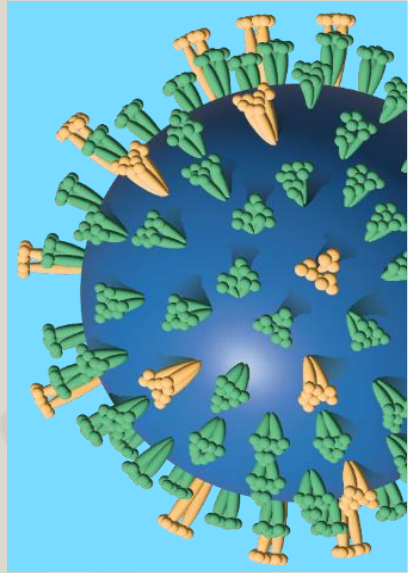


"HMPV from discovery to intervention"



Prof. Albert Osterhaus, DVM-PhD

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University of Veterinary Medicine, Hannover, Germany

Affiliations and COI

Albert Osterhaus



- Founding Director Research Centre for Emerging Infections and Zoonoses, Univ.Vet. Med. (Tiho-RIZ), Hannover
- Guest Scientist Leibniz Inst. Virology (LIV), Hamburg
- Emeritus Professor Erasmus MC, Rotterdam
- Co-founder Viroclinics Biosciences DDL, Rotterdam
- CSO and co-founder of CR2O, CRO Maarssen
- Co-chair Global One Health Community (GOHC)
- Vice chair ESWI
- Member Advice Cttee Vaccination Dutch military
- Ad-hoc consultant, invited speaker and SAB member to pharma companies

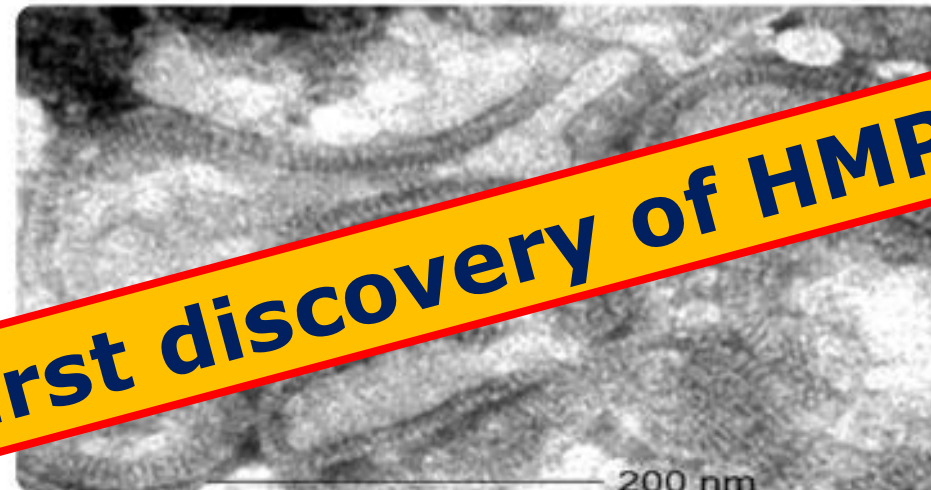
2001



A newly discovered human pneumovirus isolated from young children with respiratory tract disease

BERNADETTE G. VAN DEN HOOGEN¹, JAN C. DE JONG¹, JAN GROEN¹, THIJS KUIKEN¹, RONALD DE GROOT², RON A.M. FOUCHIER¹ & ALBERT D.M.E. OSTERHAUS¹

¹Departments of Virology and ²Pediatrics, Erasmus Medical Center, Rotterdam, the Netherlands
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First discovery of HMPV

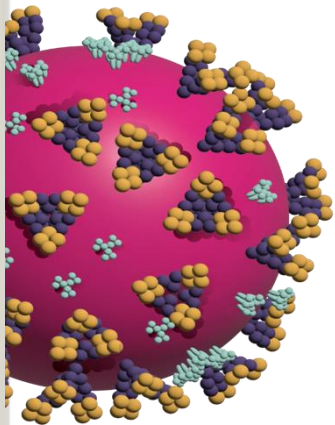


Table 1

Seroprevalence of hMPV antibodies in humans categorized by age group

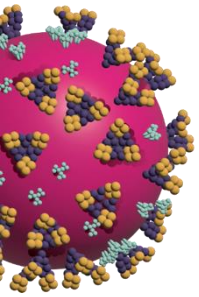


Table 1 Seroprevalence of hMPV antibodies in humans categorized by age group

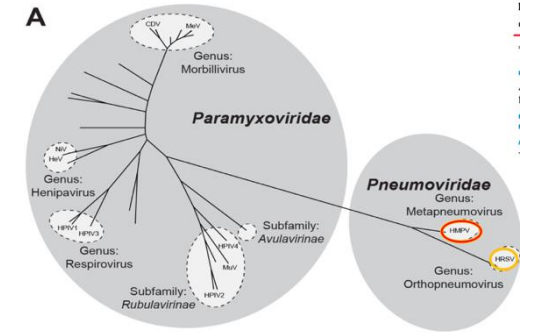
| Age (years) | Immunofluorescence assays | | Virus neutralization assays | | Titer range |
|-------------|---------------------------|-----------------------|-----------------------------|-----------------------|-------------|
| | <i>n</i> tested | <i>n</i> positive (%) | <i>n</i> tested | <i>n</i> positive (%) | |
| 0.5–1 | 20 | 5 (25) | 12 | 3 (25) | 16–32 |
| 1–2 | 20 | 11 (55) | 13 | 4 (31) | 16–32 |
| 2–5 | 20 | 14 (70) | 8 | 3 (38) | 16–512 |
| 5–10 | 20 | 20 (100) | 4 | 4 (100) | 32–256 |
| 10–20 | 20 | 20 (100) | 4 | 3 (75) | 32–128 |
| > 20 | 20 | 20 (100) | 4 | 3 (75) | 32–128 |
| 8–99* | 72 | 72 (100) | 11 | 11 (100) | 16–128 |

*, Sero-archeological analysis using sera collected in 1958 (refs. 16,17).

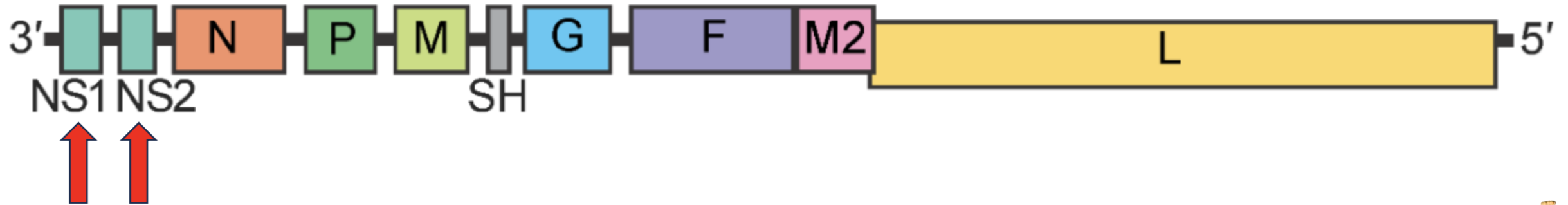
Pneumoviridae comprises large enveloped negative-sense RNA viruses. This taxon was formerly a subfamily within the *Paramyxoviridae*, but was reclassified in 2016 as a family with two genera:



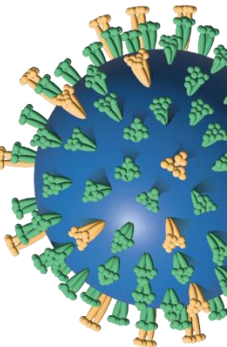
Different genome organisation

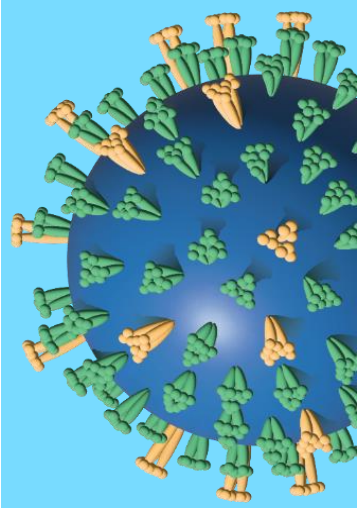
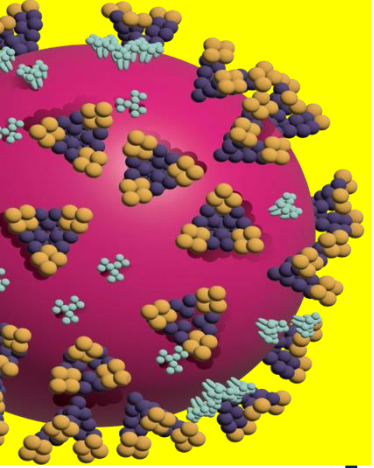


Orthopneumovirus - human respiratory syncytial virus A2 (15,222 nt)



Metapneumovirus - human metapneumovirus A1 (13,330 nt)



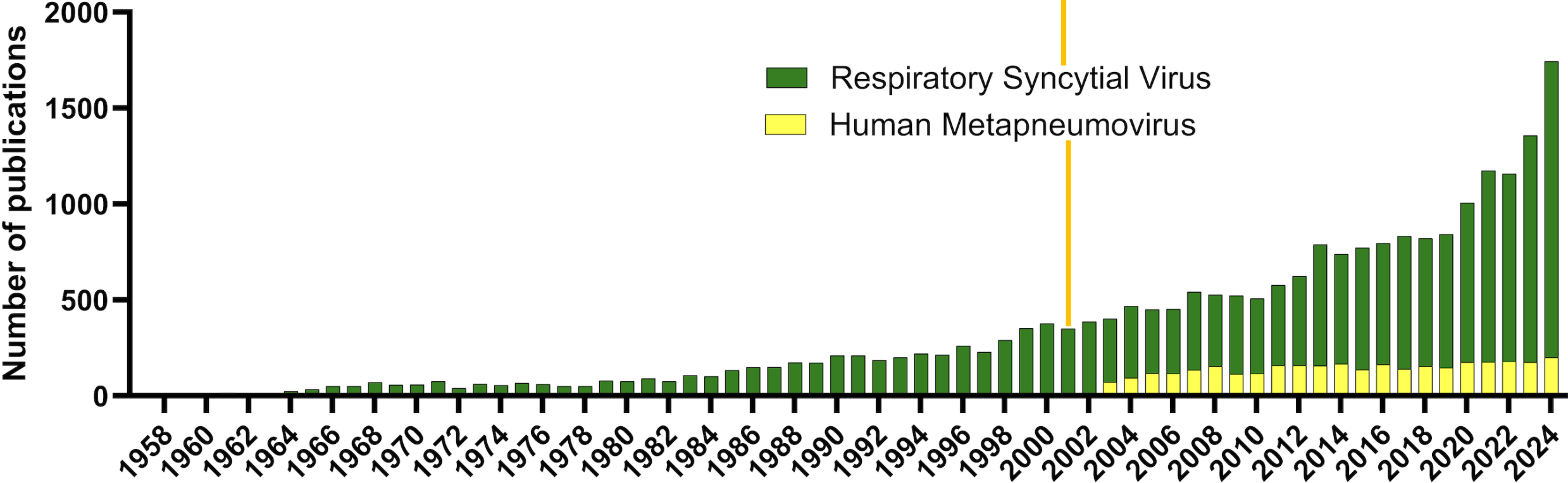


2001

Rotterdam

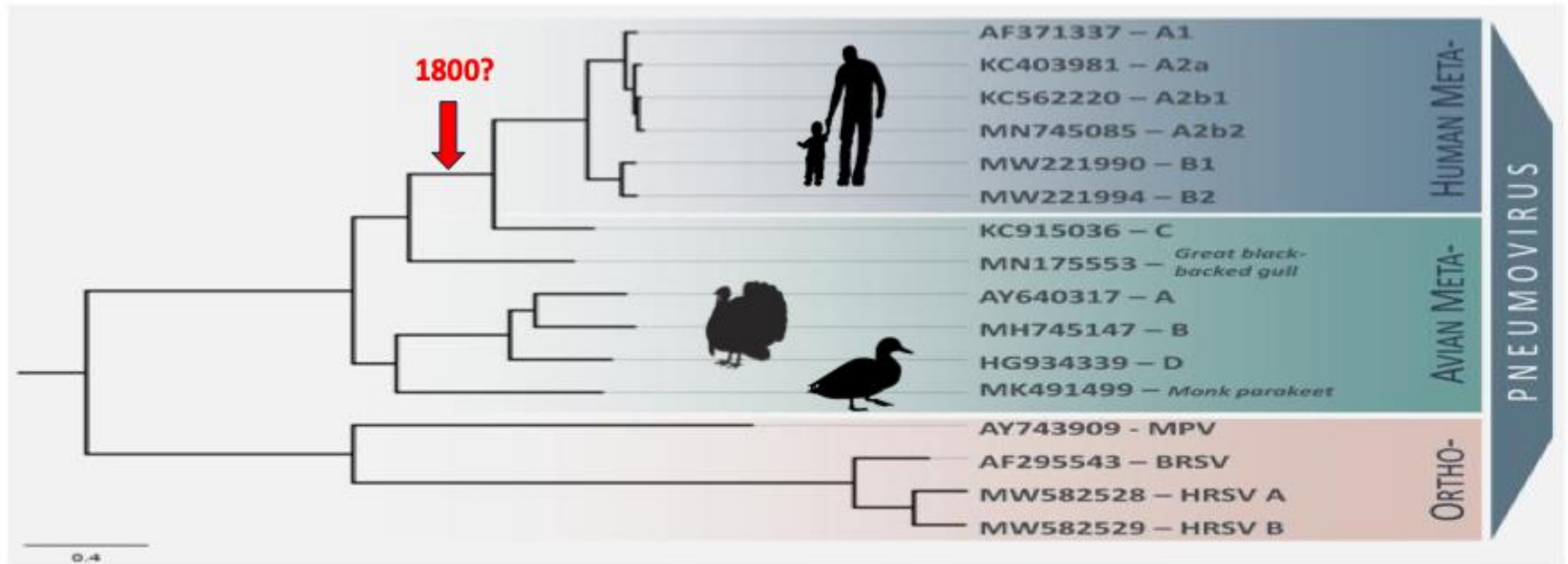
HMPV: 2.710 hits since 2001

HRSV: 10.572 hits since 1960



Zoonotic Origins of Human Metapneumovirus: A Journey from Birds to Humans

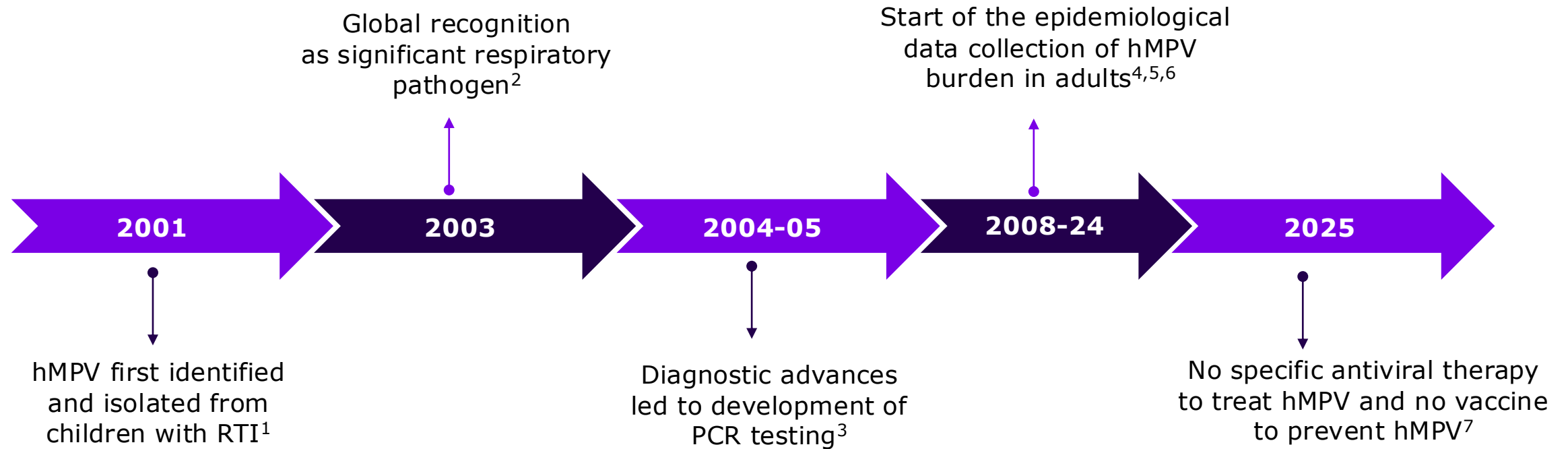
Sonja T Jesse, Martin Ludlow, Albert D M E Osterhaus



Evolutionary dynamics of human and avian metapneumoviruses
Miranda de Graaf, Albert D. M. E. Osterhaus, Ron A. M. Fouchier, Edward C. Holmes
J.Gen.Virol., 2008

MRCA for HMPV and AMPV-C was estimated to have existed **around 200 years ago**

History of hMPV



Though hMPV was first identified in 2001, the virus is circulating in humans for at least 70 years prior to its discovery, with no evidence suggesting recent zoonotic origins⁸

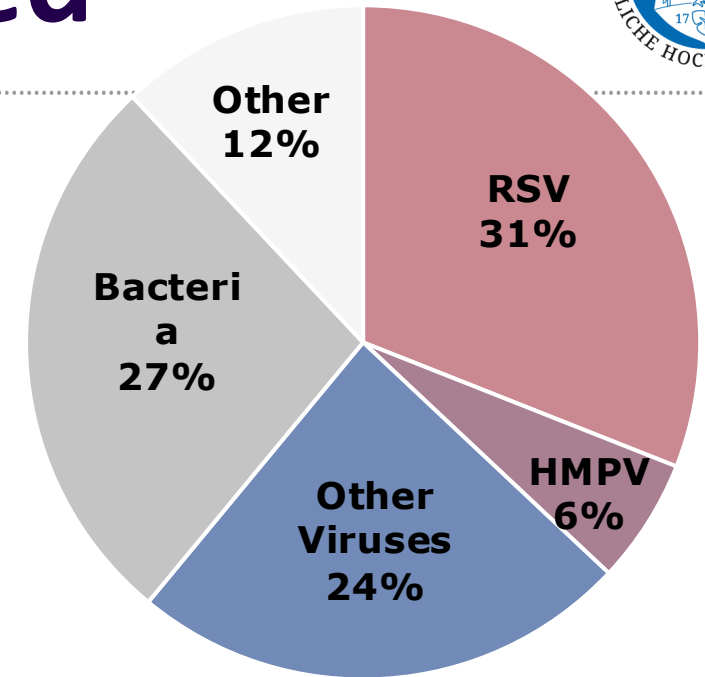
hMPV: Human Metapneumovirus; PCR: Polymerase Chain Reaction; RTI: Respiratory tract infection

References: 1. Mistry LN, et al. *Cureus*. 2025;17(3):e80964. 2. Walsh EE, et al. *Arch Intern Med*. 2008;168(22):2489-2496. 3. Maertzdorf J, et al. *J Clin Microbiol*. 2004;42(3):981-986. 4. Falsey AR, et al. *J Infect Dis*. 2010;201(10):1052-1060. 5. Walsh EE, et al. *Arch Intern Med*. 2008;168(22):2489-2496. 6. Kulkarni D, et al. *Lancet Healthy Longev*. 2025;6(2):100679. 7. Human Metapneumovirus Seasonality and Co-Circulation with Respiratory Syncytial Virus — United States, 2014–2024. Available at [MMWR, Volume 74, Issue 11 — April 3, 2025](https://doi.org/10.1007/s44162-025-00079-w) (accessed on 10 Jun). 8. Adedokun, KA, et al. *J Rare Dis* 2025. Available at <https://doi.org/10.1007/s44162-025-00079-w>. 9. Jesse ST, Ludlow M, Osterhaus ADME. *Viruses*. 2022 Mar 25;14(4):677.

hMPV remains underdiagnosed

due to:

- **limited awareness,**
- **restricted access to reliable diagnostic tools,**
- **frequent co-infections that obscure its contribution to disease severity.**



Rates of Hospitalizations for Respiratory Syncytial Virus, Human Metapneumovirus, and Influenza Virus in Older Adults

[Kyle Widmer](#),¹ [Yuwei Zhu](#),² [John V. Williams](#),^{3,5} [Marie R. Griffin](#),^{1,4,6} [Kathryn M. Edwards](#),³ and [H. Keipp Talbot](#)^{1,3}

The Journal of
Infectious Diseases

2012

A prospective study in older adults to determine the disease burden of:

- *respiratory syncytial virus (RSV)*
- *human metapneumovirus (HMPV)*
- *in comparison with influenza virus (FluV)*

Methods.

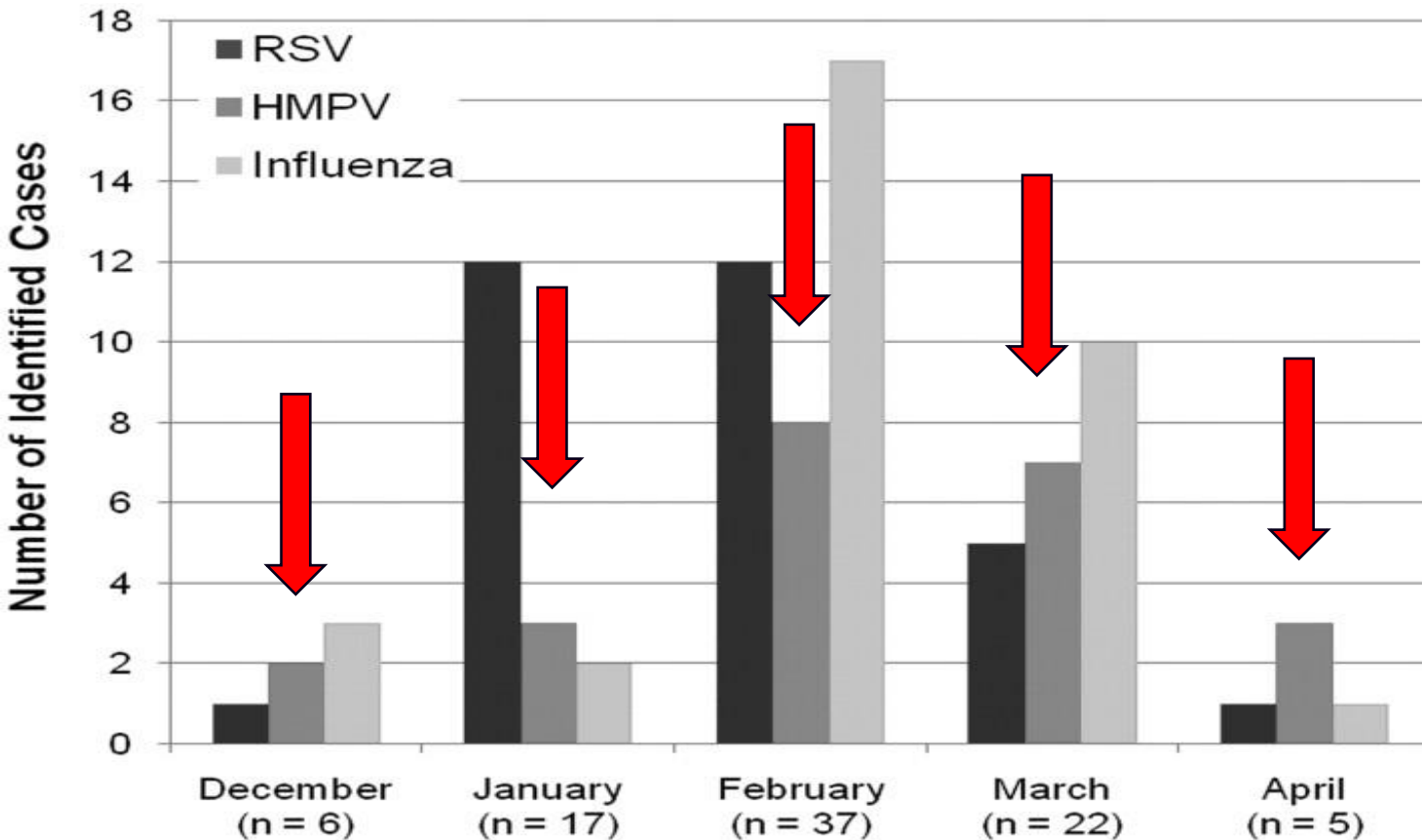
- Three consecutive winters
- Davidson County (Nashville, TN) residents aged ≥ 50 years
- admitted to 1 of 4 hospitals with ARI
- Nasal/throat swabs tested for influenza, RSV, and HMPV with RT-PCR.
- Hospitalization rates were calculated.

Rates of Hospitalizations for Respiratory Syncytial Virus, Human Metapneumovirus, and Influenza Virus in Older Adults

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The Journal of
Infectious Diseases

2012



- Data from three subsequent years
- AUCs similar

RSV

HMPV

Flu

Case report

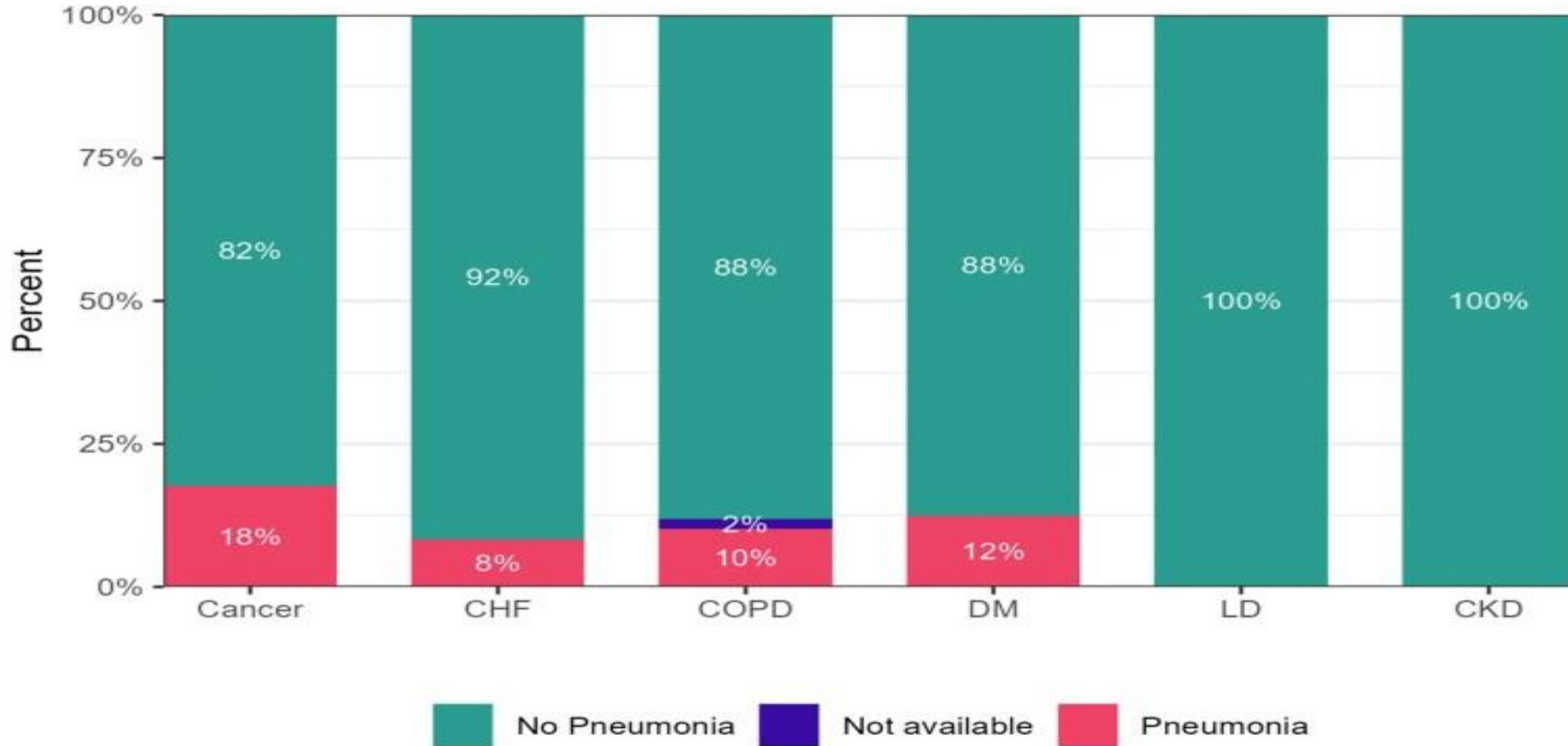
Human metapneumovirus in a haematopoietic stem cell transplant recipient with fatal lower respiratory tract disease

PA Cane¹, BG van den Hoogen², S Chakrabarti^{3,4}, CD Fegan⁴ and ADME Osterhaus²

¹*Division of Immunity & Infection, University of Birmingham Medical School, Birmingham, UK;* ²*Department of Virology, Erasmus Medical Centre, Rotterdam, The Netherlands;* ³*Bone Marrow Transplant Unit, Bristol Royal Hospital for Sick Children, Bristol, UK;* and ⁴*Department of Haematology, Heartlands Hospital, Bordesley Green East, Birmingham, UK*

Human Metapneumovirus Epidemiology Among Middle-aged and Older Adults Hospitalized With Acute Respiratory Infection

Pott H. *et al.*, JID 2025



Percentage of patients diagnosed with pneumonia due to human metapneumovirus infection, categorized by underlying comorbidities. Abbreviations: CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; LD, liver disease.

Proportion of respiratory viruses RSV+HMPV that account for ARI hospitalization in adults: 5-15%

- In 2 US studies of hospitalized adults, **4.5% to 8.5% of illnesses were identified as hMPV related**, with those infected having high rates of chronic cardiopulmonary conditions

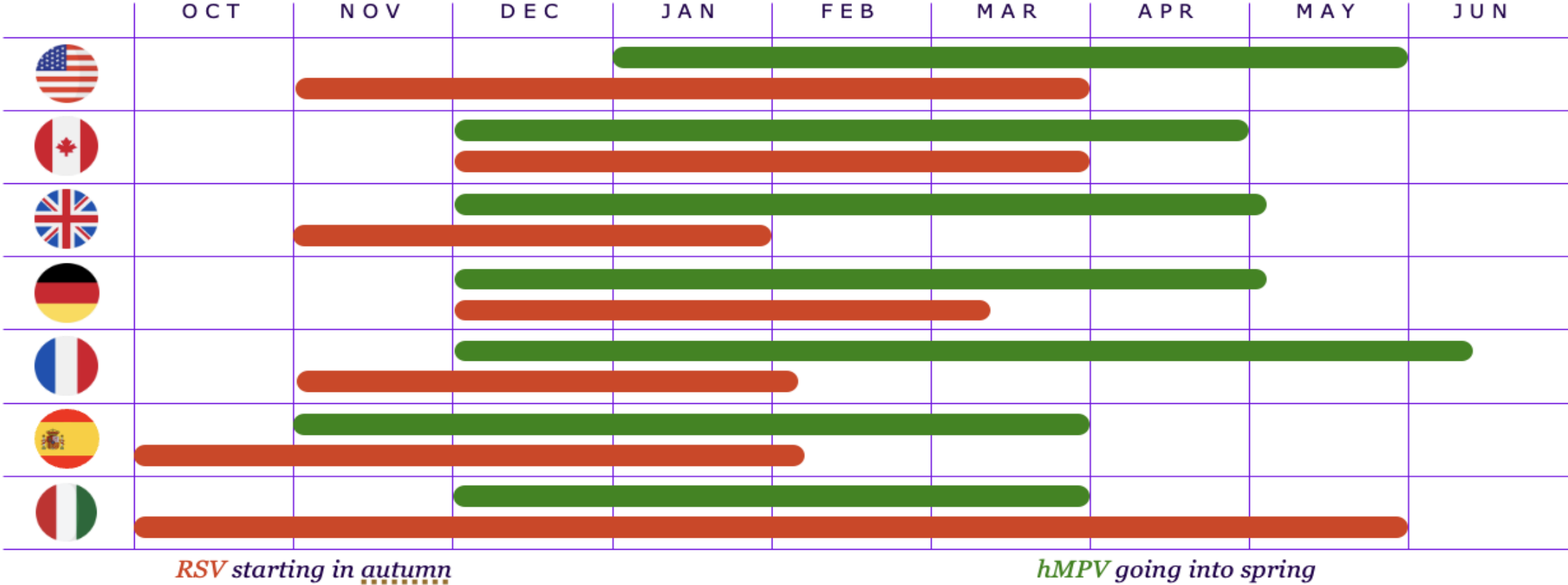
Walsh EE *et al.*, Arch Intern Med 2008

Widmer. K. *et al.*, JID 2012

- Combining 2 other USA studies resulted in a total of 1914 ARI hospitalizations evaluated, 127 **(6.6%) with RSV** and 90 **(4.7%) with HMPV** as single viral infections available for the comparative analysis.

Samoriski C. *et al.*, JID 2025

RSV+hMPV Epidemic Months Overlap in Northern Hemisphere*1-4



Although most of the data are from the pre-COVID period, a study indicates that RSV+hMPV have shown seasonal patterns in most countries, with a gradual return to pre-pandemic seasonality⁵

*Duration of epidemics is defined as the minimum number of months to account for 75% of annual positive samples, with each component month defined as an epidemic month (except for Spain and Italy). Systematic analysis of studies between 2000 and 2017
hMPV, Human Metapneumovirus; **RSV**, Respiratory Syncytial Virus; **UK**, United Kingdom; **US**, United States.
1. Li Y, Nair H et al. The Lancet Global Health Volume 7, Issue 8, August 2019, Pages e1031-e1045; **2.** Piñana M, et al. *J Clin Virol.* 2020;132:104590. ; **3.** Obando-Pacheco P, et al. *J Infect Dis.* 2018;217(9):1356-1364; **4.** Guido M, et al. *Virology.* 2011;417(1):64-70; **5.** Billard MN, et al. *Open Forum Infect Dis.* 2025 Jan 29;12(Suppl 1):ofae631.2490.

HMPV in the spotlight early 2025!



THE ECONOMIC TIMES | News

English Edition | Today's ePaper

HMPV may be rising in China, but it has been reported in US previously. The 'most important' virus, explained

Protection of infants from RSV infection

Maternal RSV Vaccine (RSVpreF)

Advantages

- Provides protection immediately after birth
- Might be more resistant to potential RSV mutation

Disadvantages

- Protection potentially reduced if fewer antibodies are produced or are transferred from mother to infant (e.g., mother is immunocompromised, infant is born soon after vaccination, or infant has prematurity)
- Potential risk for hypertensive disorders of pregnancy

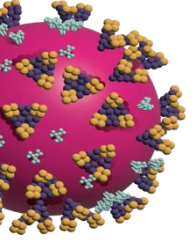
RSV Monoclonal Antibodies

Advantages

- Protection might last longer
- Ensures infant receives antibodies directly rather than relying on transplacental transfer
- No risk for adverse pregnancy outcomes

Disadvantages

- Requires infant to receive an injection
- Product might not be available



Human metapneumovirus (HMPV)



- **Discovered in 2001 in infants suspected of RSV-infection.**
- **Causes globally serious ARV in URT and LRT in:**
 - *Infants*
 - *Older adults*
 - *Immune-compromised individuals.*
- **BOD comparable to RSV and influenza in older adults.**
- **Epidemics in winter and spring (in moderate climate zones).**
- **Limited antigenic drift**
- **Still no vaccine or antiviral treatment available.**
- **MoAb and vaccine development inspired by new RSV interventions.**
- **Several antiviral and vaccine candidates in the pipeline.**