Cold, Flu, and Beyond
: The Viral Landscape of Asthma

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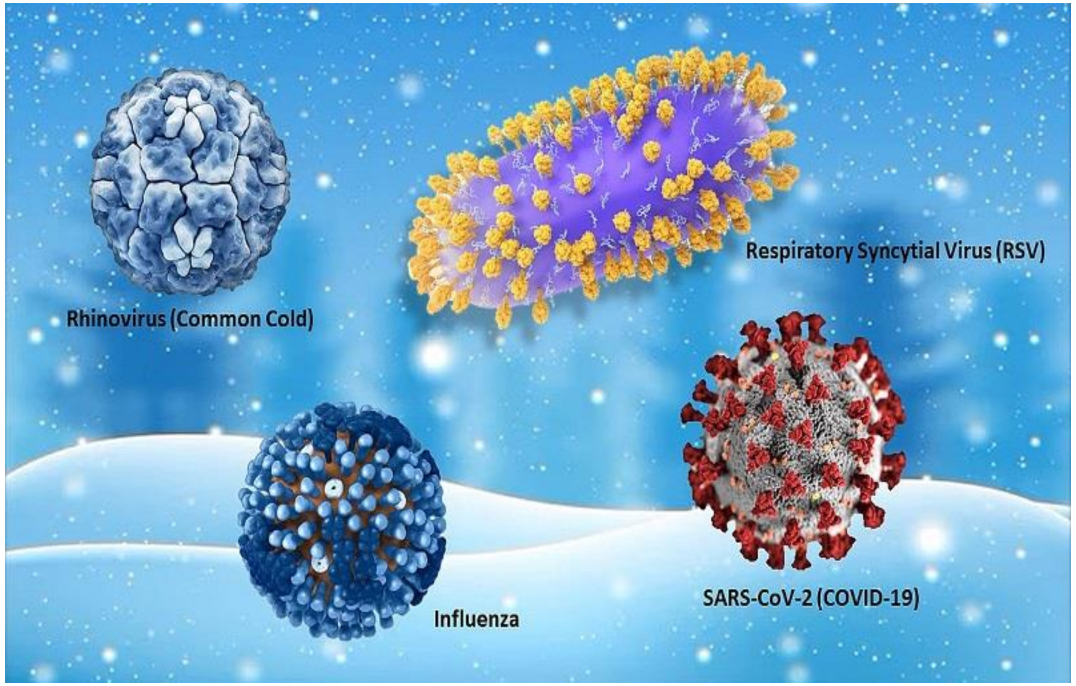
Today's Table

- Respiratory Virus
- Viral Infection and Asthma
  - Early-life Exposure
  - Exacerbation
  - Immunologic Landscape
  - Seasonality
- What should we do?

Respiratory Virus

Cold, Flu, and Respiratory Virus

- **Cold**
  - **'cald': 차가운 (고대영어)**
  - **'kaldaz': 차갑게하다 (게르만어)**
  - **'kalt': 차가운 (독일어)**
- **Flu**
  - **'influentia': 영향**
  - **L'influenza degli astir: 별의 영향→ 신체 건강**
  - **Influenza (of cold) → "Flu"**



- **감기: Common cold, catch a cold etc. → Infection of Respiratory Virus**

https://www.hopkinsmedicine.org/news/newsroom/news-releases/2025/01/know-your-respiratory-virus-enemies-this-season

Respiratory Virus and Transmission

Table 1 | **Transmissibility of, modes of transmission of and transmission-based precautions for common respiratory viruses in humans**

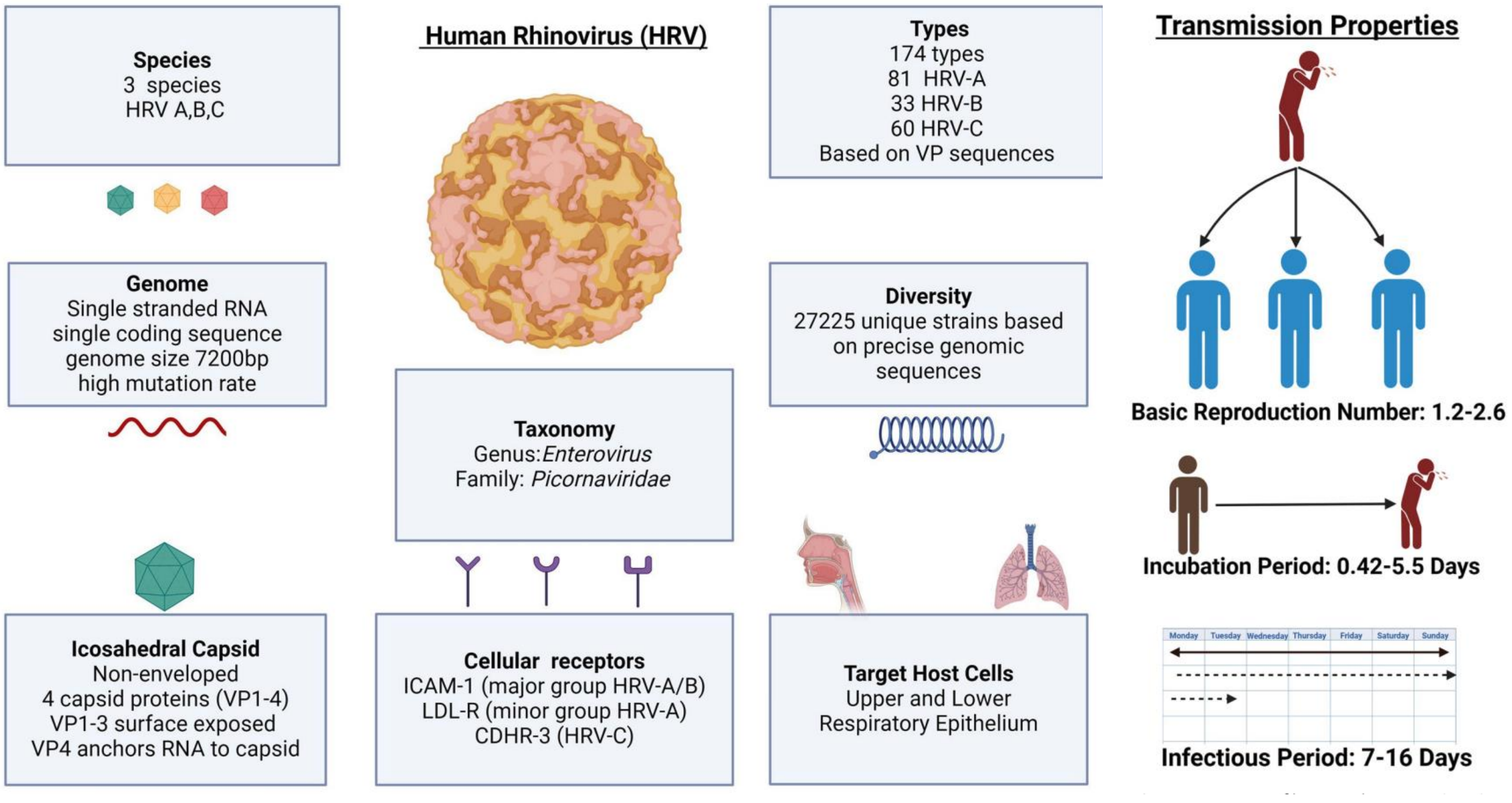
Transmissibility and transmission	**HCoV**	**IV**	**MeV**	**PIV**	**RSV**	**HMPV**	**VZV**	**RhV**	**HAdV**[a]
Transmissibility[b]									
Basic reproduction number (R_0)	0.5–8.0	1.0–21.0	1.4–770	2.3–2.7	0.9–21.9	–	1.2–16.9	1.2–2.7	2.3–5.1
Household SAR (%)	0–38.2	1.4–38.0	52.0–84.6	36.0–67.0	11.6–39.3	–	61.0–78.1	28.0–58.0	–

- **R_0 = 2**라면 → 1명이 2명을 감염시킴 → 전파 확산
- **R_0 < 1**이면 → 감염이 자연적으로 소멸함
- **R_0 > 1**이면 → 유행 가능성 있음

Household SAR (Secondary Attack Rate)
= 가정 내에서 첫 번째 감염자로부터 **같은 공간에 있는 가족 구성원에게 2차 감염이 발생한 비율**

Nat Rev Microbiol **19**, 528–545 (2021)

Rhinovirus


Species
3 species
HRV A,B,C
Genome
Single stranded RNA
single coding sequence
genome size 7200bp
high mutation rate
Icosahedral Capsid
Non-enveloped
4 capsid proteins (VP1-4)
VP1-3 surface exposed
VP4 anchors RNA to capsid
Human Rhinovirus (HRV)
Taxonomy
Genus: *Enterovirus*
Family: *Picornaviridae*
Cellular receptors
ICAM-1 (major group HRV-A/B)
LDL-R (minor group HRV-A)
CDHR-3 (HRV-C)
Types
174 types
81 HRV-A
33 HRV-B
60 HRV-C
Based on VP sequences
Diversity
27225 unique strains based on precise genomic sequences
Target Host Cells
Upper and Lower Respiratory Epithelium
Transmission Properties
Basic Reproduction Number: 1.2-2.6
Incubation Period: 0.42-5.5 Days
Monday
Tuesday
Wednesday
Thursday
Friday
Saturday
Sunday
Infectious Period: 7-16 Days

Most Common Pathogen, Wheeze

Table 2 Overview of HRV in Lower Respiratory Infections (LRI) Within Community and Primary Care Settings

Community/primary care studies highlighting prevalence of HRV LRI to LRI caused by other viruses

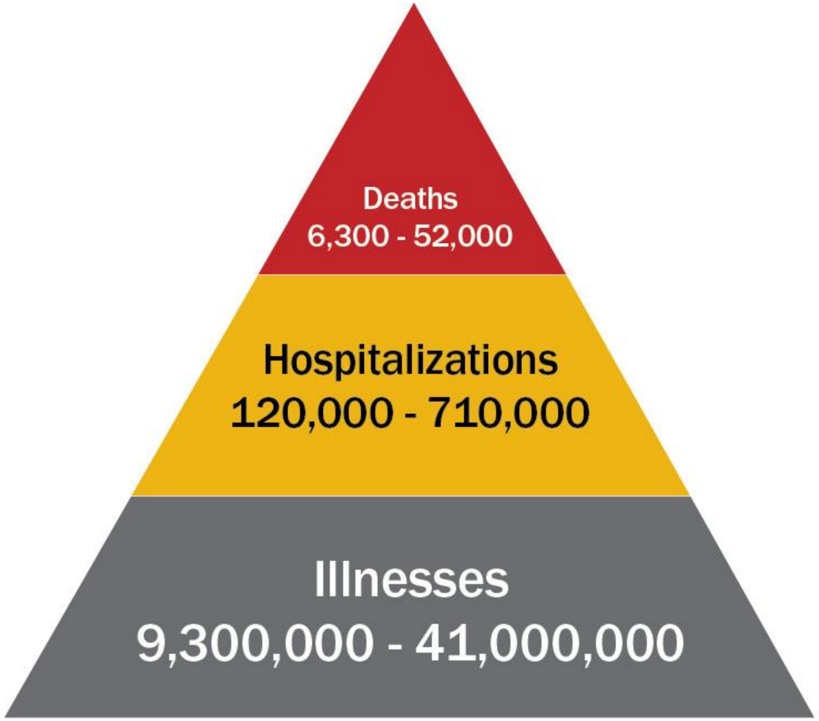
Authors/year	Patient population	HRV % Detection in RVIs and rank	% of Other common RVIs	Key points
Vos et al. [122]	Adults with acute cough/LRI,	39.7% HRV (Most common virus)	Influenza (13.6%), RSV (9.5%)	HRV associated with more severe symptoms particularly severe wheezing vs virus negative LRI
Ieven et al. [118]	Adults with LRI	20.4% HRV (Most common virus)	Influenza (9.9%), Coronavirus (7.4%)	HRV detected 14.2% of adult pneumonia cases in primary care
Falsey et al. [123]	Elderly adults (≥ 65 years) with moderate-to-severe ILI	25.6% HRV (2.nd most common virus)	Influenza A (18.7%), RSV (7.4%)	14.6% of adults over 65 with HRV LRI ultimately required hospitalisation

Community/primary care studies specific HRV LRI

Authors/year	Patient population	% HRV detected in all LRI	HRV Species data (symptomatic patients)	Common comorbidities
Zlateva et al. [61]	Adults with acute cough/LRI	19%	HRV-A (68%), HRV-B (12%), HRV-C (20%)	Asthma (12%), COPD (7%), Allergic diseases (23%), Cardiac disease (8%), Diabetes (6%)
Zlateva et al. [98]	Adults with acute cough/LRI	18%	HRV-A (51%), HRV-C (7%), HRV-C (42%)	COPD (29%), Asthma (24%), Allergic disease (29%), Cardiovascular disease (8%)

Influenza virus

- 외피 RNA 바이러스
- Influenza A: H1-18 + N1-11 아형
- Influenza B: B/Victoria, B/Yamagata
- Transmission: Droplet, air borne
- Tx: Oseltamivir, Peramivir, Baloxavir



2010~2024

WHO, CDC

Preliminary 2024–2025 U.S. Flu In-Season Disease Burden Estimates

Since October 1, 2024, CDC estimates there have been between:

47 Million - 82 Million	21 Million - 37 Million	610,000 - 1.3 Million	27,000 - 130,000
Flu Illnesses	**Flu Medical Visits**	**Flu Hospitalizations**	**Flu Deaths**

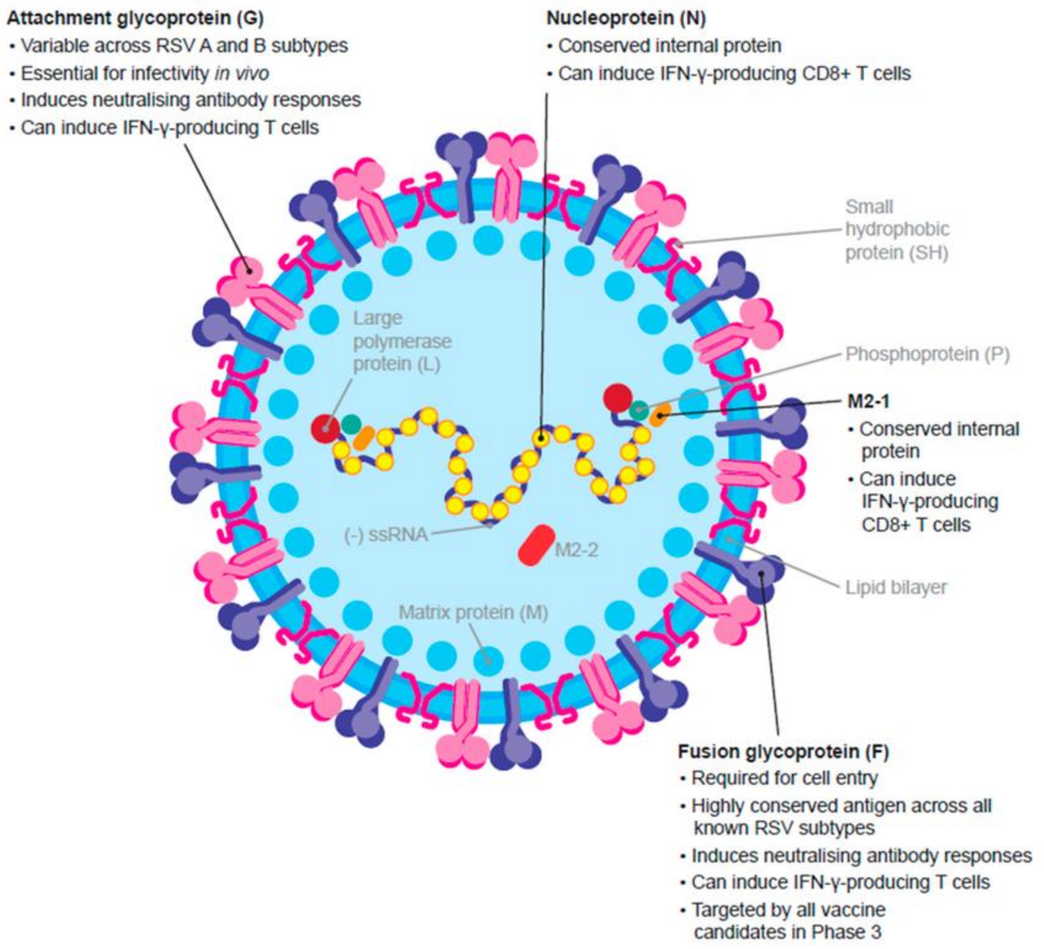
Based on data from October 1, 2024, through May 17, 2025

Because influenza surveillance does not capture all cases of flu, CDC provides these estimated ranges to better reflect the full burden of flu in the United States. These estimates are calculated using a mathematical model based on CDC's weekly influenza surveillance data and are preliminary and are updated weekly throughout the season.

FluVIEW CDC

Respiratory Syncytial Virus, RSV

- **Pneumoviridae 과 Mononegavirales 목 Orthopneumovirus속**
- **단일가닥 비분절 음성센스 RNA 바이러스**
- **바이러스 진입과 함께 합포체 (syncytium)을 형성**
- **RSV A, RSV B subtype**



Vaccines **2023**, *11*(2), 382

RSV - Disease Burden

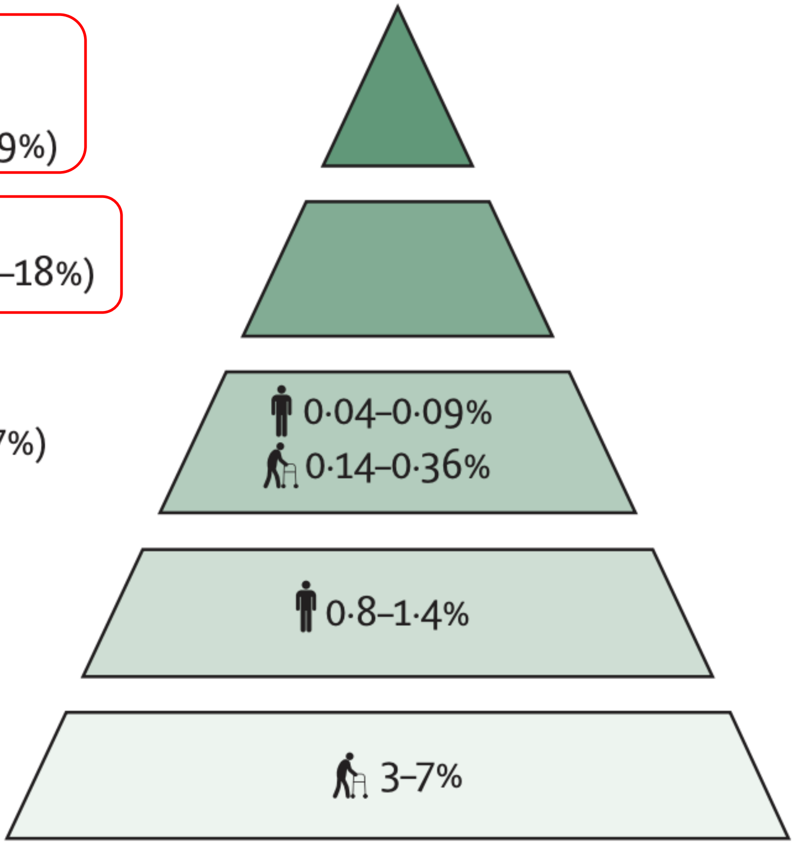
RSV mortality
- Among all adults hospitalised with RTI: 0·2–0·6%
- Among all adults hospitalised with RSV RTI: 1–12% (older adults 6–9%)

RSV admission to ICU
- Among all adults hospitalised with RSV RTI: 6–15% (older adults 11–18%)

RSV admission to hospital
- Among all adults hospitalised with RTI: 4–11% (older adults 2·6–6·7%)
- Among medically attended older adults with RSV infection: 12%

Medically attended RSV infection
- Among older adults with RSV infection: 17–28%

Symptomatic RSV infection (community)
- Among all adults at high risk for severe RSV infection: 4–10%



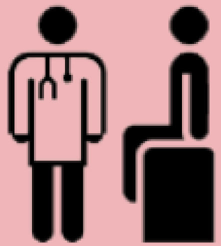
Adults (≥18 years)
Older adults (≥60 years or ≥65 years, depending on study)

Lancet Respir Med 2024;12:822-36

Preliminary 2024-2025 U.S. RSV Burden Estimates

CDC estimates* that, from October 1, 2024 through December 7, 2024, there have been:

470,000-950,000

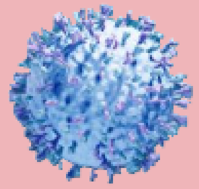


RSV Outpatient Visits

22,000-45,000

RSV Hospitalizations

980-2,300



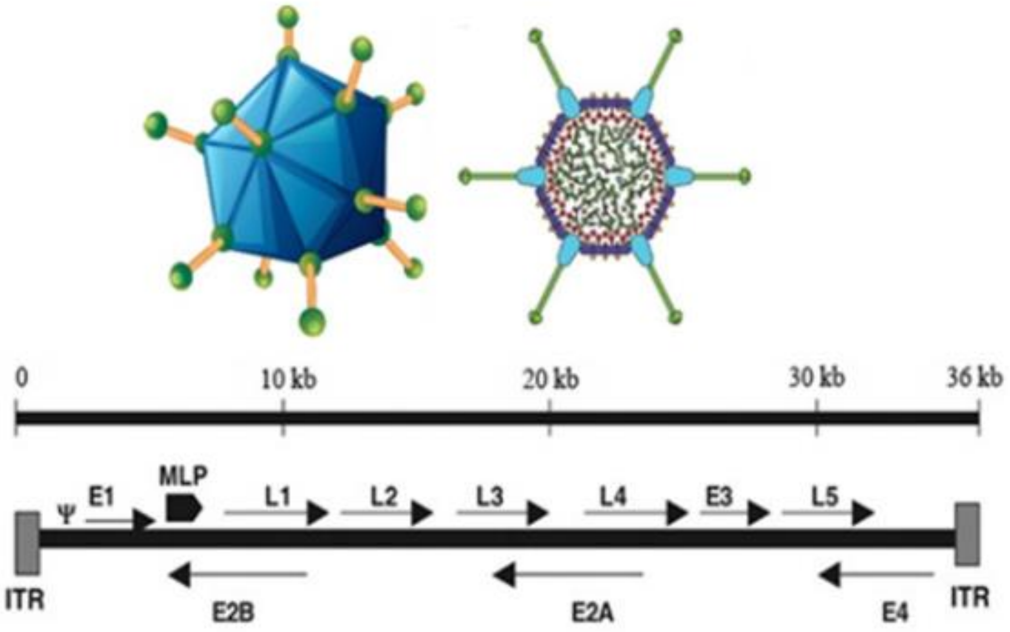
RSV Deaths

*Based on data from September 29, 2024 through December 7, 2024.

Adenovirus

- Adenoviridae
- Subtype: A~G

  → 116+ more genetic mutation
- All year, all ages
  - Pediatric: 5~10%
  - Adults: 1~4%
- Used as vectors in genetic Tx



Wild-Type Adenovirus (WTAd) e.g., Adv5: Natural, unmodified adenoviruses

Prevalence and burden of human adenovirus-associated acute respiratory illness in the Republic of Korea military, 2013 to 2022

JKMS

Reviewed data from patients who underwent PCR test for respiratory viruses in all Korean military hospitals between January 2013 and July 2022

10,670 Positive

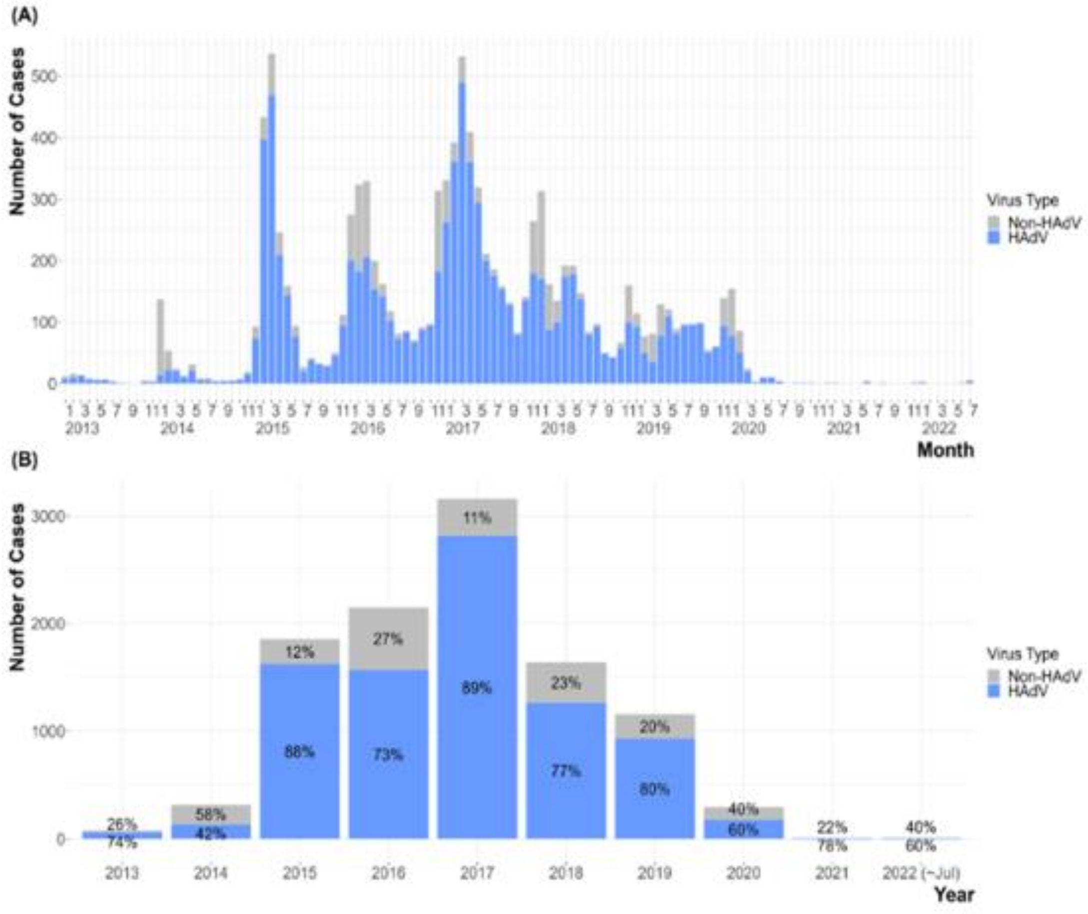
- 8,580 (80.41%) tested positive for HAdV
- 2,090 (19.59%) tested positive for non- HAdV (IFV, HMPV, HPIV, HRSV)

Comparison of Healthcare Utilization

		HAdV	Non-HAdV
Emergency	N (%)	2,969 (34.60)	625 (29.90)
	No.of visits/patient	1.04	1.02
Outpatient	N (%)	4,396 (51.24)	1,075 (51.44)
	No.of visits/patient	1.31	1.27
Hospitalization	N (%)	5,884 (68.58)	1,193 (57.08)
	Length of stay (days)	8.14	6.84
ICU	N (%)	177 (2.06)	16 (0.77)
	Length of stay (days)	5.21	3.38
Transfer	N (%)	235 (2.74)	10 (0.48)

Comparison of Prognosis N (%)

	HAdV	Non-HAdV
Oxygen therapy	164 (1.91)	18 (0.86)
HFNC	6 (0.07)	0 (0.00)
MV	20 (0.23)	1 (0.05)
ECMO	7 (0.08)	0 (0.00)
CRRT	2 (0.02)	0 (0.00)
Pneumonia	5,645 (65.79)	1,010 (48.33)
Severe ARD	25 (0.29)	1 (0.05)

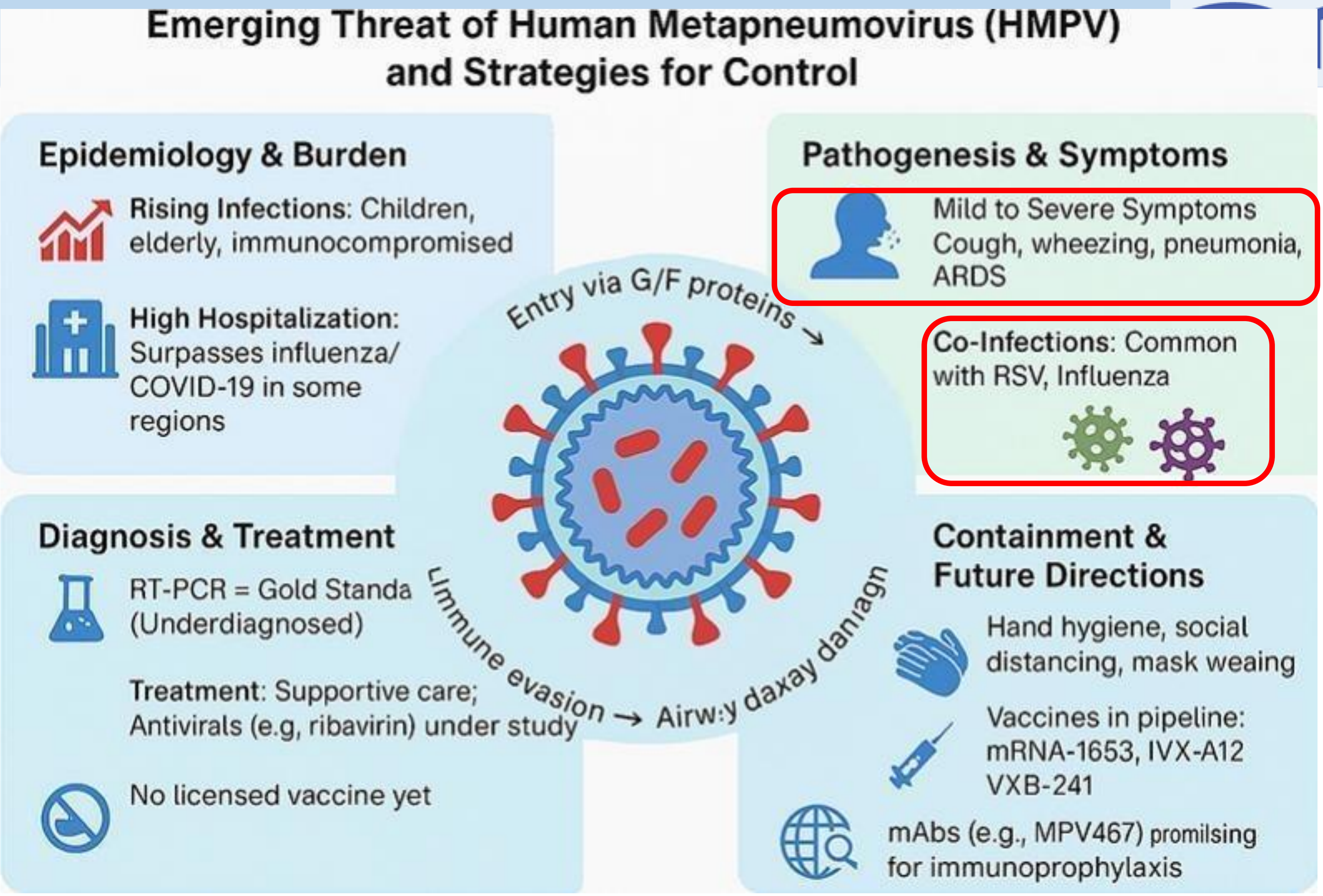


Conclusions

HAdV posed a significant public health concern within the Korean military prior to the COVID-19 pandemic

Metapneumovirus

- Found in 2001
- Paramyxoviridae, Pneumovirinae, Metapneumovirus 속
- Droplet transmission
- Usually in child and older age


Emerging Threat of Human Metapneumovirus (HMPV) and Strategies for Control
Epidemiology & Burden
Rising Infections: Children, elderly, immunocompromised
High Hospitalization: Surpasses influenza/ COVID-19 in some regions
Pathogenesis & Symptoms
Mild to Severe Symptoms Cough, wheezing, pneumonia, ARDS
Co-Infections: Common with RSV, Influenza
Entry via G/F proteins →
Immune evasion → Airw:y daxay daniagn
Diagnosis & Treatment
RT-PCR = Gold Standa (Underdiagnosed)
Treatment: Supportive care; Antivirals (e.g, ribavirin) under study
No licensed vaccine yet
Containment & Future Directions
Hand hygiene, social distancing, mask weaing
Vaccines in pipeline: mRNA-1653, IVX-A12 VXB-241
mAbs (e.g., MPV467) promilsing for immunoprophylaxis

The global burden of human metapneumovirus-associated acute respiratory infections in older adults: a systematic review and meta-analysis

	HICs	LMICs	Global*
Number of data points	6	10	NA
Pooled hMPV-proportion positive, %	2·46 (1·33–4·51)	2·01 (1·69–2·40)	NA
Number of all-cause LRI hospital admissions (thousands)†	7507 (7151–7938)	14 377 (11 356–18 227)	21 897 (18 702–25 744)
Number of hMPV- associated hospital admissions (thousands)	185 (105–340)	288 (193–436)	473 (396–777)

Data in parentheses are 95% CIs. HICs=high-income countries. hMPV=human metapneumovirus. LMICs=low-income and middle-income countries. LRI=lower respiratory infection. NA=not applicable. *Global estimates are sum of estimates from HICs and LMICs. †Estimated using Global Burden of Disease Study 2017 data (applied to 2019 population estimates); both are from the Institute For Health Metrics and Evaluation.

Table 1: **Number of hMPV-associated LRI hospitalisation episodes in individuals aged ≥65 years in 2019 based on data from proportion-positive studies**

HMPV Hospitalization Risks/10K

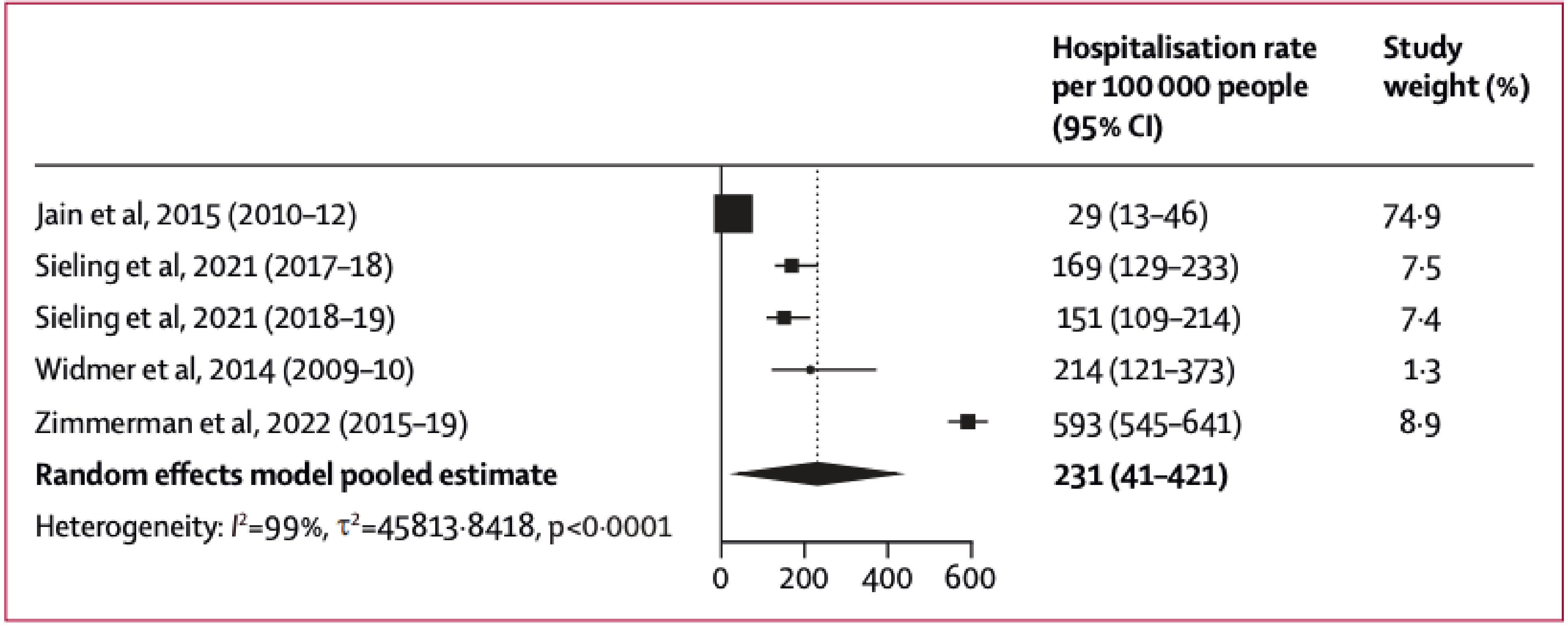
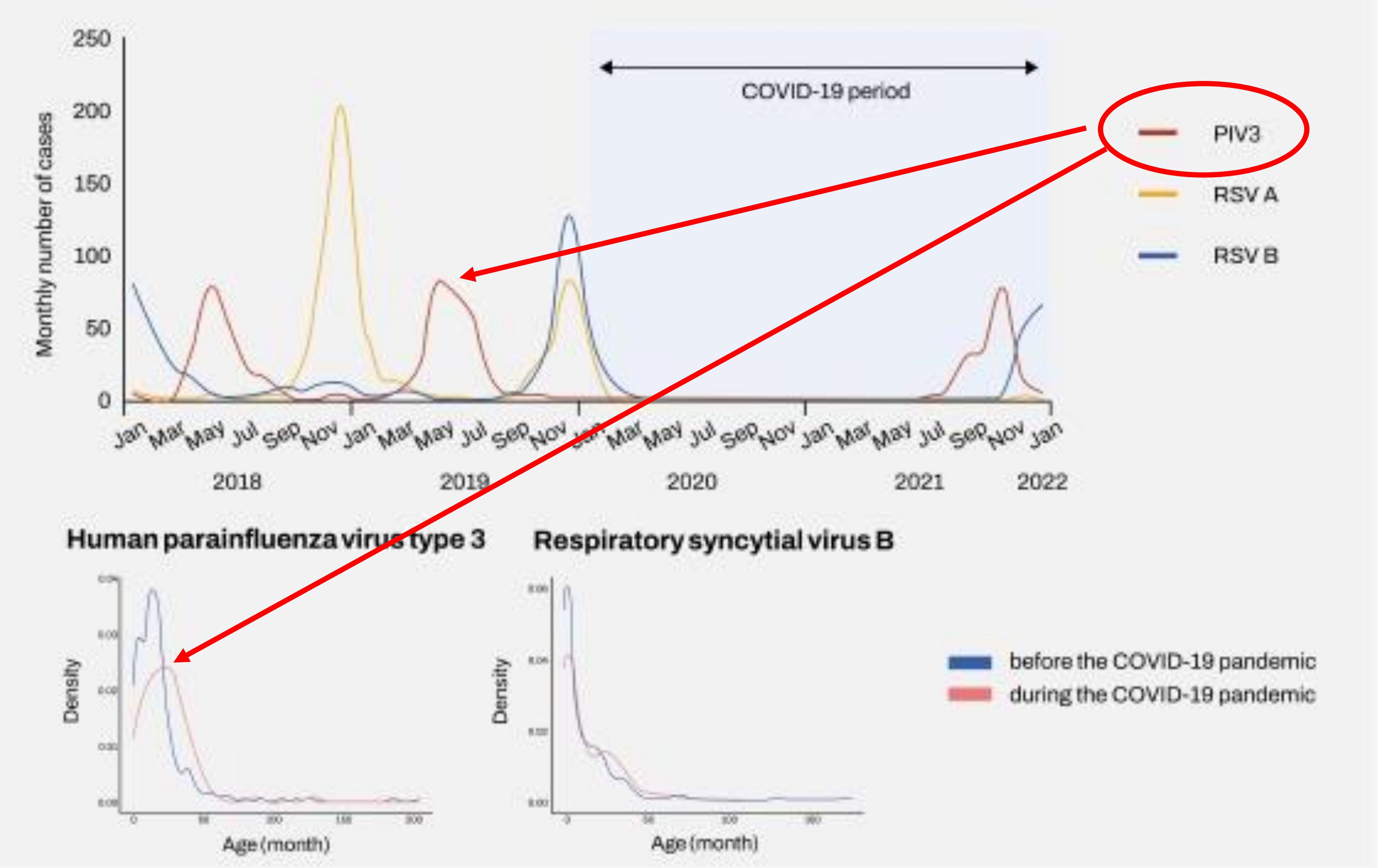


***Figure 3*: Forest plot of meta-analysis of hMPV-associated hospitalisation rate in the USA**
For each study, the years of data collection are shown in parentheses. hMPV=human metapneumovirus.

Parainfluenza virus

- Found in 1955
- Mononegavirales 목 Paramyxoviridae 과
- HPIV1, HPIV2, HPIV3, HPIV4의 네 가지 유형
- Upper RTI usually
- Lower RTI in some cases → < 5-year-old/older age/immunocompromised
- HPIV3 → 생후초기, HPIV1/2 2~6세 사이 감염


COVID-19 period
PIV3
RSV A
RSV B
Monthly number of cases
250
200
150
100
50
0
Jan Mar May Jul Sep Nov Jan Mar May Jul Sep Nov Jan Mar May Jul Sep Nov Jan Mar May Jul Sep Nov Jan
2018
2019
2020
2021
2022
Human parainfluenza virus type 3
Respiratory syncytial virus B
Density
Age (month)
before the COVID-19 pandemic
during the COVID-19 pandemic

Coronavirus

항목	일반 코로나바이러스 (Human CoVs)	SARS-CoV-2 (코로나19 바이러스)
정의	주로 감기 유사 증상을 유발	COVID-19를 유발하는 특수한 Betacoronavirus
대표 바이러스	HCoV-229E, HCoV-NL63 (Alphacoronavirus) HCoV-OC43, HCoV-HKU1 (Beta)	SARS-CoV-2 (2019-nCoV)
분류	Alphacoronavirus 또는 Beta coronavirus	Beta coronavirus
감염 특성	상기도 감염 중심, 감기 유사한 경증 증상	상·하기도 감염 모두, 고령자 중증 위험
세포 수용체	229E: APN, NL63: ACE2 등 다양	ACE2 수용체
변이 특성	돌연변이 빈도 낮음	돌연변이 매우 잦음 (Alpha, Delta, Omicron 등)
면역 회피 및 반응	면역 반응 경미, 후유증 거의 없음	면역 회피 능력 강화, 항체 회피
임상 양상	콧물, 기침, 인후통 등 경증	발열, 기침, 호흡곤란, 무증상 감염도 많음

Preliminary 2024-2025 U.S. COVID-19 Burden Estimates

CDC estimates* that, from October 1, 2024 through December 7, 2024, there have been:

2.5 million - 4.4 million
COVID-19 Illnesses

610,000 - 1.0 million
COVID-19 Outpatient Visits

72,000 - 120,000
COVID-19 Hospitalizations

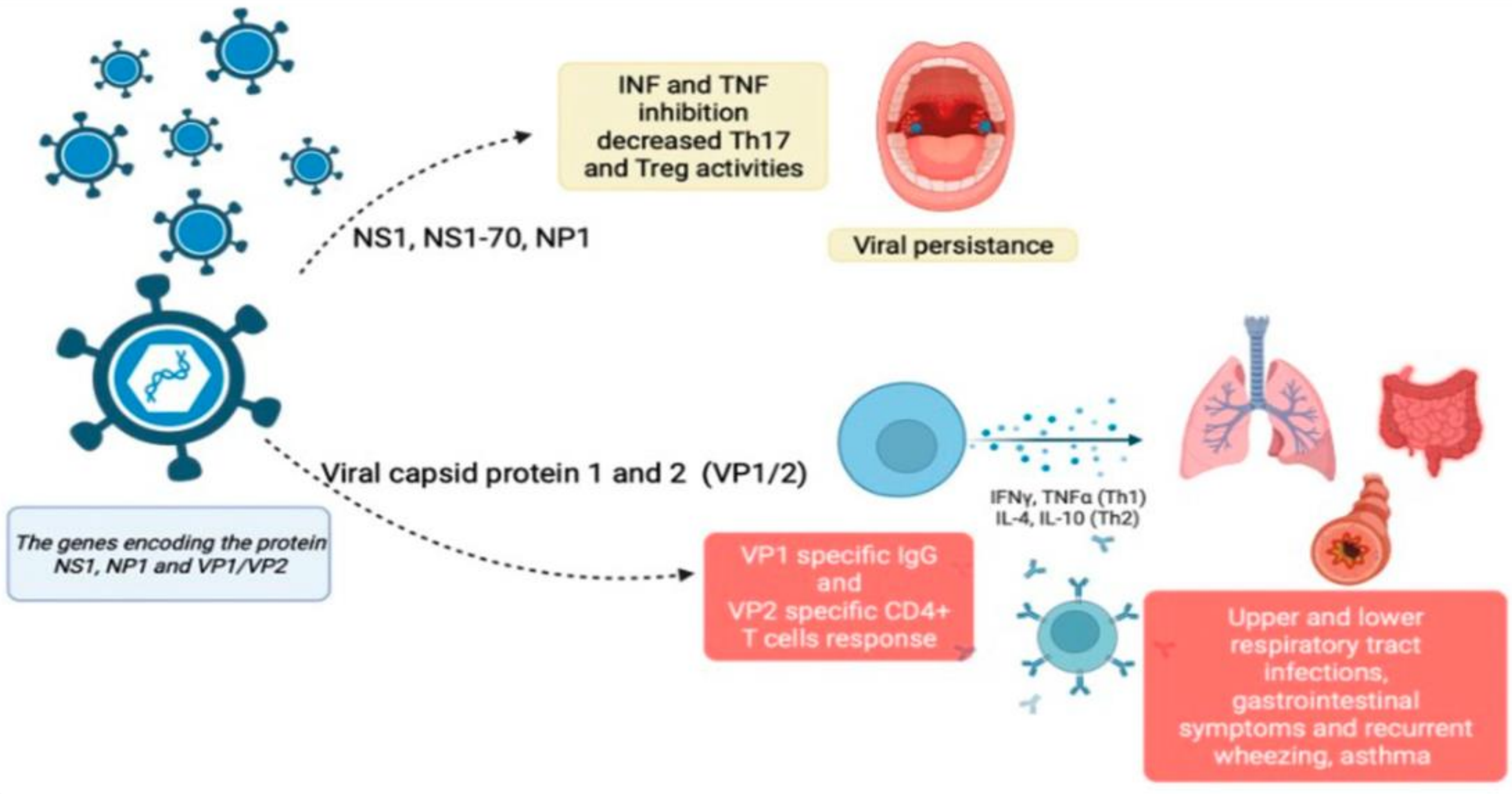
8,200 - 13,000
COVID-19 Deaths

*Based on data from September 29, 2024 through December 7, 2024.

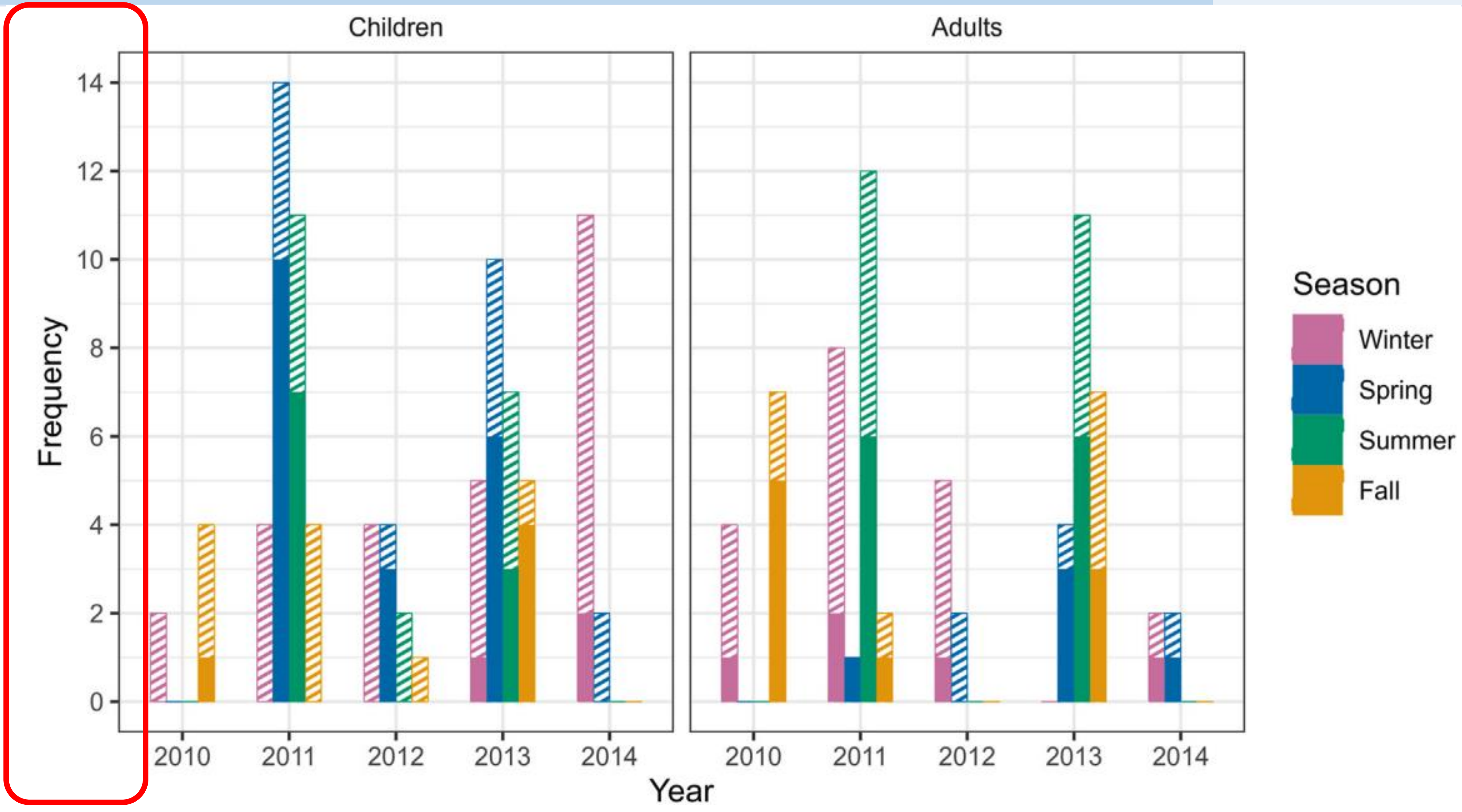
Bocavirus

- 2005 첫 분리
- Parvovirus
- HBoV 1,2,3,4

Figure 1. Immune response to HBoV infection: from viral persistence to acute and long consequences. Created with **BIORender.com** (last updated: 19 March 2023).



Microorganisms **2023**, *11*(5), 1243



Children
Adults
Frequency
14
12
10
8
6
4
2
0
2010
2011
2012
2013
2014
Year
Season
Winter
Spring
Summer
Fall


RESPIRATORY
VIRUS

Viral Infection and Asthma

Today's Table

- Respiratory Virus
- Viral Infection and Asthma
  - Early-life Exposure
  - Exacerbation
  - Immunologic Landscape
  - Seasonality
- What should we do?

How Respiratory Viruses Impact Asthma?

- **Triggering Exacerbations**

: Major cause of asthma exacerbations

- **Inflammation and Mucus**

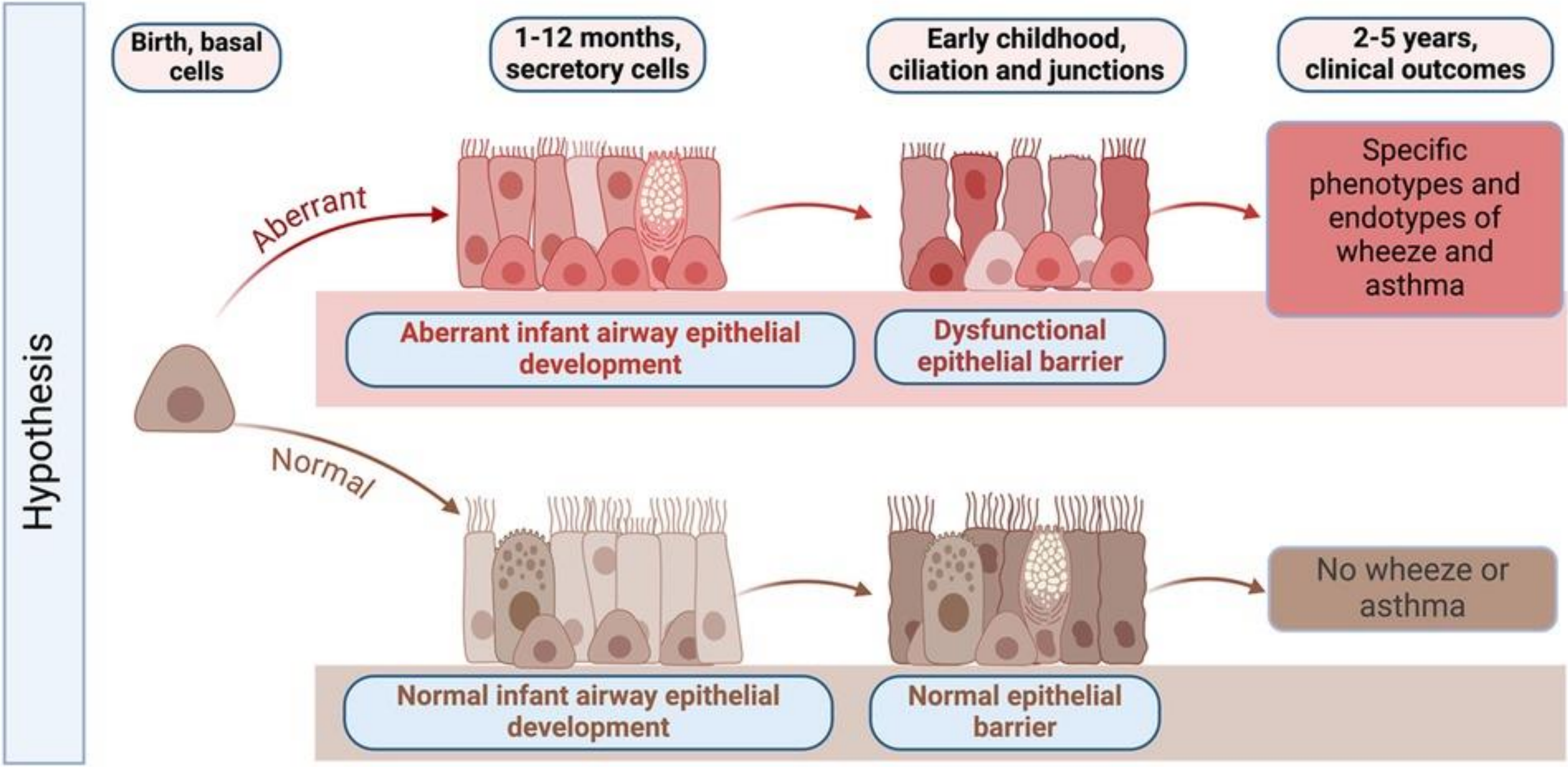
- **Increased Susceptibility**

: People with asthma may have altered immune responses and a compromised airway barrier

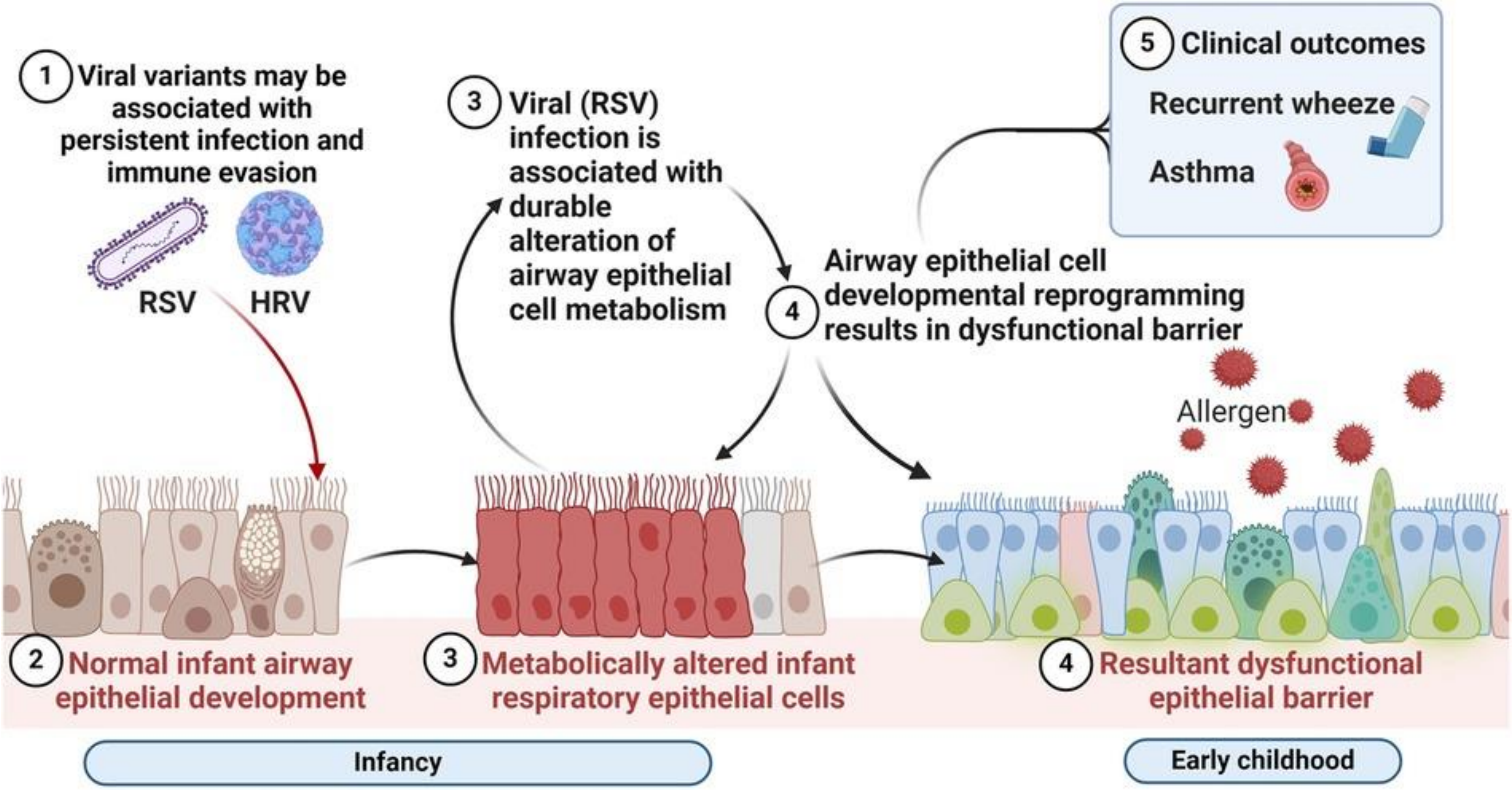
- **Potential for Long-Term Impact**

: Early childhood infections with viruses like RSV and rhinovirus can be associated with developing asthma later in life.

Viral Infection and Asthma
1) Early-life Exposure



Hypothesis
Birth, basal cells
1-12 months, secretory cells
Early childhood, ciliation and junctions
2-5 years, clinical outcomes
Aberrant
Aberrant infant airway epithelial development
Dysfunctional epithelial barrier
Specific phenotypes and endotypes of wheeze and asthma
Normal
Normal infant airway epithelial development
Normal epithelial barrier
No wheeze or asthma



1 Viral variants may be associated with persistent infection and immune evasion
RSV
HRV
3 Viral (RSV) infection is associated with durable alteration of airway epithelial cell metabolism
5 Clinical outcomes
Recurrent wheeze
Asthma
4 Airway epithelial cell developmental reprogramming results in dysfunctional barrier
Allergen
2 Normal infant airway epithelial development
3 Metabolically altered infant respiratory epithelial cells
4 Resultant dysfunctional epithelial barrier
Infancy
Early childhood

Birth Cohorts and Viral Exposure

- COAST (Childhood Origins of Asthma)
- COPSAC (Copenhagen Prospective Study on Asthma in Childhood
  - Most powerful predictor of “pediatric asthma”
    - by wheeze RV infection
  - Inducing T2 inflammation → increased IL-22/IL-33
  - Allergic sensitization → Atopic asthma
  - Loss of innate immunity of airway epithelial cells to RV in asthma patients

Birth Cohorts and Viral Exposure

- COAST (Childhood Origins of Asthma)
- COPSAC (Copenhagen Prospective Study on Asthma in Childhood
  - Most common pathogen of Asthma AE (~70%)
  - By inducing airway hyperresponsiveness → airway inflammation
  - RV-C receptor → CDHR3 mutation (rs6967330)
  - Aggravated by air pollution, smoking exposure, NO_2, and O_3
  - Co-infection with bacteria

Virus infection → Development of Asthma

Rhinovirus-induced wheezing in infancy—the first sign of childhood asthma?

Anne Kotaniemi-Syrjänen, MD,[a] Raija Vainionpää, PhD,[b] Tiina M. Reijonen, MD,[a] Matti Waris, PhD,[b] Kaj Korhonen, MD,[a] and Matti Korppi, MD[a] *Kuopio and Turku, Finland*

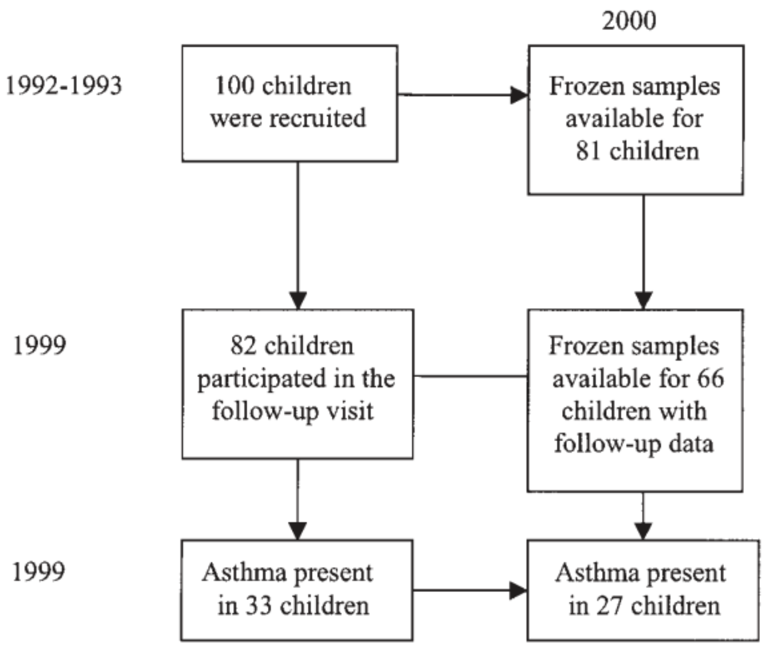


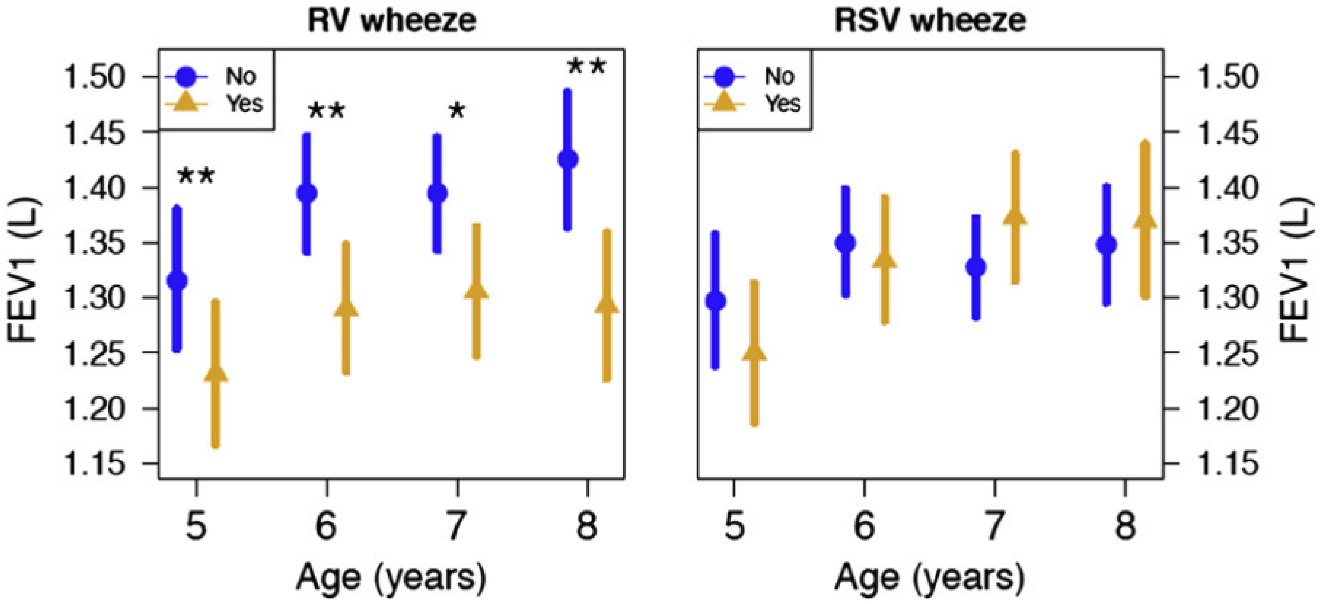
TABLE IV. Viruses associated with wheezing in infancy and the presence of asthma at early school age

	Asthma at early school age: no. of subjects (%)	
Viral identifications	**Present (n = 27)**	**Not present (n = 39)**
Single identification	18 (67)	24 (62)
RV	14 (52)*	6 (15)
Enterovirus	0 (0)	5 (13)
RSV/other respiratory viruses	1 (4)/3 (11)	9 (23)/4 (10)
Multiple identifications	2† (7)	8‡ (21)
No viral identifications	7 (26)	7 (18)

RV → Preschool wheeze → ↓FEV1

Decreased lung function after preschool wheezing rhinovirus illnesses in children at risk to develop asthma

Theresa W. Guilbert, MD, MS,[a] Anne Marie Singh, MD,[a,b] Zoran Danov, MD,[e] Michael D. Evans, MS,[c] Daniel J. Jackson, MD,[a,b] Ryan Burton, BS,[a,b] Kathy A. Roberg, RN,[a] Elizabeth L. Anderson, RN,[a] Tressa E. Pappas, BS,[a] Ronald Gangnon, PhD,[c,d] James E. Gern, MD,[a] and Robert F. Lemanske, Jr, MD[a,b] *Madison, Wis, and Lexington, Ky*



Everyone? No, someone is weak

- 17q21 locus
  - RV infection → ORMLD3, GSDMB, IKZF3

- CDHR3 (Cadherin-related family member 3)
  - rs6967330 → Severe AE pediatric asthma
  - RV 결합 증가, RV 관련 호흡기질환 중증도 증가

- STAT4, JAK2, MX1, DDX58

Ann Allergy Asthma Immunol 123 (2019)
N Engl J Med 2013;368:1398-407.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Rhinovirus Wheezing Illness and Genetic Risk of Childhood-Onset Asthma

Minal Çalışkan, B.S., Yury A. Bochkov, Ph.D., Eskil Kreiner-Møller, M.D., Klaus Bønnelykke, M.D., Michelle M. Stein, B.S., Gaixin Du, M.S., Hans Bisgaard, D.M.Sci., M.D., Daniel J. Jackson, M.D., James E. Gern, M.D., Robert F. Lemanske, Jr., M.D., Dan L. Nicolae, Ph.D., and Carole Ober, Ph.D.

Study Population: COAST/COPSAC
Methods: 17q21 genotypes in RV/RSV wheezing illness vs. unstimulated

N Engl J Med 2013;368:1398-407.

17q21 locus variant is only in RV wheezing

Table 1. **Associations of 17q21 Single-Nucleotide Polymorphisms (SNPs) with Asthma, Allergic Sensitization, and Viral Wheezing Illness Phenotypes in the Childhood Origins of Asthma (COAST) Cohort.***

SNP	Gene	Location	Minor Allele	Minor-Allele Frequency	P Value					
					Asthma	Allergic Sensitization†	HRV Wheezing Illness	No. of HRV Wheezing Illnesses	RSV Wheezing Illness	No. of RSV Wheezing Illnesses
rs9303277	*IKZF3*	Intron	C‡	0.488	0.03	0.86	0.01	<0.001	0.25	0.51
rs11557467	*ZPBP2*	Intron	T‡	0.498	0.05	0.98	0.02	<0.001	0.30	0.63
rs12936231	*ZPBP2*	Exon	C‡	0.493	0.07	0.95	0.02	<0.001	0.22	0.57
rs2290400	*GSDMB*	Intron	A∫	0.500	0.08	0.90	0.02	<0.001	0.17	0.47
rs7216389	*GSDMB*	Intron	T∫	0.500	0.04	0.90	0.01	<0.001	0.22	0.54

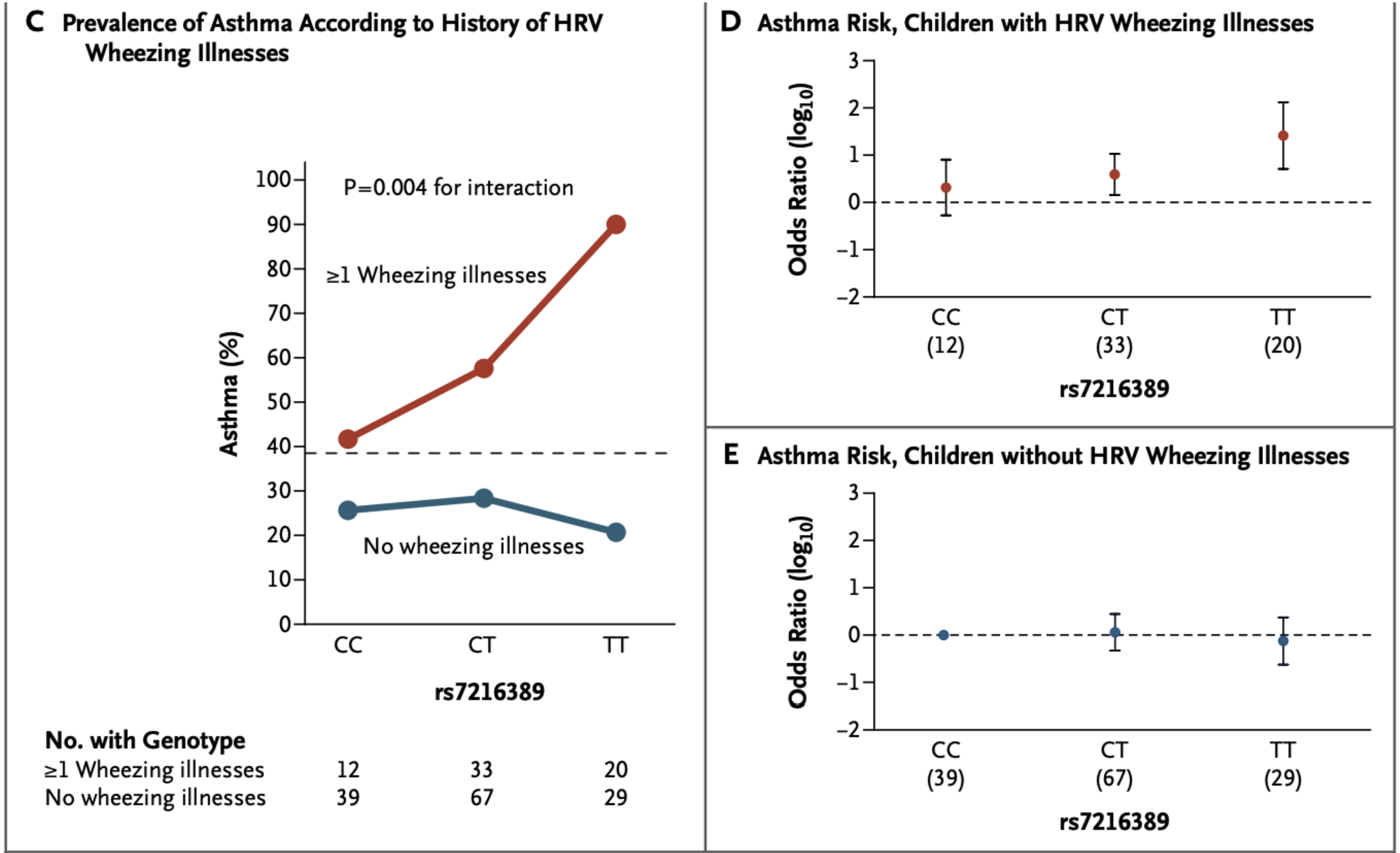


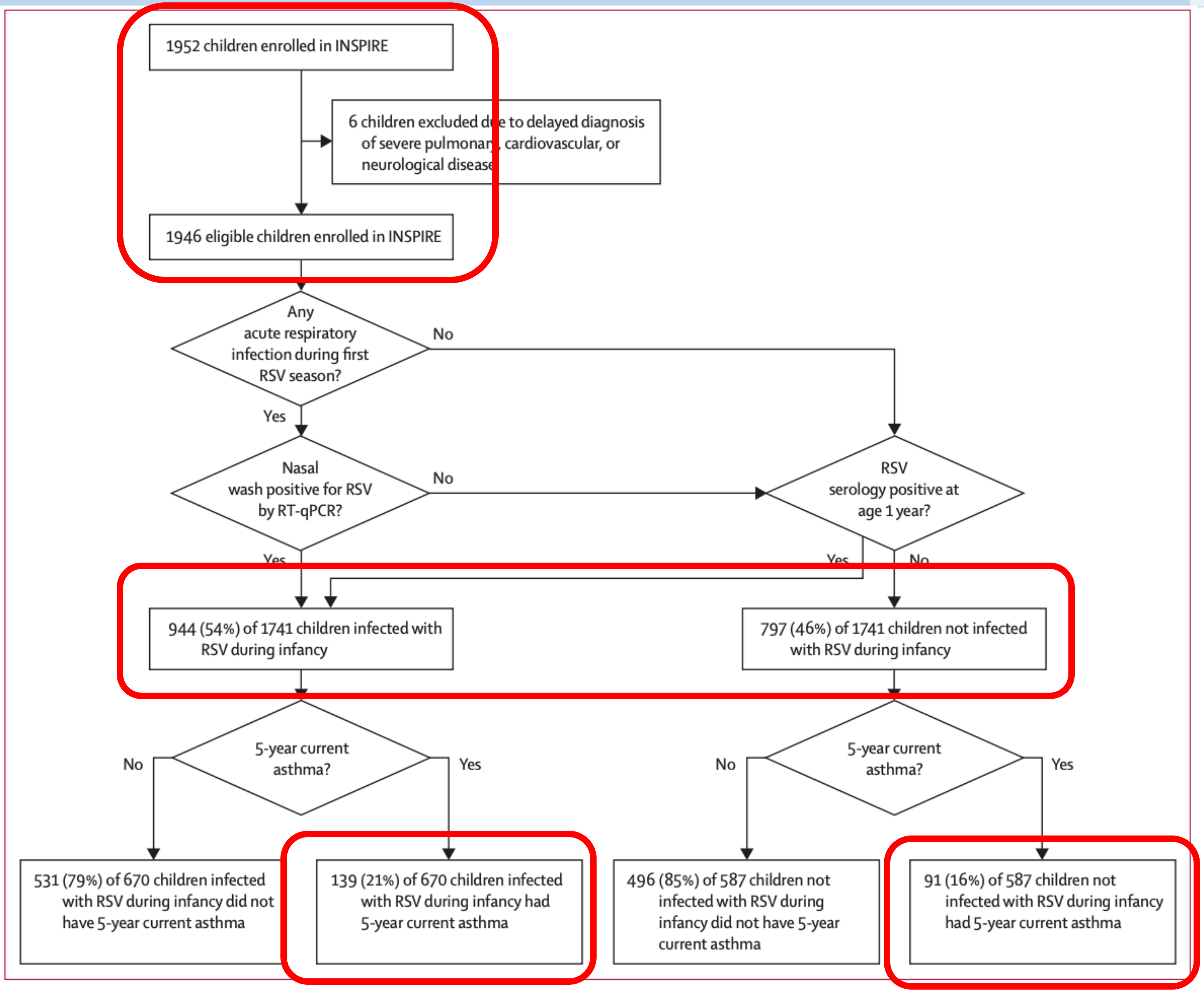
Figure 1. Effects of 17q21 Genotype on Asthma and Human Rhinovirus (HRV) Wheezing Illnesses in the Childhood Origins of Asthma (COAST) Cohort.

RSV

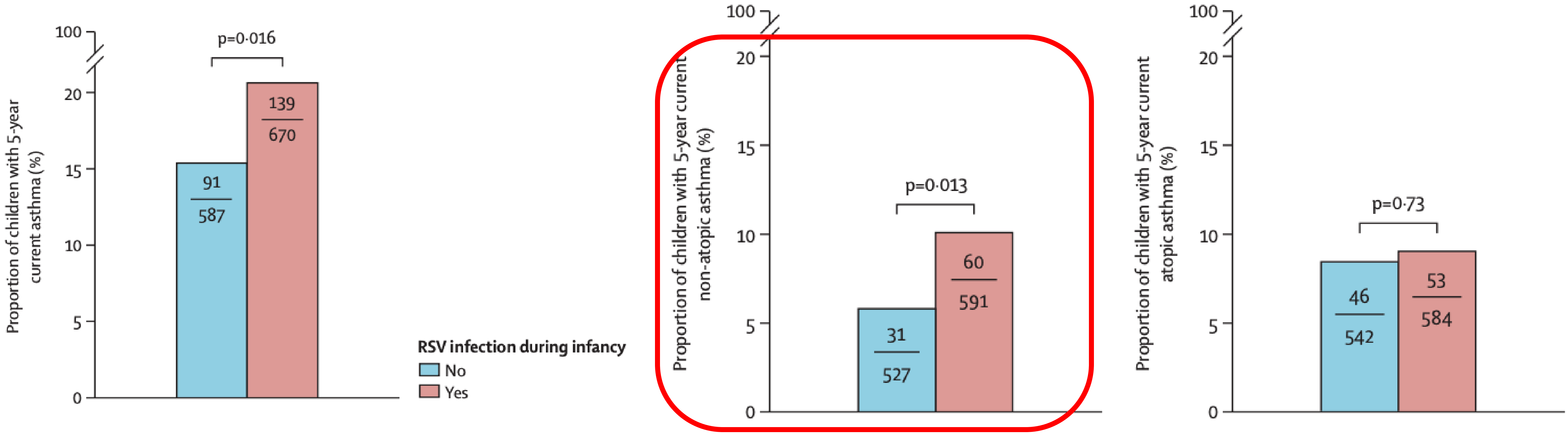
Respiratory syncytial virus infection during infancy and asthma during childhood in the USA (INSPIRE): a population-based, prospective birth cohort study

Christian Rosas-Salazar, Tatiana Chirkova, Tebeb Gebretsadik, James D Chappell, R Stokes Peebles Jr, William D Dupont, Samadhan J Jadhao, Peter J Gergen, Larry J Anderson, Tina V Hartert

Lancet. 2023 May 20;401(10389):1669-1680


1952 children enrolled in INSPIRE
6 children excluded due to delayed diagnosis of severe pulmonary, cardiovascular, or neurological disease
1946 eligible children enrolled in INSPIRE
Any acute respiratory infection during first RSV season?
No
Yes
Nasal wash positive for RSV by RT-qPCR?
No
Yes
RSV serology positive at age 1 year?
Yes
No
944 (54%) of 1741 children infected with RSV during infancy
797 (46%) of 1741 children not infected with RSV during infancy
5-year current asthma?
No
Yes
5-year current asthma?
No
Yes
531 (79%) of 670 children infected with RSV during infancy did not have 5-year current asthma
139 (21%) of 670 children infected with RSV during infancy had 5-year current asthma
496 (85%) of 587 children not infected with RSV during infancy did not have 5-year current asthma
91 (16%) of 587 children not infected with RSV during infancy had 5-year current asthma

RSV during infancy → Non-atopic Asthma



The Earlier, the Riskier

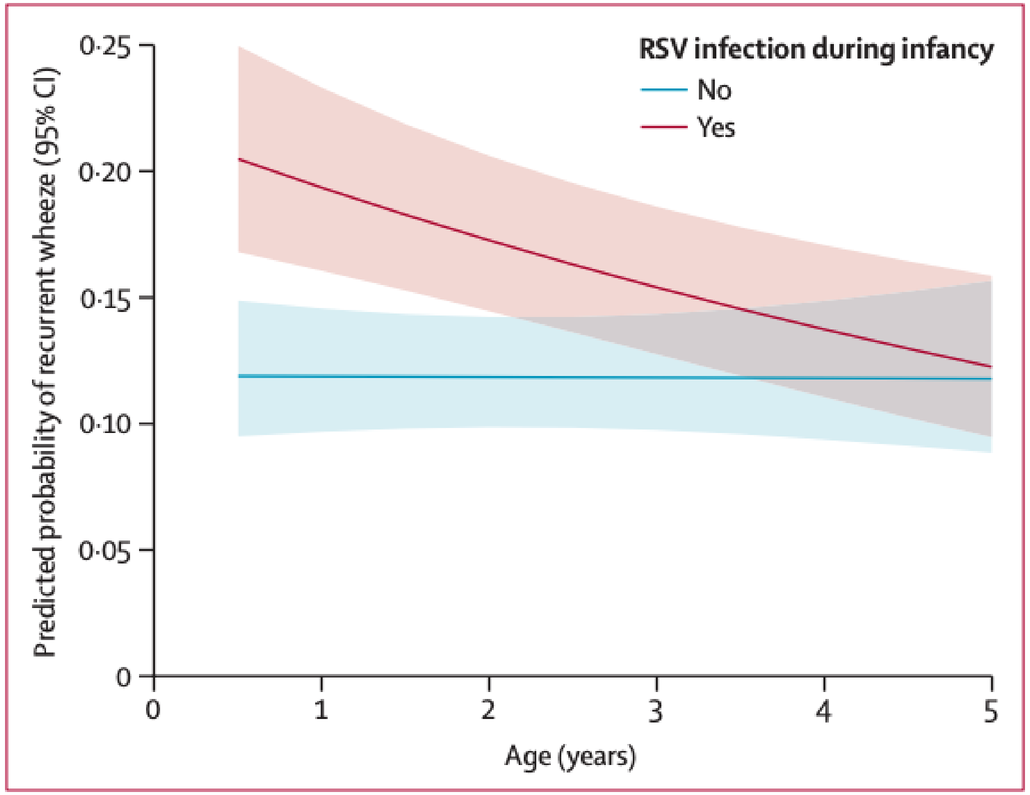


Figure 4: **Predicted probability of recurrent wheeze in the first 4 years of life by RSV infection during infancy**

Lancet. 2023 May 20;401(10389):1669-1680

Metapneumovirus is also asthma risk factor

ERJ OPEN RESEARCH
ORIGINAL RESEARCH ARTICLE
Å. MYKLEBUST ET AL.

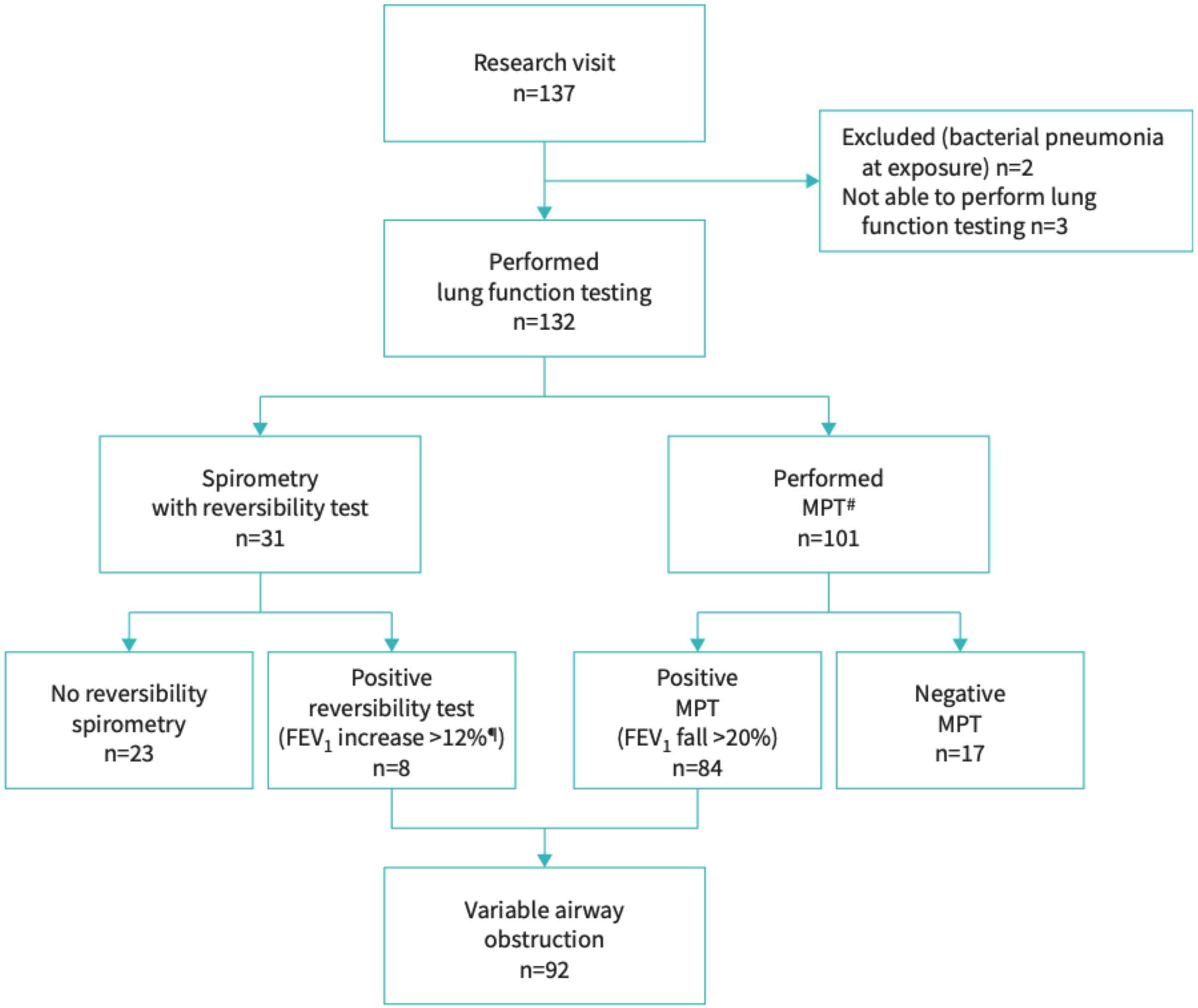
Bronchial reactivity and asthma at school age after early-life metapneumovirus infection

Åsne Myklebust[1,2], Melanie Rae Simpson[3], Jonas Valand[1], Vibeke Stenhaug Langaas[4], Tuomas Jartti[5,6,7], Henrik Døllner[1,2] and Kari Risnes[1,2]

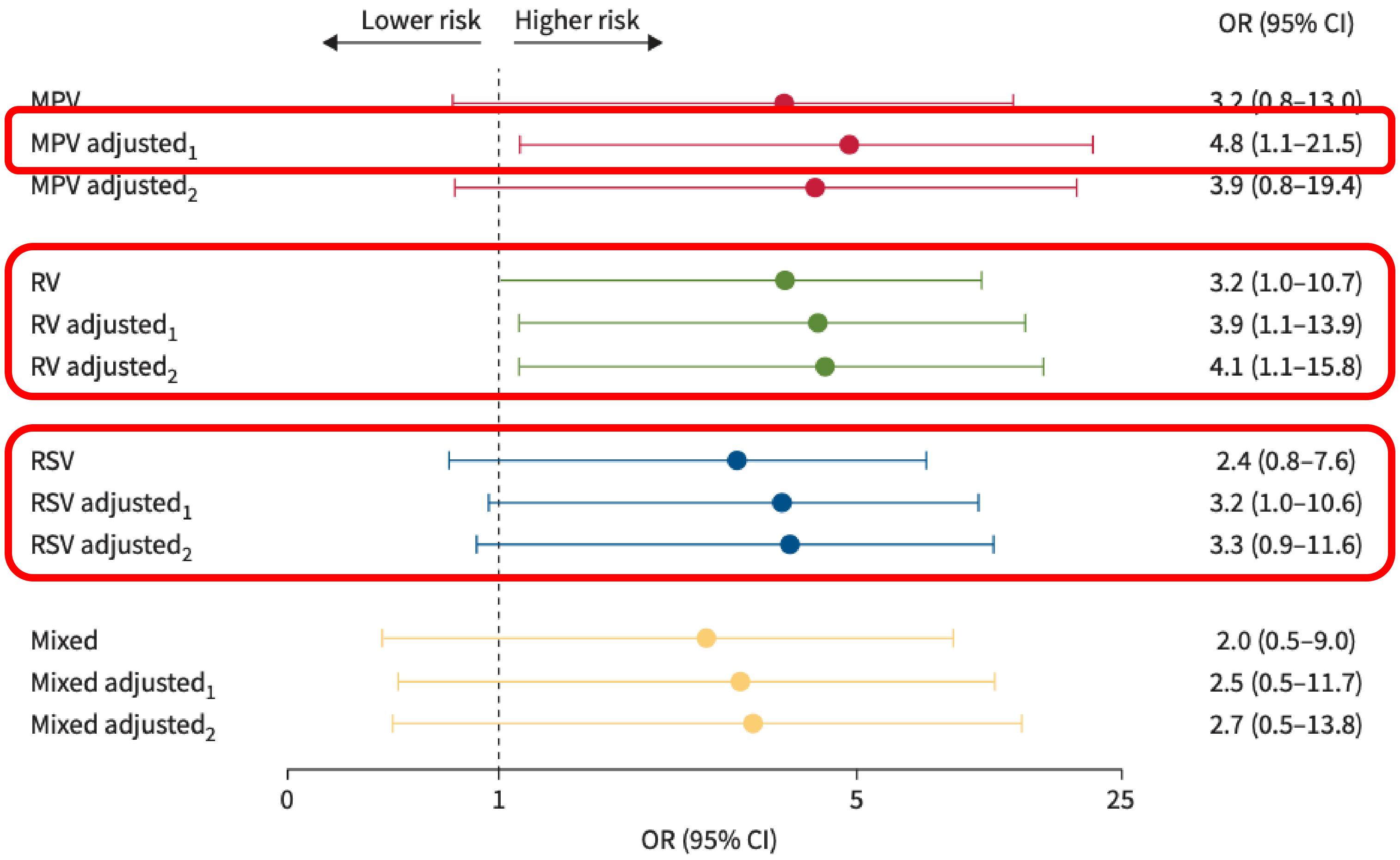
Original cohort: 2006~2012

Follow-up at school age: 2017~2019 (7~10 yrs after)

St Olavs Hospital (Trondheim, Norway)



Metapneumovirus



ERJ Open Res 2024; 10: 00832-2023

Adenovirus, Coronavirus, Bocavirus, Parainfluenza virus

- Acute wheezing (+) in some cases
- Not associated long term development, YET

Viral Infection and Asthma
2) Exacerbation

REVIEW ARTICLE

Viruses and bacteria in acute asthma exacerbations – A GA²LEN-DARE* systematic review

Table 1 Reported prevalence of individual microbial agents in AAE, according to data from the literature reviewed in this manuscript

Pathogen	Prevalence (%) in AAE: Infants and pre-school-age children	Children (6–17 years)	Adults	Higher frequency in AAE than control populations
Rhinovirus	17–78 (33)	42–82 (55)	8–65 (29)	Yes
Enterovirus	12–25 (18)	5–16 (7)	?	?
Coronavirus	0–5 (2)	0–13 (1)	4–21 (12)	No
Influenza virus	1–20 (3)	0–7 (2.5)	8–25 (23)	Yes (adults only)
Parainfluenza virus	4–12 (7.5)	0–7 (2)	0–18 (0)	No
Respiratory Syncytial virus	2–68 (19)	1.5–12 (4)	0–39 (3)	Yes (infants only)
Metapneumovirus	1.5–9 (4)	4–7.5 (4.5)	?	?
Adenovirus	1.5–8 (4.5)	0–71 (0)	1–3 (2)	No
Bocavirus	7.5–19 (11)	?	?	?
Chlamydophila Pn	0–45 (4)	4–23 (11)	0–73 (13)	?
Mycoplasma Pn	1–10 (2)	0–50 (14)	0–8 (4)	Yes (children only)

Allergy 66 (2011) 458–468

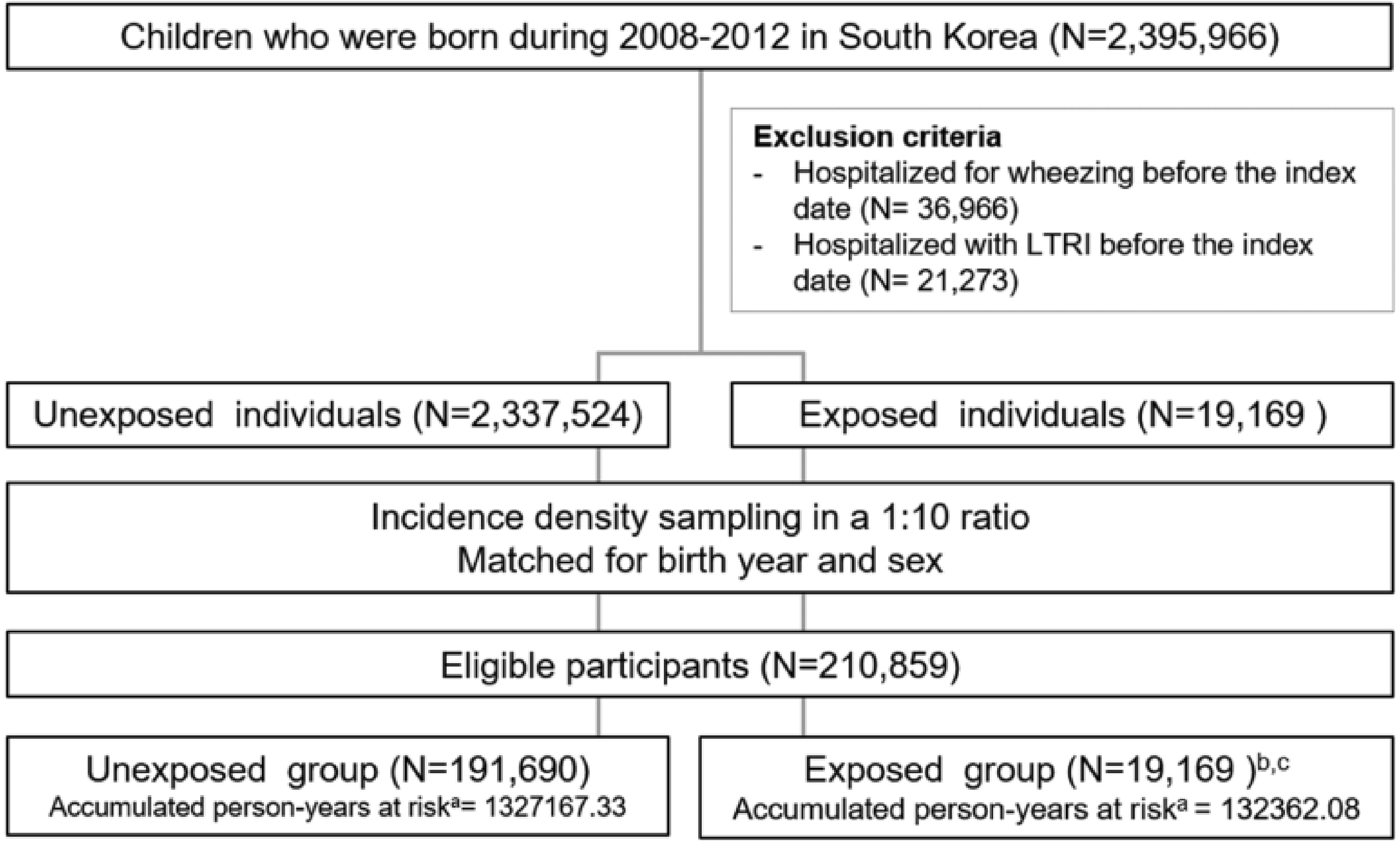
Asthma AE in Pediatrics

RESEARCH ARTICLE

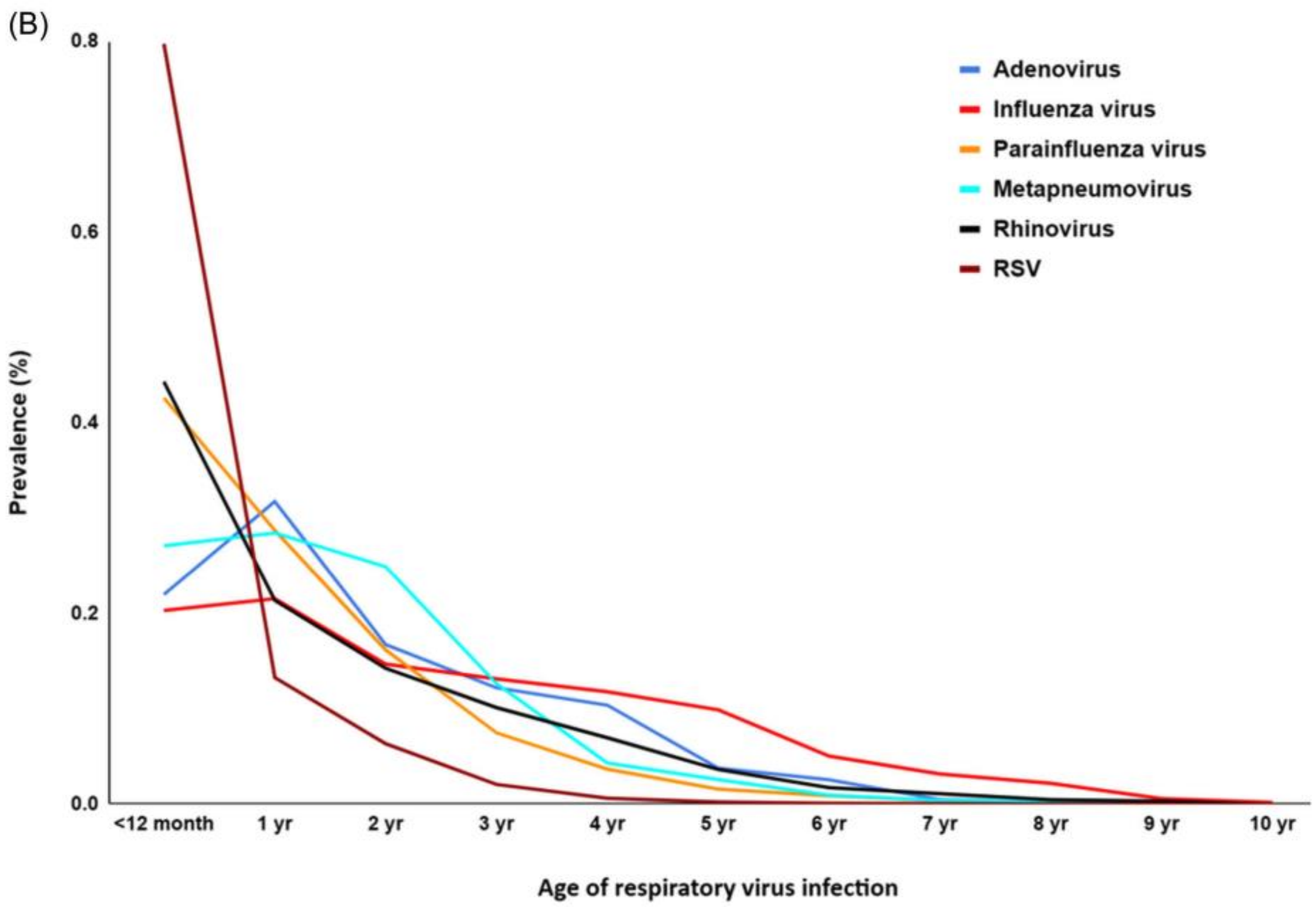
JOURNAL OF MEDICAL VIROLOGY WILEY

Viral respiratory infections requiring hospitalization in early childhood related to subsequent asthma onset and exacerbation risks

Eun Kyo Ha[1] | Ju Hee Kim[2] | Boeun Han[3] | Jeewon Shin[4] | Eun Lee[5] | Kee-Jae Lee[6] | Youn Ho Shin[2] | Man Yong Han[3]

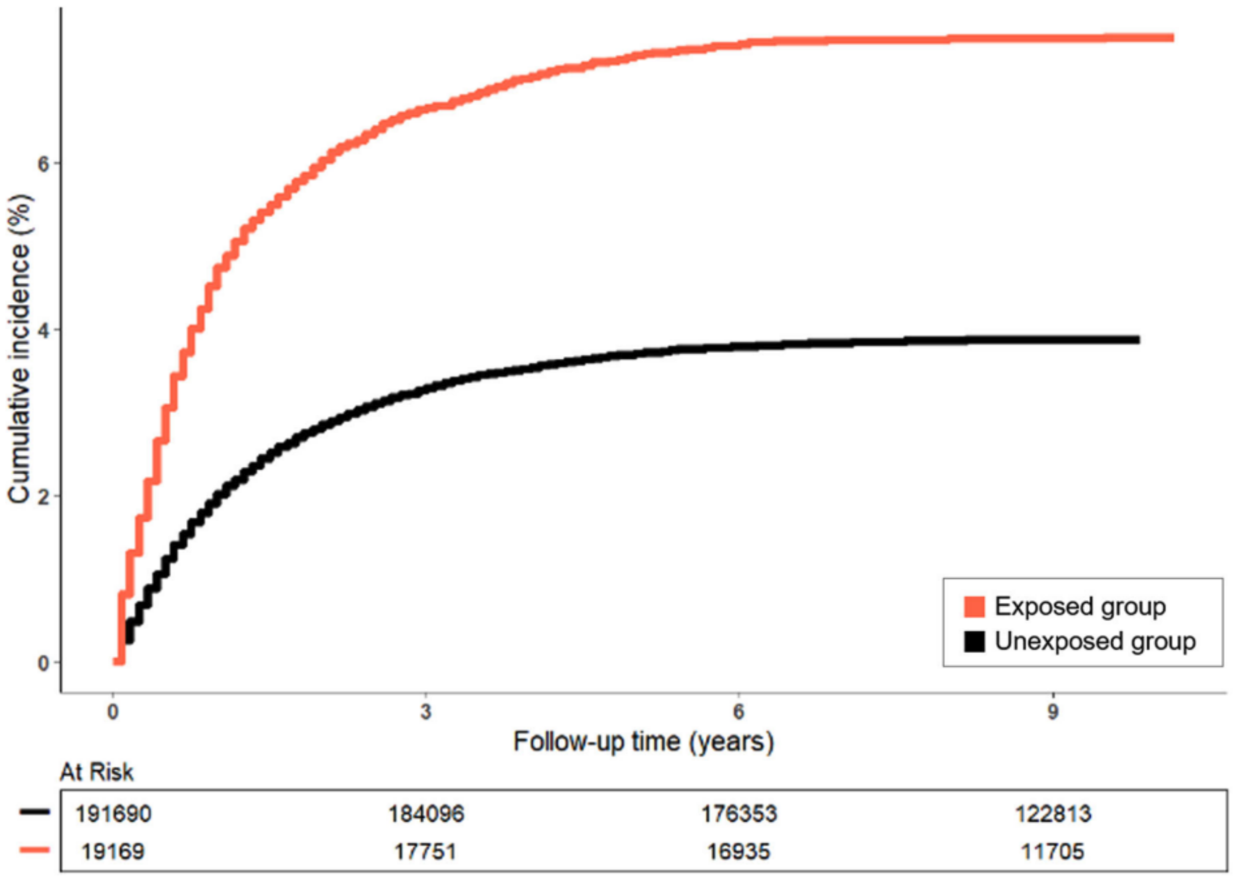


Asthma AE in Pediatrics



J Med Virol. 2024;96:e29876.

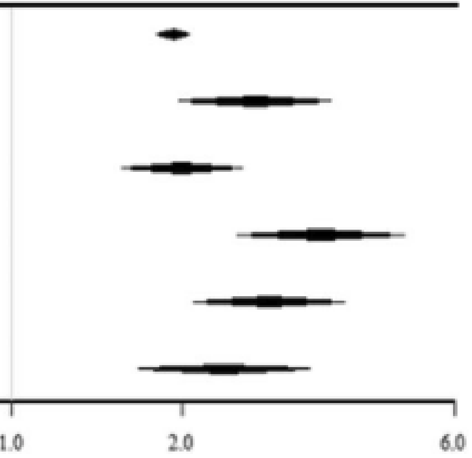
Asthma AE in Pediatrics



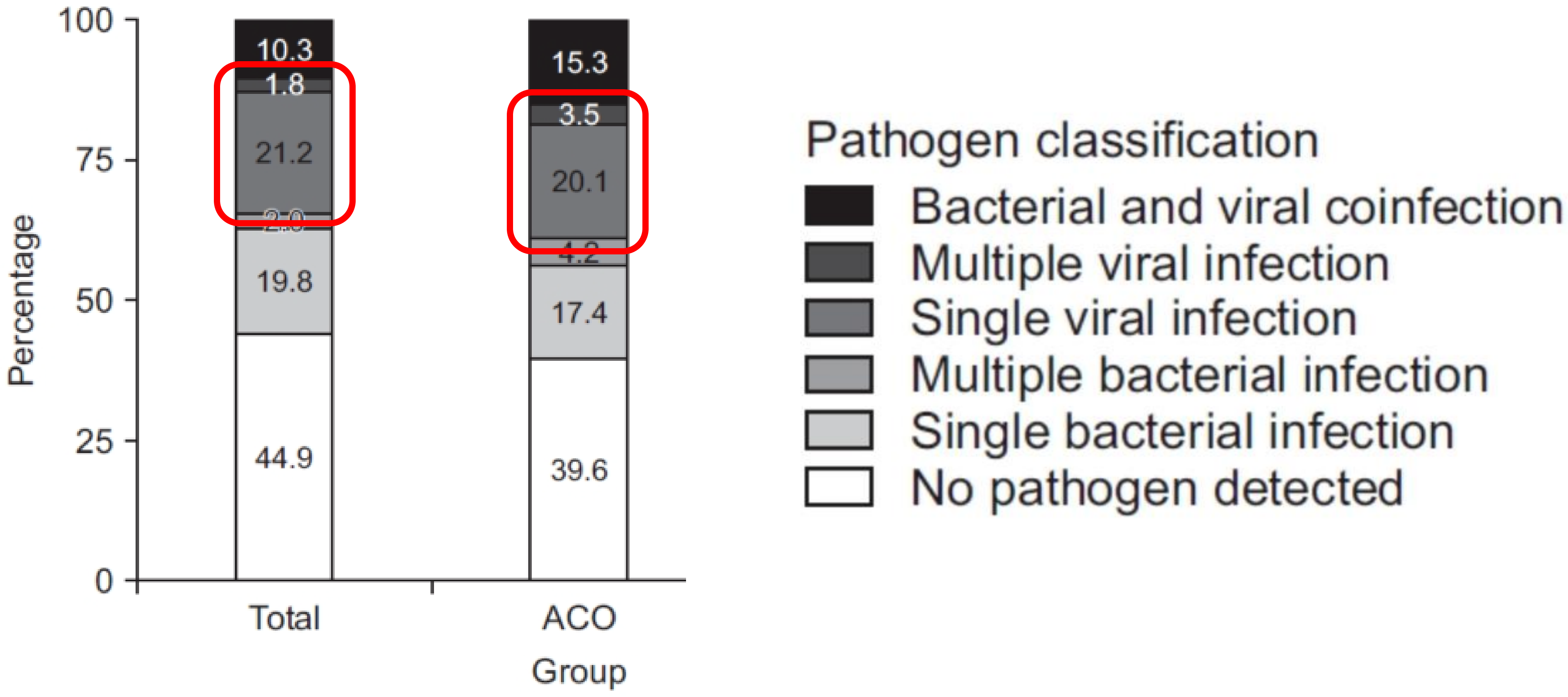
J Med Virol. 2024;96:e29876.

Asthma AE in Pediatrics

Identified pathogen	Number of Event/Total Number (Incidence rate/10,000 person-years)		Hazard Ratio (95% CI)
	Exposed cohort	Unexposed cohort	
RSV	1,190/14,669 (140.0)	6,324/146,690 (70.9)	1.926 (1.806-2.054)
Influenza virus	53/1,313 (97.7)	205/13,130 (36.4)	2.677 (1.972-3.635)
Parainfluenza virus	82/1,386 (119.7)	422/13,860 (59.5)	1.989 (1.559-2.538)
Metapneumovirus	48/806 (142.4)	148/8,060 (41.8)	3.500 (2.496-4.908)
Rhinovirus	57/779 (158.5)	213/7,790 (56.3)	2.834 (2.095-3.834)
Adenovirus	41/795 (113.0)	181/7,950 (47.8)	2.358 (1.672-3.325)



Insight from COPD data



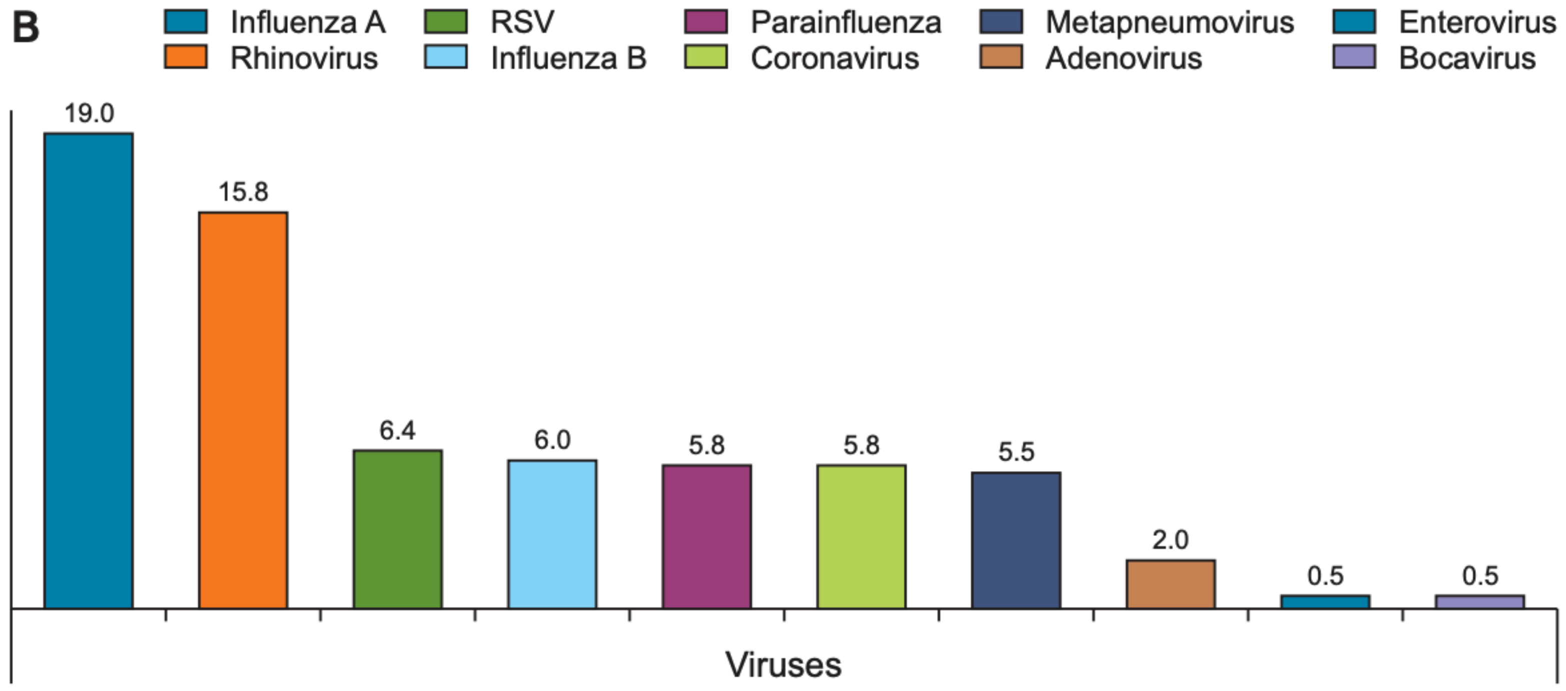
Tuberc Respir Dis 2025;88:292-302

Insight from COPD data

Original Article

Clinical Significance of Various Pathogens Identified in Patients Experiencing Acute Exacerbations of COPD: A Multi-center Study in South Korea

https://doi.org/10.4046/trd.2024.0089
ISSN: 1738-3536(Print)/
2005-6184(Online)
Tuberc Respir Dis 2025;88:292-302

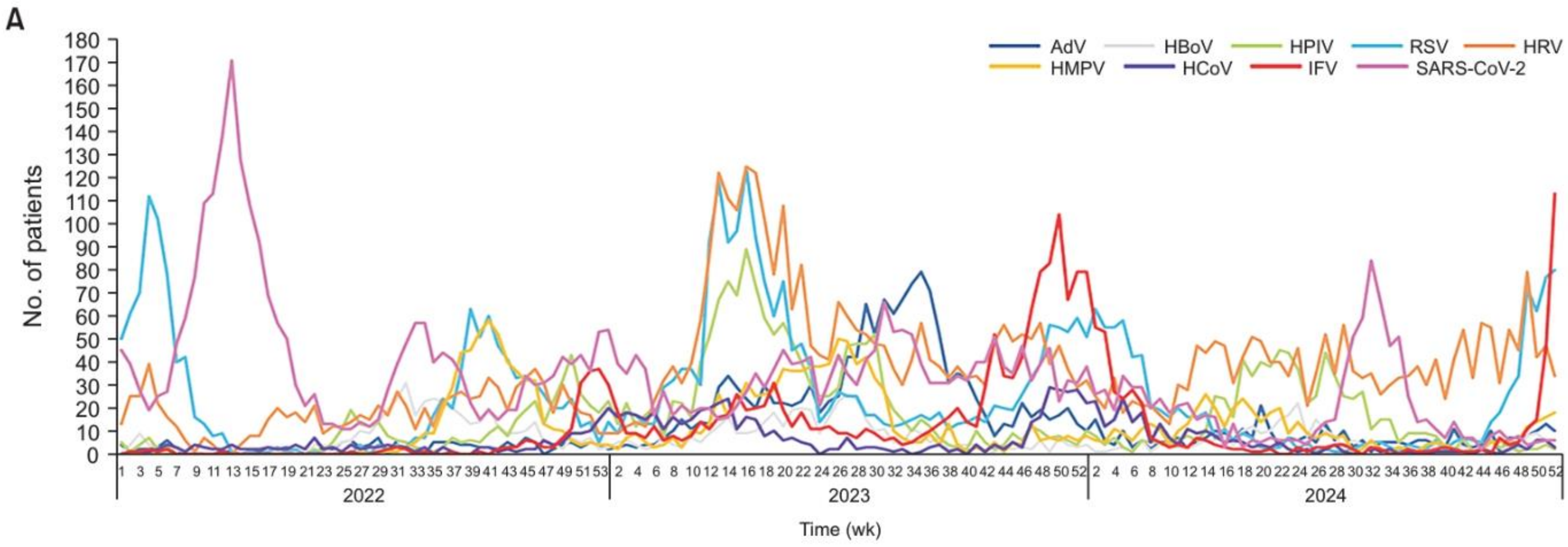


Insight from SARI data

Letter to the Editor

Epidemiology of Severe Acute Respiratory Infection in Korea: 2022 to 2024 Surveillance Data

https://doi.org/10.4046/trd.2025.0043
ISSN: 1738-3536(Print)/
2005-6184(Online)
Tuberc Respir Dis 2025;88:610-613



Prediction by using Respiratory Virus Detection Rate

Journal of Asthma and Allergy

Dovepress
open access to scientific and medical research

Open Access Full Text Article

SHORT REPORT

Predicting Asthma Exacerbation Risk in the Adult South Korean Population Using Integrated Health Data and Machine Learning Models

Joon Young Choi[1], Chin Kook Rhee[2]

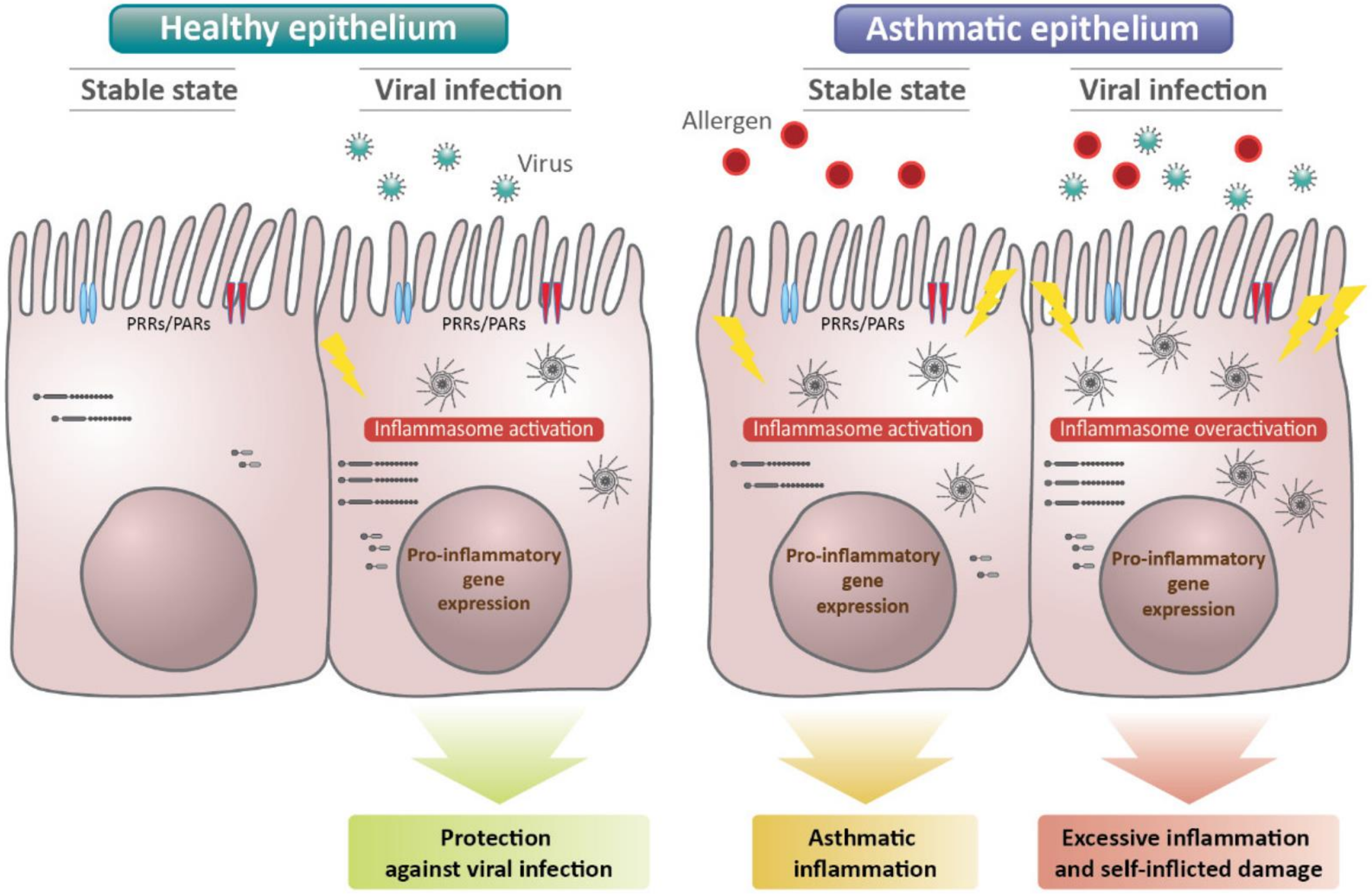
Total virus detection, total virus detection rate, adenovirus/bocavirus/coronavirus/enterovirus/human metapneumovirus/rhinovirus/influenza virus/ parainfluenza virus/RSV detection rate for the week, adenovirus/bocavirus/coronavirus/enterovirus/human metapneumovirus/rhinovirus/influenza virus/ parainfluenza virus/RSV detection rate in the previous week, sum of 2-4-week adenovirus/bocavirus/coronavirus/enterovirus/human metapneumovirus/rhinovirus/influenza virus/ parainfluenza virus/RSV detection rate,

Table 2 Model Evaluation Results Using Test Data

Method	Sampling Method	Feature Selection	AUC
1) Logistic regression	Under	No	0.59
2) penalized logistic regression (L1)	Under	No	0.59
3) penalized logistic regression (L1)	Hybrid	Yes	0.66
4) Random Forest	Hybrid	No	0.67
5) Random Forest	Hybrid	Yes	0.71
6) Adaboost	Under	No	0.64
7) Adaboost	Hybrid	No	0.70
8) Adaboost	Hybrid	Yes	0.71
9) light GBM	Under	No	0.67
10) light GBM	Hybrid	Yes	0.69
11) XGBoost	Under	No	0.68
12) XGBoost	Hybrid	No	0.68
13) XGBoost	Hybrid	Yes	0.68

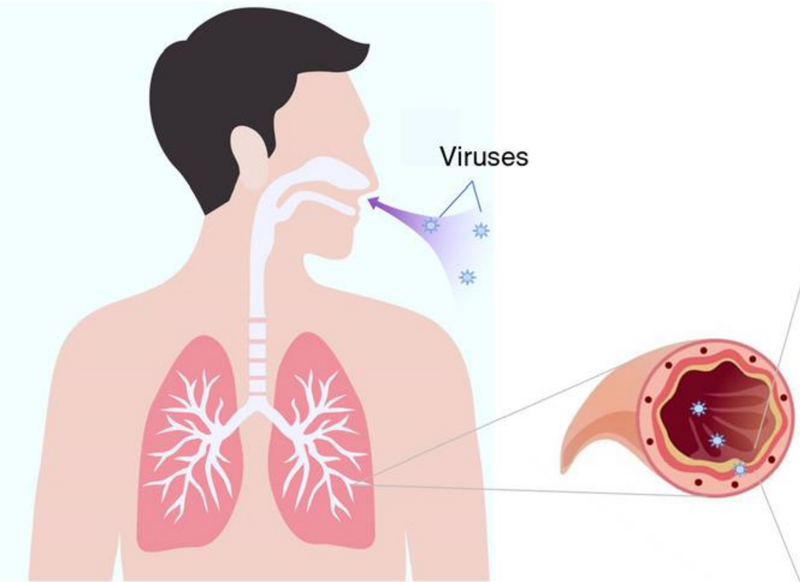
Viral Infection and Asthma
3) Immunologic Landscape

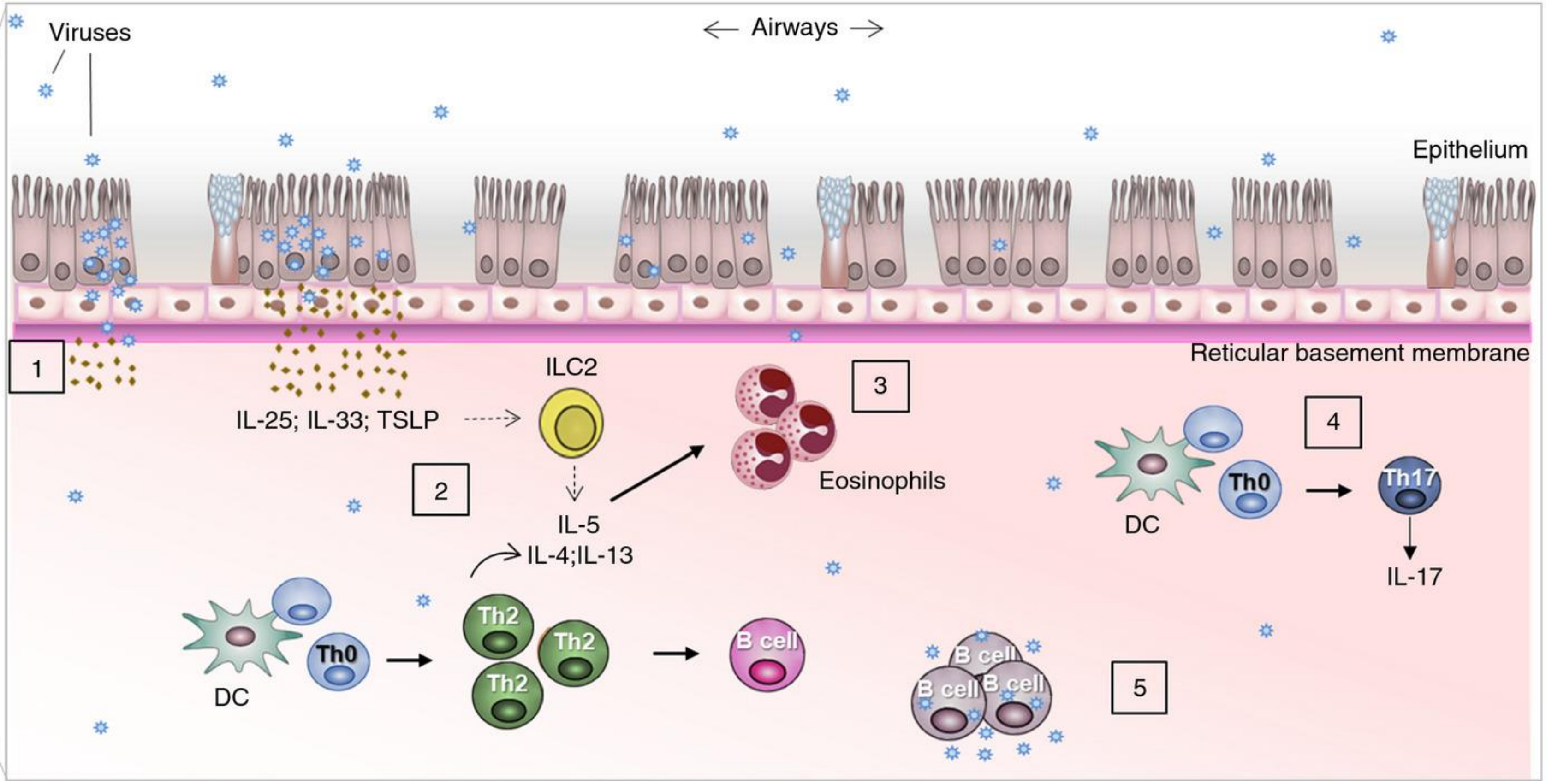
Viral infection led to epithelial damage



Int. J. Mol. Sci. **2022**, *23*(17), 9914

Increased Alarmin and T2 immune reaction





Immunology, 161: 83-93.

Examples of RV

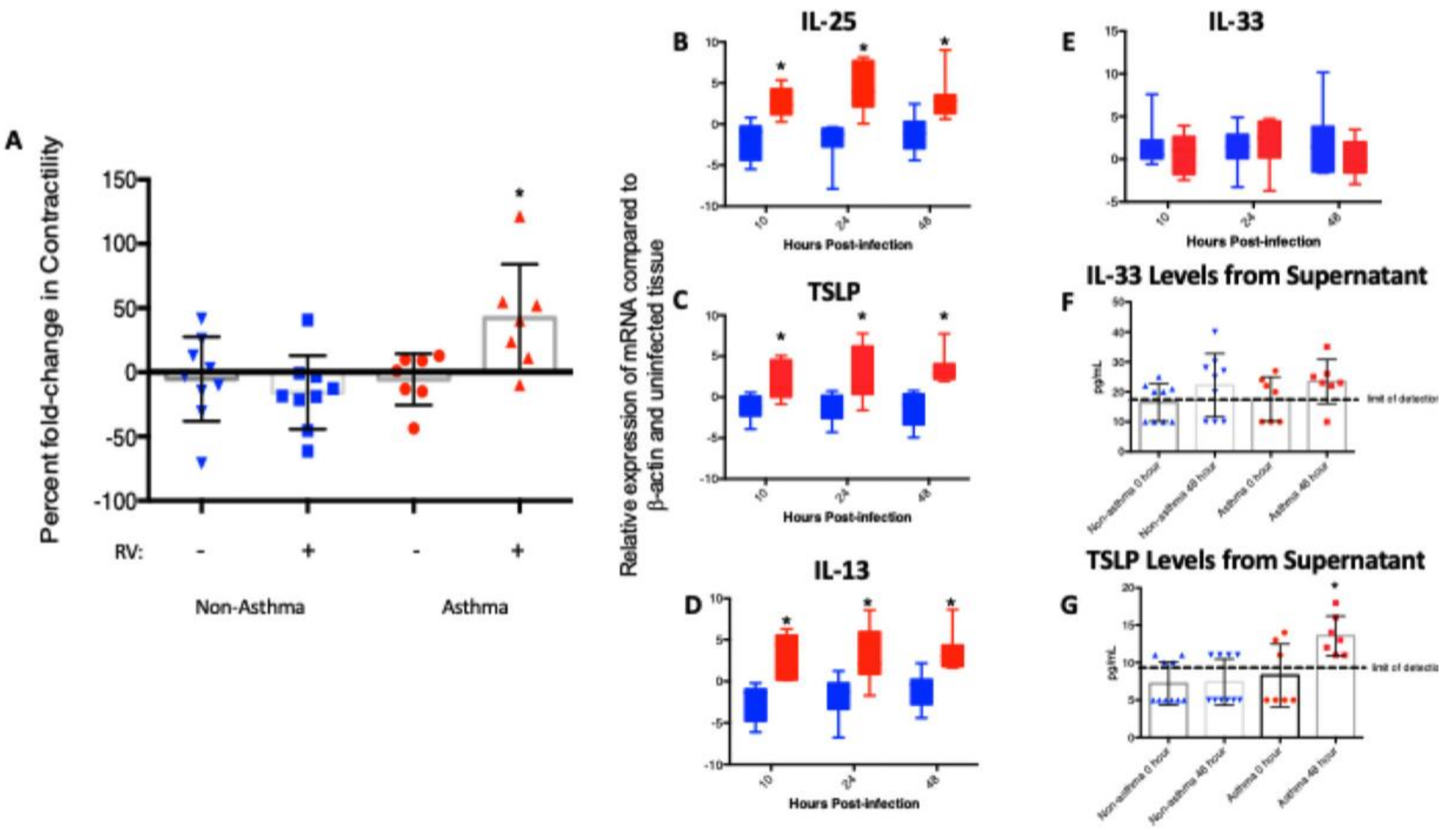
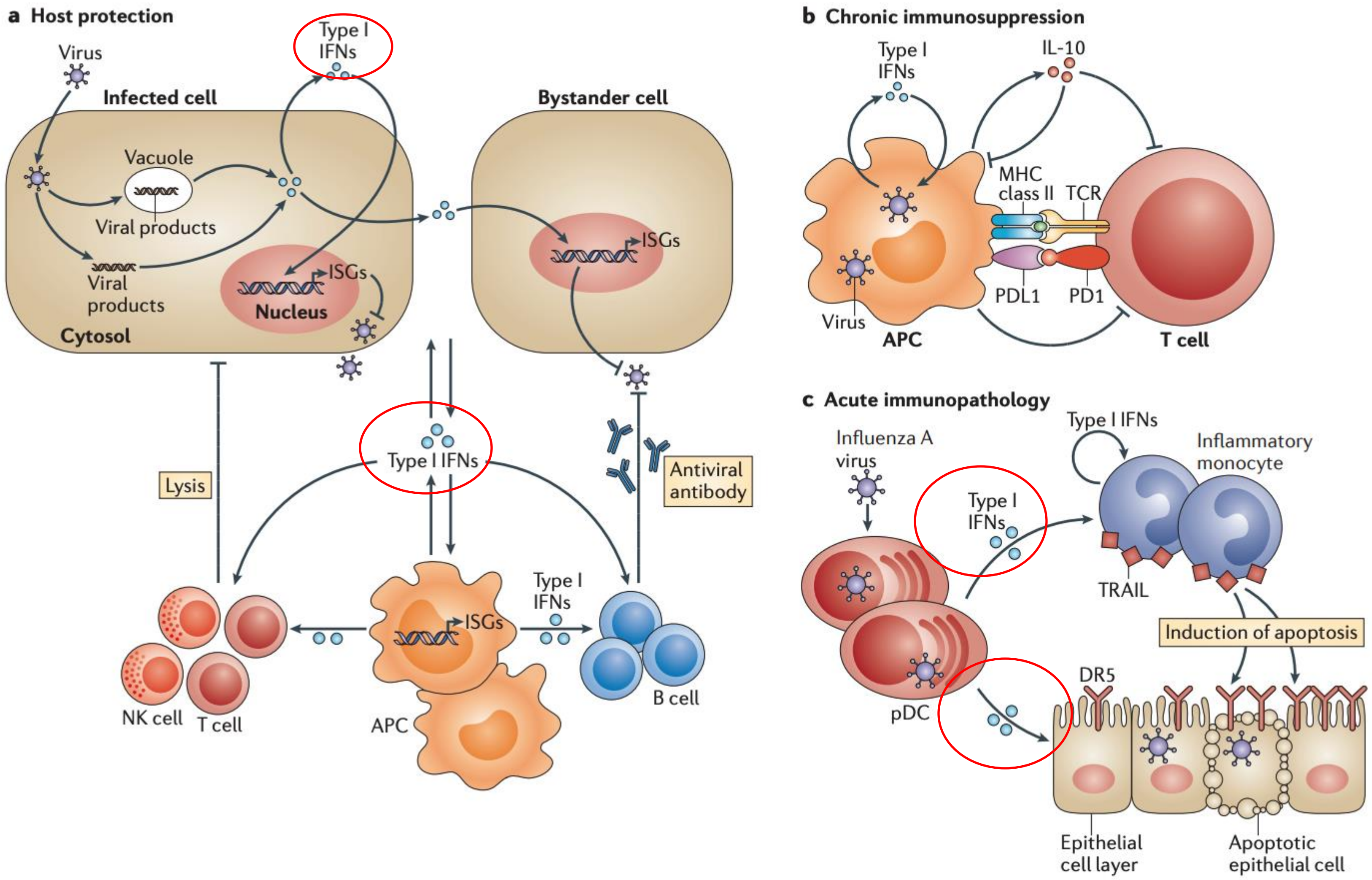


Figure 1: RV39 infection of Human Precision Cut Lung Slices (PCLS) from Asthma Donors.

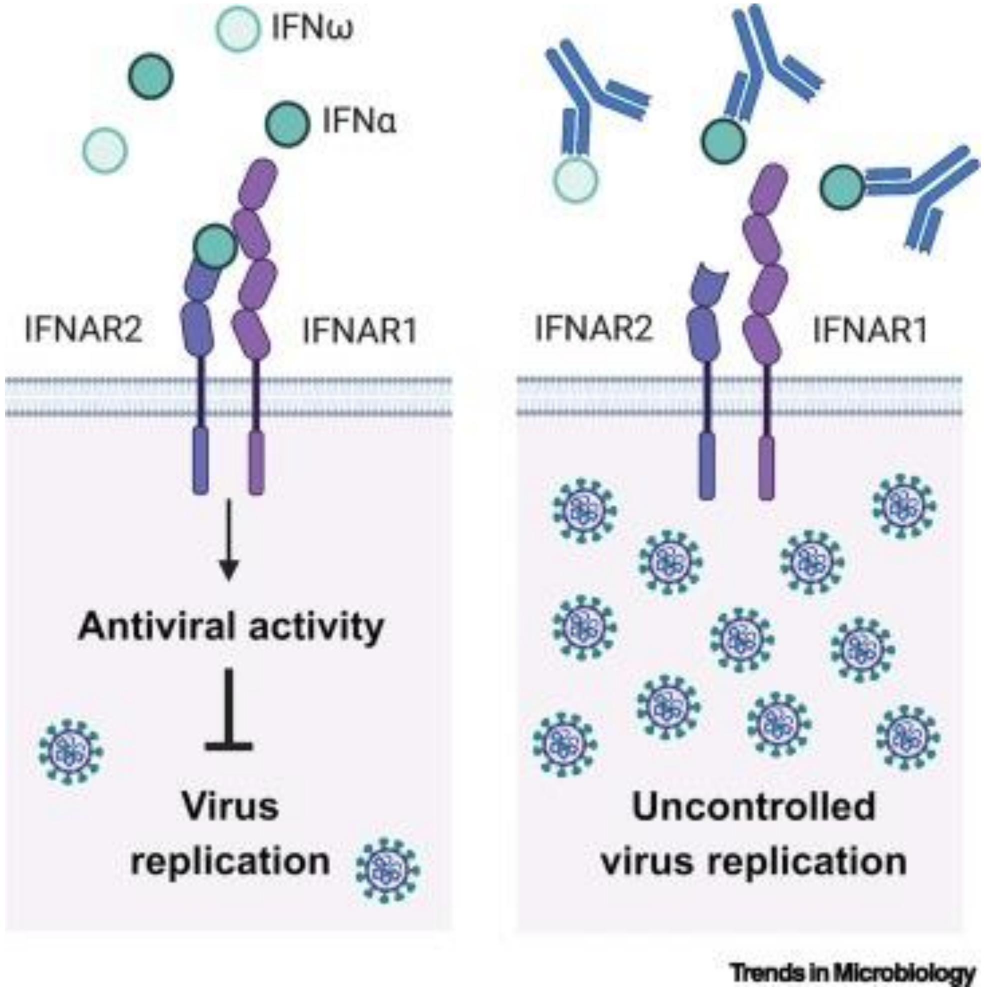
Immunol Allergy Clin North Am. 2019 Aug;39(3):335-344.

Decreased Type 1 IFN in Asthma (non-T2)



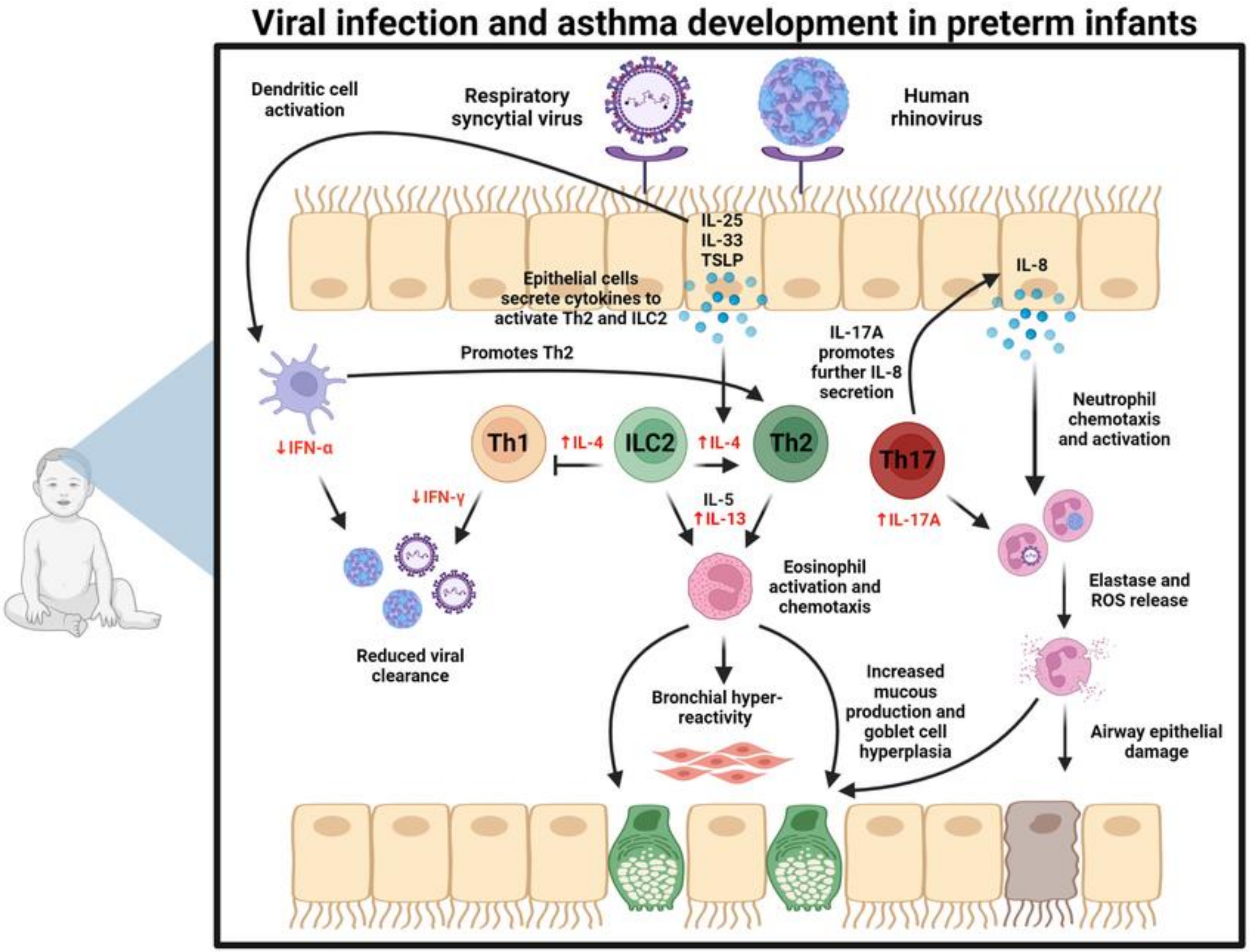
Nature Reviews Immunology 2015

Decreased Type 1 IFN in Asthma (Non-T2)



Persistent Infections

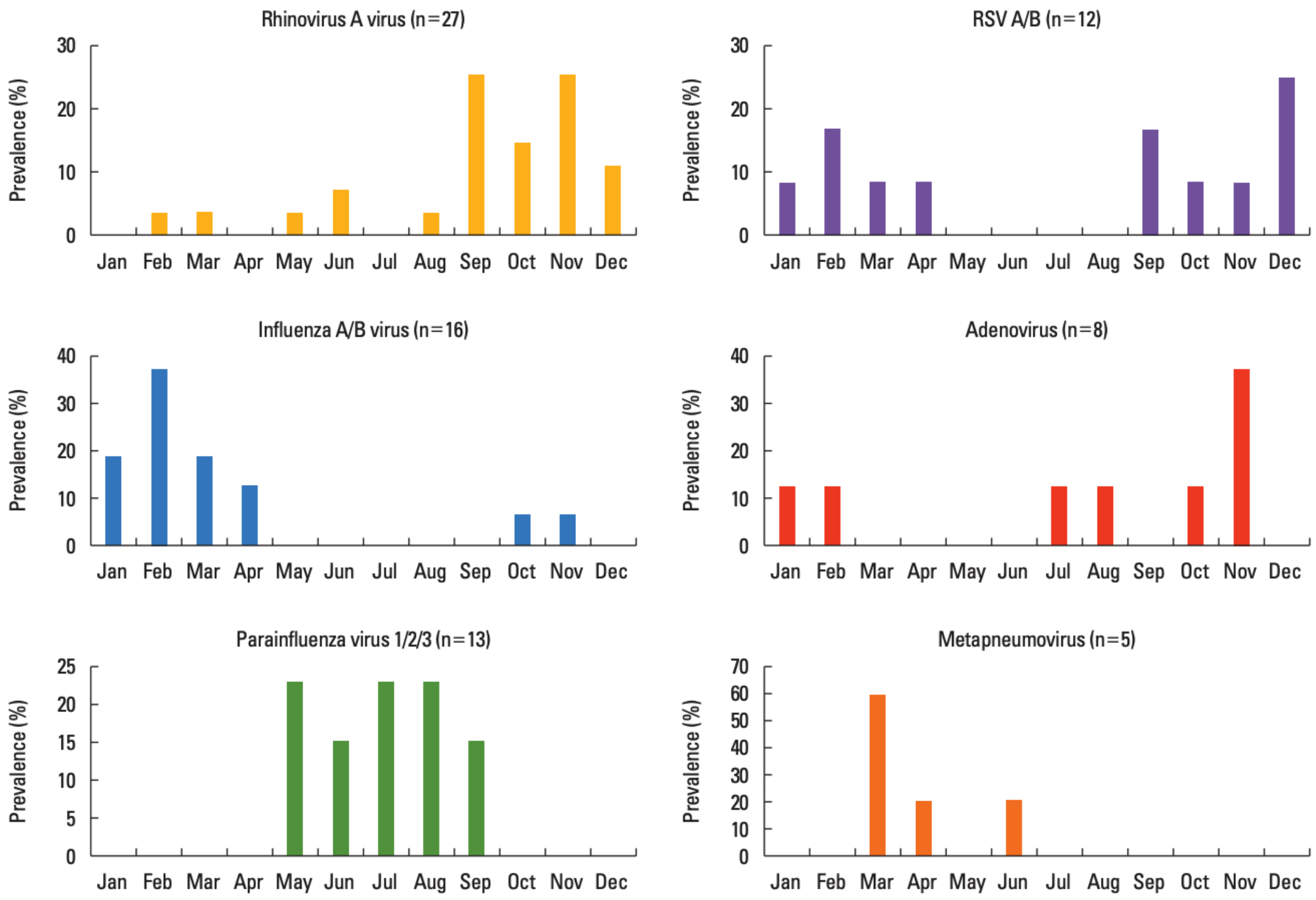
Not always in same ways…



Viral Infection and Asthma
4) Seasonality

Single center study

Prevalence of Respiratory Viral Infections in Korean Adult Asthmatics With Acute Exacerbations: Comparison With Those With Stable State



AAIR 2017 November;9(6):491-498

Seasonality of Causative Pathogen in Korea

An et al. BMC Pulmonary Medicine (2024) 24:474
https://doi.org/10.1186/s12890-024-03298-x

BMC Pulmonary Medicine

RESEARCH **Open Access**

Check for updates

Similarity analyses of causative viruses for chronic obstructive pulmonary disease and asthma exacerbations

Author

Tai Joon An[1], Jangwon Lee[2], Myoungin Shin[3], Kwang Ha Yoo[4], Yong Il Hwang[5], Kyung Hoon Min[6], Deog Kyeom Kim[7], Yun Su Sim[8], Ji Ye Jung[9] and Chin Kook Rhee[10*] on behalf of the Korean Asthma Study Group and the Korean COPD Study Group in The Korean Academy of Tuberculosis and Respiratory Diseases (KATRD)

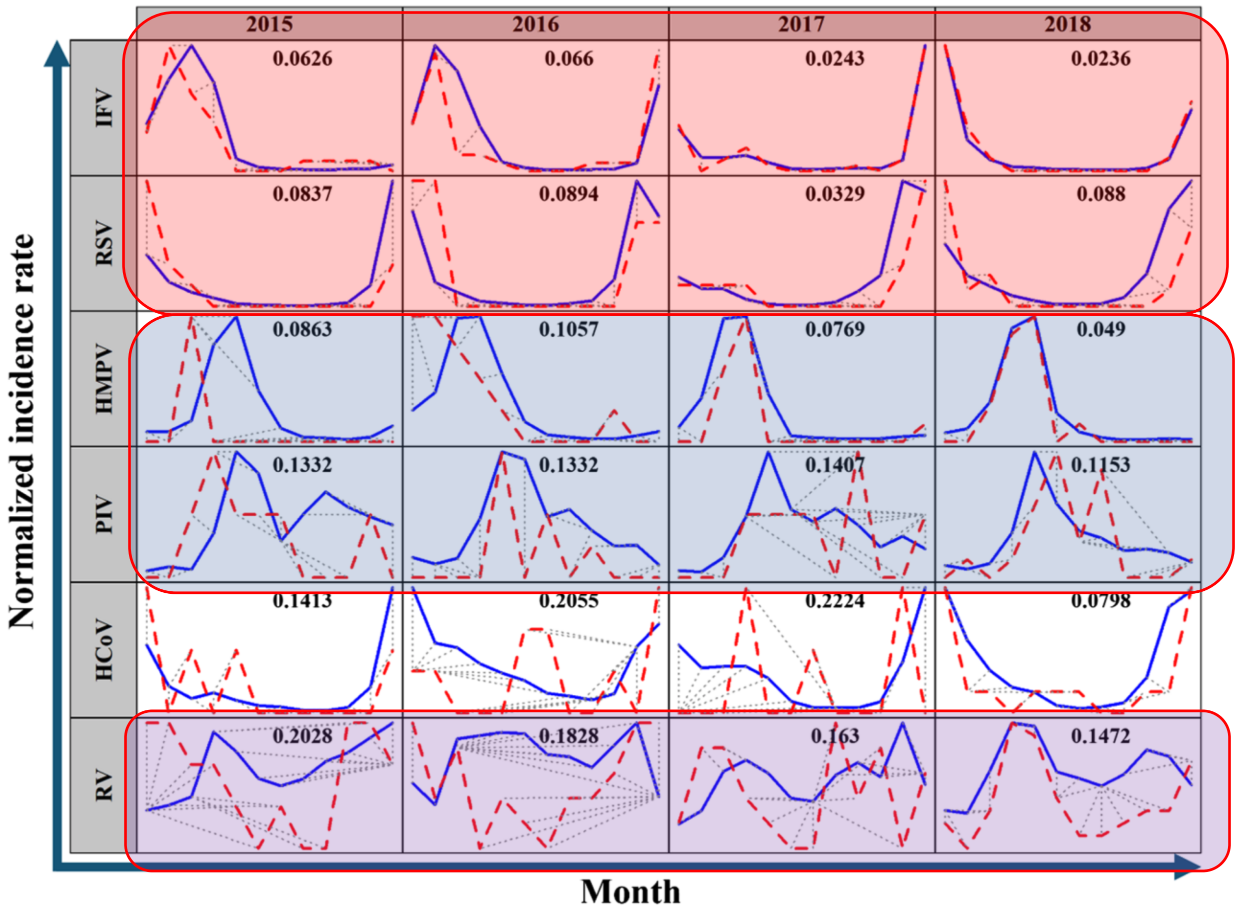
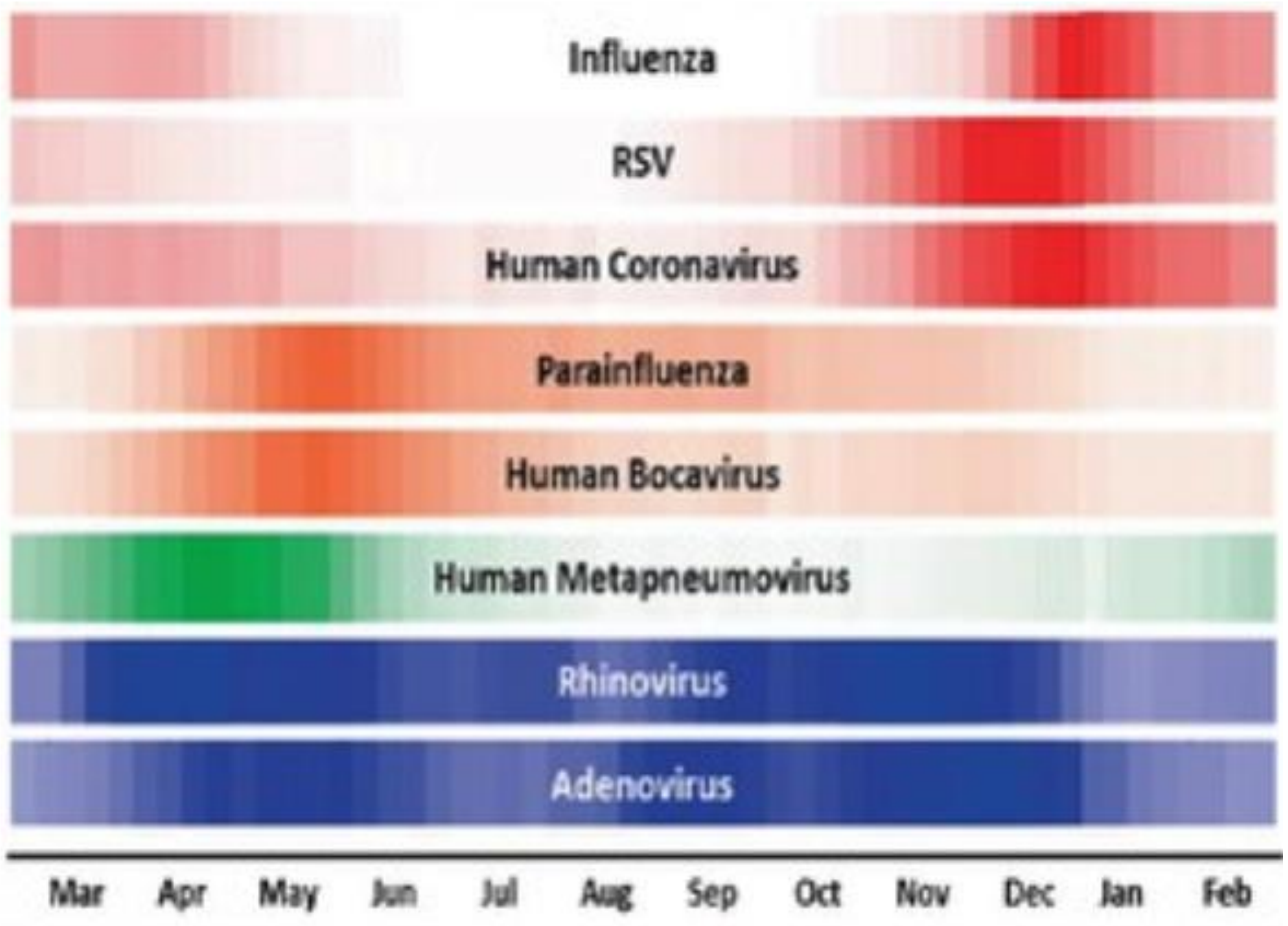


Fig. 1 The results of dynamic time warping (DTW). Figure 1 provides results of the dynamic time warping analyses. Blue line means positivity trends of KDCA data and red dash line means those of multicenter retrospective cohort data in each year. IFV, RSV, HMPV, and PIV showed synchronicity

Common Respiratory Viruses in Korea



Respirology. 2024 Nov;29(11):985-993

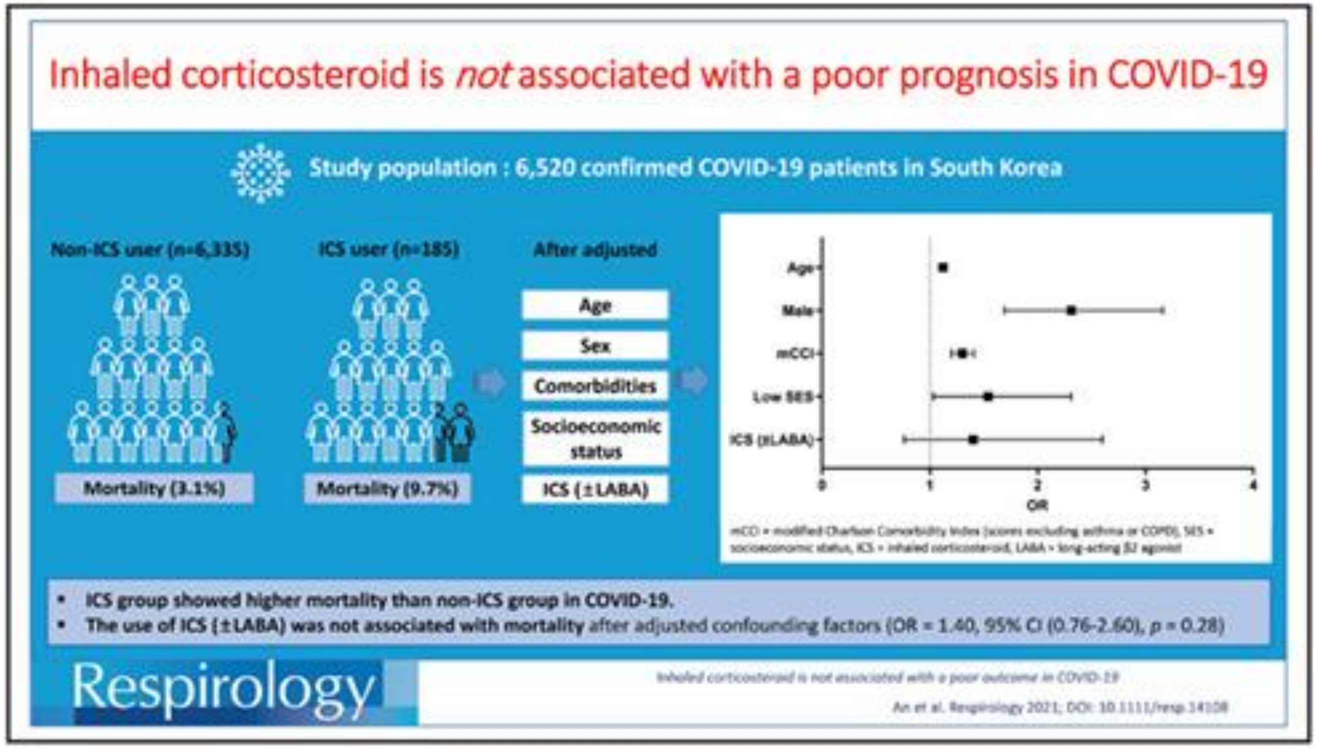
What should we do?

ICS and Asthma

SCIENTIFIC LETTER

Respirology WILEY

Inhaled corticosteroid is not associated with a poor prognosis in COVID-19



Effect of asthma and asthma medication on the prognosis of patients with COVID-19

Yong Jun Choi [1], Ju-Young Park [2], Hye Sun Lee [2], Jin Suh [1], Jeung Yoon Song [1], Min Kwang Byun [1], Jae Hwa Cho [1], Hyung Jung Kim [1], Jae-Hyun Lee [3,4], Jung-Won Park [3,4] and Hye Jung Park [1]

TABLE 3 Significant factors associated with mortality

	Univariate		Multivariate		VIF
	OR (95% CI)	p-value	OR (95% CI)	p-value	
Among all COVID-19 patients#					
Asthma	2.885 (1.726–4.822)	<0.001**	1.317 (0.708–2.451)	0.385	
Among asthma patients¶					
ICS alone					
Past year	1.685 (0.612–4.637)	0.313	11.741 (0.765–180.151)	0.077	1.630
Past 2 months	2.059 (0.745–5.691)	0.164	17.810 (0.944–336.092)	0.055	1.822
ICS–LABA					
Past year	1.462 (0.541–3.951)	0.454	1.444 (0.130–16.103)	0.765	1.425
Past 2 months	1.663 (0.615–4.502)	0.316	3.493 (0.242–50.396)	0.358	1.551
Oral LABA					
Past year	0.747 (0.253–2.204)	0.597	0.890 (0.113–7.023)	0.912	1.238
Past 2 months	0.872 (0.295–2.578)	0.804	0.685 (0.085–5.508)	0.722	1.341
Patch LABA					
Past year	0.252 (0.032–1.954)	0.187	0.139 (0.003–6.226)	0.309	1.583
Past 2 months	0.296 (0.038–2.309)	0.246	1.358 (0.016–112.584)	0.892	1.799
LTRA					
Past year	1.194 (0.373–3.821)	0.765	1.203 (0.070–20.631)	0.899	1.278
Past 2 months	1.699 (0.534–5.408)	0.370	1.795 (0.086–37.650)	0.707	1.428
Inhaled SABA					
Past year	2.505 (0.941–6.862)	0.074	1.925 (0.172–21.588)	0.595	1.686
Past 2 months	2.989 (1.089–8.208)	0.034*	1.273 (0.112–14.420)	0.846	1.924
Oral SABA					
Past year	1.382 (0.372–5.125)	0.629	1.836 (0.154–21.926)	0.631	1.193
Past 2 months	1.509 (0.405–5.621)	0.540	1.626 (0.113–23.347)	0.721	1.284
Xanthine					
Past year	1.114 (0.413–3.003)	0.831	0.464 (0.072–2.997)	0.420	1.208
Past 2 months	1.360 (0.504–3.667)	0.544	0.753 (0.121–4.690)	0.761	1.287
Inhaled LAMA					
Past year	5.225 (1.737–15.716)	0.003*	0.515 (0.051–5.193)	0.574	1.593
Past 2 months	5.225 (1.737–15.716)	0.003*	0.371 (0.038–3.643)	0.395	1.617
Severity of asthma (reference step 1)					
Step 2	0.428 (0.079–2.323)	0.325	0.068 (0.005–1.002)	0.050	1.668
Step 3	0.400 (0.044–3.627)	0.415	0.055 (0.001–2.059)	0.117	1.397
Step 4	0.974 (0.308–3.078)	0.964	0.409 (0.042–3.955)	0.440	1.759
Step 5	0.000 (0.000–999.999)	0.987	0.000 (0.000–999.999)	0.978	1.171

Biologics, Virus, and Asthma AE

Table 1. Proposed mechanisms of how asthma biologics can increase antiviral responses

Biologic	Target	Proposed mechanism of boosting antiviral responses
Omalizumab	IgE	Allergen-bound immunoglobulin E (IgE) inhibits antiviral type I interferons produced by plasmacytoid dendritic cell (pDC). Blocking IgE prevents inhibition of pDC and enhances type I interferon secretion.
Mepolizumab (IL-5), reslizumab (IL-5), benralizumab (IL-5Ra)	IL-5/IL-5Ra	Toll-like receptor-7 (TLR-7) is crucial in recognizing viral single stranded RNA in endosomes. Interleukin-5 (IL-5) reduces expression of toll-like recptor-7 (TLR-7). Blocking IL-5 or its receptor (IL-5Ra) restores TLR-7 expression.
Dupilumab	IL-4Ra	Suppressor of cytokine signaling-1 (SOCS-1) inhibits Th1 responses and is stimulated by Th2 cytokines in particular interleukin 4 (IL-4). By blocking IL-4 pathway there is a reduces production of SOCS-1 and therefore a stronger antiviral Th1 response. Additionally, IL-4 is necessary for IgE class switching of B cells and IgE plasma cell differentiation. By inhibiting IL-4, dupilumab reduces IgE levels and boosts type I interferon production by pDC.
Tezepelumab	TSLP	Thymic stromal lymphopoietin (TSLP) is an upstream alarmin secreted with the respiratory epithelial cells in the presence of infection or allergen. Inhibiting TSLP reduces downstream Th2 inflammation and might help stabilize the respiratory epithelium but does not change interferon levels. Unlike the other asthma biologics that increase interferon levels and therefore antiviral immunity, it seems that tezepelumab may have a more neutral effect towards viral infections.

Curr Opin Pulm Med 2024, 30:287–293

In near future, we hope…

Global epidemiology of non-influenza RNA respiratory viruses: data gaps and a growing need for surveillance

*Julian W Tang, Tommy T Lam, Hassan Zaraket, W Ian Lipkin, Steven J Drews, Todd F Hatchette, Jean-Michel Heraud, Marion P Koopmans, and the INSPIRE investigators**

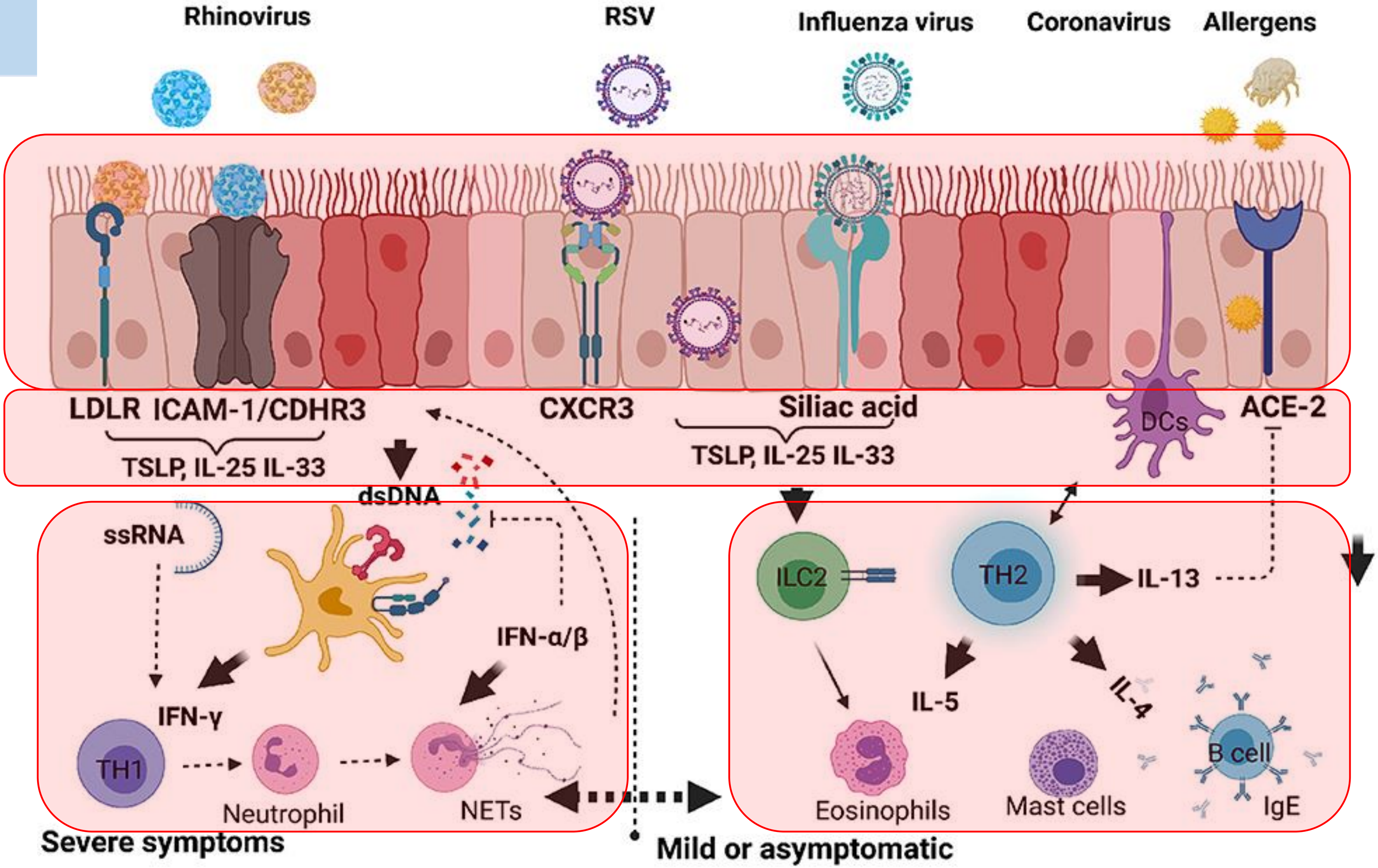
	Influenza	Respiratory syncytial virus	Human parainfluenze virus	Human metapneumovirus	Coronavirus	Rhinovirus
USA	1561 vaccine trials; 190 antiviral drug trials	49 vaccine trials; 33 antiviral drug trials	13 vaccine trials; 0 antiviral drug trials	3 vaccine trials; 0 antiviral drug trials	4 vaccine trials; 4 antiviral drug trials	12 vaccine trials; 3 antiviral drug trials
European Union	357 vaccine trials; 11 antiviral drug trials	4 vaccine trials; 13 antiviral drug trials	1 vaccine trial; 0 antiviral drug trials	0 vaccine trials; 0 antiviral drug trials	0 vaccine trials; 0 antiviral drug trials	1 vaccine trial; 0 antiviral drug trials

***Table*: Ongoing clinical trials associated with vaccine and antiviral drug development for the different respiratory viruses**

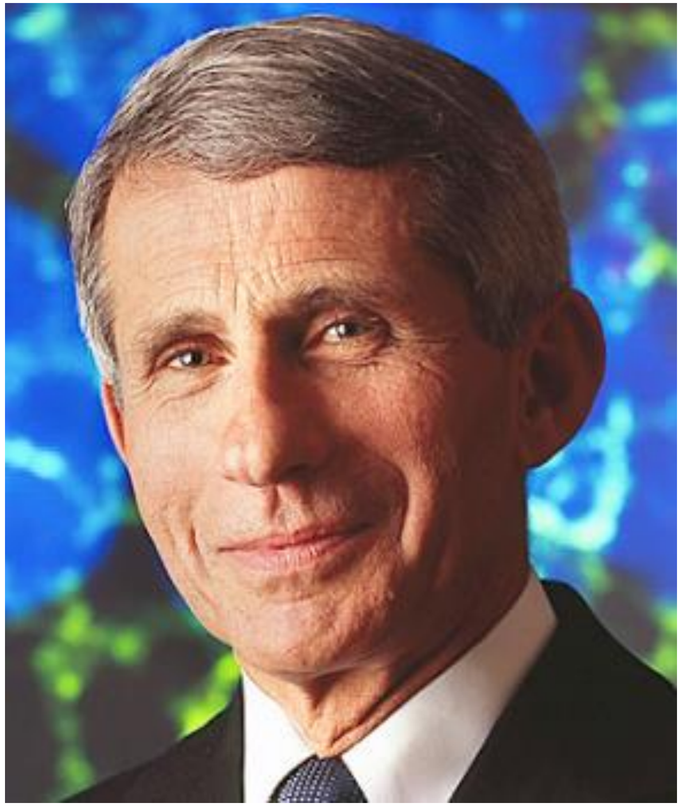
Summary

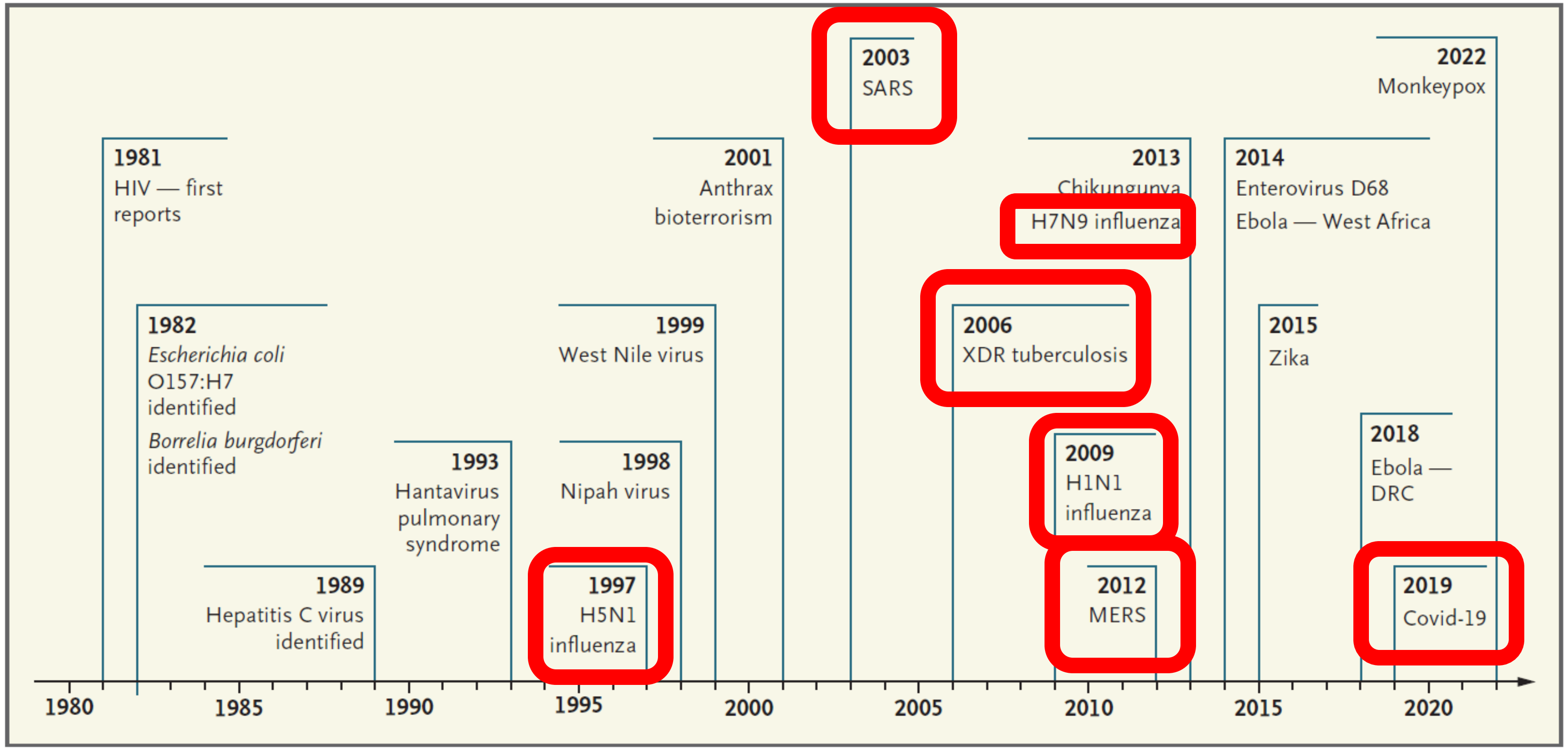
Summarized Tables

Seasonality	Virus	Evidence	Key Findings
All Year Virus	Rhinovirus	Very strong	영유아기 wheezing 동반 감염이 향후 천식의 가장 강력한 예측인자. 알레르기 감작 동반 시 위험 증가.
	Adenovirus	Limited	중증 호흡기 감염 및 wheezing과 일부 연관, 장기적 천식 위험은 불확실.
Winter Virus	Influenza	Limited/Unclear	3세 미만에서 wheezing 유발, 팬데믹 H1N1은 합병증 위험↑. 장기적 천식 발생과의 직접적 연관성은 명확하지 않음.
	RSV	Strong	중증 감염(입원 필요) 후 천식 및 반복적 wheezing 위험 증가.
	Coronavirus	Not supported	최근 연구에서 천식 발생 위험 증가 근거 없음.
Spring/Summer/Fall	Parainfluenza	Limited	급성 wheezing 원인, 장기적 천식 위험 근거 부족.
	Bocavirus	Moderate/Limited	일부 연구에서 위험 증가 보고, 근거 제한적.
	Metapneumovirus	Moderate/Emerging	RSV, rhinovirus와 유사하게 천식 위험 증가 보고.


Rhinovirus
RSV
Influenza virus
Coronavirus
Allergens
LDLR ICAM-1/CDHR3
TSLP, IL-25 IL-33
CXCR3
Siliac acid
TSLP, IL-25 IL-33
DCs
ACE-2
dsDNA
ssRNA
IFN-α/β
IFN-γ
TH1
Neutrophil
NETs
ILC2
TH2
IL-13
IL-5
IL-4
Eosinophils
Mast cells
B cell
IgE
Severe symptoms
Mild or asymptomatic

Respiratory virus: It ain't over.





Selected Landmark Events in Infectious-Disease Emergence Leading up to and during the Author's Four-Decade Tenure as NIAID Director.
DRC denotes Democratic Republic of Congo, MERS Middle East respiratory syndrome, SARS severe acute respiratory syndrome, and XDR extensively drug-resistant.

It ain't over = "아직 끝나지 않았다", " 끝난게 아니다", "이제 시작일 뿐이다"

Thank you