offered, despite that 71% of them believe that COVID-19 might be a serious illness in pregnant women. The most important obstacle in having better acceptance of the vaccines is in the assumption that the vaccines are not safe for pregnant women (73%) or the fetus (75%), or that the vaccines are not effective (41%). The relationship exists between acceptance of vaccination in general and willingness to get other vaccines in pregnancy and readiness to be vaccinated against COVID-19 in pregnancy. Only one out of 55 women who were not adherent to the current vaccination recommendations in Croatia would accept the COVID-19 vaccine during pregnancy if offered. 21 (5%) women stated that vaccination against influenza and pertussis during pregnancy is necessary and 13 (62%) of them would get vaccinated against COVID-19 if offered.

