# Respiratory Virus

**14.05.2025**

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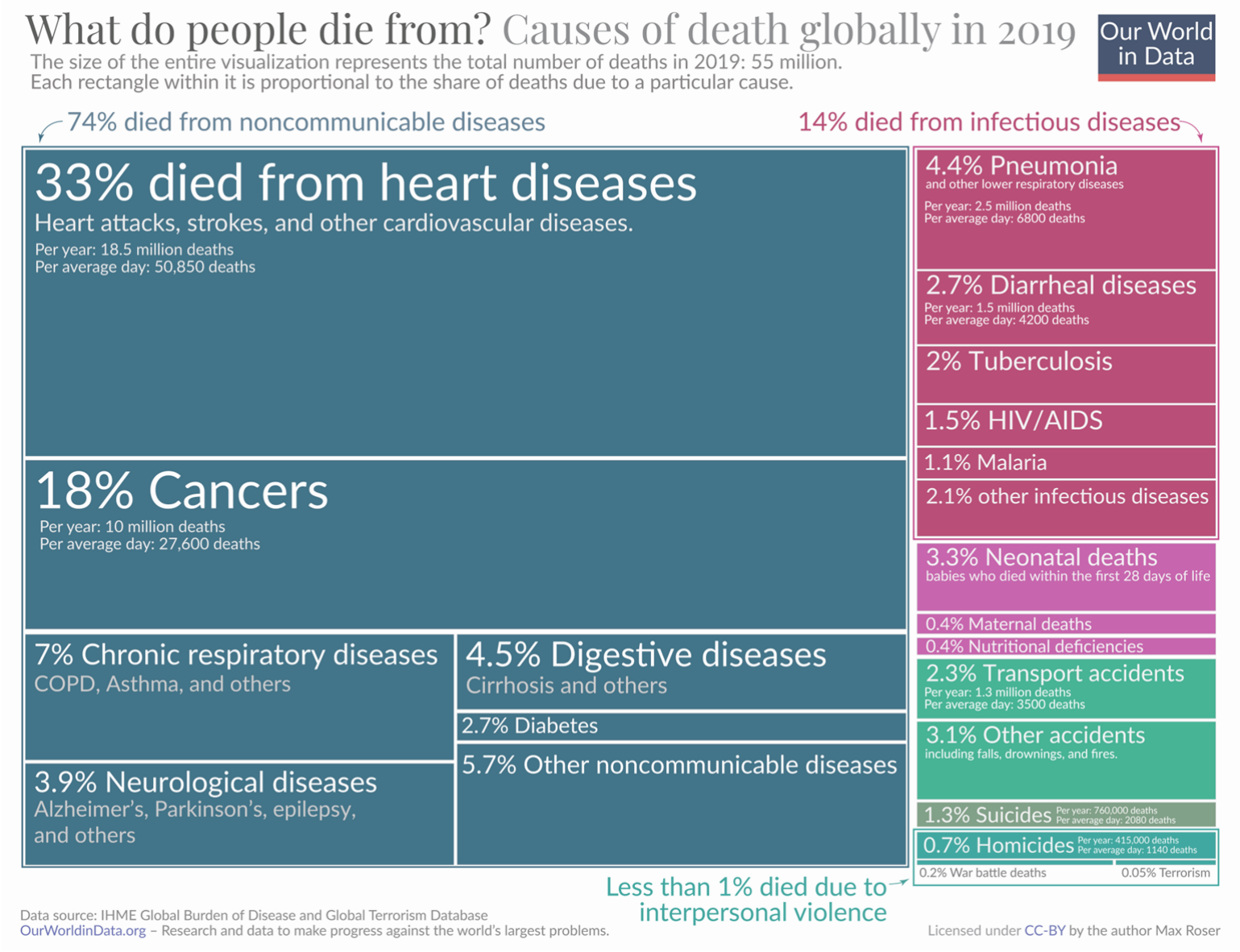
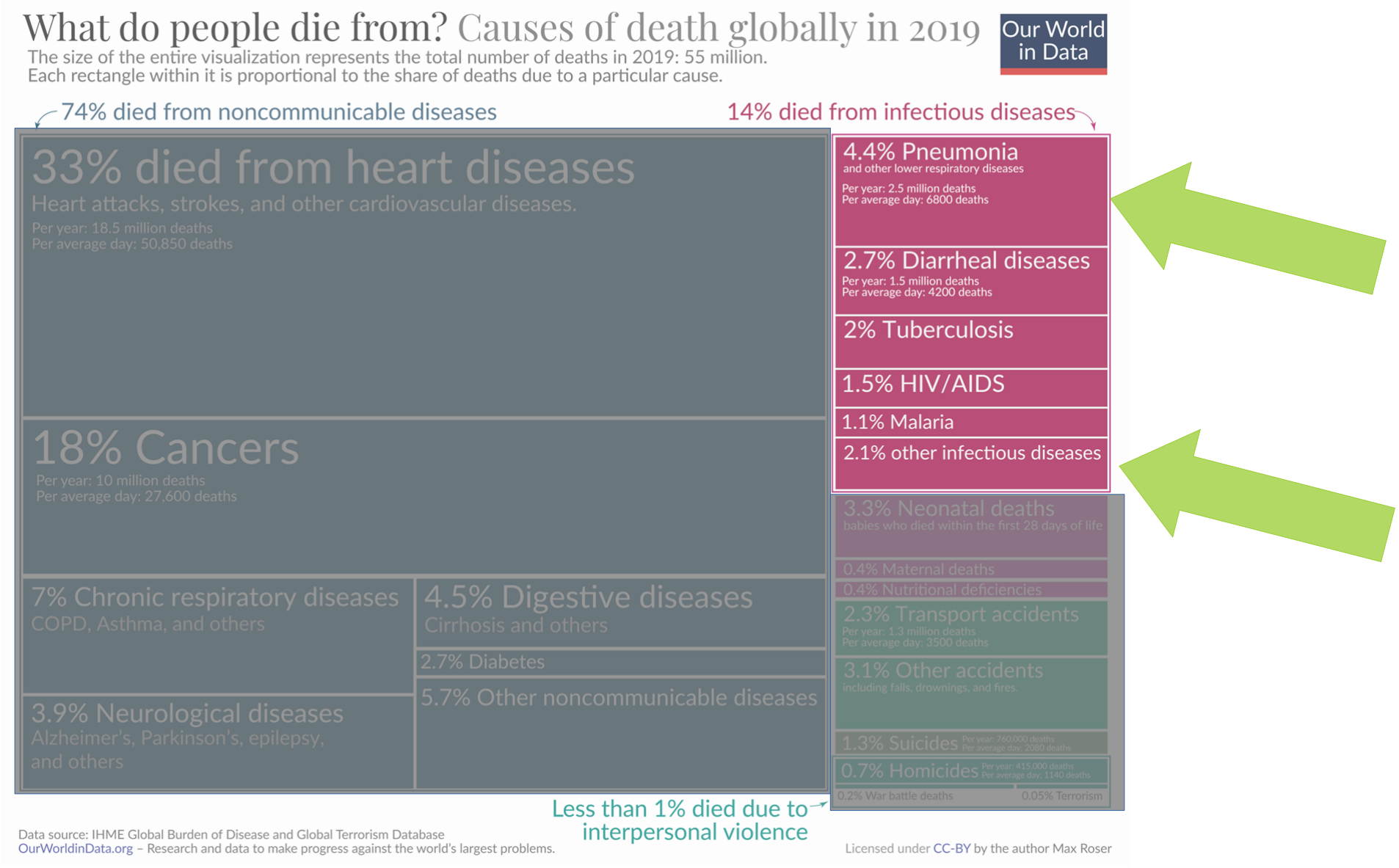
# Structure and Objectives

- Global burden of respiratory virus infections
- Seasonality of respiratory virus
- Respiratory tract
- Reservoir drops: Influenza
- Goopfellas: RSV
- Natural born killer: SARS
- Pulp afflictions: Other respiratory virus

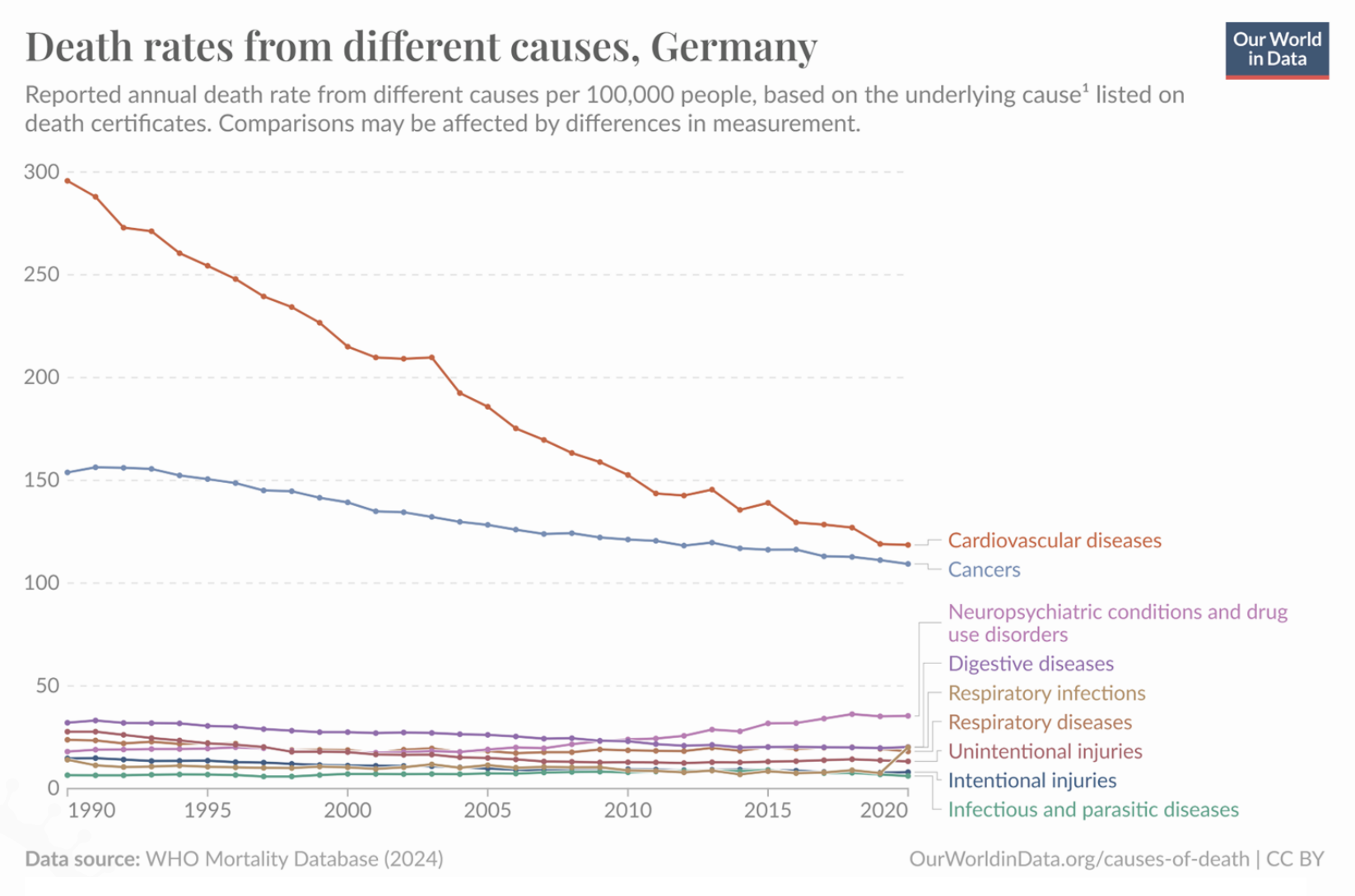
# Global burden of respiratory virus



# Global burden of respiratory virus

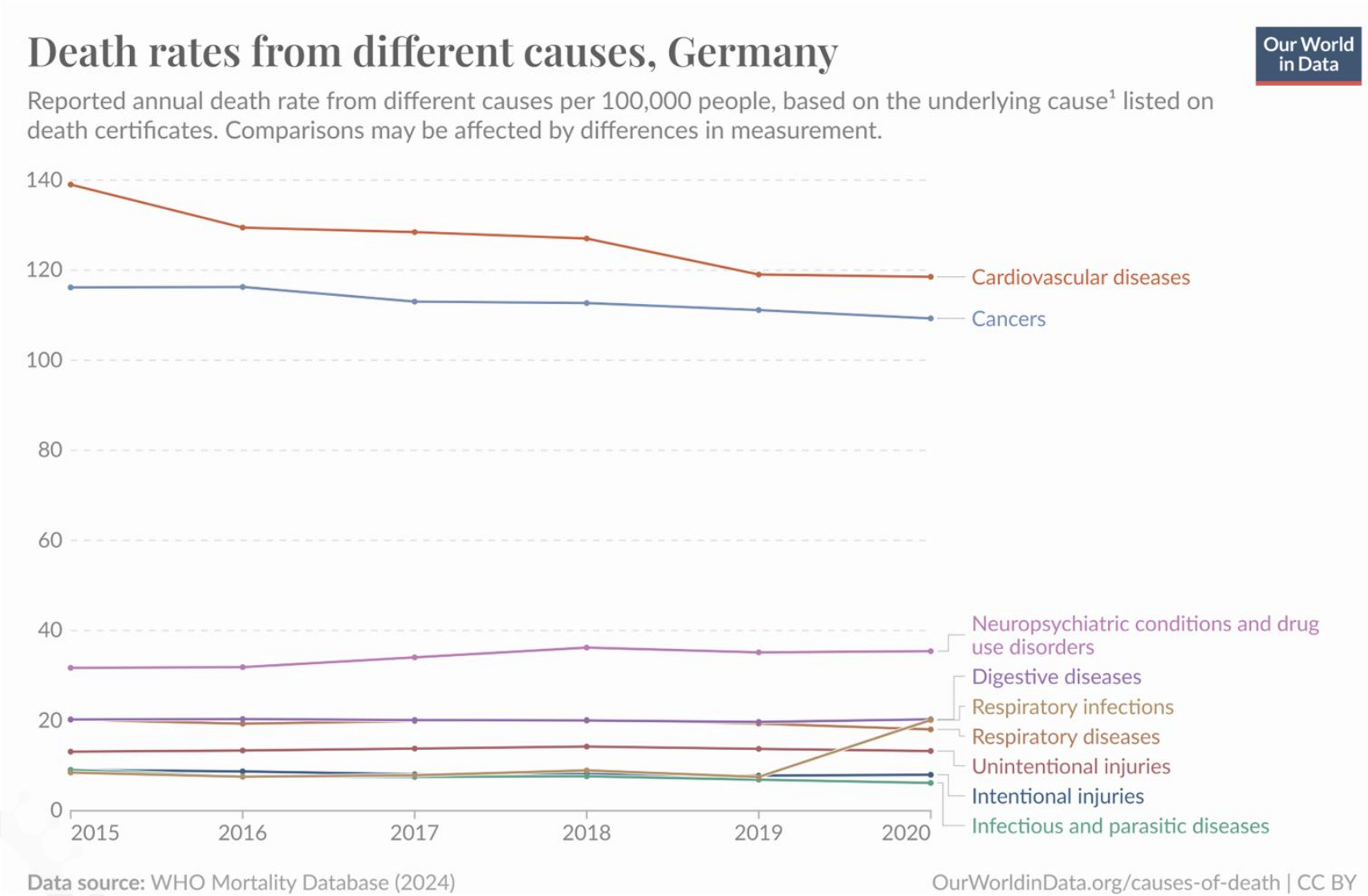


# Global burden of respiratory virus



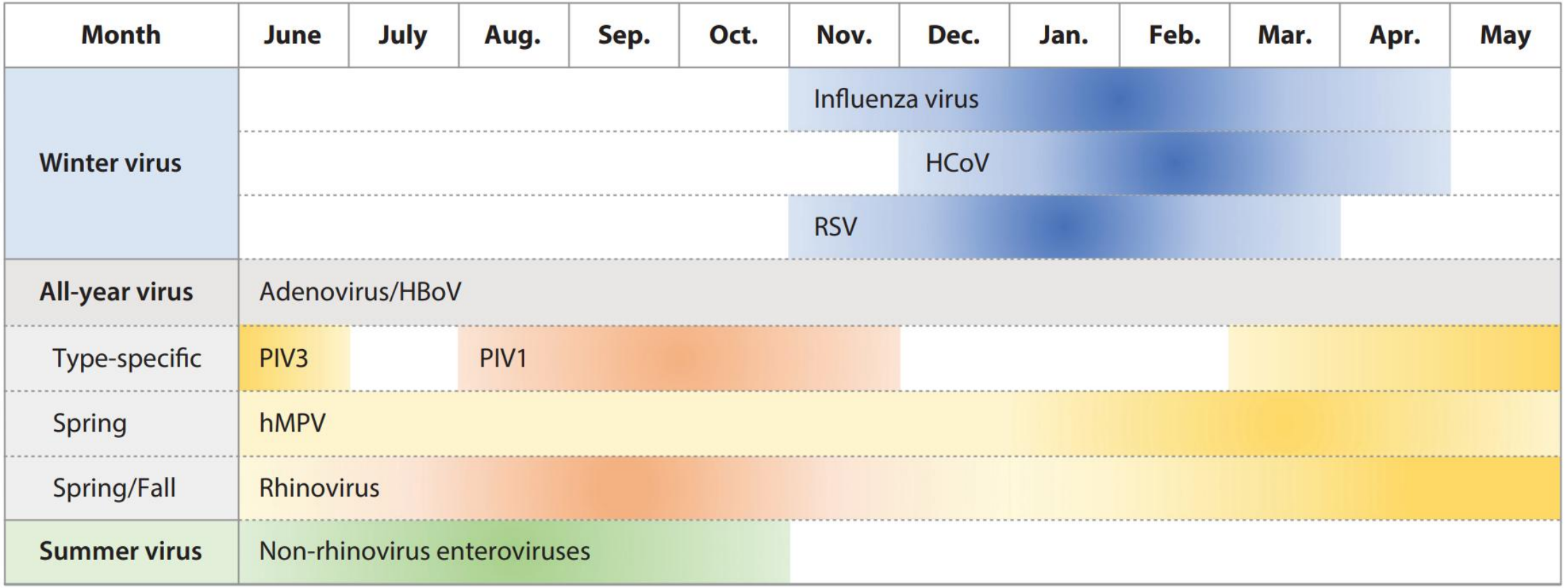

Top 4 cause of death in Germany

# Global burden of respiratory virus



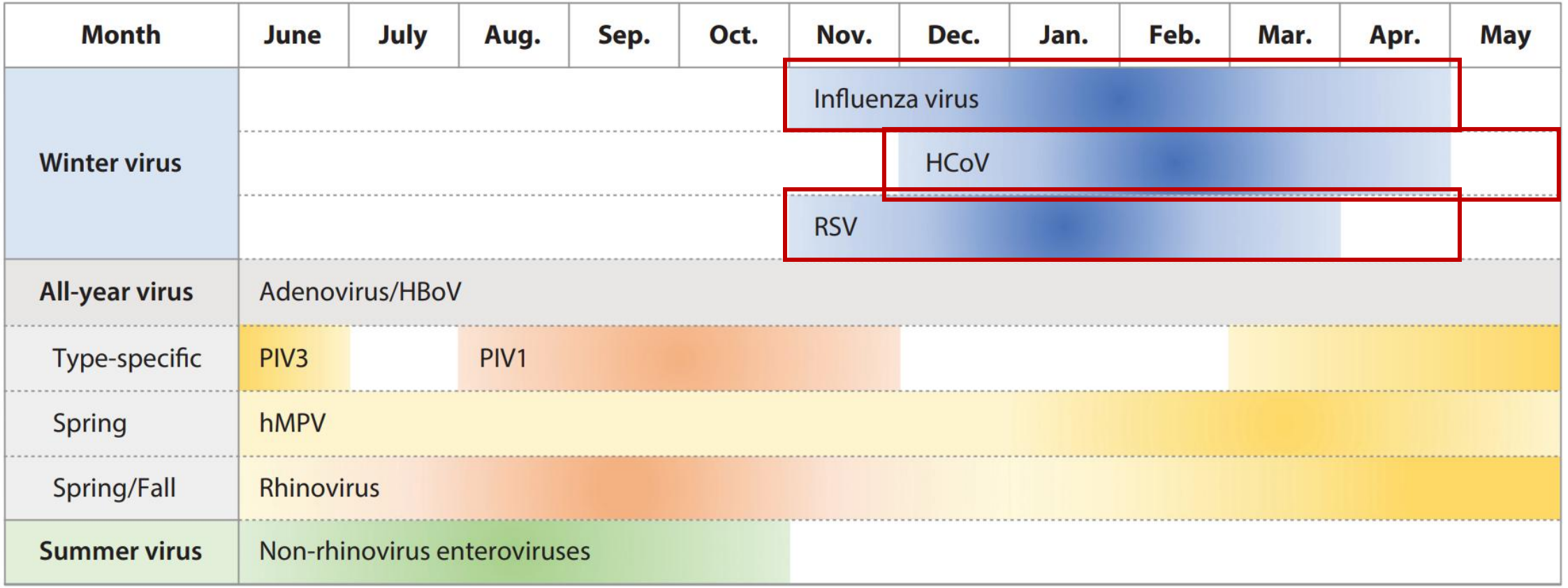

Main cause of death via communicable diseases

# Seasonality of respiratory virus




*Annual Review of Virology*, 2020

# Seasonality of respiratory virus

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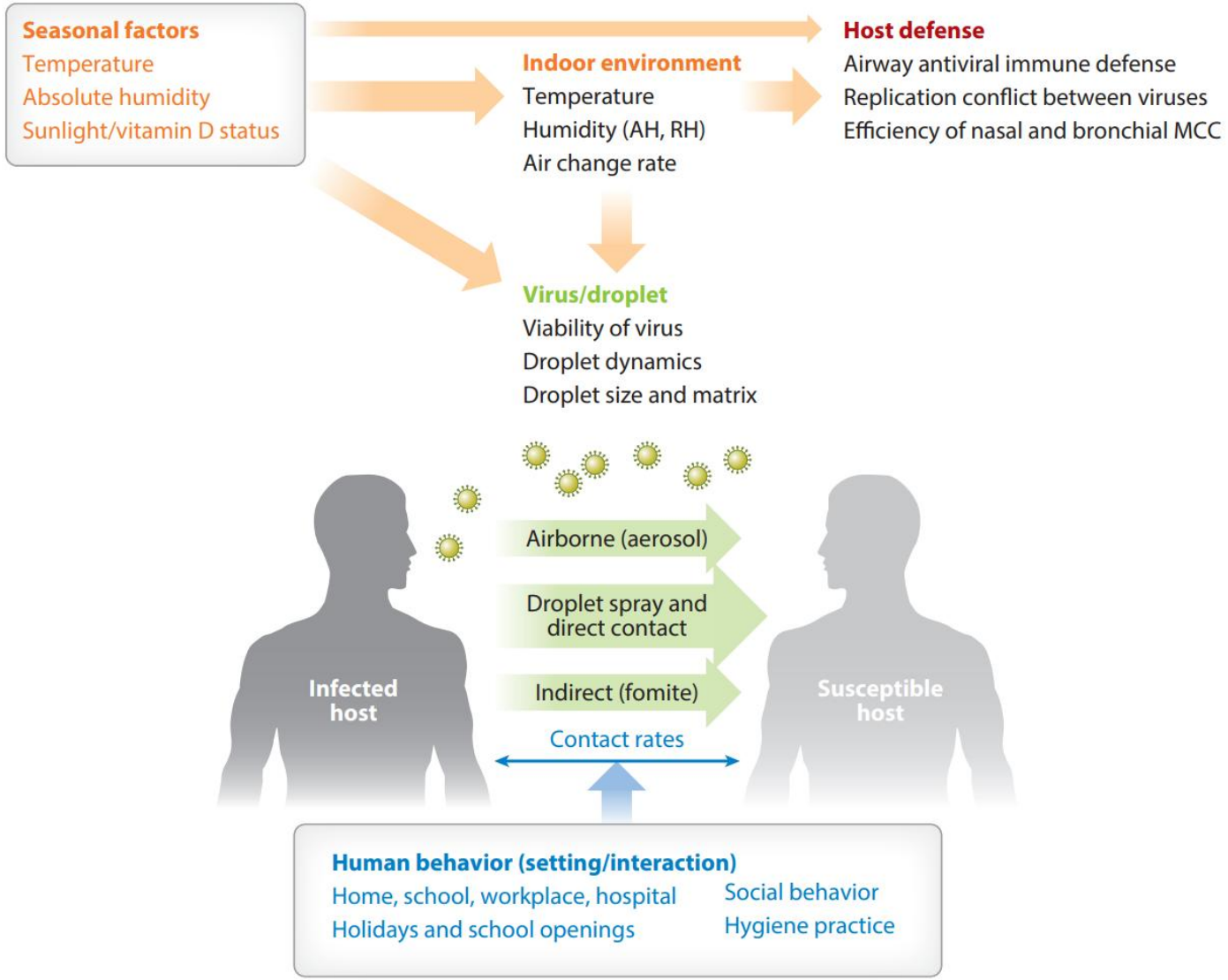
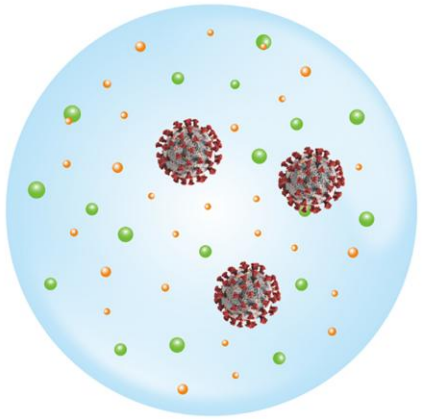


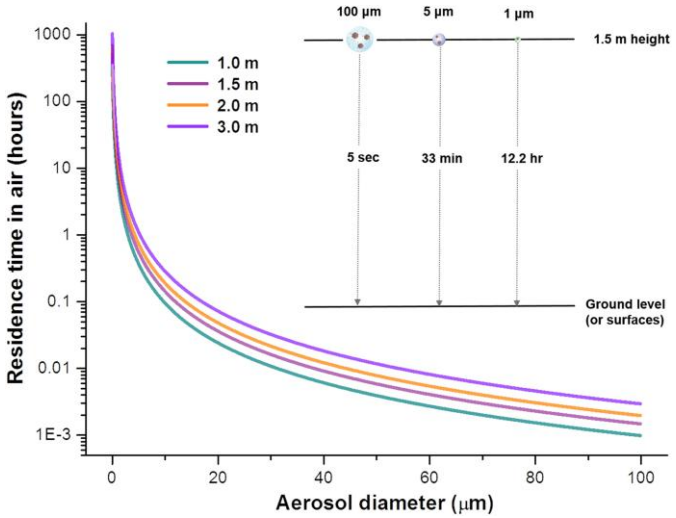

*Annual Review of Virology*, 2020

# Seasonality of respiratory virus

## Physicochemical properties of virus-laden aerosols:



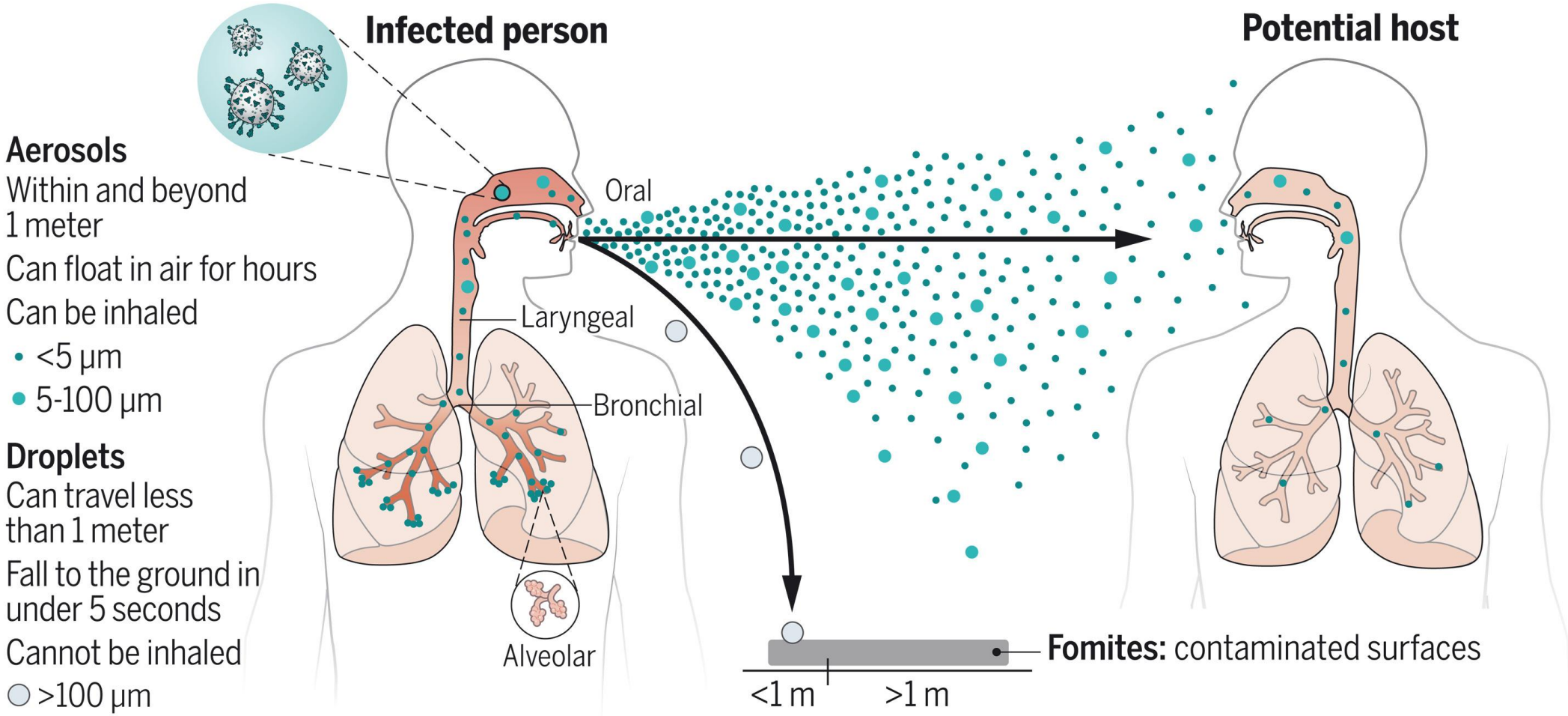
- Size
- Viral load and infectivity
- Other chemical components:
  - electrolytes, proteins, surfactants
- pH value
- Electrical charge
- Air/liquid interfacial properties




| Climate/season | Outdoor absolute humidity | Indoor relative humidity (%) | Respiratory virus stability | Proportion of droplet nuclei | Viability of respiratory viruses | Predominant transmission |
|---|---|---|---|---|---|---|
| Tropical | High | 60–100 | High | Low | High | Fomite, direct and indirect contact |
| Temperate: spring, fall | Intermediate | 40–60 | Low | Low | Low | All transmission ways possible |
| Temperate: winter | Low | 10–40 | High | High | High | Predominantly airborne |

*Annual Review of Virology*, 2020
Science 2021

# Seasonality of respiratory virus




*Science*, 2021

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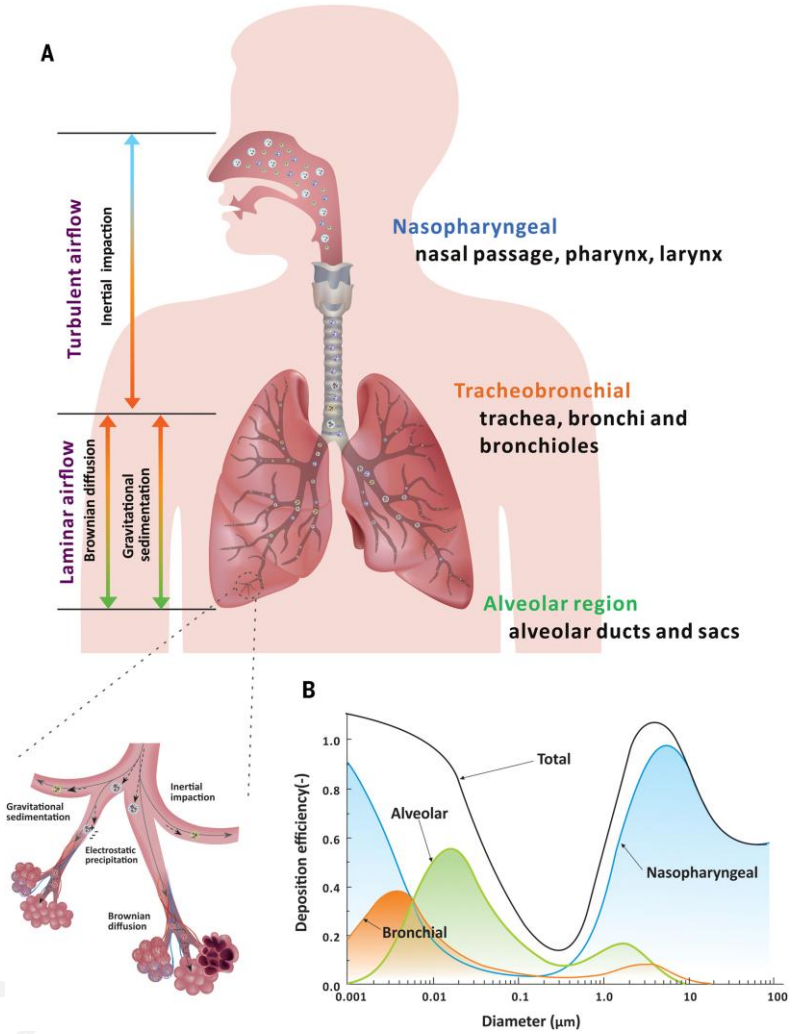
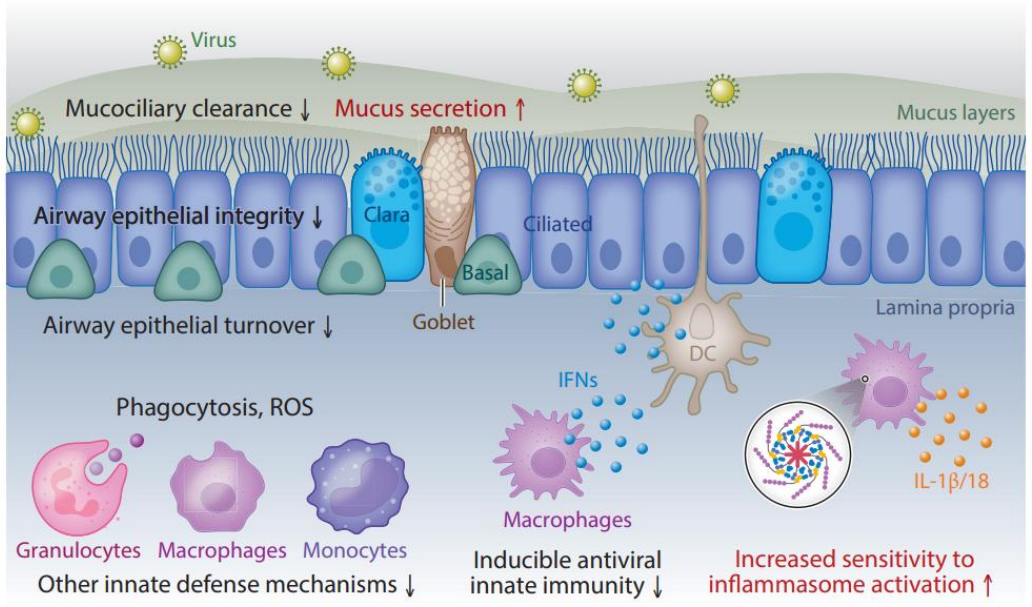
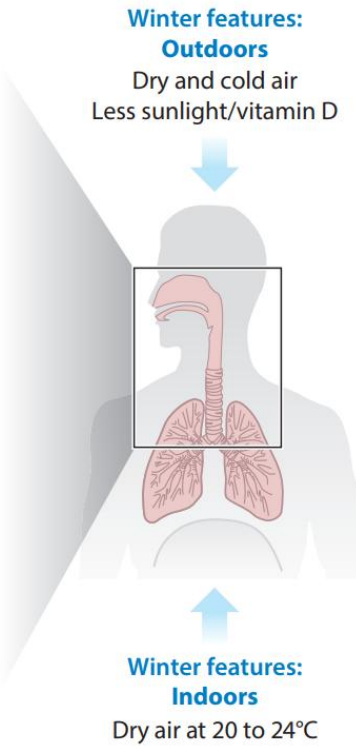


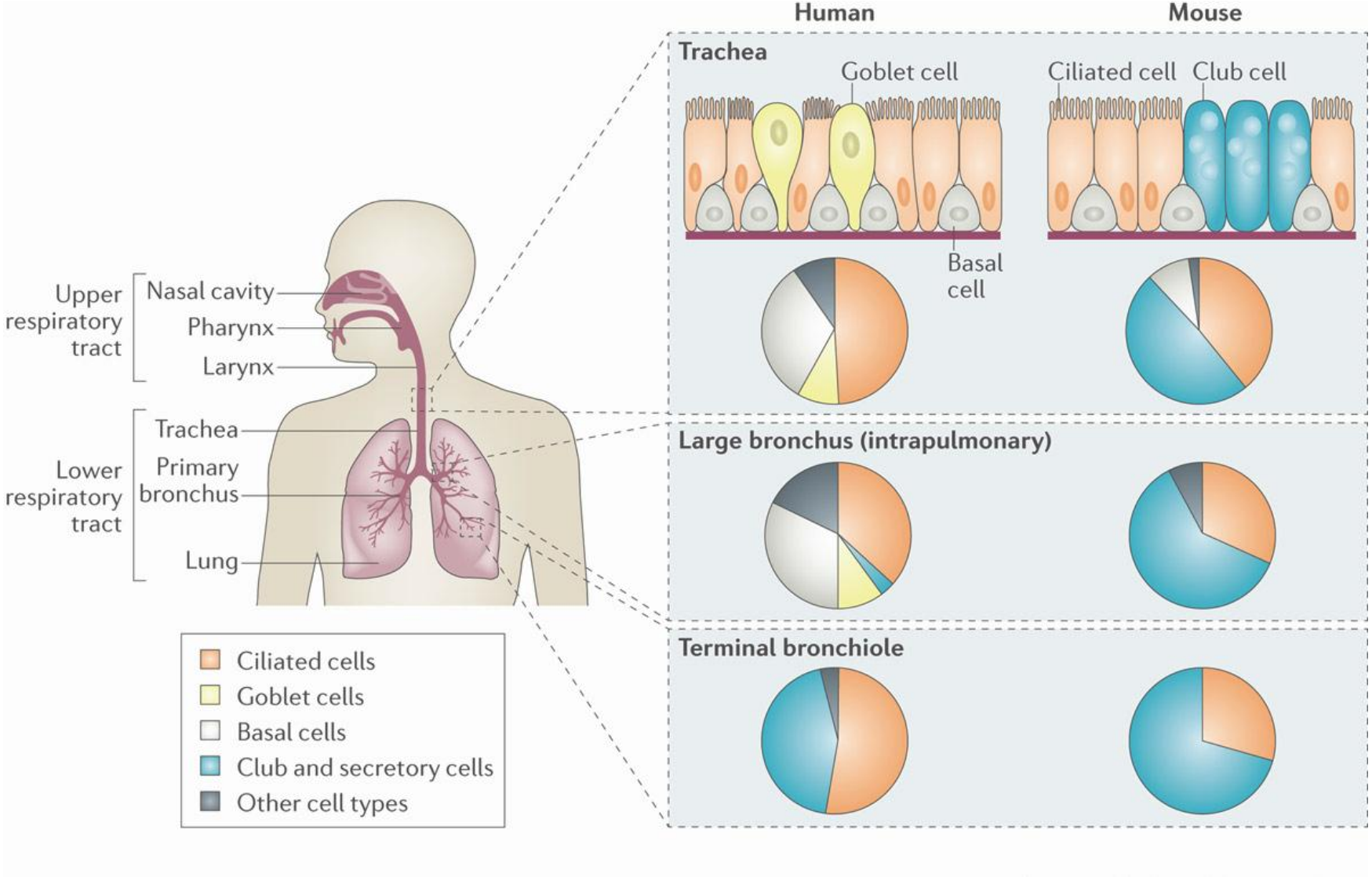




*Annual Review of Virology*, 2020
Science 2021

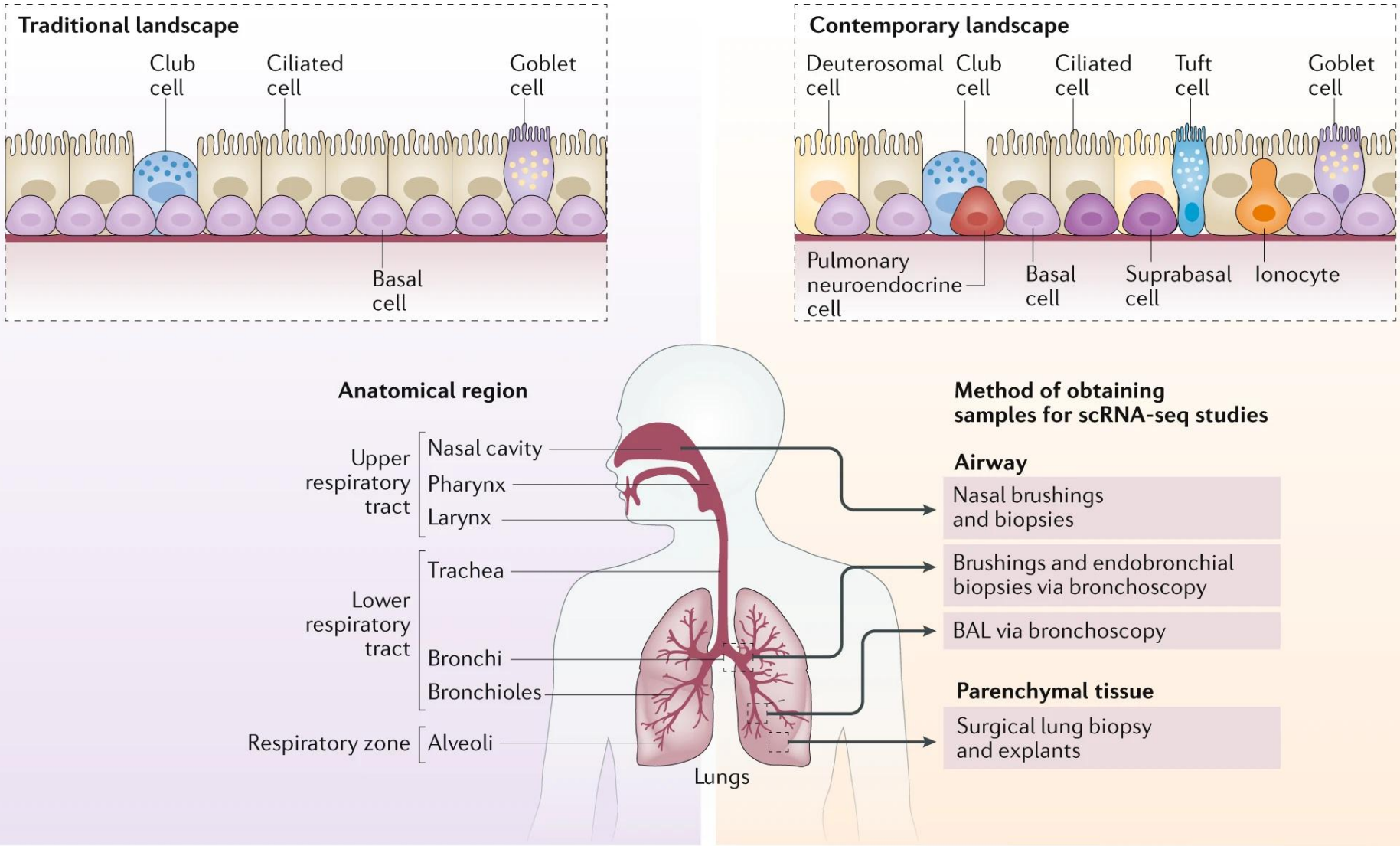
# The human respiratory tract

# Respiratory tract



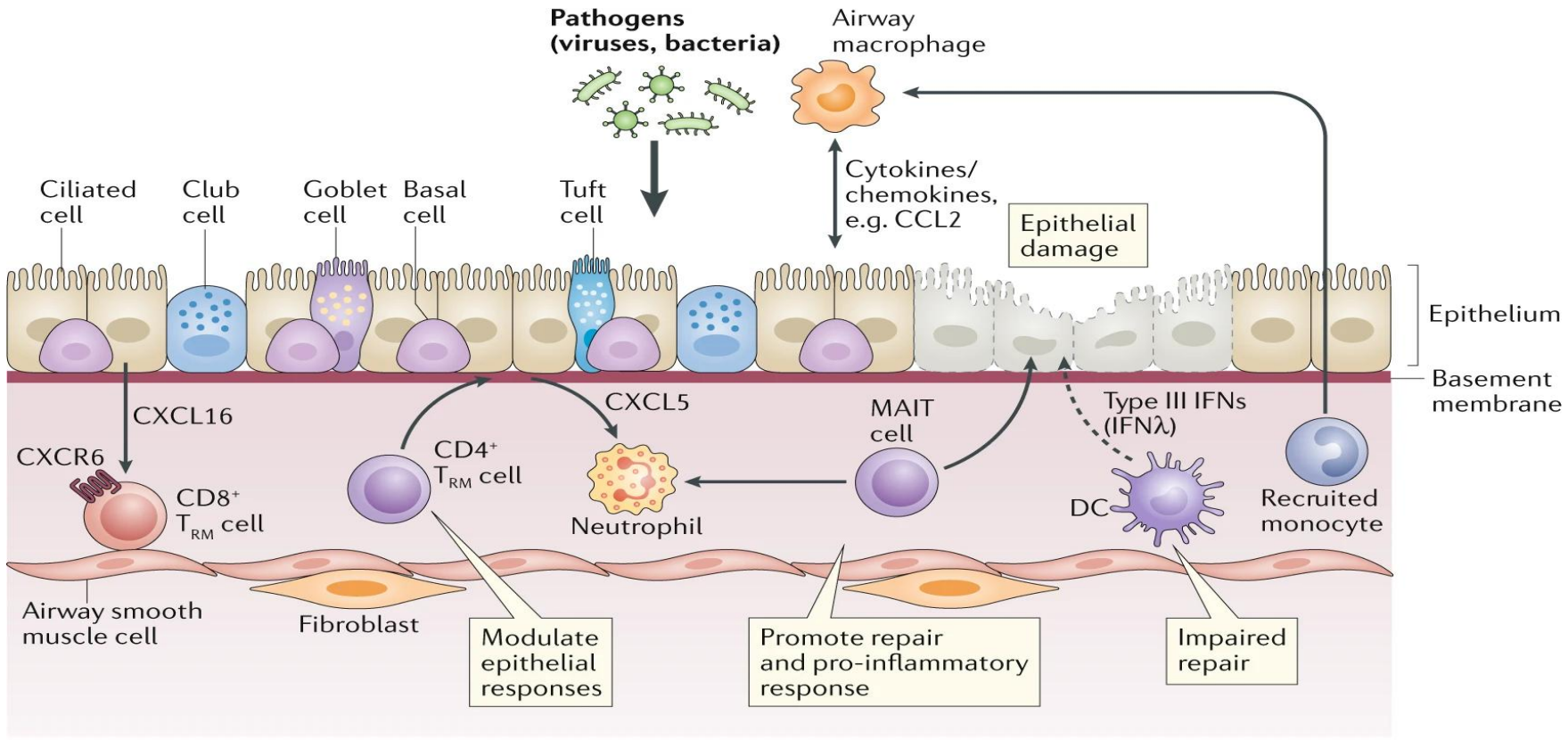

*Nature Reviews, Immunology*, 2021

# Respiratory tract

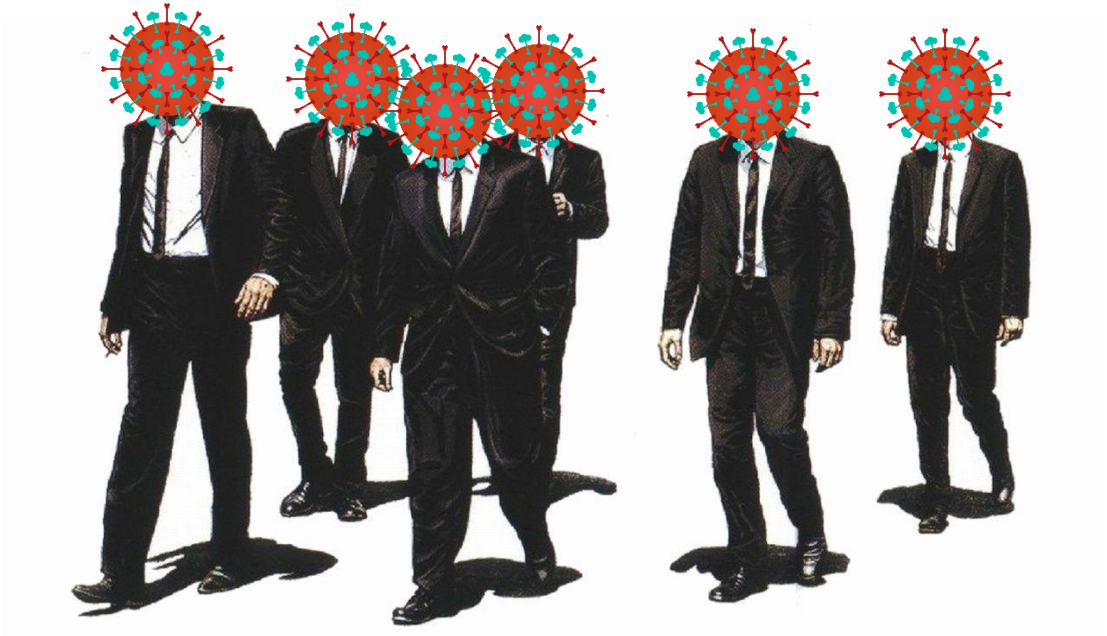



*Nature Reviews, Immunology*, 2024

# Respiratory tract




*Nature Reviews, Immunology*, 2021



# The cast:

## Reservoir drops

# Influenza (“Flu”)

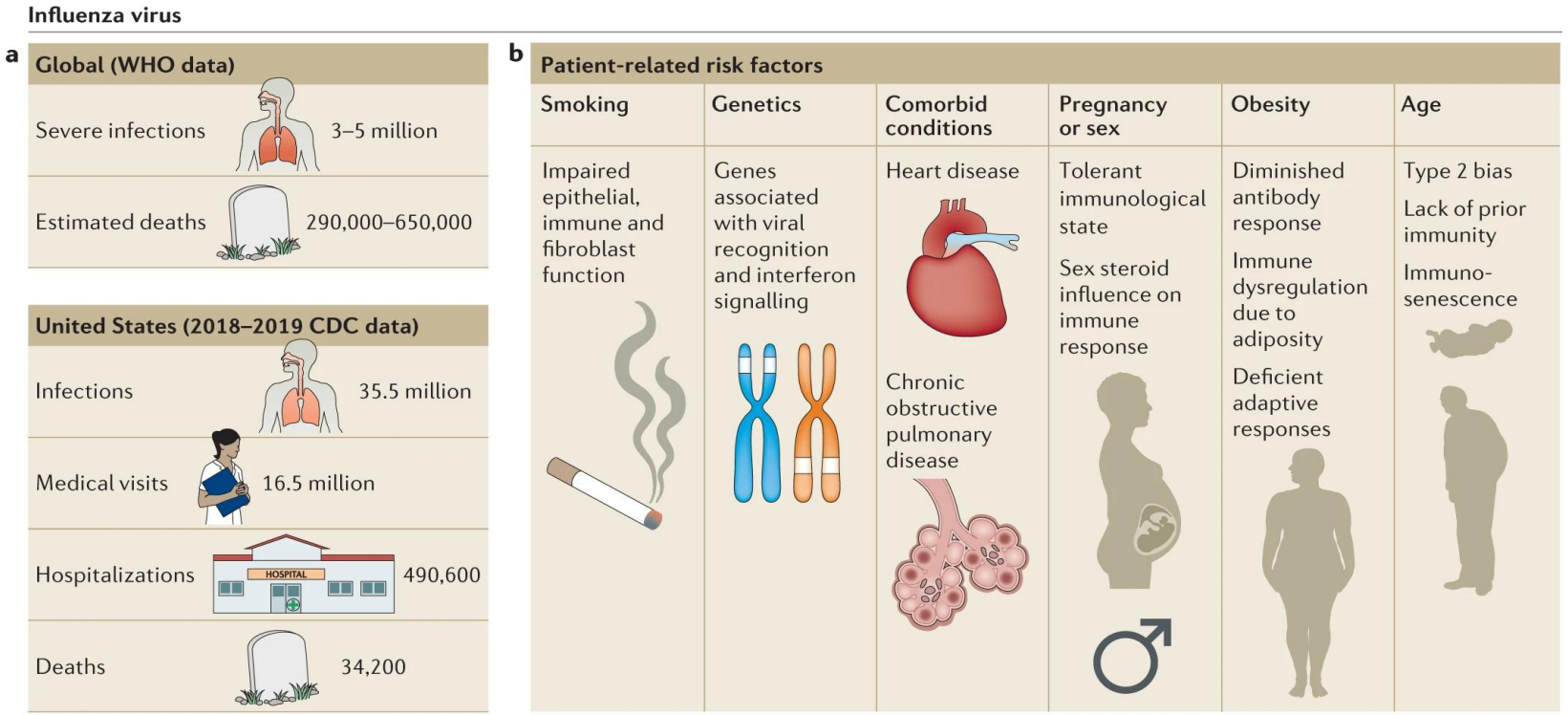
Infectious respiratory disease
(mild to severe illness)

Annual seasonal epidemic
General population: 5–20%
Children: 20–35%

Sporadic pandemic

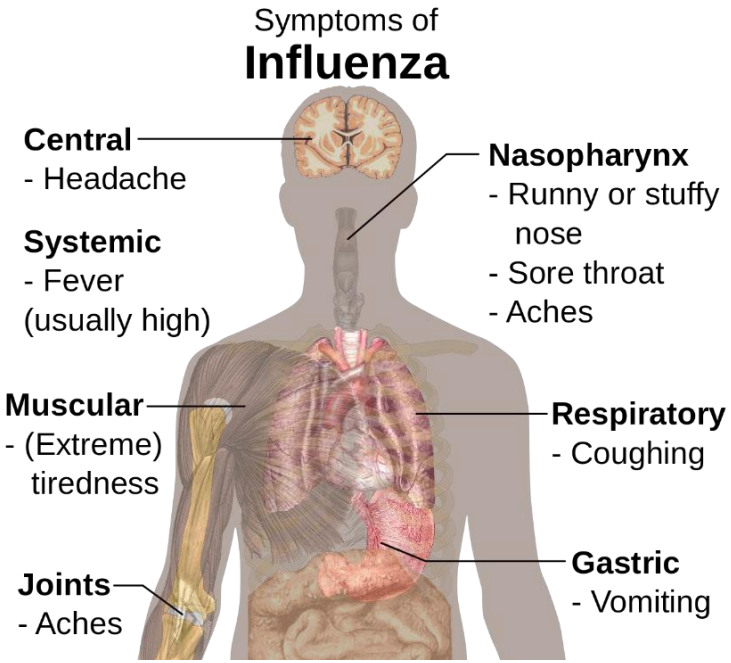
Circulates in humans and animals

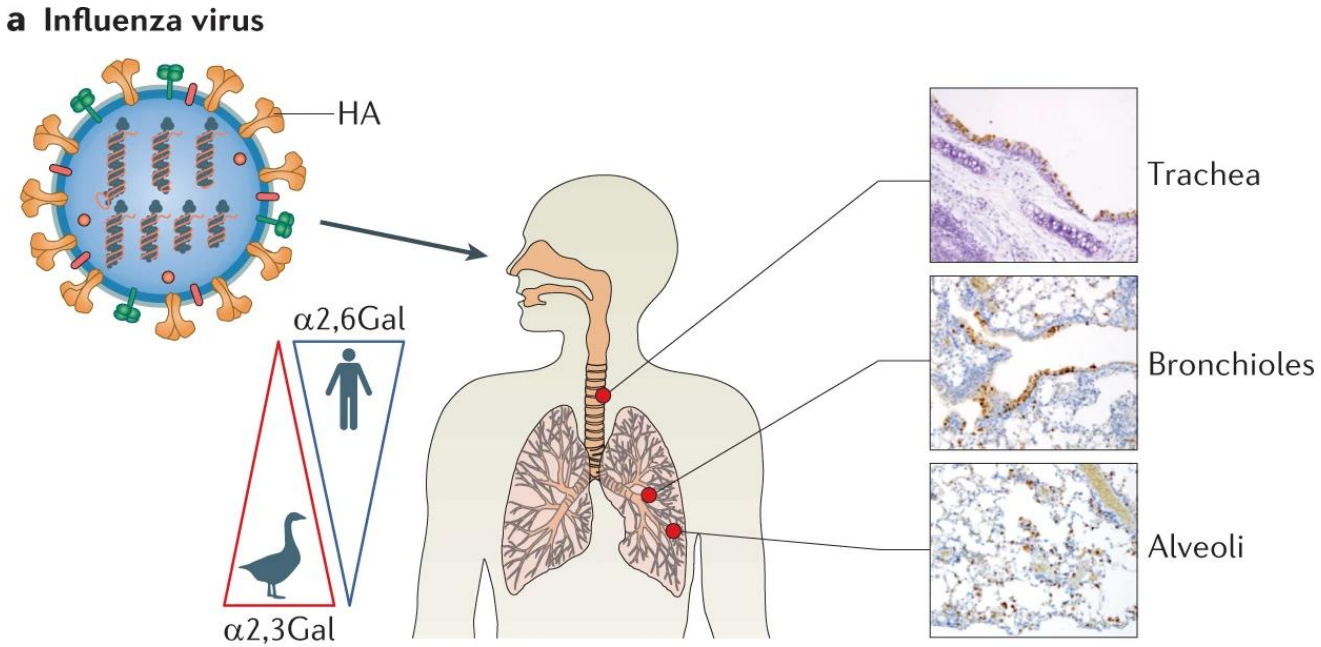
Vaccines are available




*Nature Reviews, microbiology*, 2021

# Influenza: pathophysiology




Infects **upper** and **lower** respiratory tract (epithelial cells)

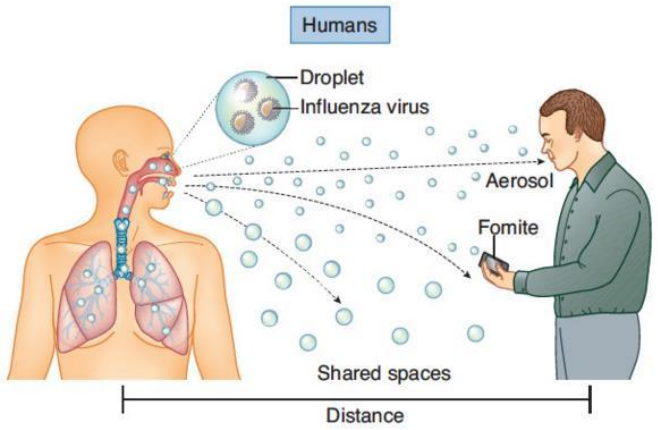
Symptoms arise after 1-2 days after infection

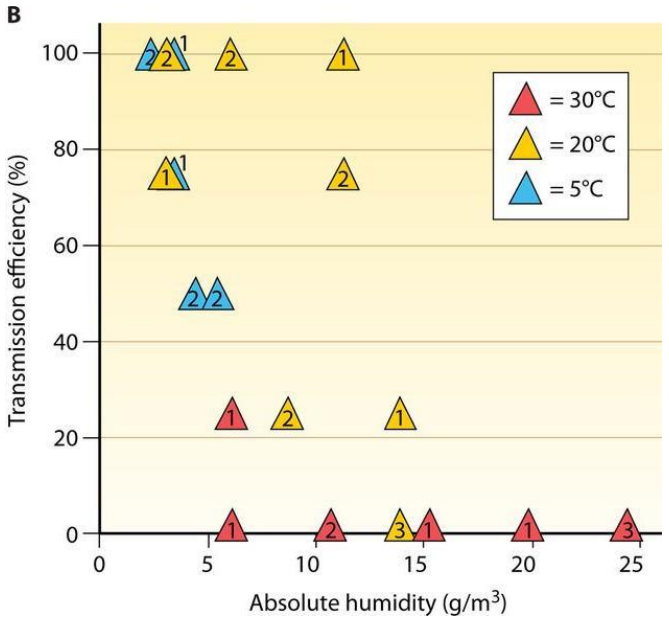
Infected cells produce proinflammatory cytokines (cytokine storm)

Severity of disease is the result of the interplay between viral virulence, host resistance and infection tissue

*Nature Reviews, microbiology*, 2021

# Influenza: transmission



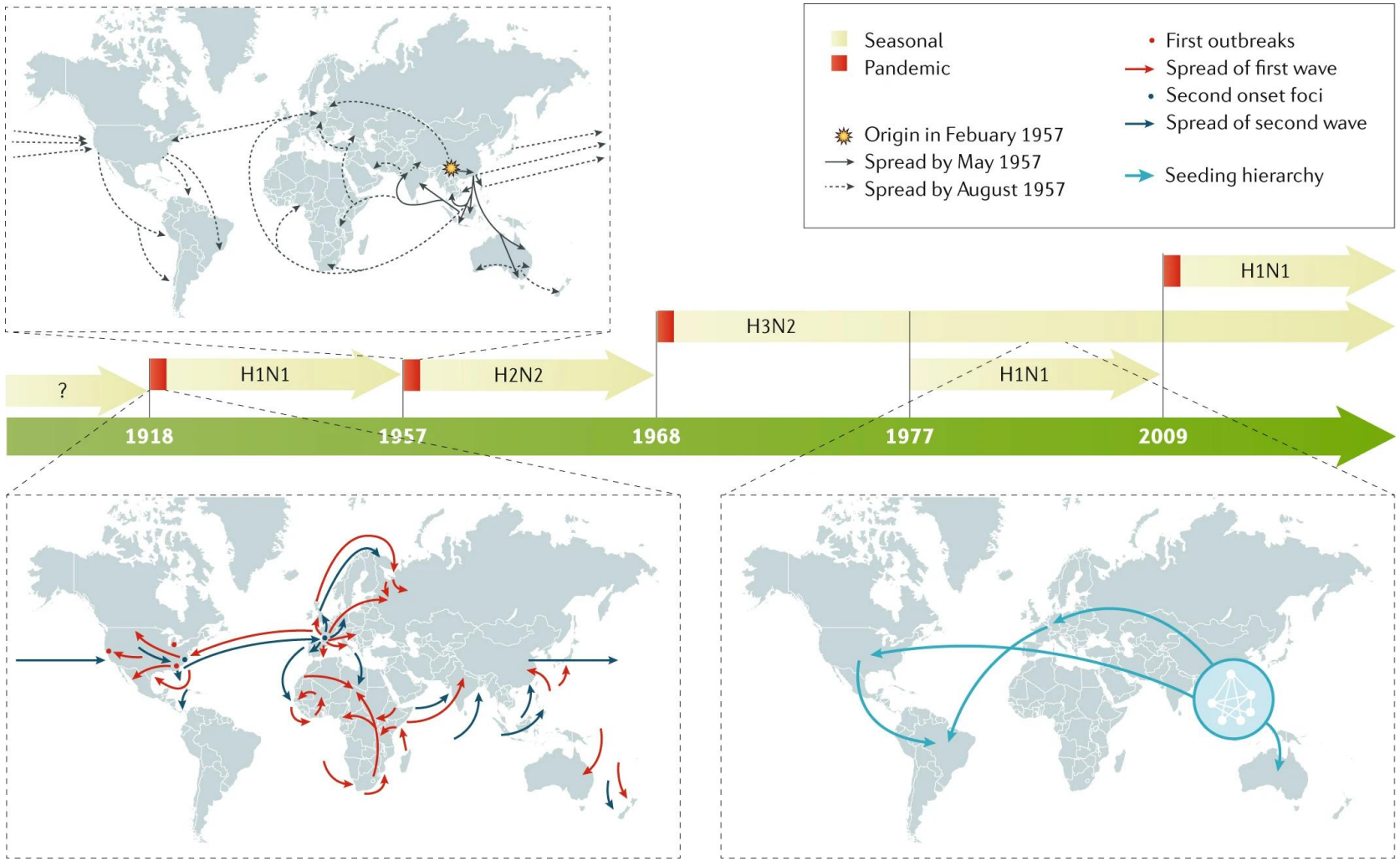




Respiratory droplets (main mechanism)
- Short distance (1m or less)

(In-)Direct contact
- infected individuals
- Fomites

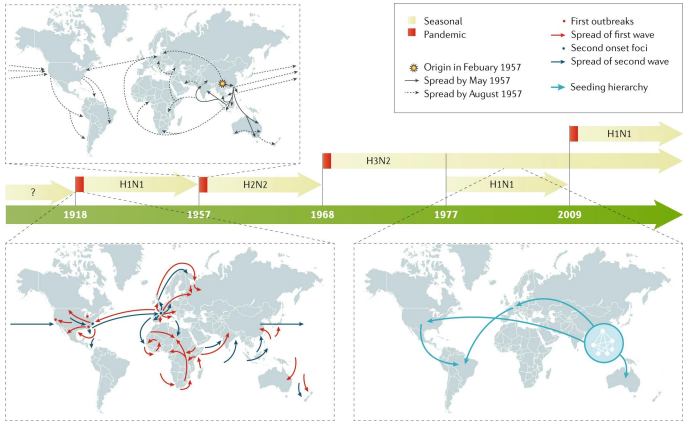
| Climate/season | Outdoor absolute humidity | Indoor relative humidity (%) | Respiratory virus stability | Proportion of droplet nuclei | Viability of respiratory viruses | Predominant transmission |
|---|---|---|---|---|---|---|
| Tropical | High | 60–100 | High | Low | High | Fomite, direct and indirect contact |
| Temperate: spring, fall | Intermediate | 40–60 | Low | Low | Low | All transmission ways possible |
| Temperate: winter | Low | 10–40 | High | High | High | Predominantly airborne |

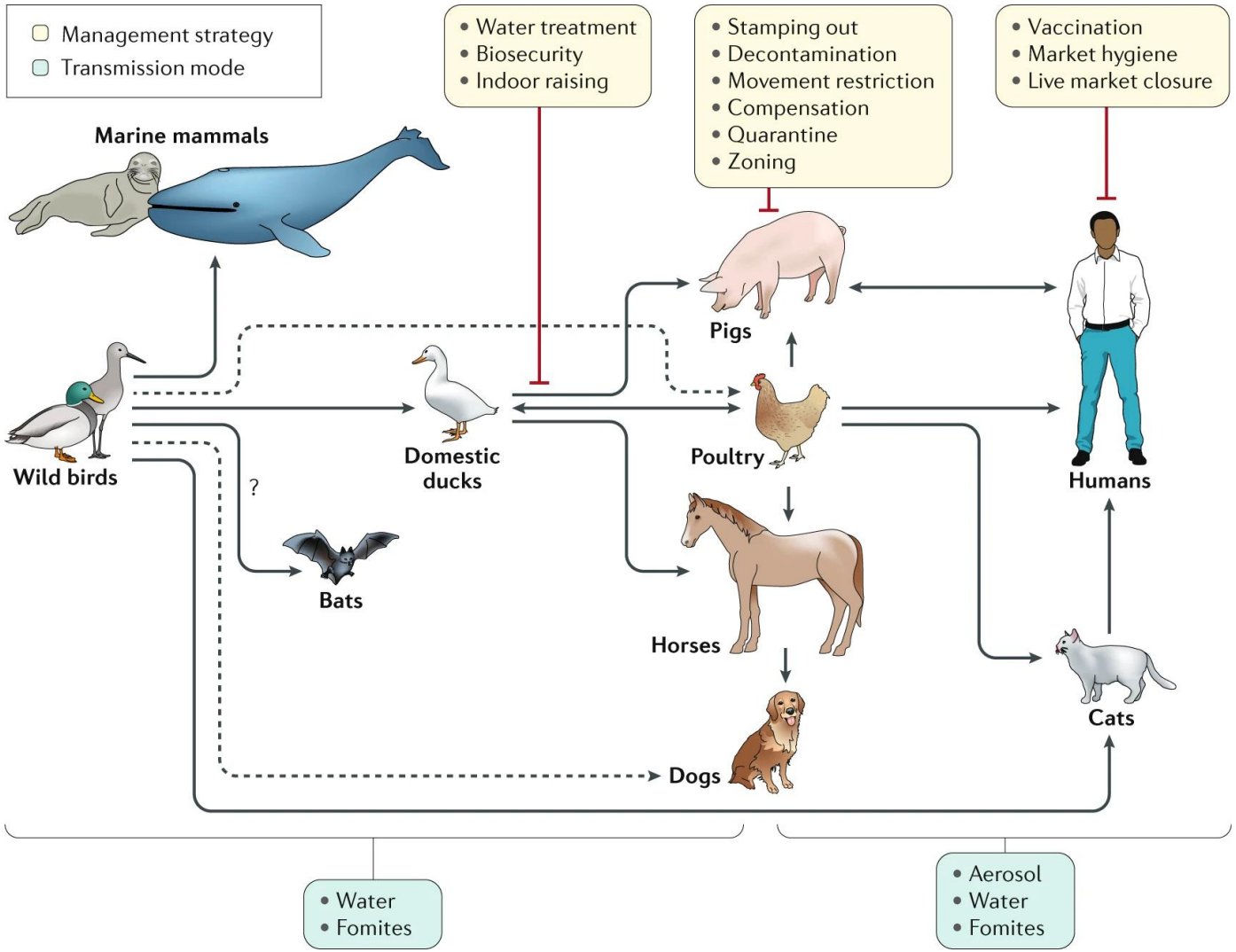
# Influenza: Global distribution




*Nature Reviews, microbiology*, 2021

# Influenza: Global distribution




*Nature Reviews, microbiology*, 2021

# Influenza: Host range

**A**

- Most common
- Infects humans and animals
- Can cause pandemics
- Different subtypes
- 18 HA and 11 NA

**B**

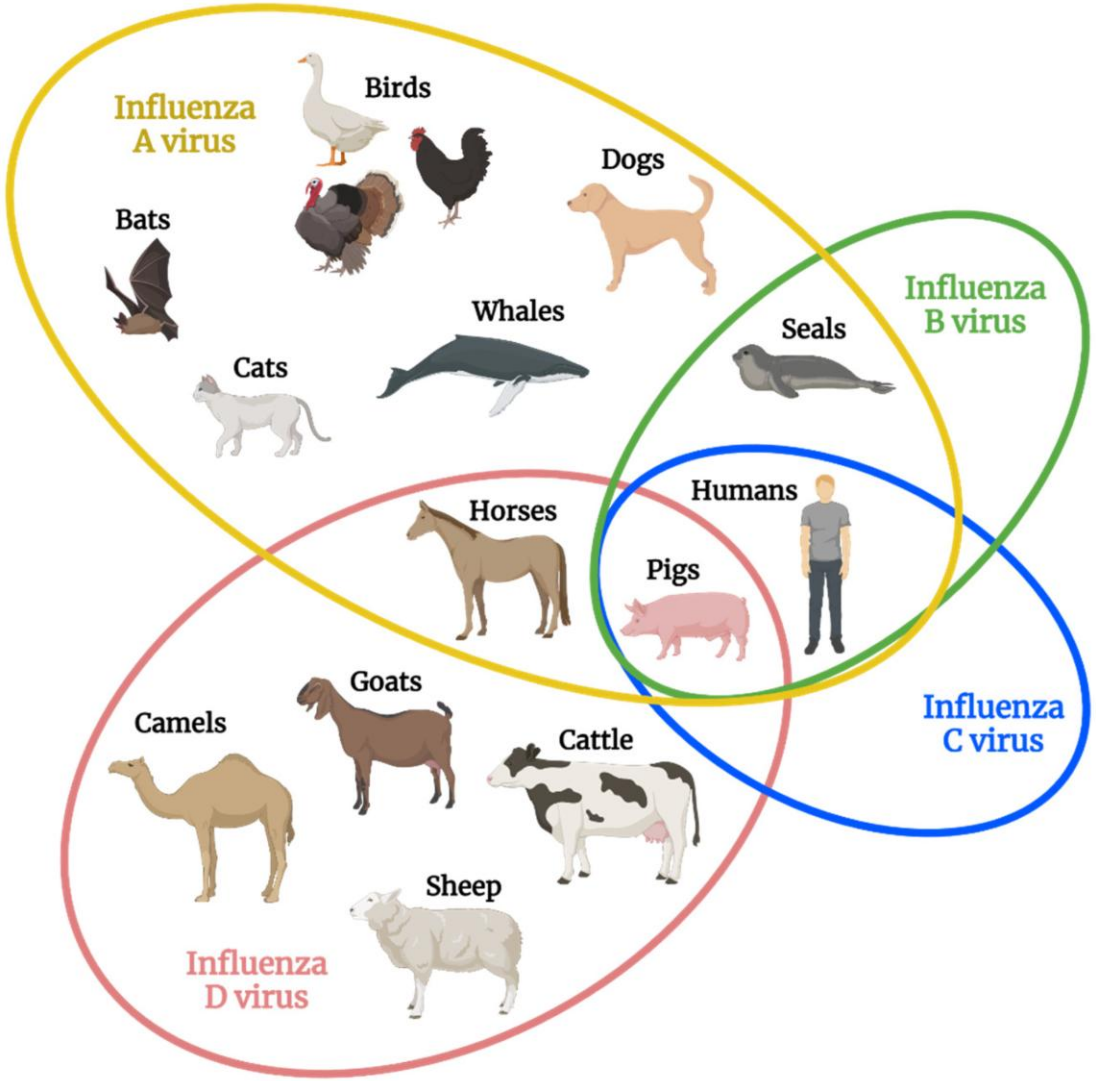
- Infects humans
-

**C**

- Mostly infects humans
- Causes mild symptoms

**D**

- Identified in 2011 from pigs
- No human infections described




*Viruses*, 2022

# Influenza: Biology

Order: Articulavirales

Family: Orthomyxoviridae

Genus: Alphainfluenzavirus

Betainfluenzavirus

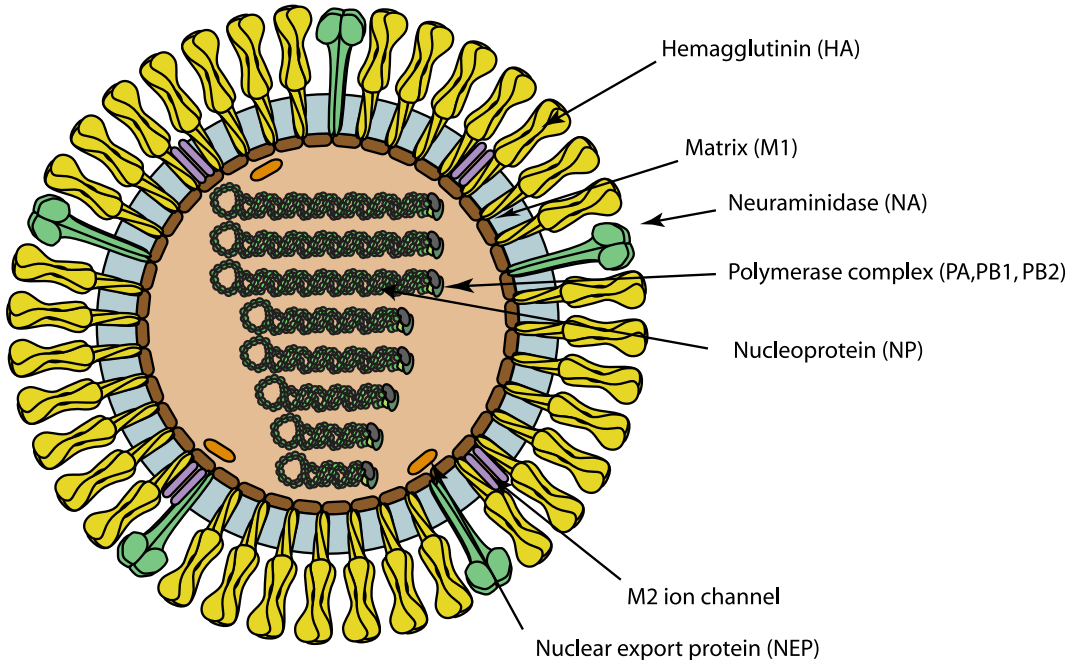
Gammainfluenzavirus

Deltainfluenzavirus

Enveloped

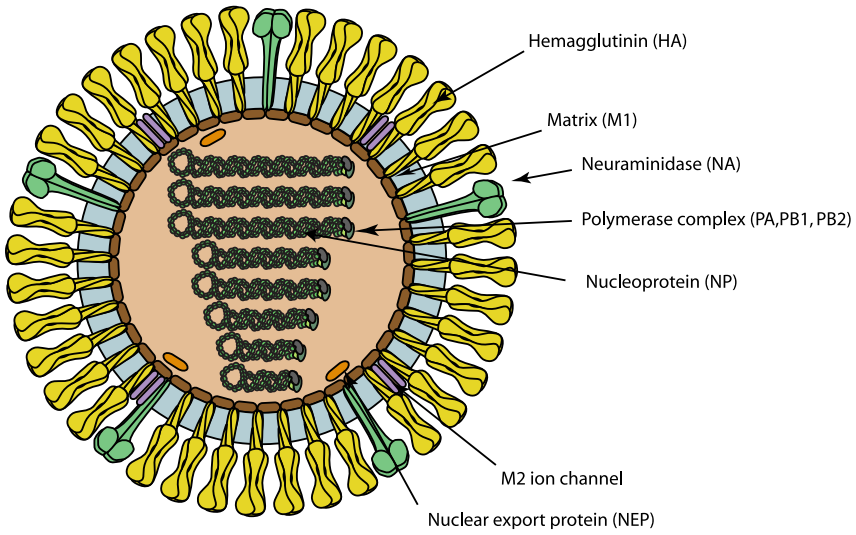
Diameter of 80-120nm

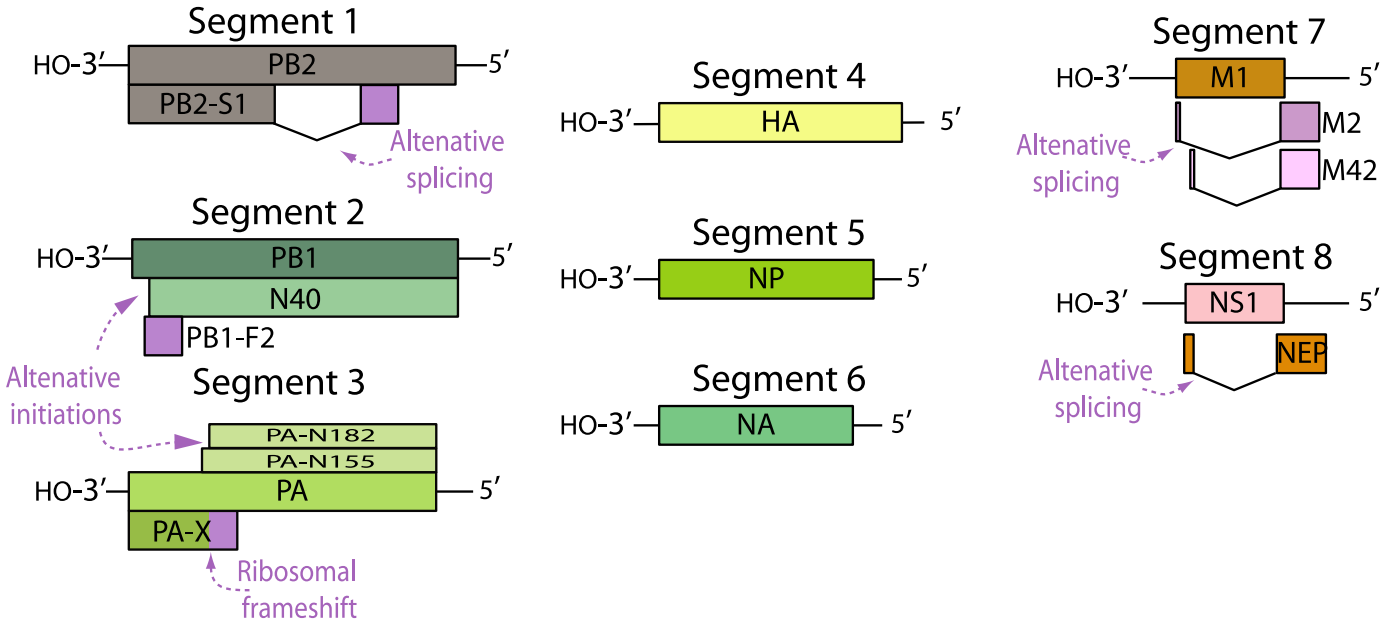
Segmented (8AB – 7CD)



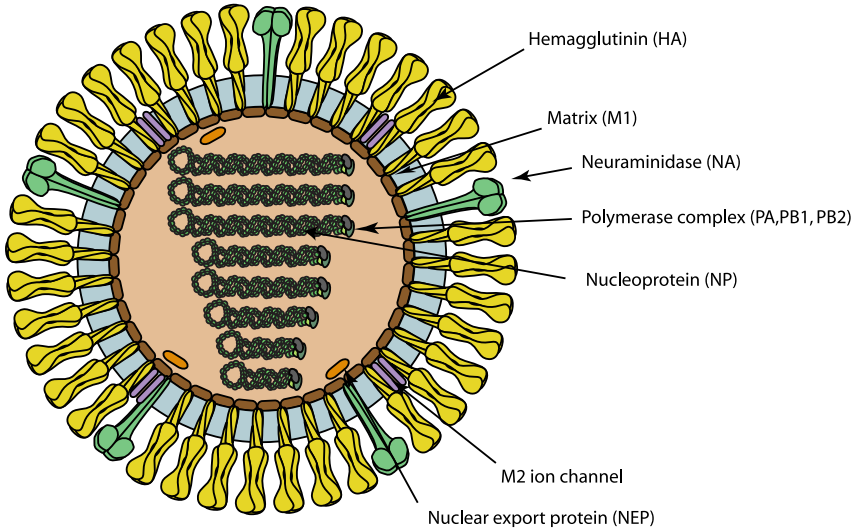

Viral Zone, Expasy

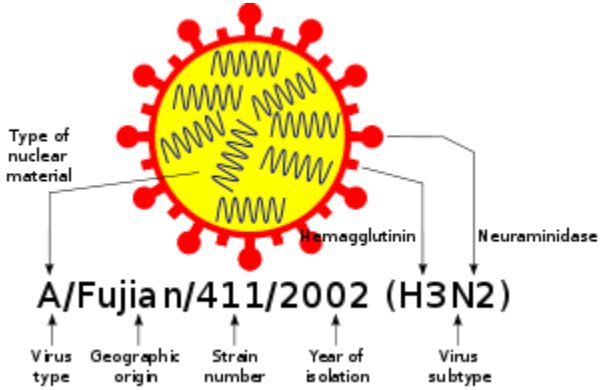
# Influenza: Biology



# Influenza: Nomenclature




Viral Zone, Expasy
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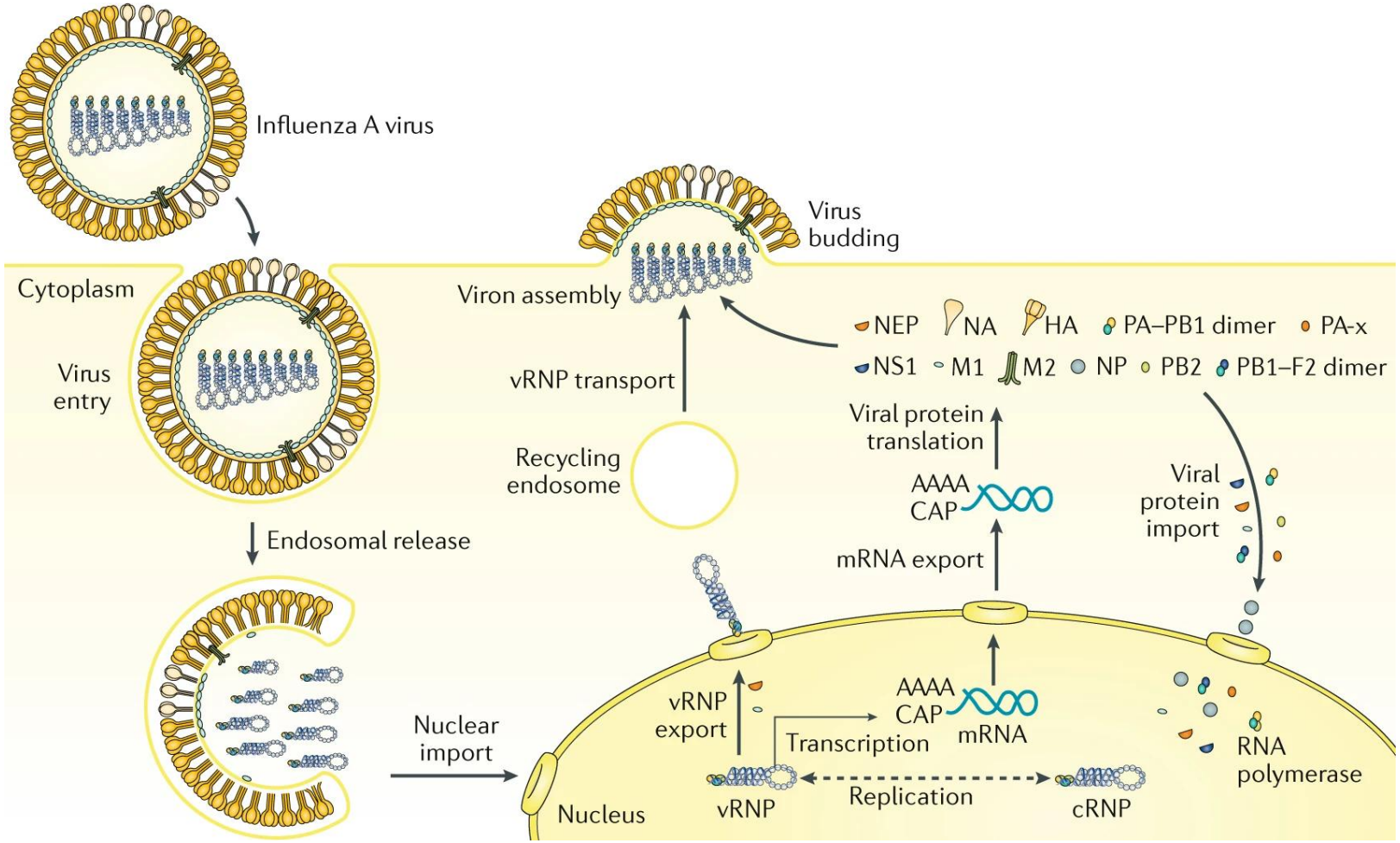
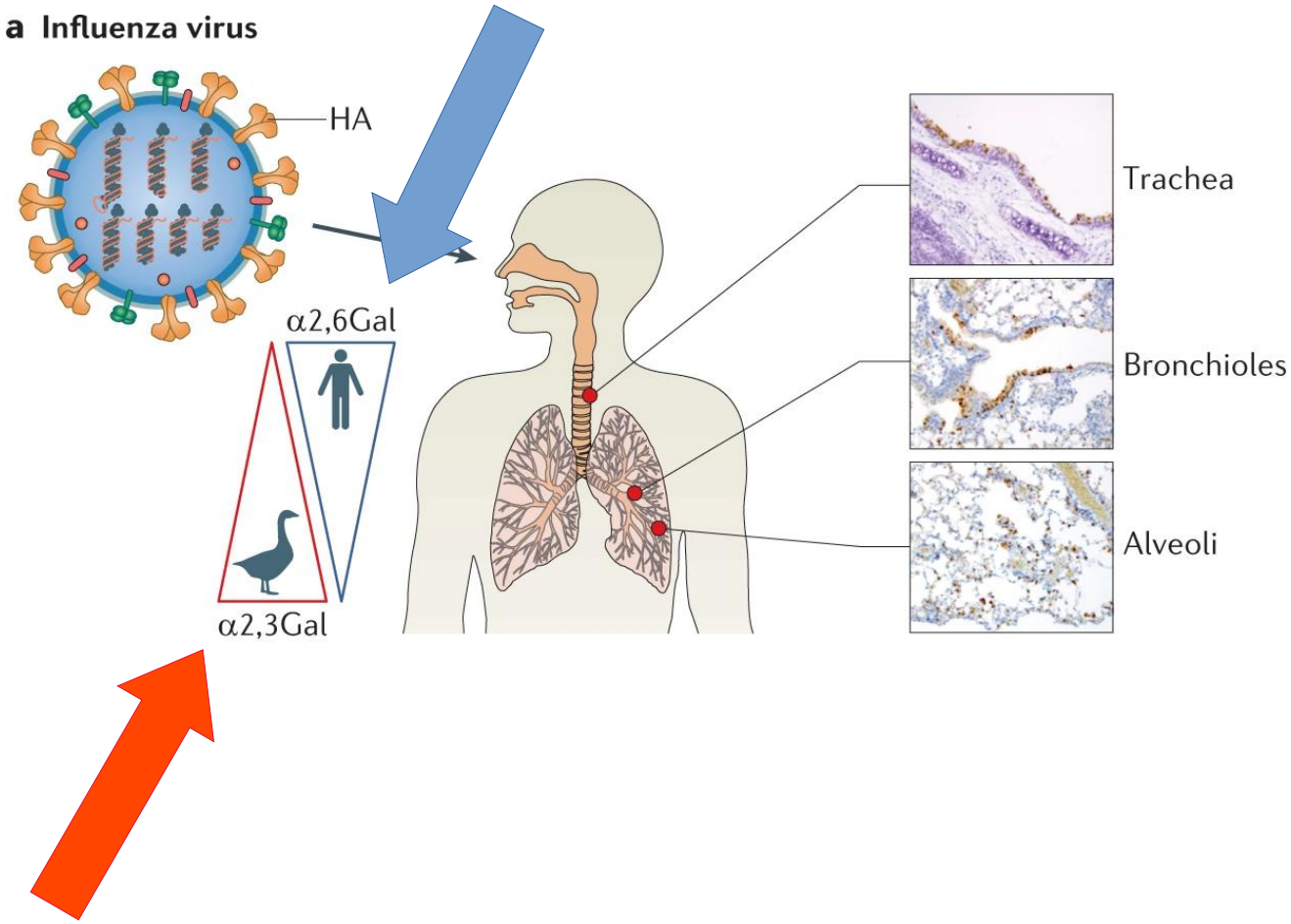
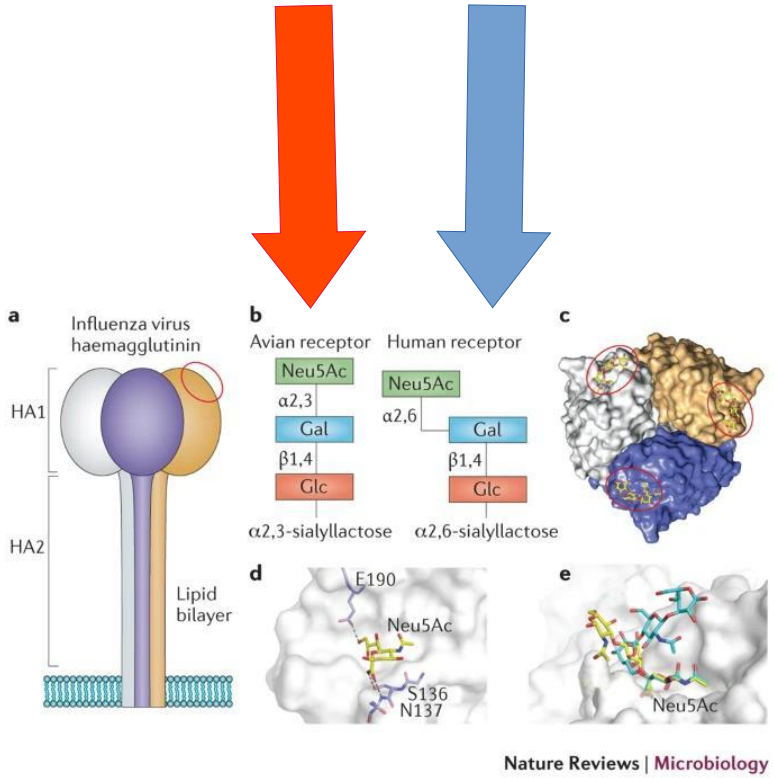
# Influenza: replication




*Nature Reviews, microbiology*, 2021

# Influenza: binding

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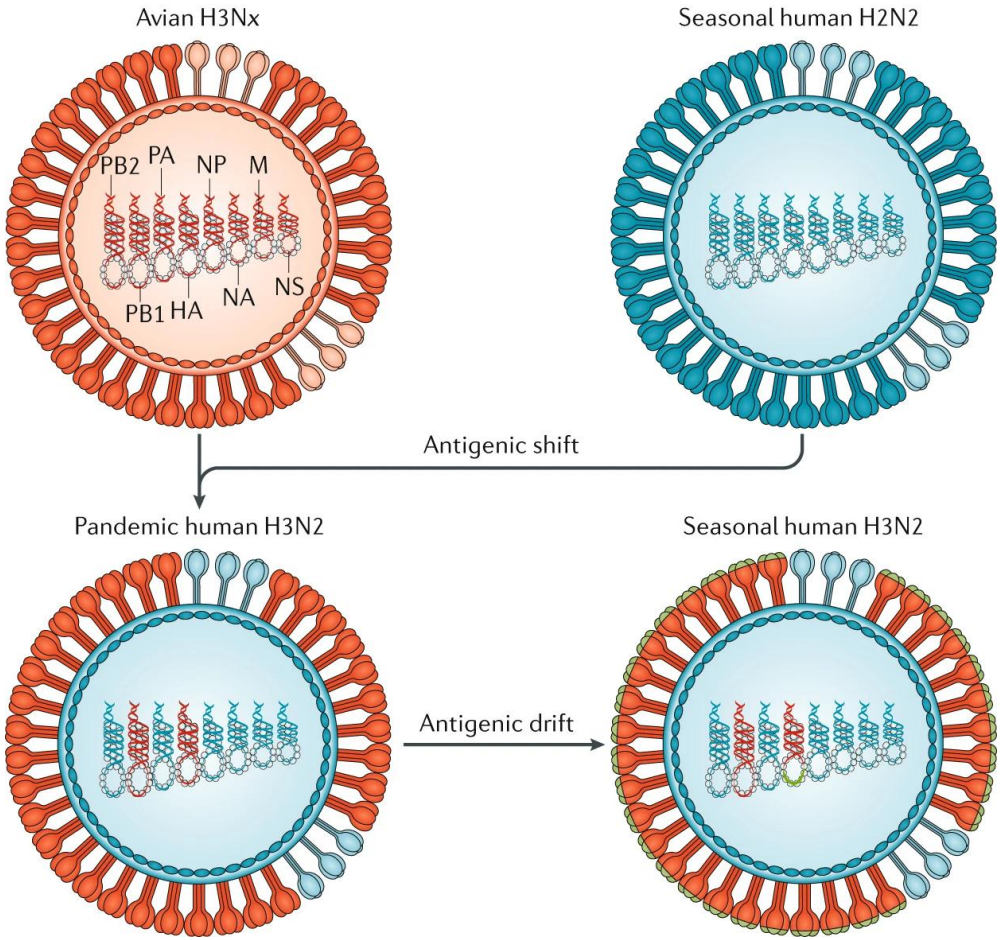
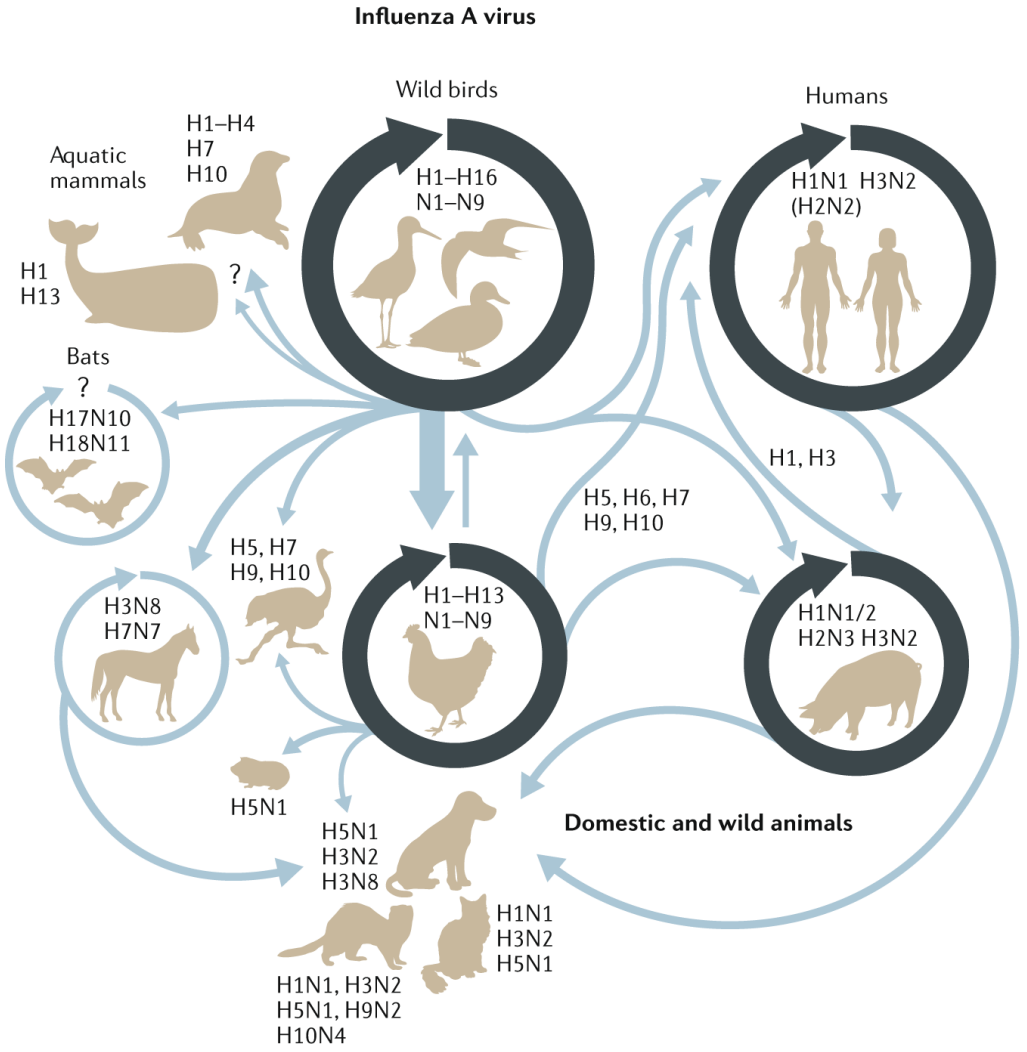
# Influenza: Antigenic „schwifrt”

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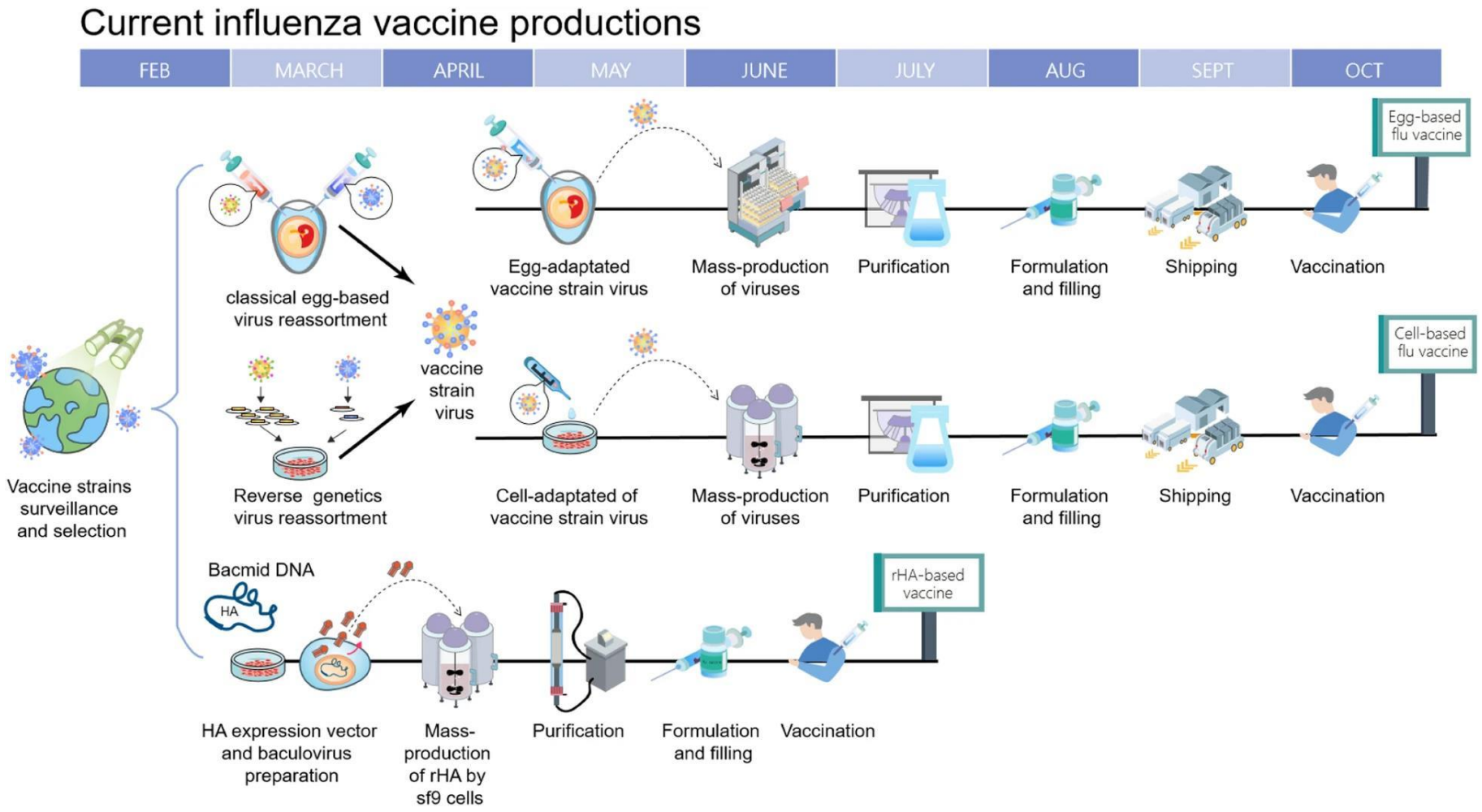
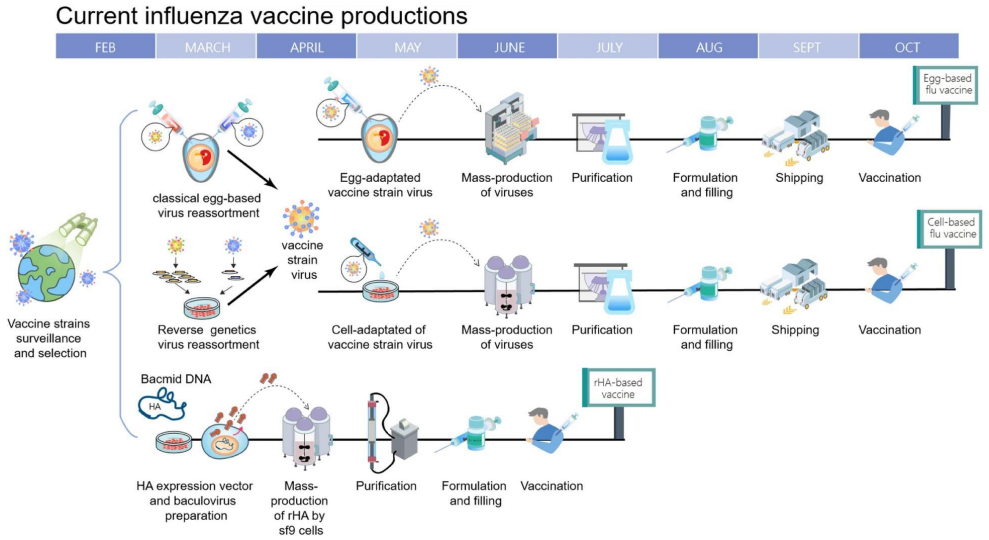
# Influenza: Vaccination




*JBS*, 2020

# Influenza: Vaccination & Drugs




| Drug | Route of administration | Approved age of use |
|---|---|---|
| Oseltamivir | Oral | At least two weeks old |
| Zanamivir | Inhalation | At least five years old |
| Peramivir | Intravenous injection | At least 18 years old |
| Laninamivir | Inhalation[1] | 40 milligrams (mg) dose for people at least 10 years old, 20 mg for those under 10[66] |
| Baloxavir marboxil | Oral[4] | At least 12 years old[46] |

*JBS*, 2020
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# Influenza: Vaccination & Drugs

Neuraminidase

Cap endonuclease activity

| Drug | Route of administration | Approved age of use |
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*JBS*, 2020
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# The cast:

## Goopfellas

# RSV (Respiratory syncytial virus)

Infectious respiratory disease

(mild to severe illness)

Dangerous to vulnerable populations:

Older adults: 6/10000 in rich countries

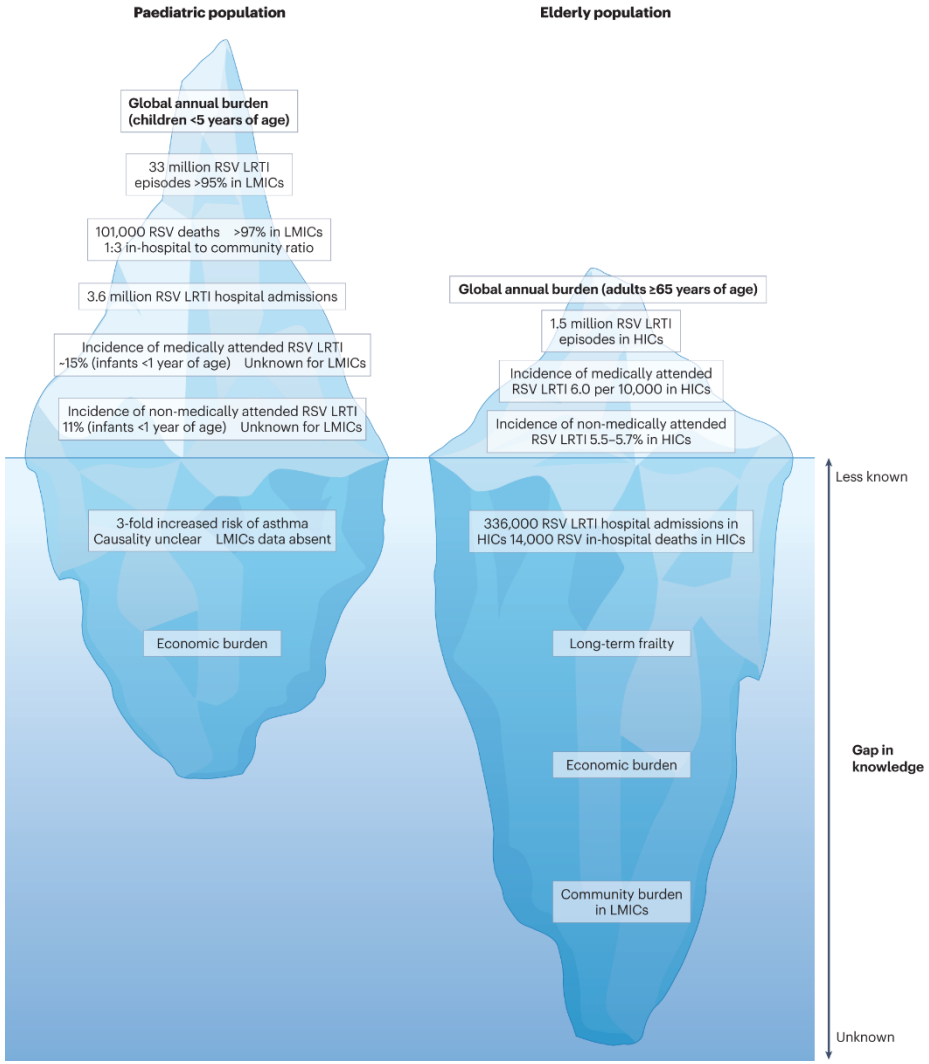
Children up to 5y: 33M annually LMIC

Leading cause of bronchiolitis and pneumonia in young children

Circulates in humans

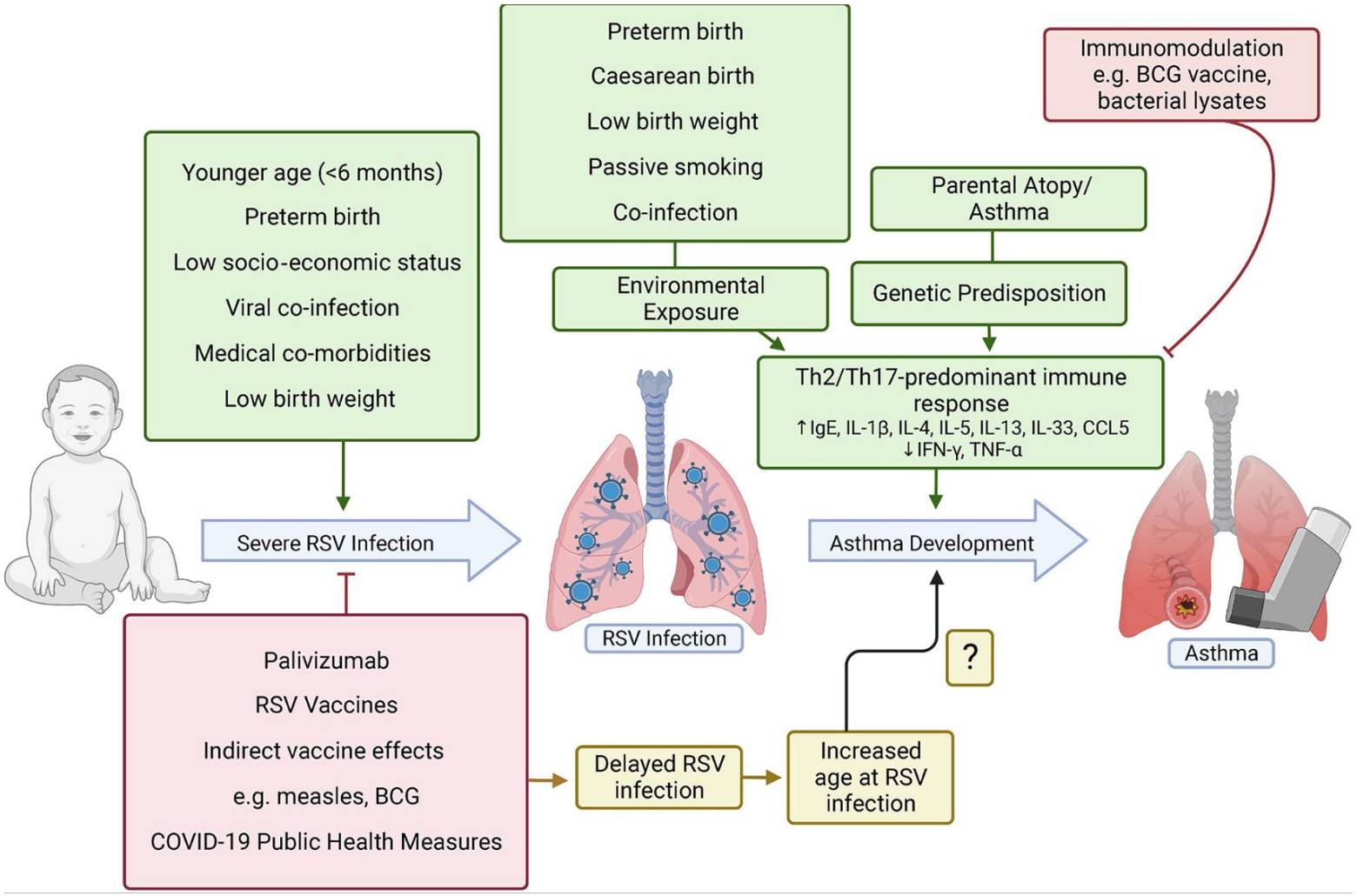
Vaccines: Arexvy (GSK) (EU-US), Abrysvo (Pfizer) (US), and Mresvia (Moderna)(US)

Normaly, seasonal



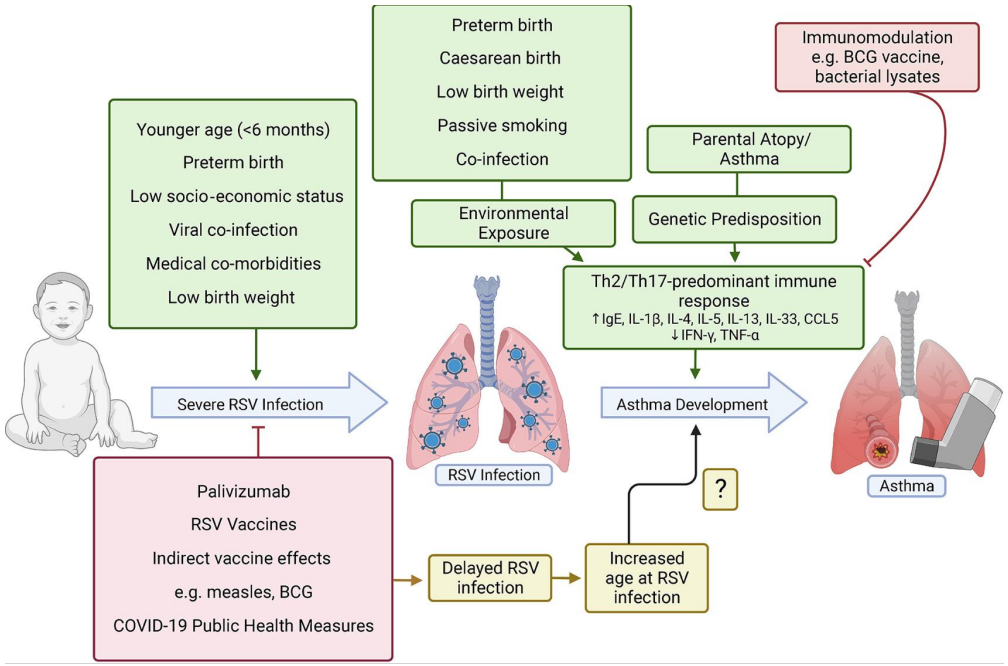

*Nature Reviews, microbiology*, 2023

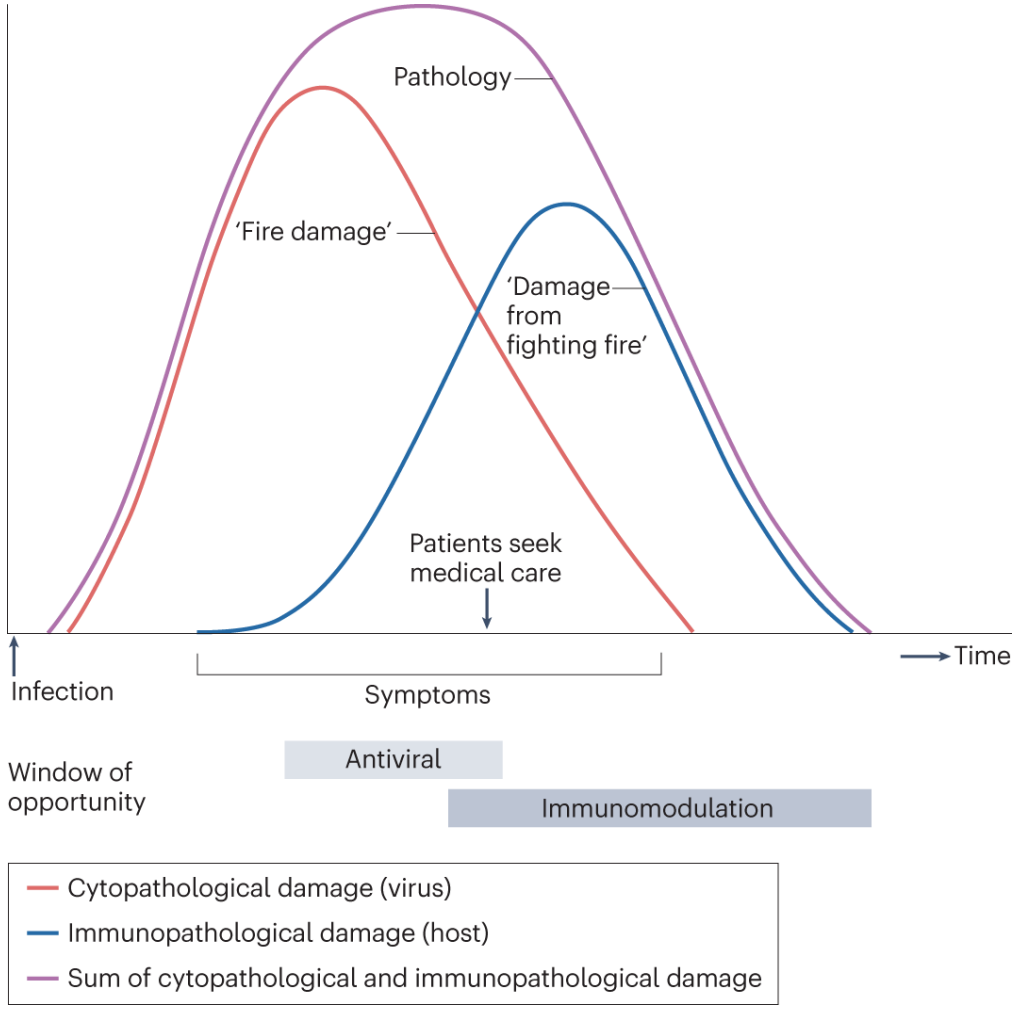
# RSV: Pathophysiology




*JPCH, Wiley*, 2022

# RSV: Pathophysiology




*JPCH, Wiley*, 2022
*Nature Reviews, microbiology*, 2023

# RSV: Biology

Order: Mononegavirales

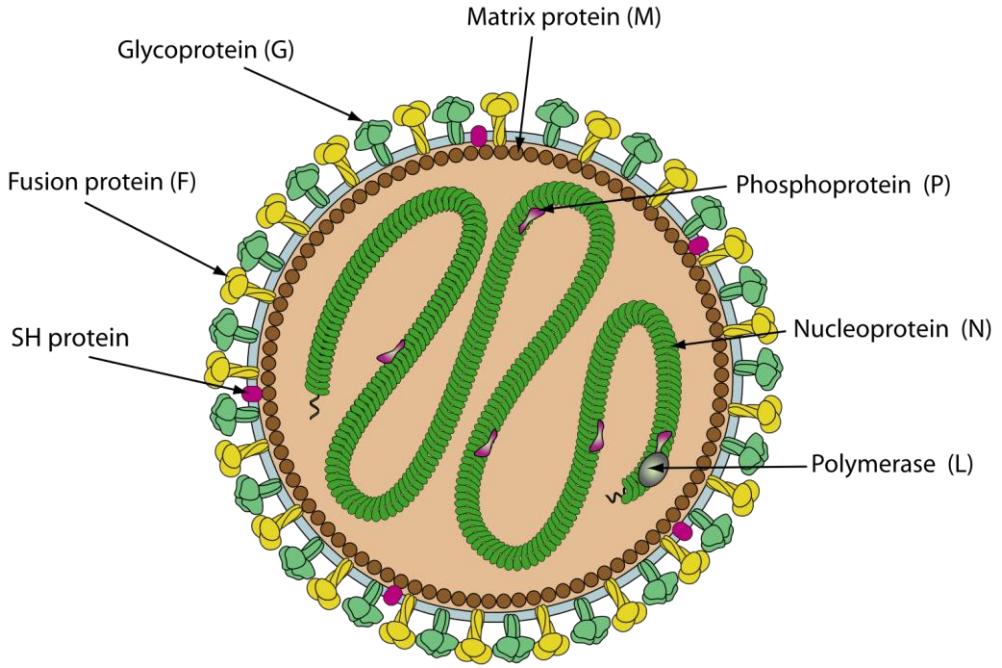
Family: Pneumoviridae

Genus: Orthopneumovirus

Enveloped, spherical.

Diameter ~ 150nm nm

Subtypes RSV-A and RSV-B

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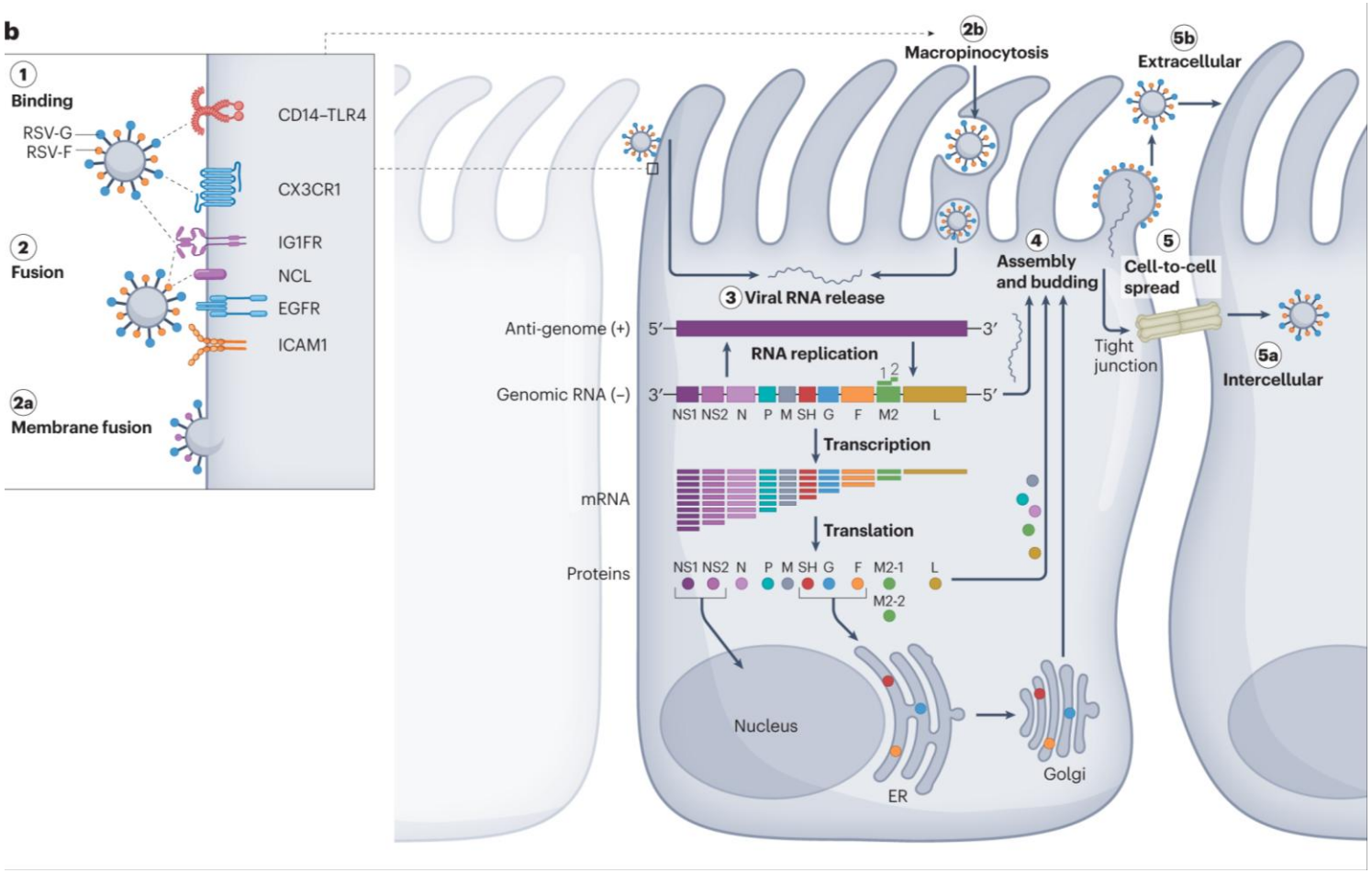
# RSV: Biology




| Location in the Virion | Protein | Alternative Name | Function | Additional Information |
|---|---|---|---|---|
| Lipid envelope (transmembrane surface proteins) | G | Glycoprotein | Viral attachment to ciliated cells of the host airway | F and G glycoproteins are the two major surface proteins that control viral attachment and the initial stages of infection. F and G proteins are also the primary targets for neutralizing antibodies during natural infection. |
| | F | Fusion protein | Fusion of viral and host cell membranes; syncytium formation | |
| | SH | Small hydrophobic protein | Viroporin; ion channel | Participates in cell fusion, but no known neutralizing epitope |
| Inner envelope face | M | Matrix protein | Assembly | |
| Ribonucleocapsid | N | Nucleoprotein | RNA-binding | Involved in genome transcription, RNA replication, and particle budding |
| | P | Phosphoprotein | Phosphorylation | |
| | L | "Large" protein | RNA-dependent RNA polymerase | |
| | M2-1 | - | Transcription processivity factor | |
| Regulatory | M2-2 | - | Regulation of transcription / RNA replication | |
| Nonstructural | NS-1 | - | Involved in evasion of the innate immune system | Act by inhibiting apoptosis and inhibiting Type I IFN signaling |
| | NS-2 | - | | |

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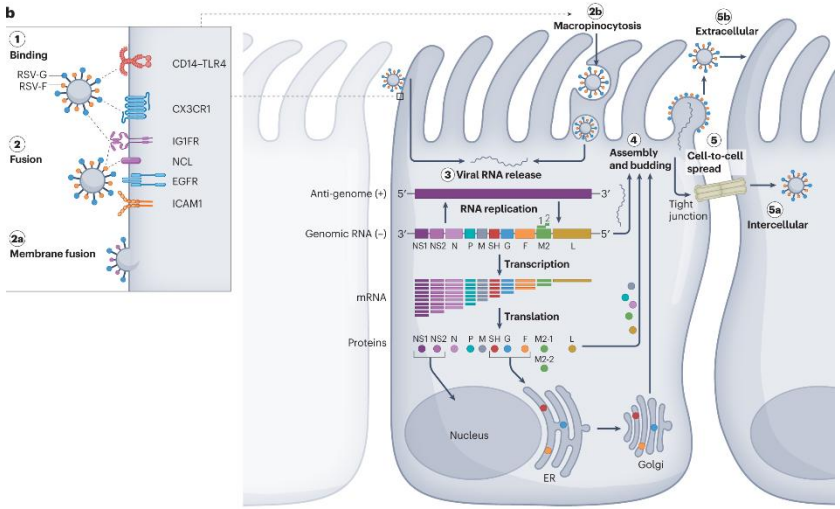
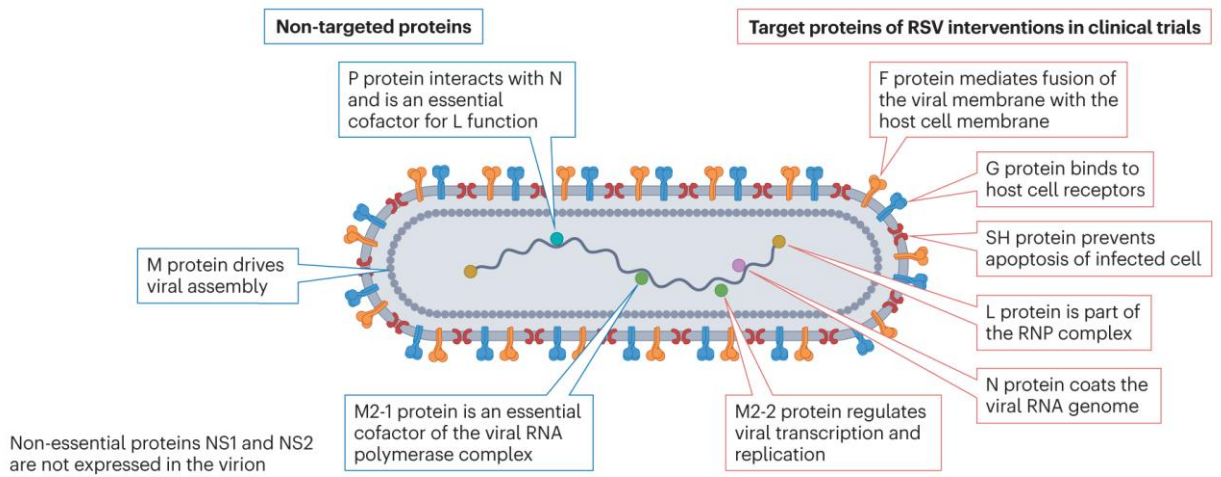
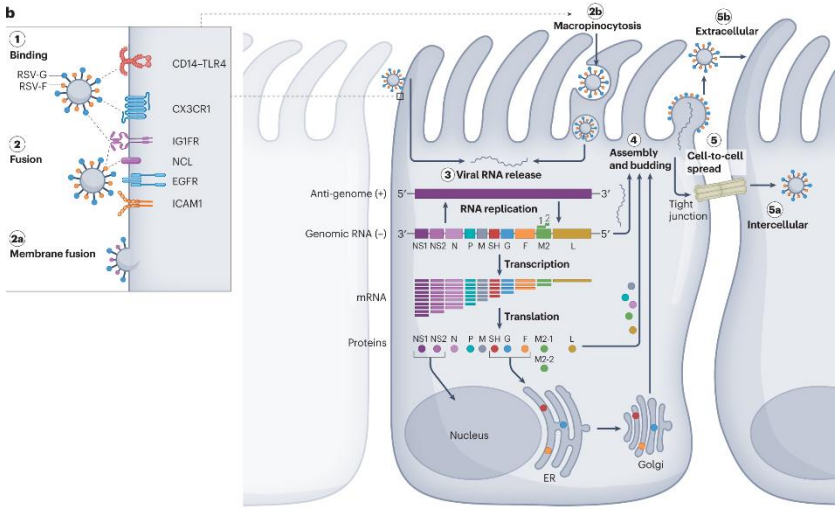
# RSV: Biology

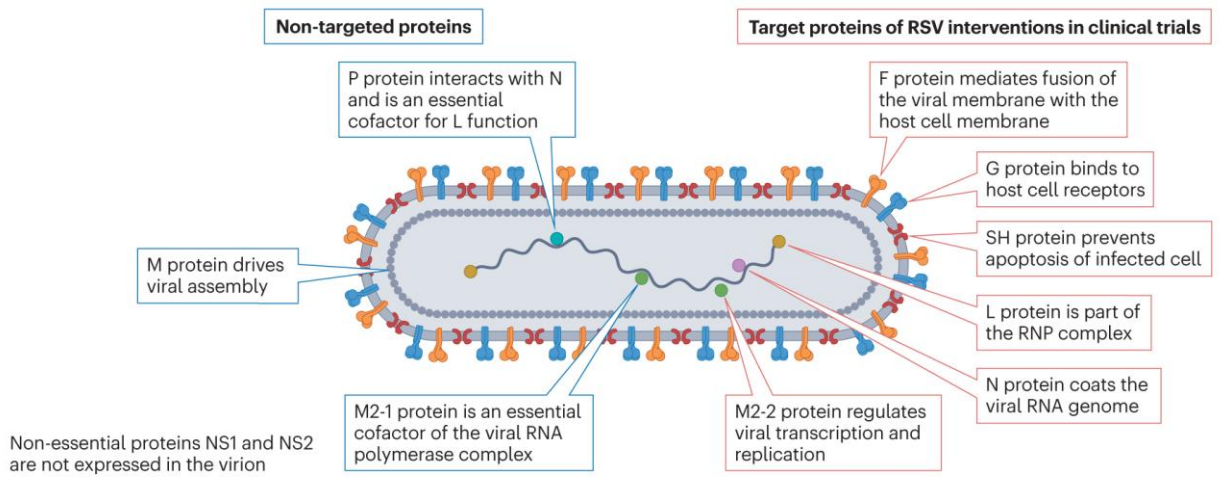



*Nature Reviews, microbiology*, 2023

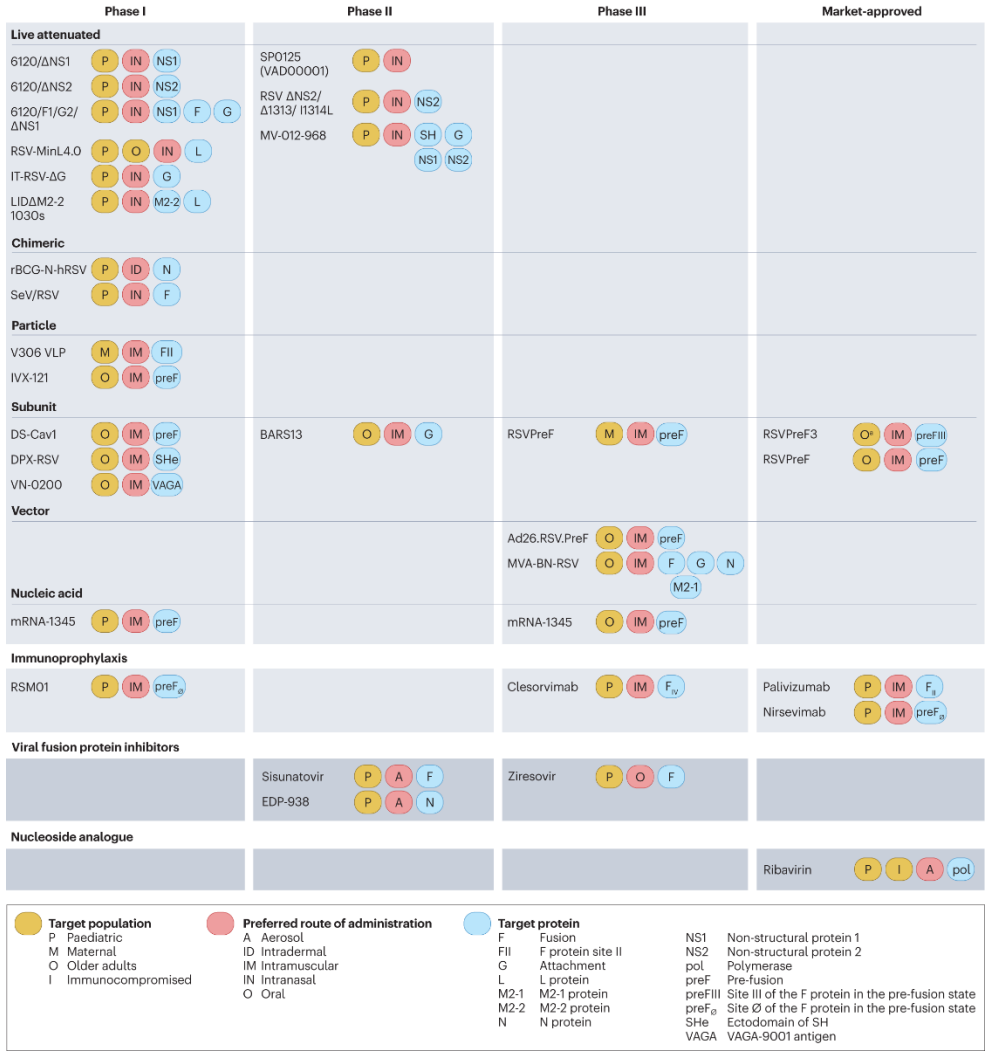
# RSV: Biology



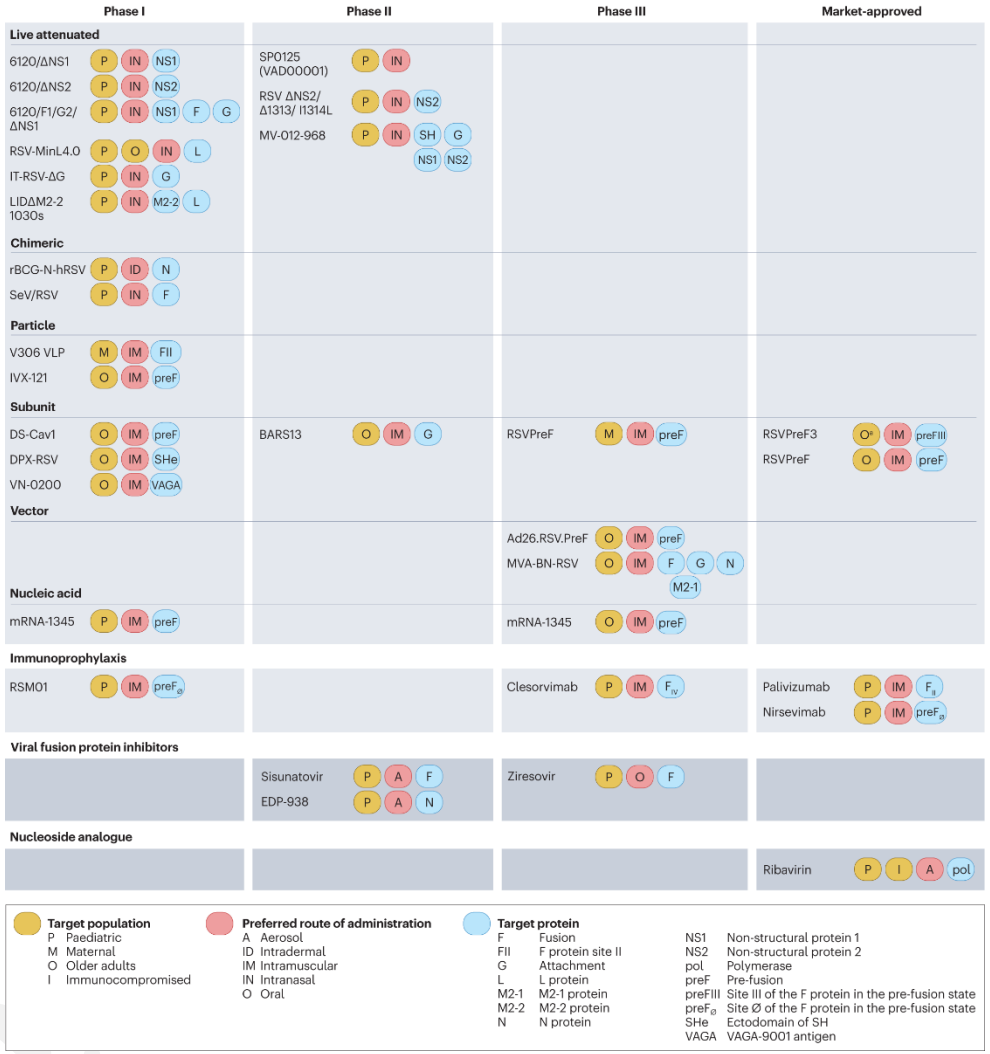

*Nature Reviews, microbiology*, 2023

# RSV: Treatment




*Nature Reviews, microbiology*, 2023

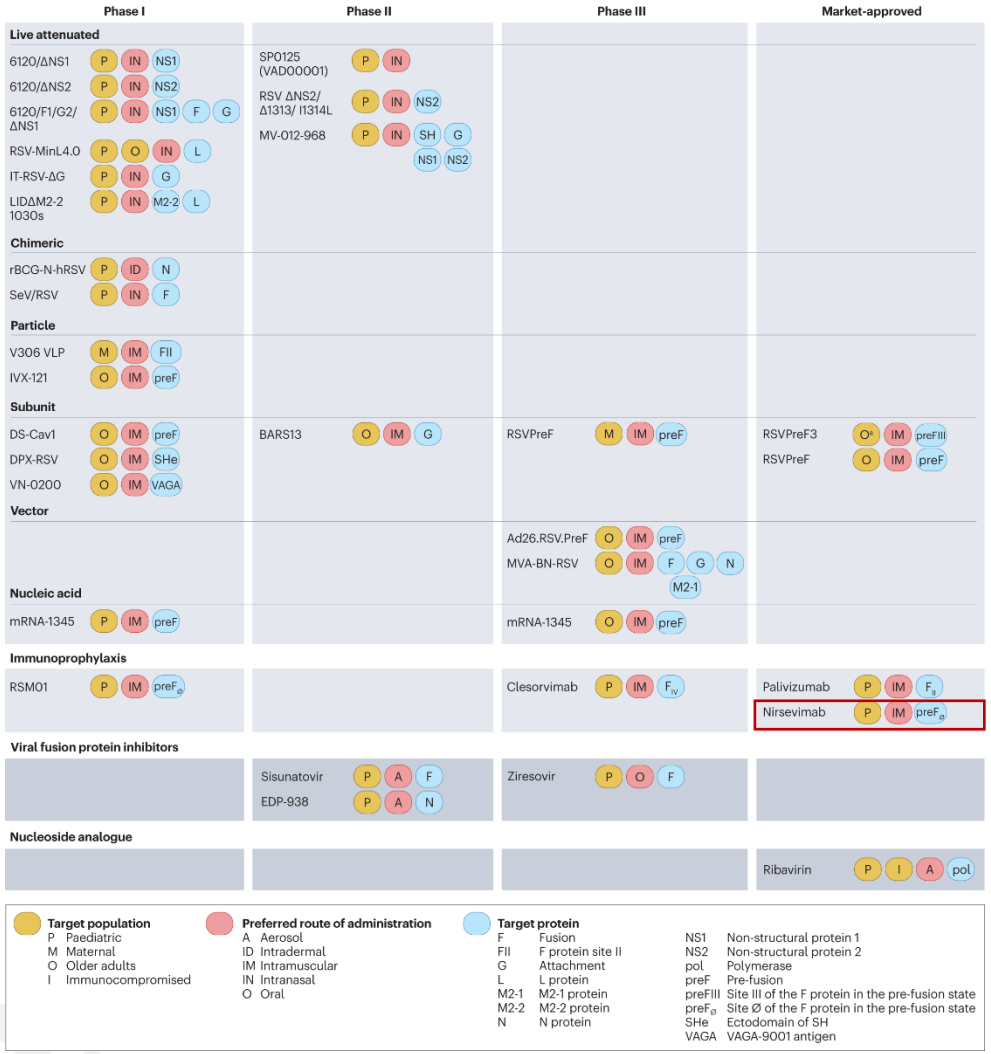
# RSV: Treatment & Prophylaxis




| Name | Description | Marketing Authorisation Holder | Kind of Vaccine | License Number | License Date | Further Information |
|---|---|---|---|---|---|---|
| Abrysvo | Respiratorischer Synzytial-Virus-Impfstoff (rekombinant)<br><br>Verwendung ab einem Lebensalter von 60 Jahren / Use from 60 years of age onwards<br><br>Verwendung bei schwangeren Personen zum Schutz des Säuglings ab der Geburt bis zu einem Alter von 6 Monaten / Use in pregnant persons to protect the infant from birth to 6 months of age | Pfizer Europe MA EEIG, Belgien | Bivalent | EU/1/23/1752 | 23.08.2023 | EPAR: Abrysvo |
| Arexvy | Respiratorischer Synzytial-Virus-Impfstoff (rekombinant, adjuvantiert)<br><br>Verwendung ab einem Lebensalter von 60 Jahren / Use from 60 years of age onwards | GlaxoSmithKline Biologicals S.A. | Mono | EU/1/23/1740 | 06.06.2023 | EPAR: Arexvy |
| mResvia | Respiratorisches-Synzytial-Virus-mRNA-Impfstoff<br><br>Verwendung ab einem Lebensalter von 60 Jahren / Use from 60 years of age onwards | Moderna Biotech Spain S.L. | Mono | EU/1/24/1849 | 22.08.2024 | EPAR: mResvia |

*Nature Reviews, microbiology*, 2023

# RSV: Treatment & Prophylaxis

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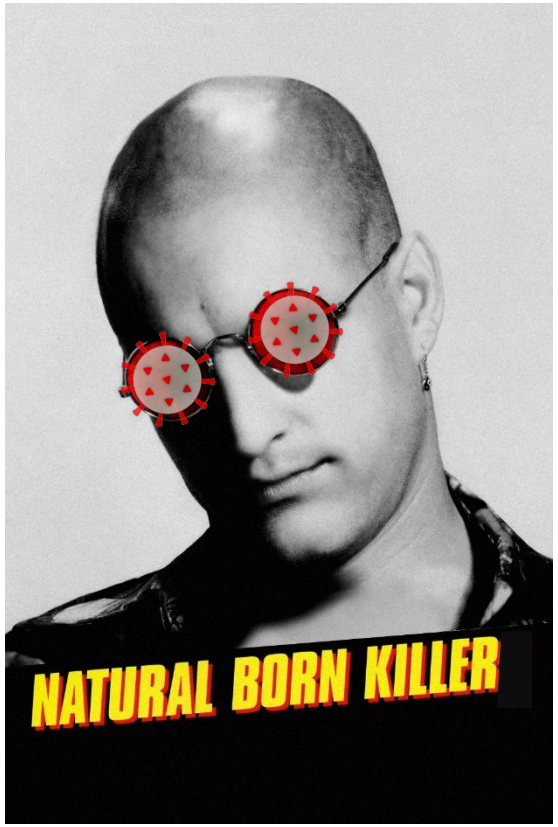
*Nature Reviews, microbiology*, 2023




# The cast:

## Natural born killer Episodes I & II

# SARS Coronavirus: Episode I

Infectious respiratory disease

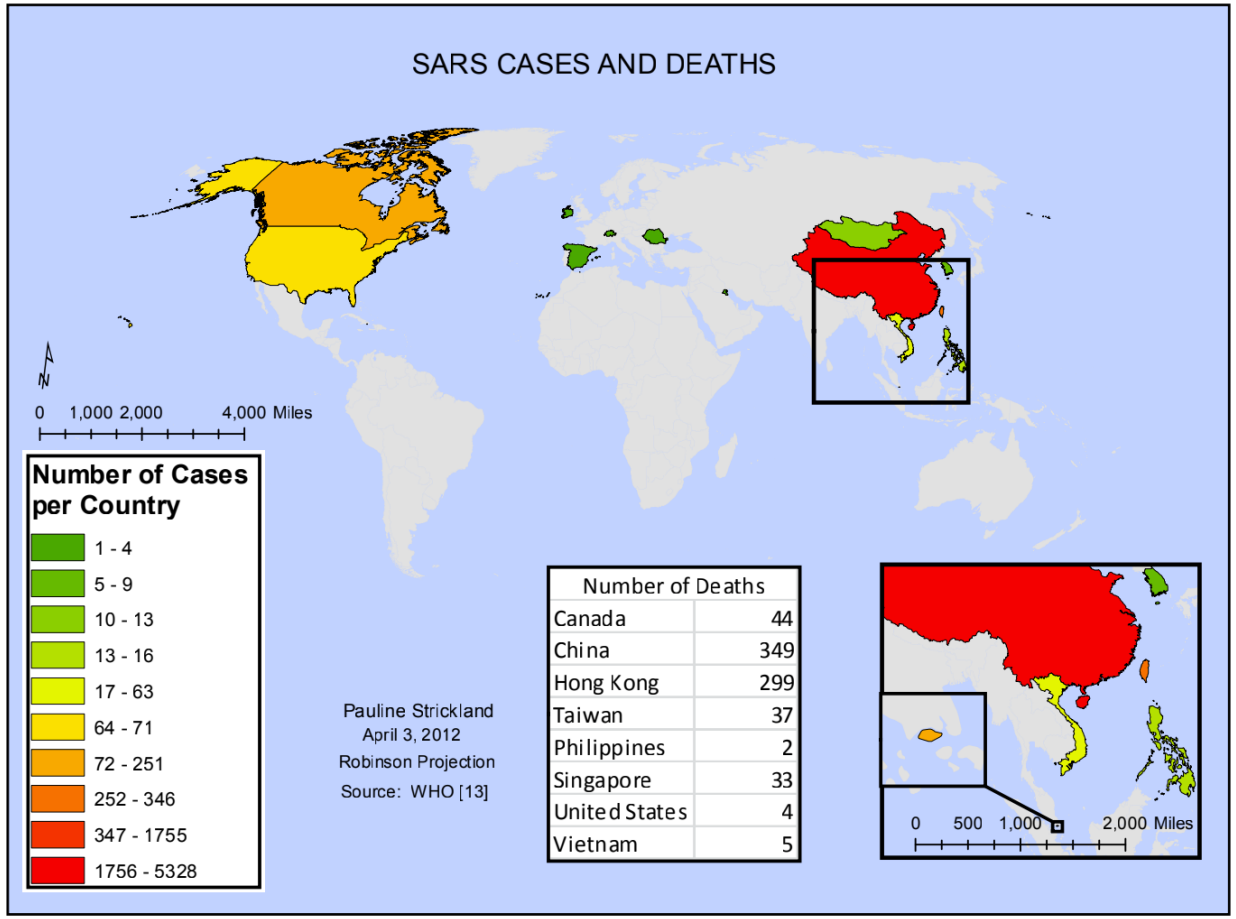
(mild to severe illness)

Dangerous to the population

Pangolin natural reservoir

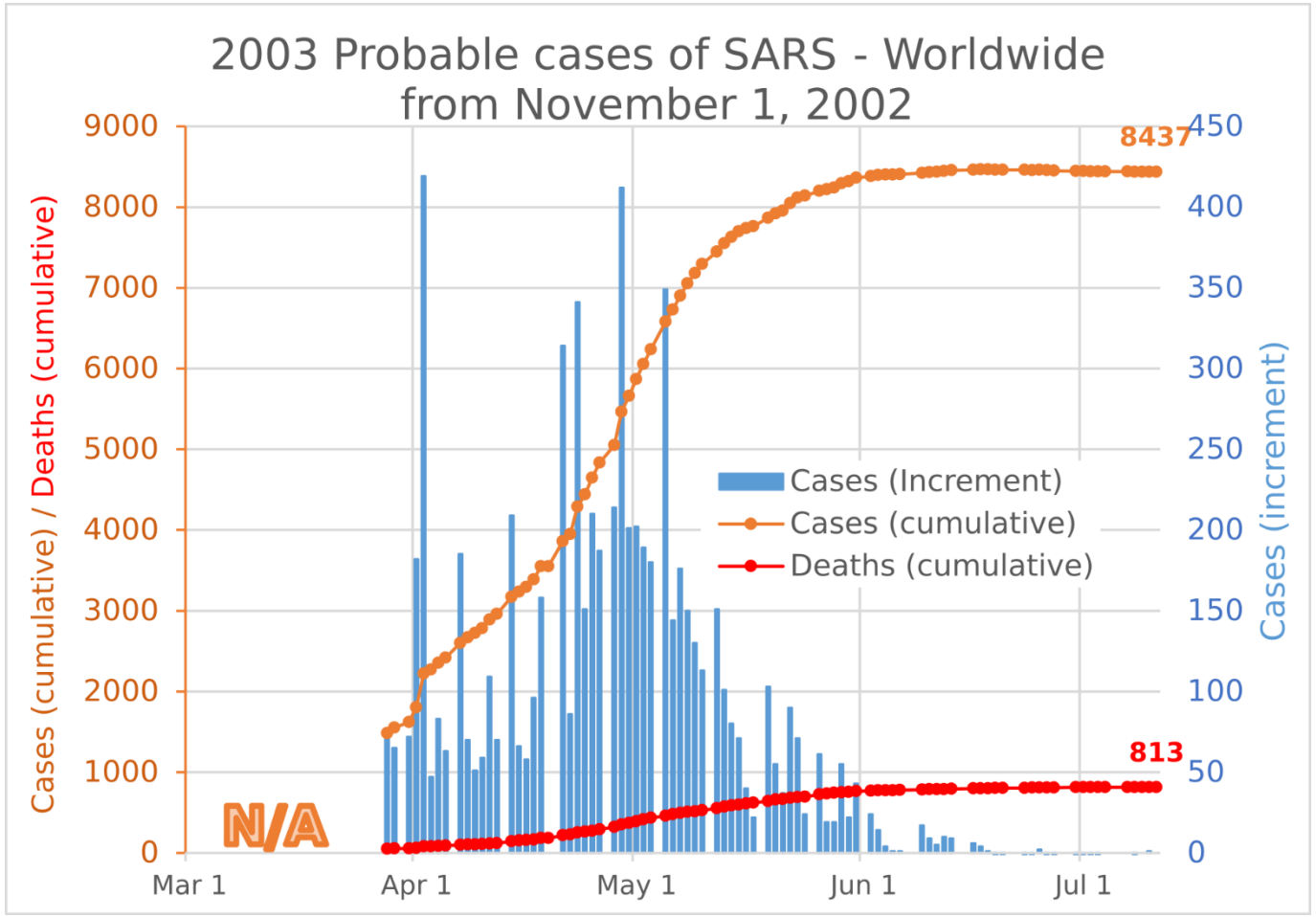
infected over 8,000 people (30 countries)

~800 deaths worldwide




*Wikimedia Foundation*

# SARS Coronavirus: Episode I



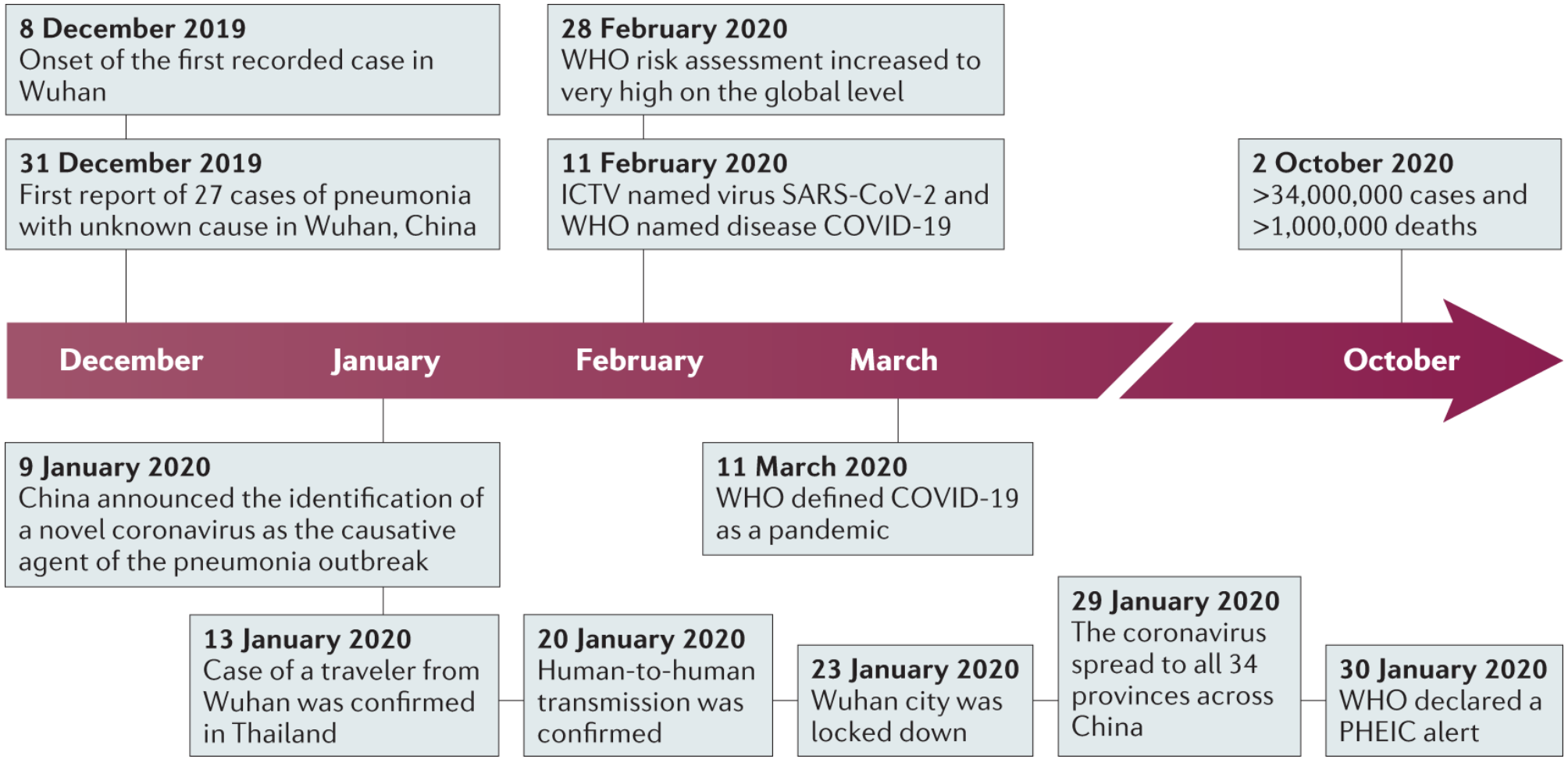

May 2004 last registered case

*Wikimedia Foundation*

# SARS Coronavirus: Episode I

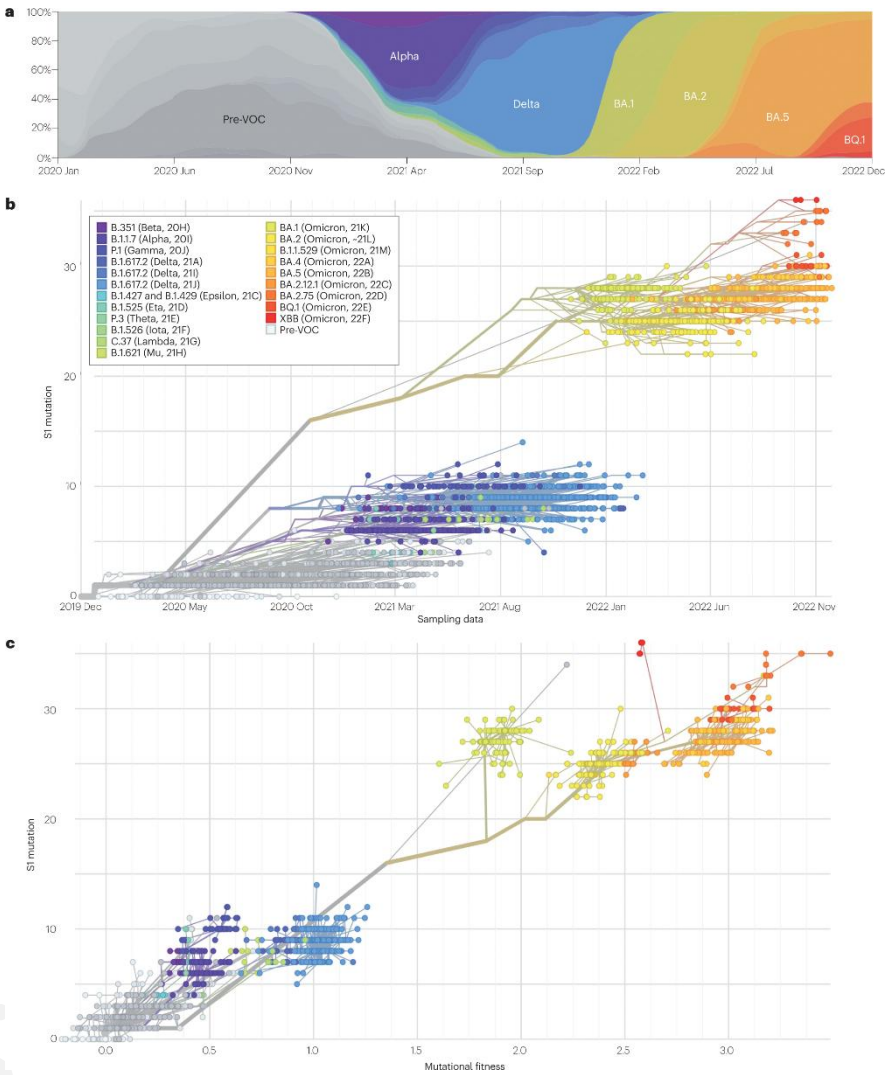
Well, this will never happen again… EVER!

# SARS Coronavirus 2: Episode II




*Nature reviews, microbiology, 2021*

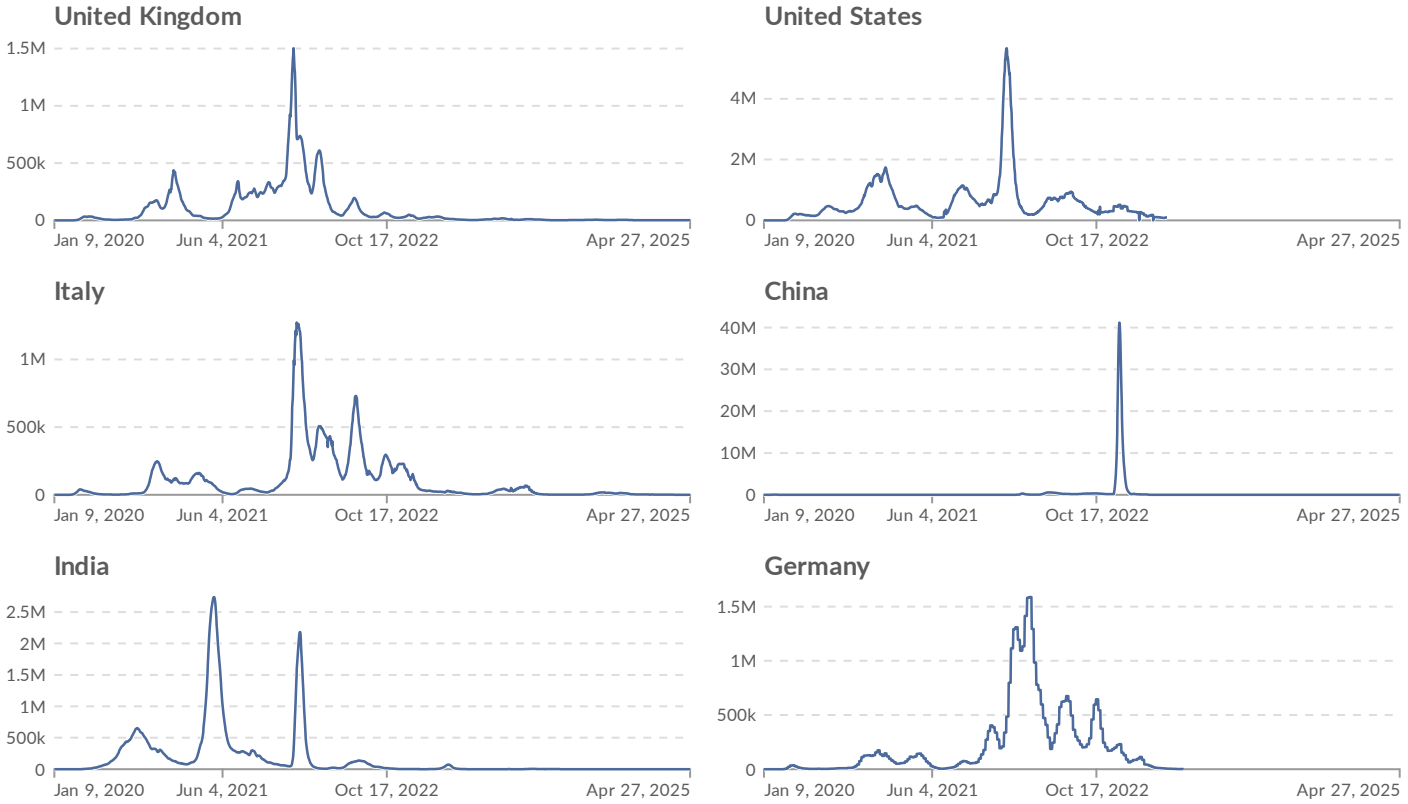
# SARS Coronavirus 2: Episode II




## Weekly confirmed COVID-19 cases

Our World in Data

Weekly confirmed cases refer to the cumulative number of cases over the previous week.

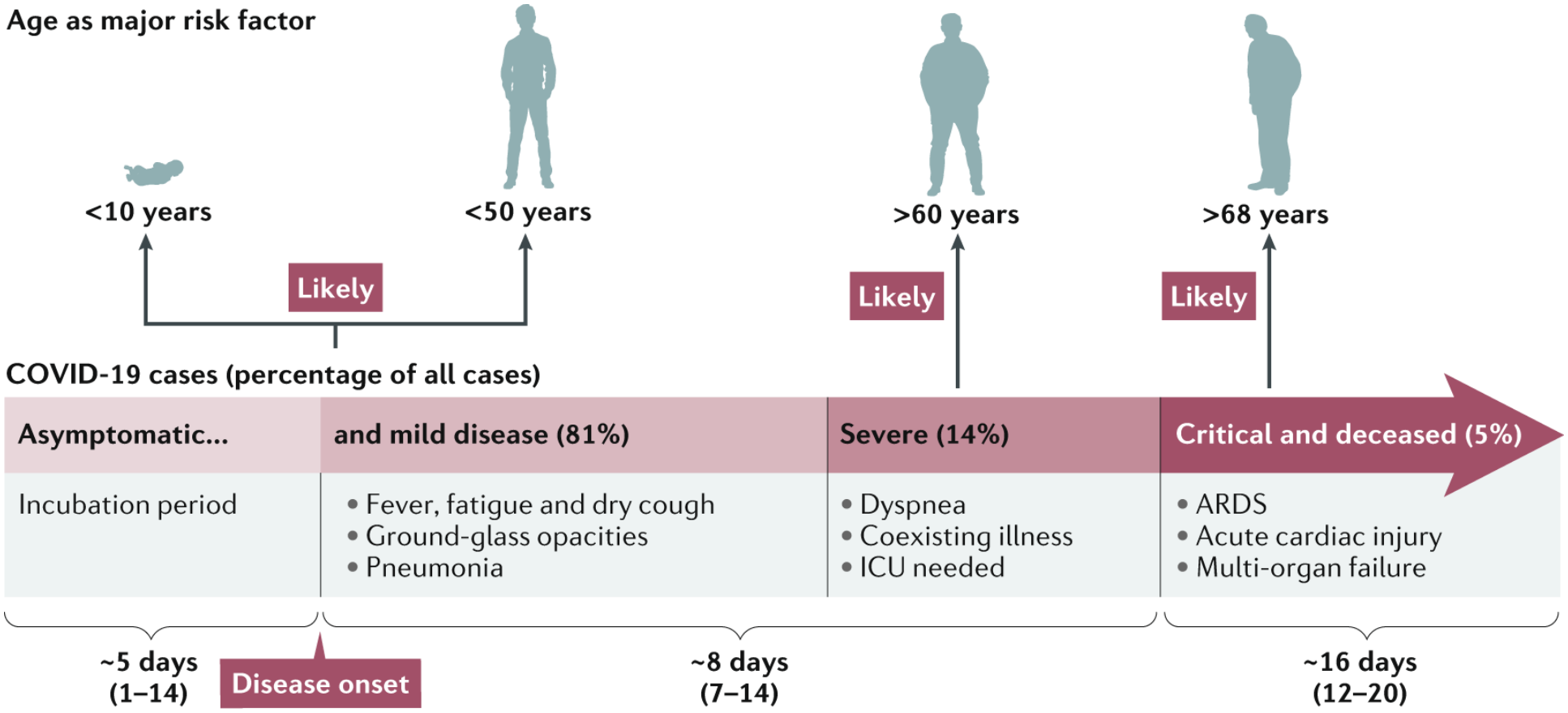



**Data source:** World Health Organization (2025)

OurWorldinData.org/coronavirus | CC BY

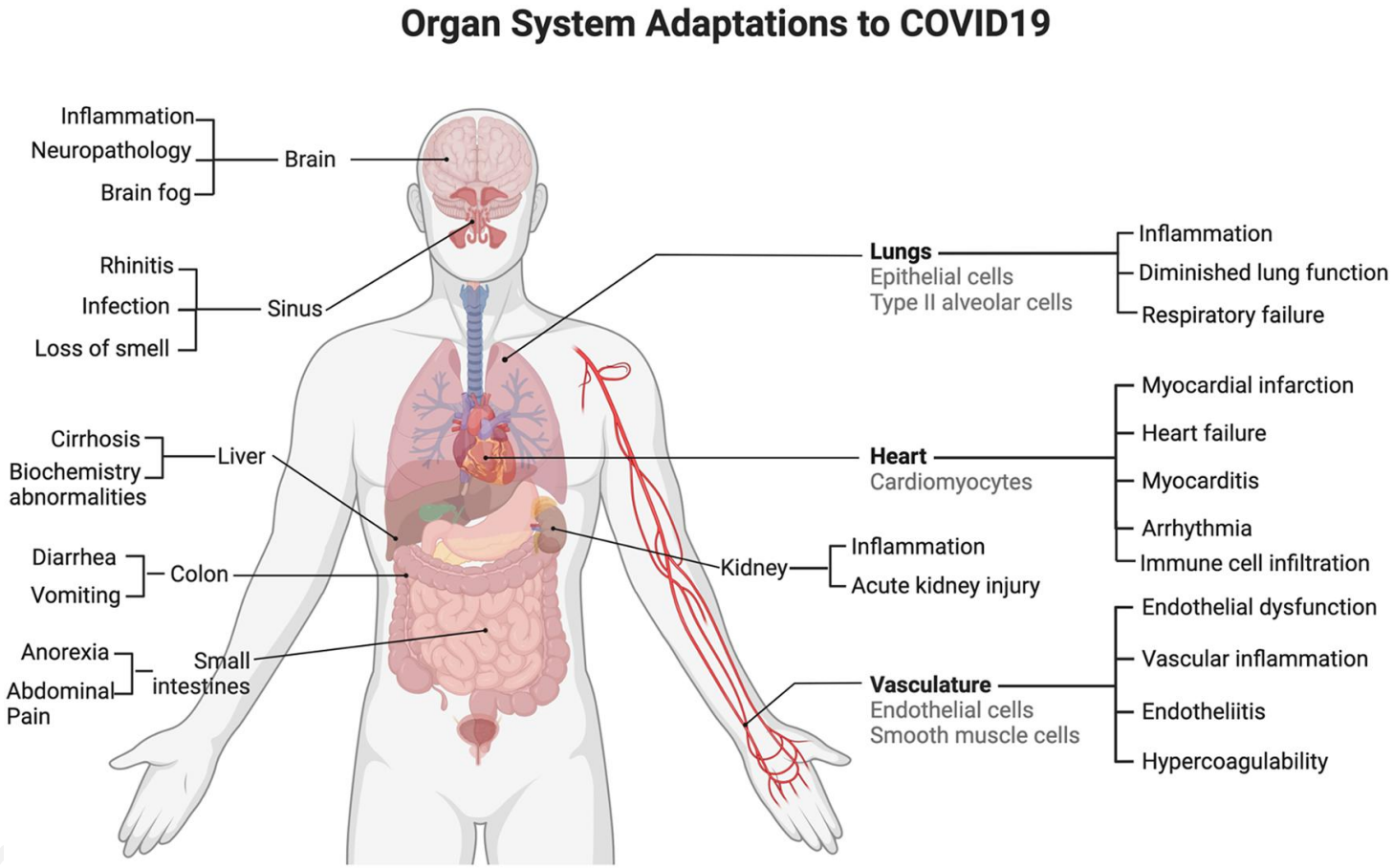
*Nature reviews, microbiology, 2023*
*Our World in Data*

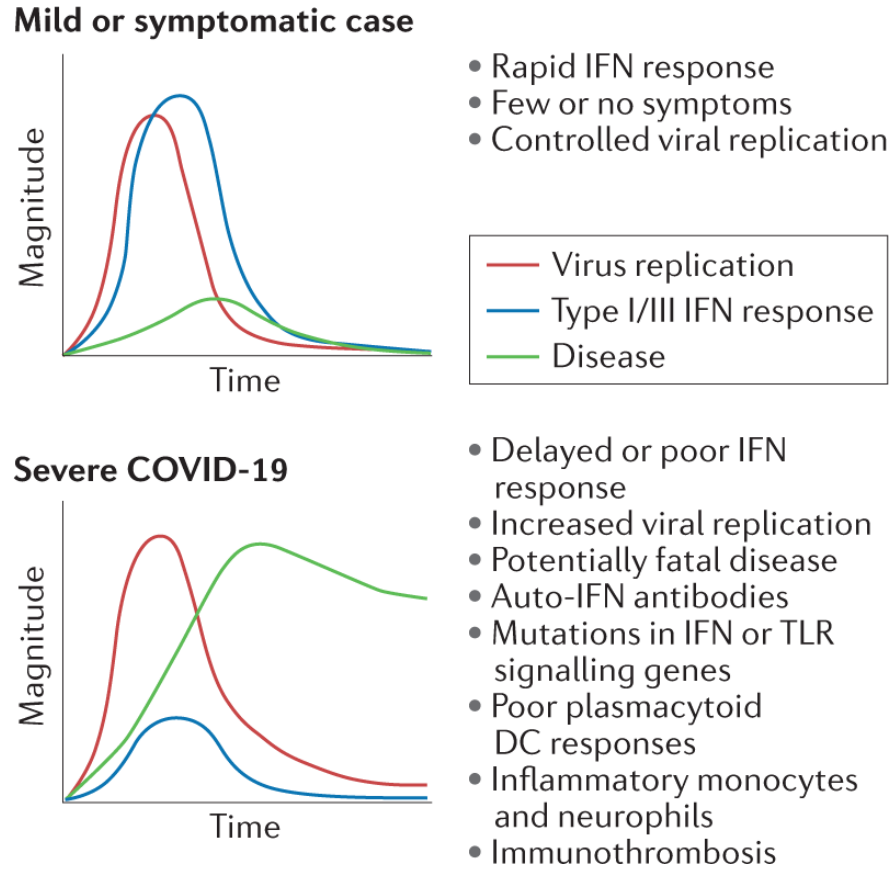
# SARS Coronavirus 2: Pathophysiology




*Nature reviews, microbiology, 2021*

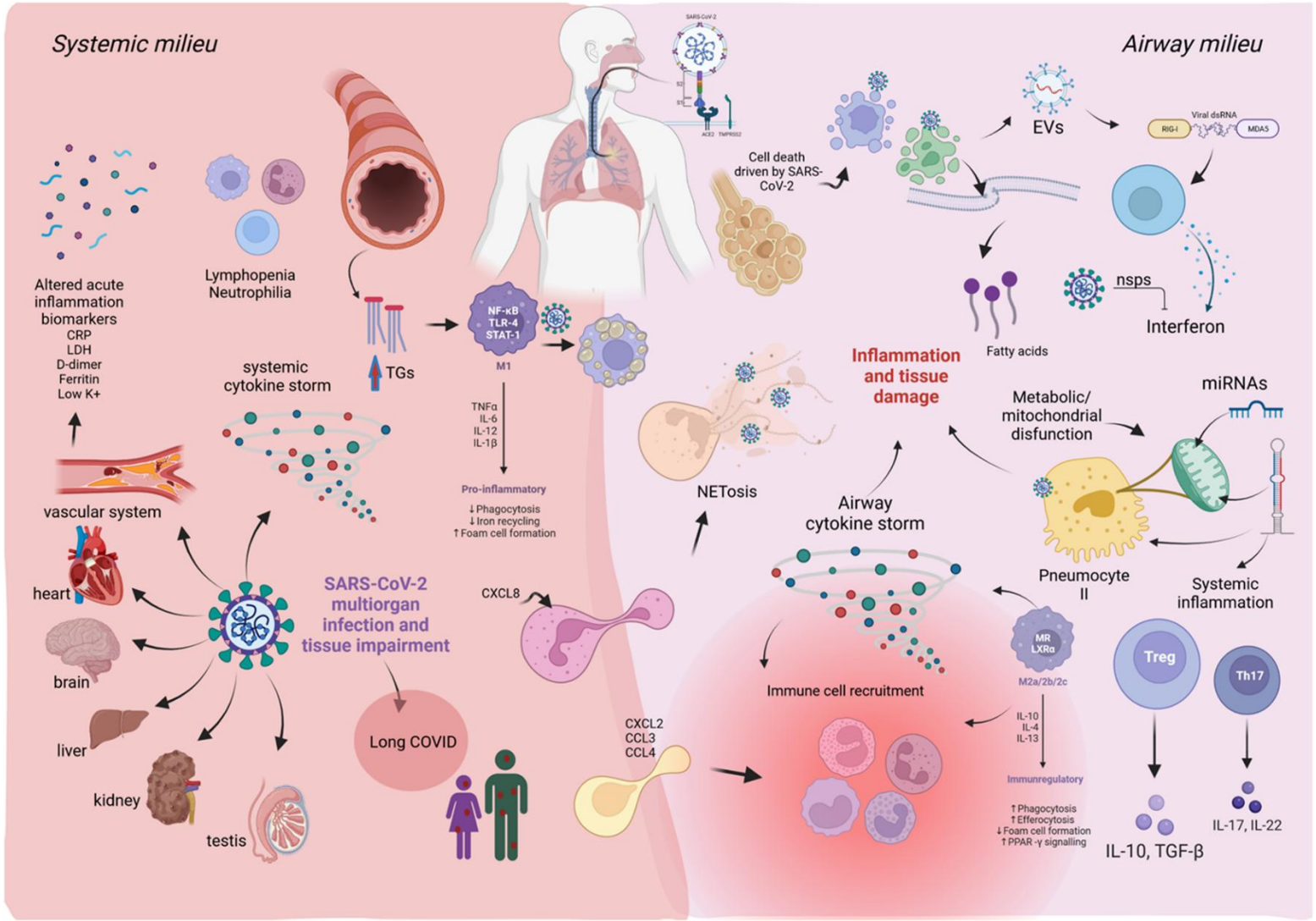
# SARS Coronavirus 2: Pathophysiology




*Nature reviews, microbiology, 2024*

# SARS Coronavirus 2: Pathophysiology




*Nature reviews, microbiology, 2024*

# SARS Coronavirus 2: Biology

Realm: Riboviria

Order: Nidovirales

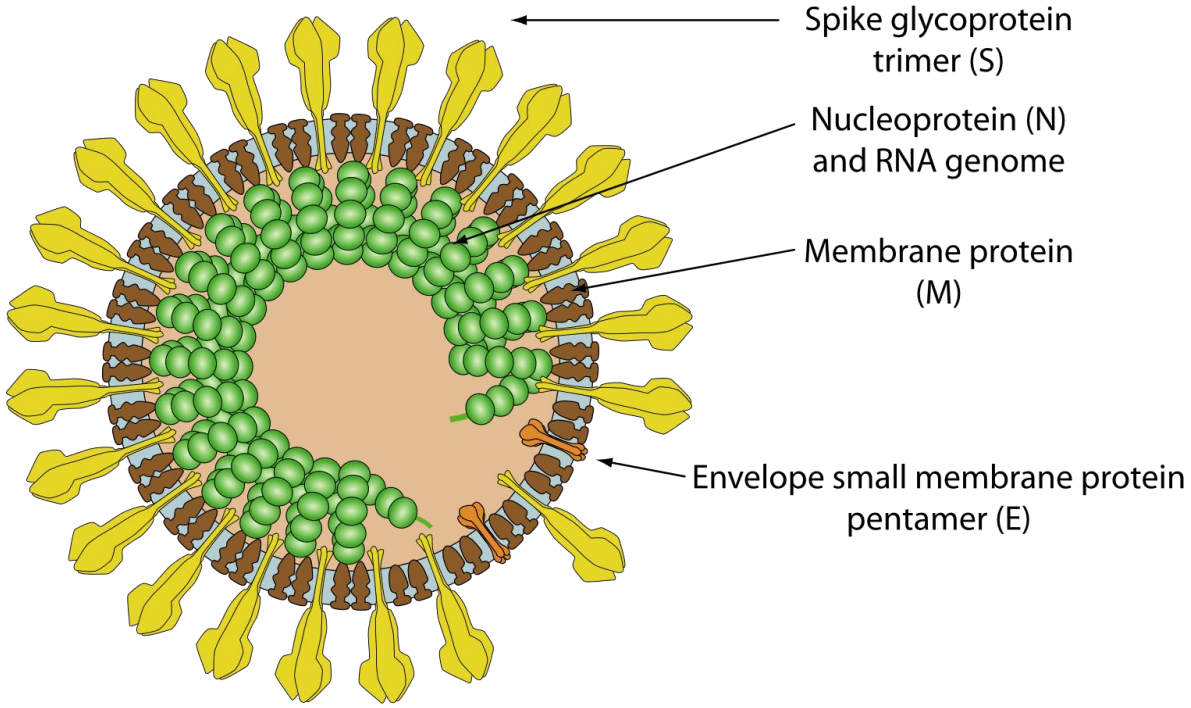
Family: Coronaviridae

Subfamily: Orthocoronavirinae

Genus: Betacoronavirus

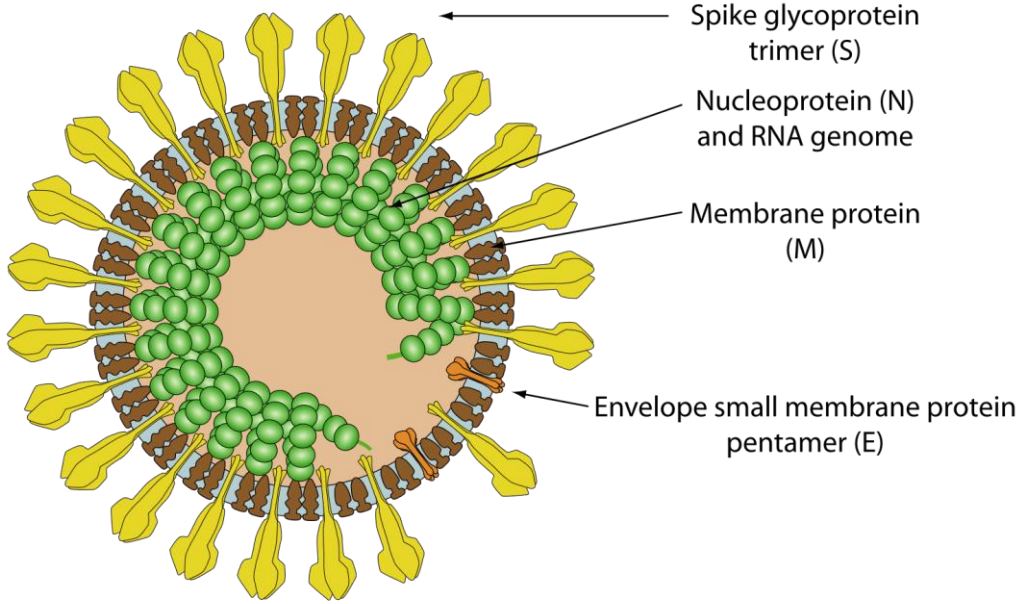
Several human pathogens:

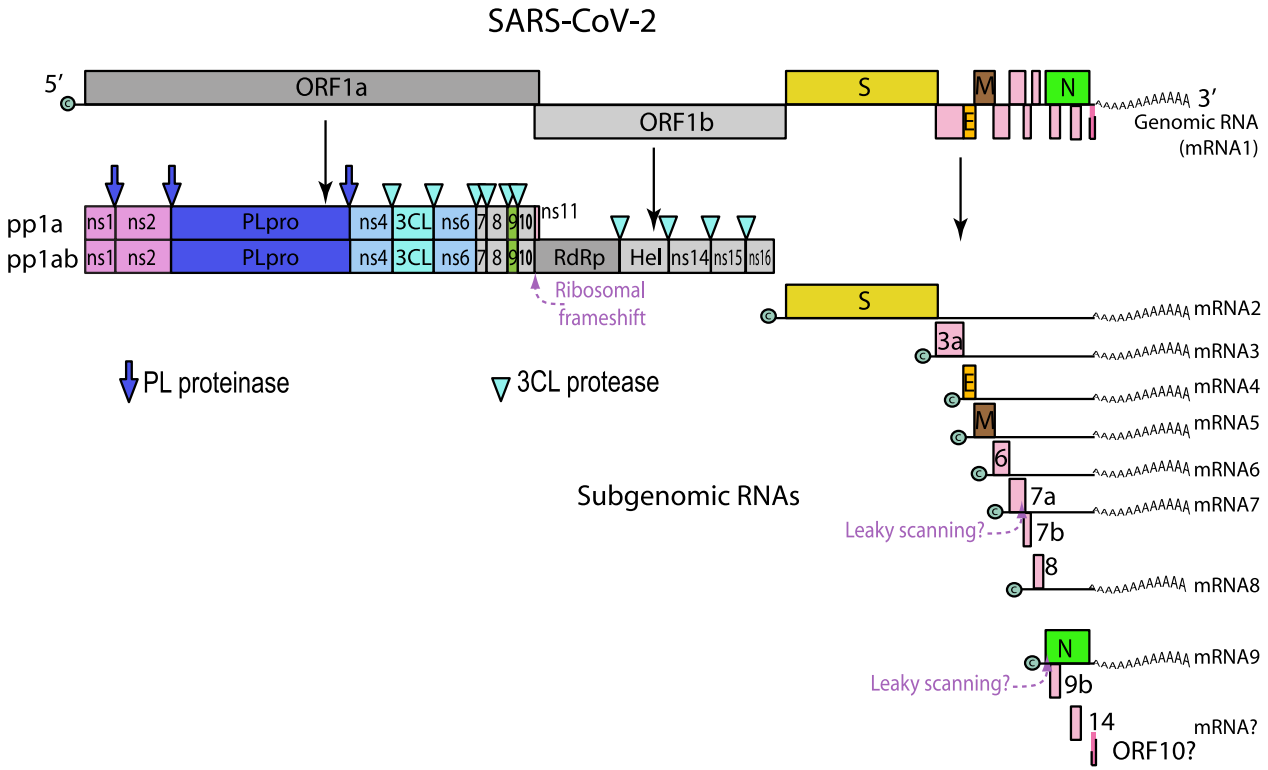
SARS-Cov, SARS-Cov-2, HCov-OC43, MERS…




*Viral Zone, Expasy*

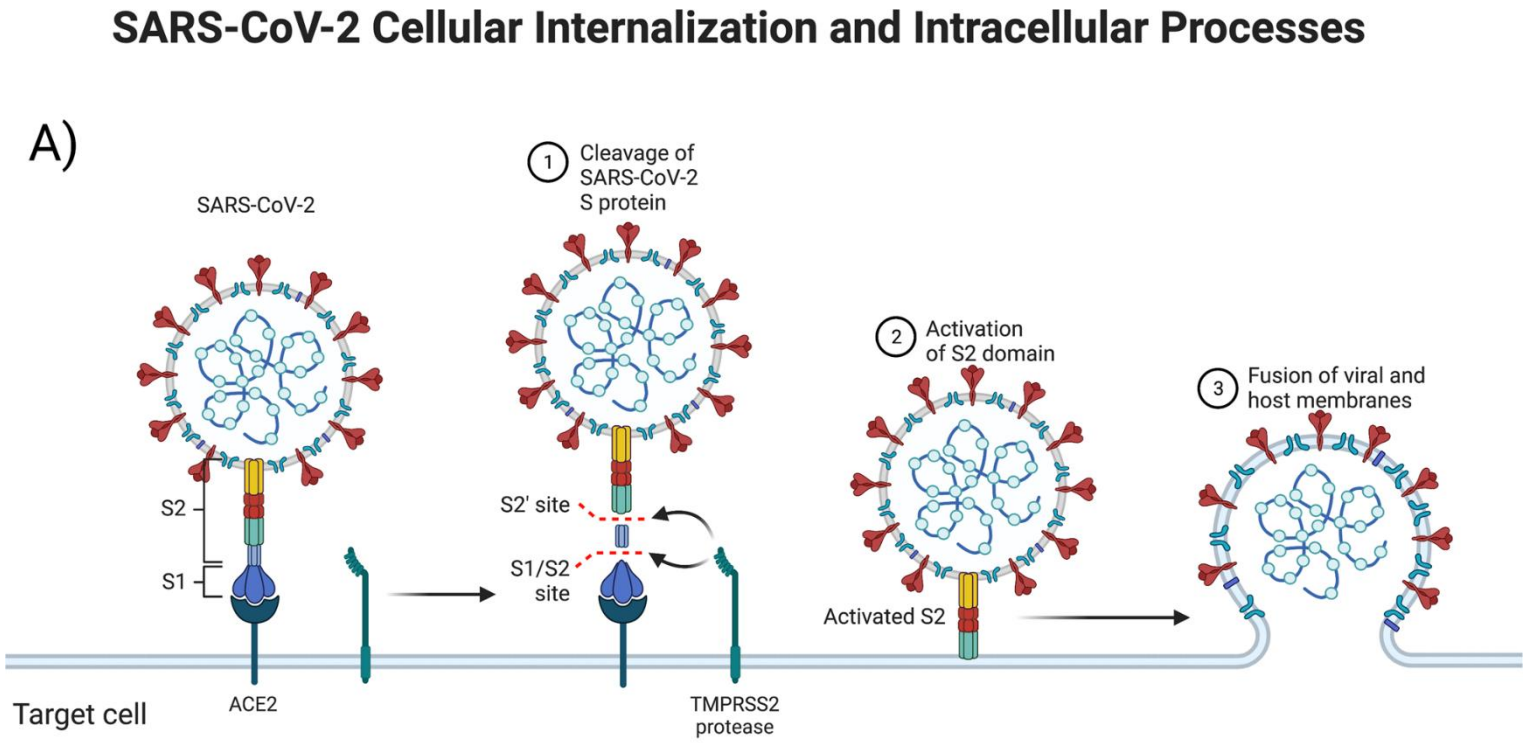
# SARS Coronavirus 2: Biology



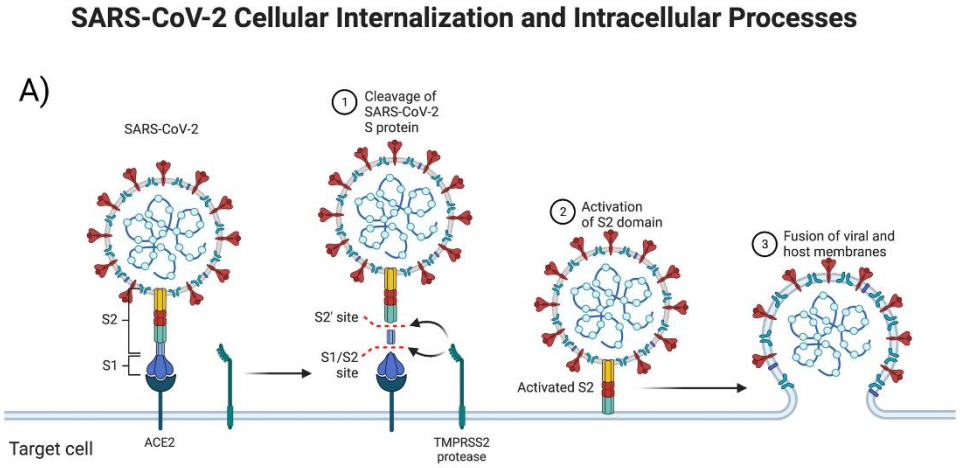

*Viral Zone, Expasy*

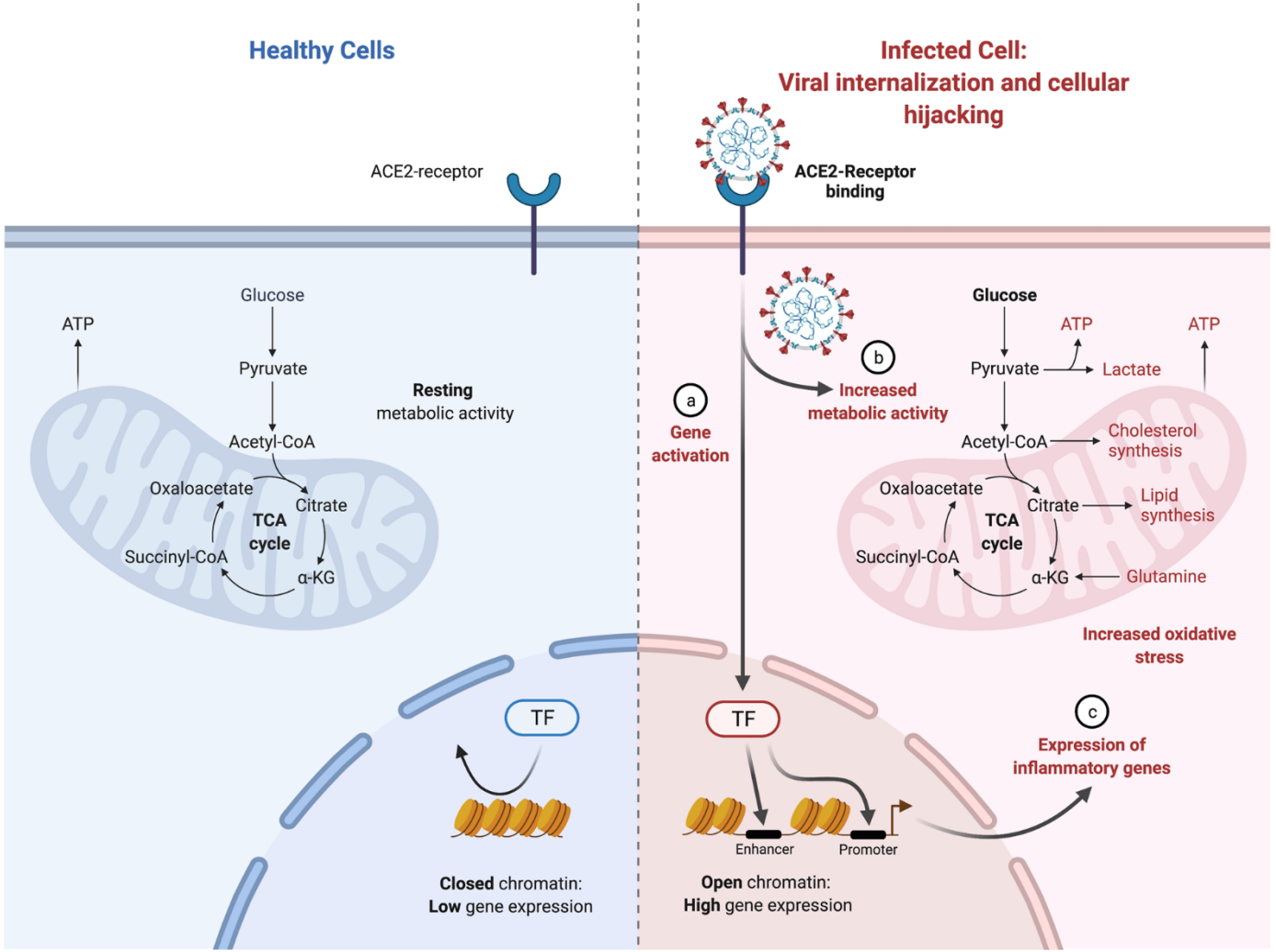
# SARS Coronavirus 2: Biology




*Nature reviews, microbiology, 2020*
*Nature reviews, microbiology, 2021*

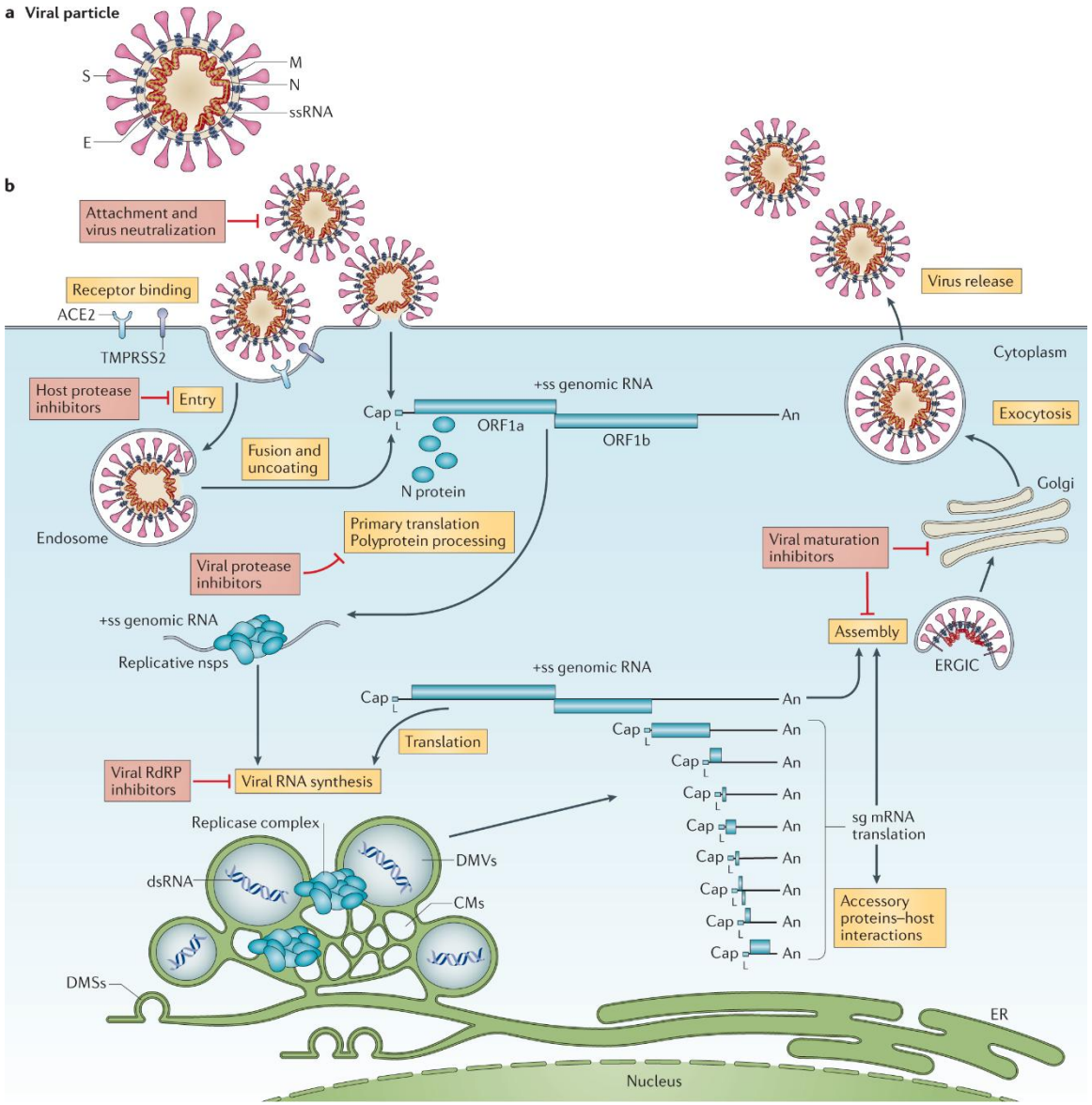
# SARS Coronavirus 2: Biology



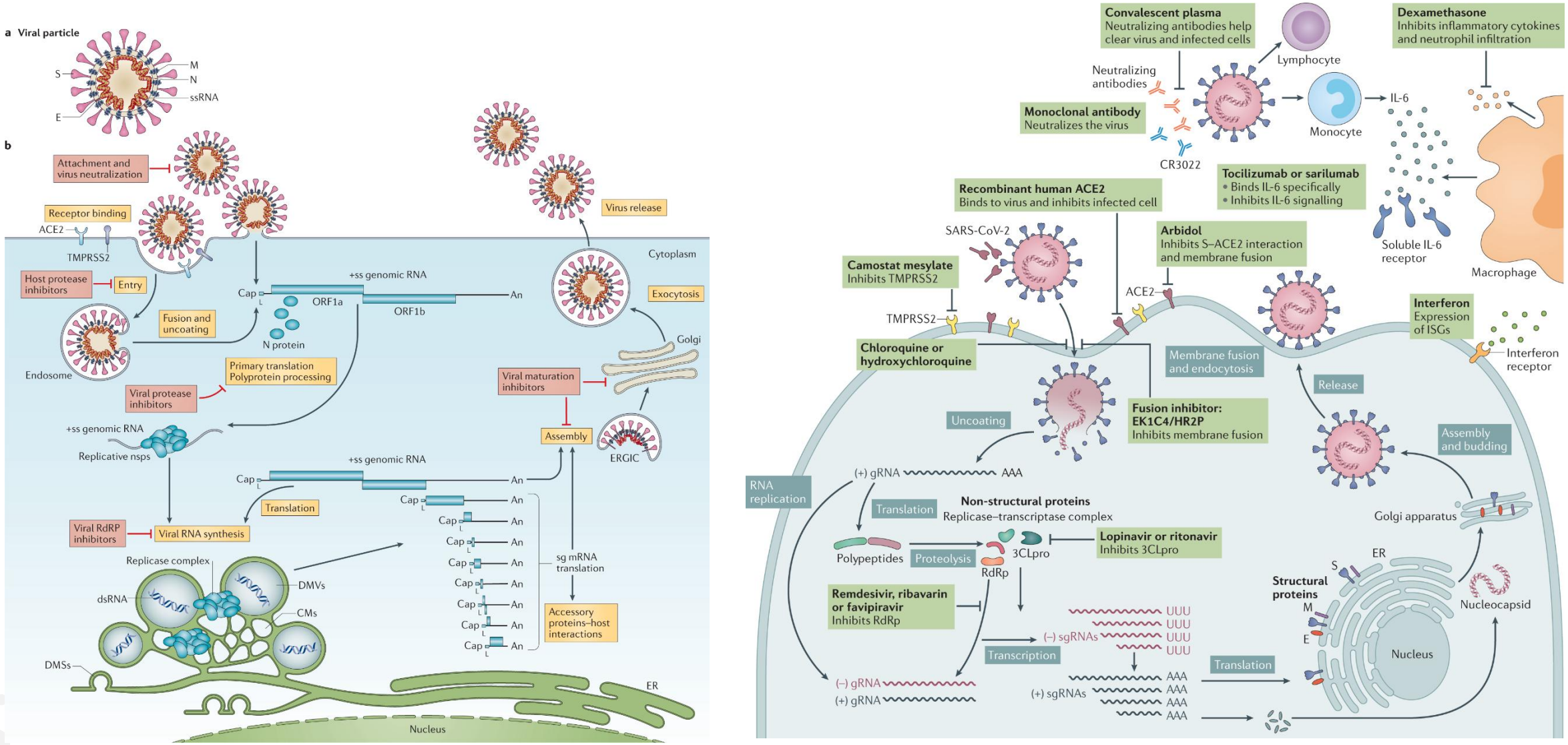

*Nature reviews, microbiology, 2020*
*Nature reviews, microbiology, 2021*

# SARS Coronavirus 2: Biology




*Nature reviews, microbiology, 2024*

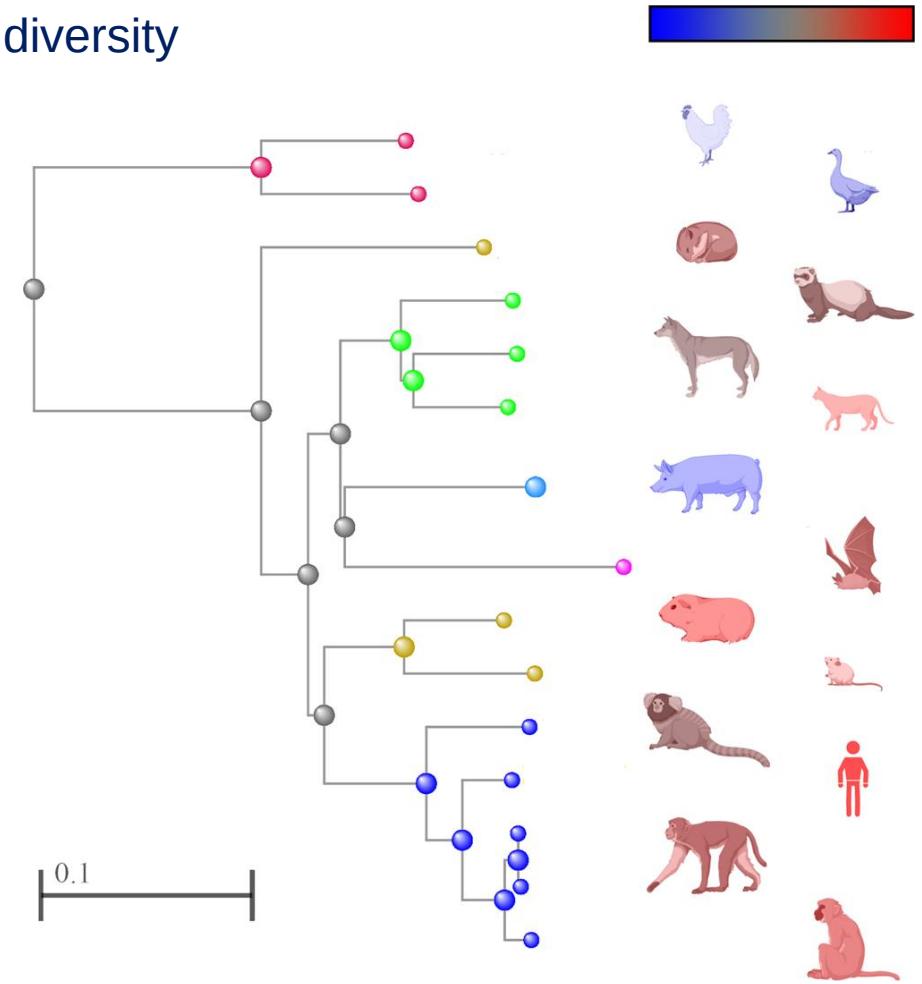
# SARS Coronavirus 2: Biology

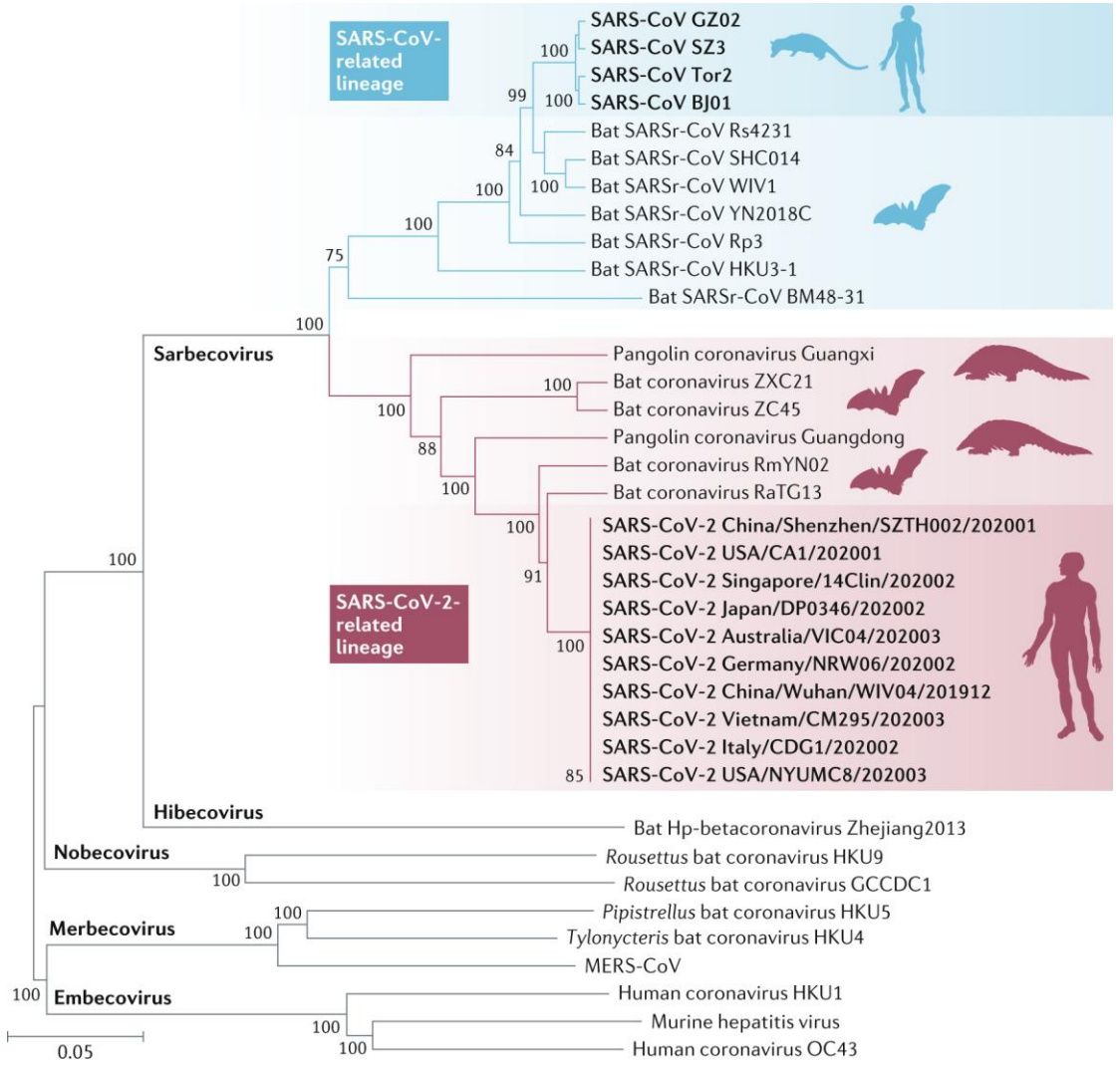



*Nature reviews, microbiology, 2024*

# SARS Coronavirus 2: Distribution

## ACE2 diversity

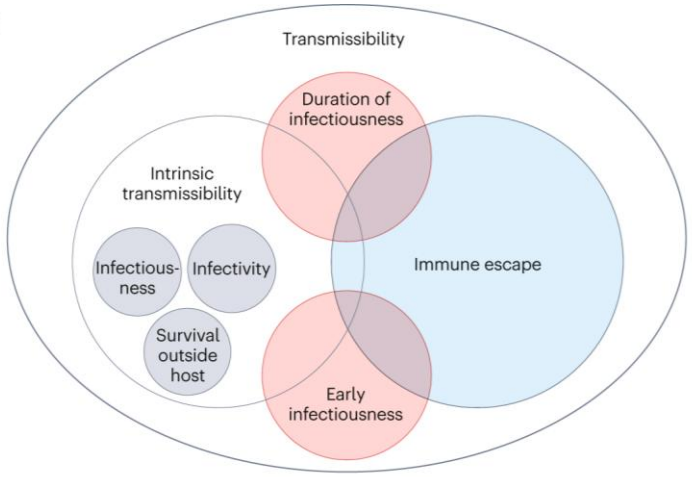



*Nature reviews, microbiology, 2020*
*Nature reviews, microbiology, 2021*

# SARS Coronavirus 2: Distribution

a




b

**Stages of viral transmission**

| Shedding from infectious host | | Survival outside host | | Establishment in a new host | |
|---|---|---|---|---|---|
| **Factors favouring virus shedding** | **SARS-CoV-2 evolvable traits** | **Factors favouring virus survival** | **SARS-CoV-2 evolvable traits** | **Factors favouring establishment of virus** | **SARS-CoV-2 evolvable traits** |
| • High viral loads | • Optimized ACE2 receptor interaction<br>• Cleavage of spike protein<br>• Immune escape | • Ability to survive in aerosol | • Virion stability<br>• Resistance to temperature, humidity, UV radiation, pH | • Ease of cell entry | • Optimized ACE2 receptor interaction<br>• Optimized cleavage of spike |
| • Presence at sites favouring transmission | • Change in tissue tropism | • Environmental conditions<br>• Host density | • Not influenced by virus evolution | • Weakened host resistance due to loss of antigen recognition | • Immune escape |
| • Infection-promoting symptoms (cough, sneeze, increased mucosal secretion) | • Change in clinical presentation | | | • Weakened host resistance due to waning immunity | • Not influenced by virus evolution |

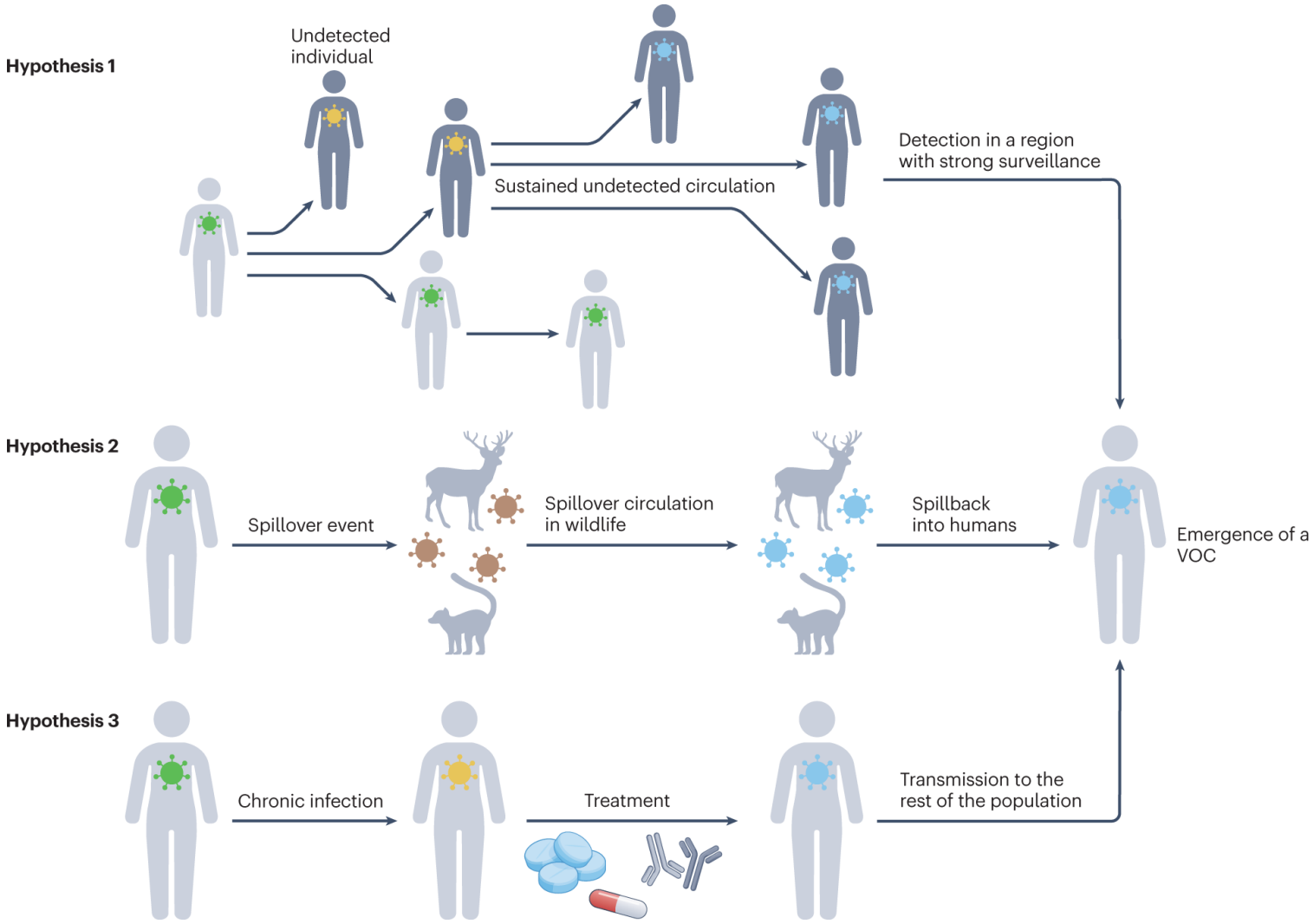
c

| Elements of transmissibility affected by viral evolution | Effects on SARS-CoV-2 epidemiological outcomes | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | $R_0$ | $R_t$ | Generation interval | Incidence of infection | Prevalence of infection | Reinfection rates | Epidemic growth rate | Burden of disease |
| Intrinsic transmissibility | ✓ | ✓ | ✗ | ✓ | ✓ | ✓[a]/✗ | ✓ | ✓ |
| Duration of infectiousness | ✓ | ✓ | ✗ | ✓ | ✓ | ✓[a]/✗ | ✓ | ✓ |
| Early onset of infectiousness | ✗ | ✗ | ✓ | ✓ | ✓ | ✓[a]/✗ | ✓ | ✓ |
| Immune escape | ✗ | ✓ | ✗ | ✓ | ✓ | ✓ | ✓ | ✓ |

✓ = Effect ✗ = No effect

*Nature reviews, microbiology, 20204*

# SARS Coronavirus 2: Distribution




*Nature reviews, microbiology, 20204*

# We‘re forgetting something - 😳

| Month | June | July | Aug. | Sep. | Oct. | Nov. | Dec. | Jan. | Feb. | Mar. | Apr. | May |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **All-year virus** | Adenovirus/HBoV | | | | | | | | | | | |
| Type-specific | PIV3 | | PIV1 | | | | | | | | | |
| Spring | hMPV | | | | | | | | | | | |
| Spring/Fall | Rhinovirus | | | | | | | | | | | |
| **Summer virus** | Non-rhinovirus enteroviruses | | | | | | | | | | | |

*Annual Review of Virology*, 2020

# We‘re forgetting something - 😳

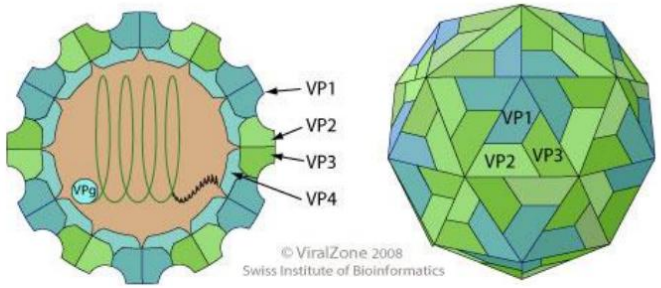
| Pathogen | Virus | Genome |
|---|---|---|
| Influenzavirus | Orthomyxoviruses | ss (-) RNA |
| Respiratory Syncitialvirus | Pneumoviruses | ss (-) RNA |
| HumanesMetapneumovirus | Pneumoviruses | ss (-) RNA |
| Parainfluenzavirus | Paramyxoviruses | ss (-) RNA |
| Human Rhinovirus | Picornaviruses | ss (+) RNA |
| Coronavirus | Coronaviruses | ss (+) RNA |
| Adenoviruses | Adenoviruses | ds DNA |

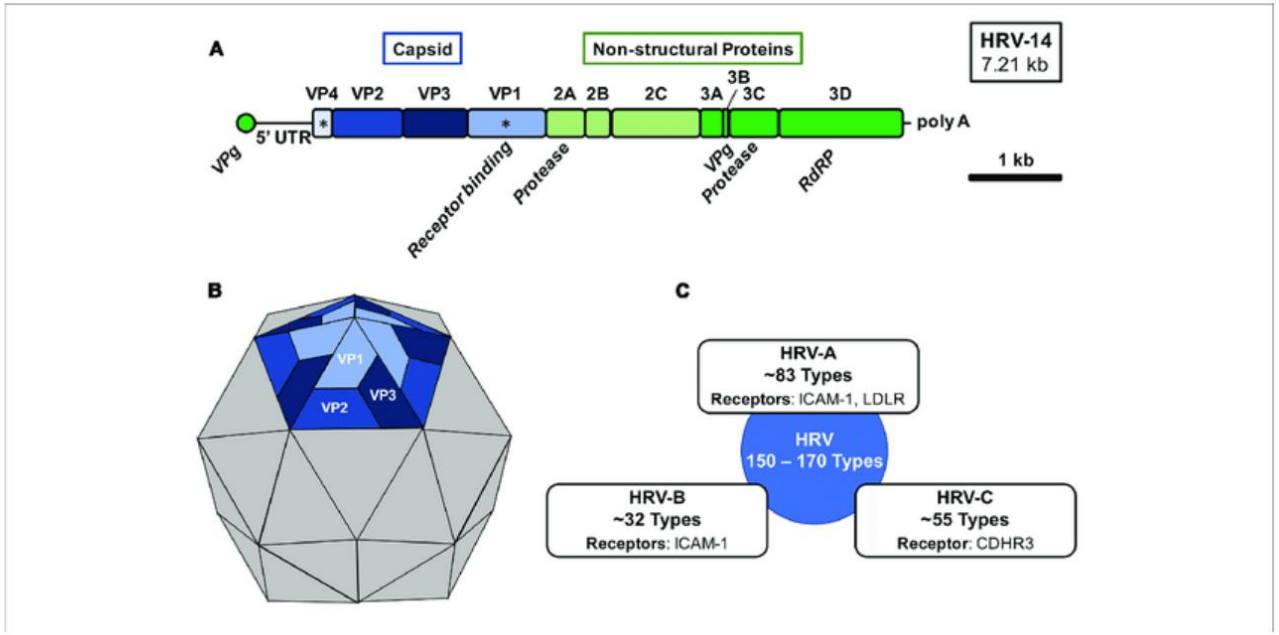
# The cast:

## Pulp afflictions
## “we badass too”

# Picornaviridae - Human Rhinovirus (HRV)

| | |
|---|---|
| **Family** | Picornaviridae |
| **Genus** | Enterovirus |
| **Genotypes / Serotypes** | 3 Genotypes<br>• HRV-A (~83 Serotypes)<br>• HRV-B (~32 Serotypes)<br>• HRV-C (~ 55 Serotypes) |
| **Genome** | 7.2 kb; (+)ssRNA; non-enveloped (icosahedric capsid) |
| **Target cells** | Epithel-, Endothel-, Mucosal cell, Fibroblasts, Lymphocytes, Monocytes / Macrophages |

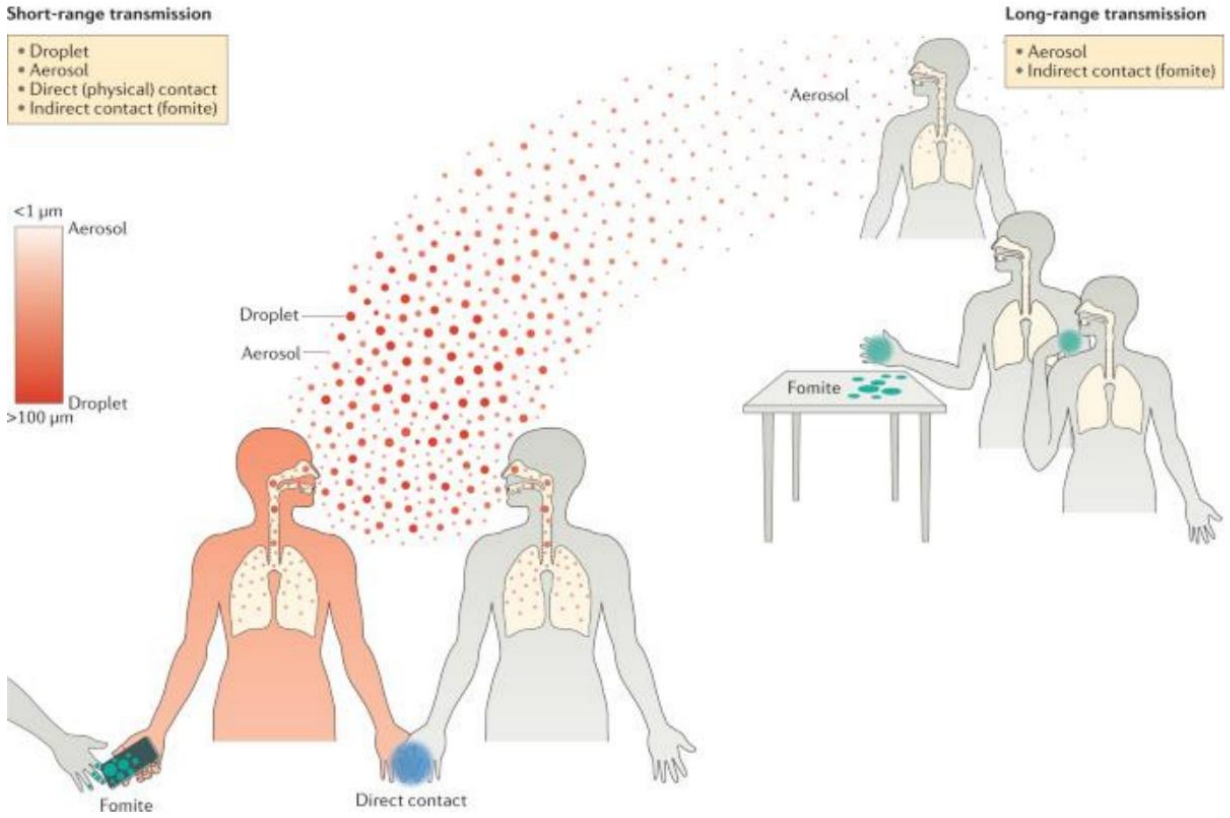



- Genotype? Genomic differences
- Serotype? Surface antigen

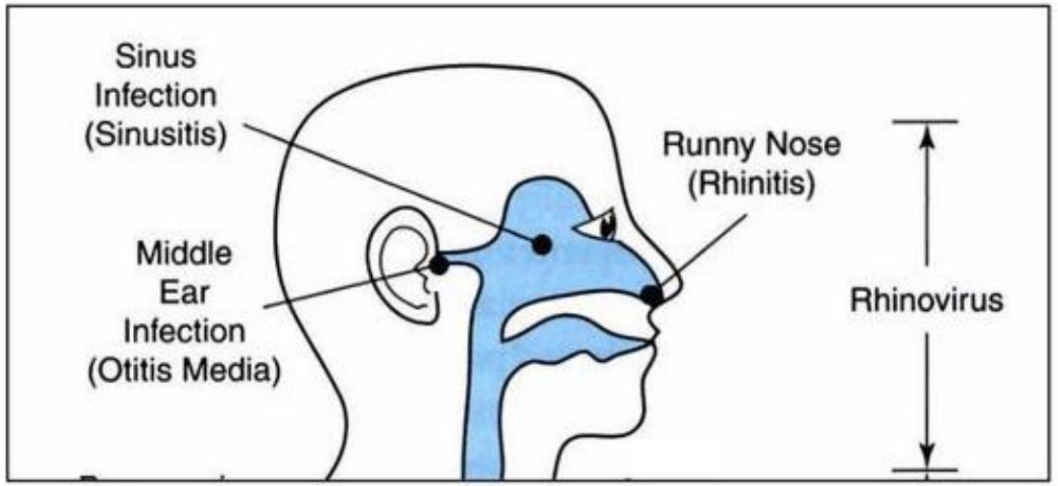
# Picornaviridae - Human Rhinovirus (HRV)

| | |
|---|---|
| **Transmission** | Droplet infection / smear infection<br>Mostly direct transmission (contaminated hands, fomites)<br>Dry air inactivates them quickly<br>Large droplets: stable (half-life 14h) |
| **Incubation periode** | 1-4 Days |
| **Epidemiology** | 25-50% of all **upper respiratory** tract infections |

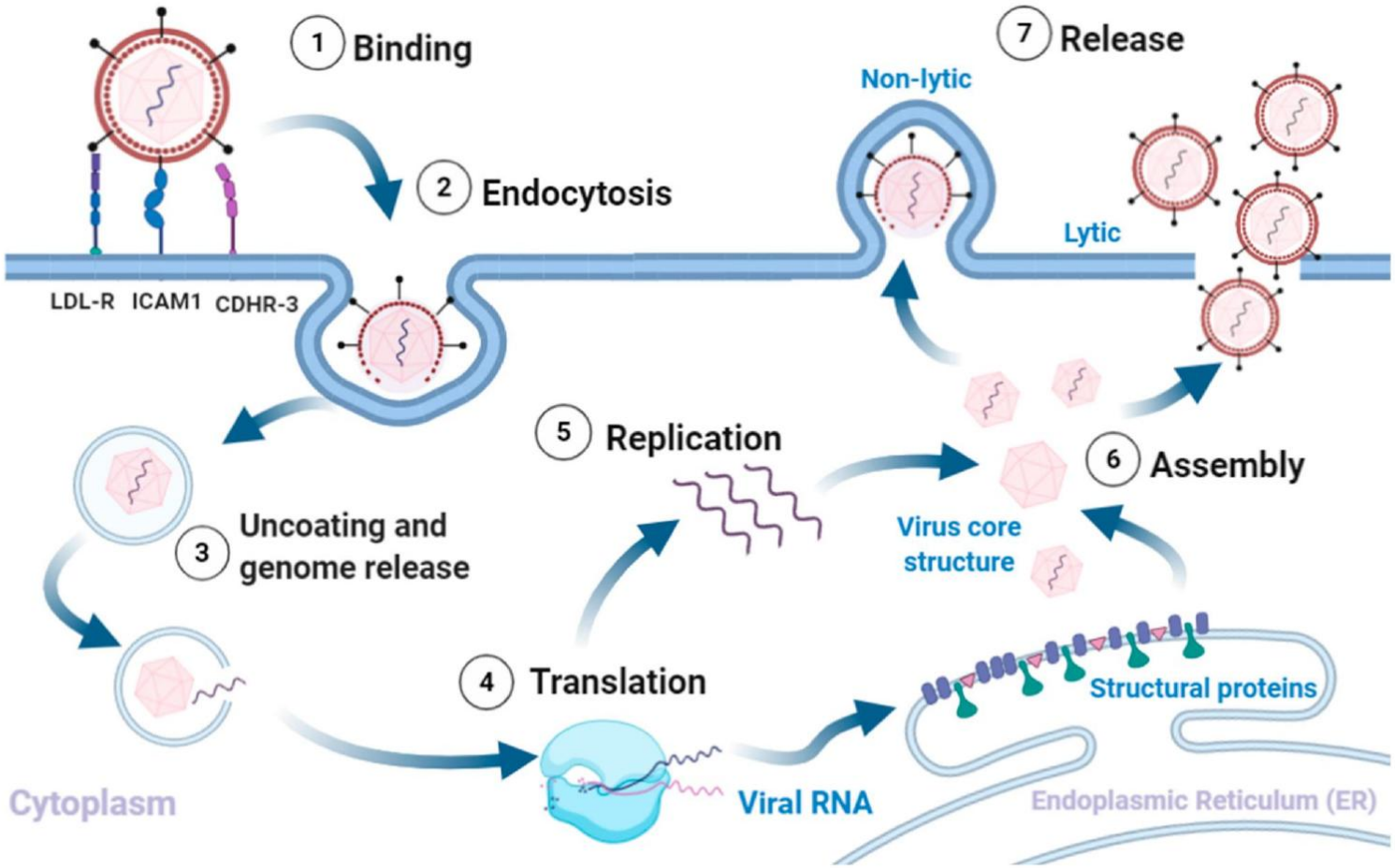


# Picornaviridae - Human Rhinovirus (HRV)

| | |
|---|---|
| **Clinic** | Common cold (e.g. fever, cough, runny nose) |
| **Pathogenesis** | Focal desctruction of the epithelium<br>• Strictly localized<br>• Inflammatory reaction of nasal mocous membrane<br>• Vessels become permeable, fluid escapes<br>• Nasal mucous membrane swells up<br>• Breathing through the nose restricted<br>• Often secondary bacterial infection |
| **Diagnosis** | Not performed |
| **Therapy** | Symptomatic |
| **Prophylaxis** | Hygienic measures |

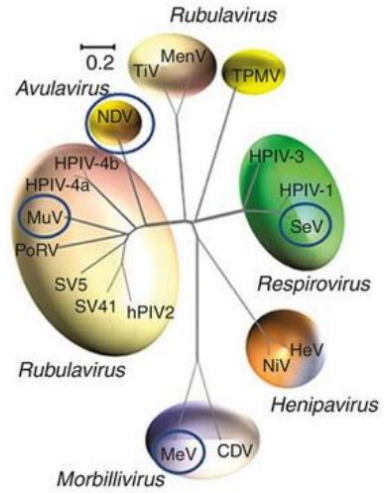


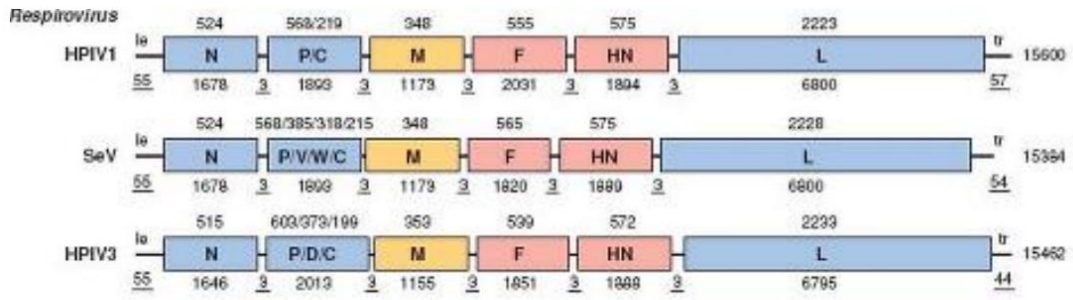
# Picornaviridae - Human Rhinovirus (HRV)

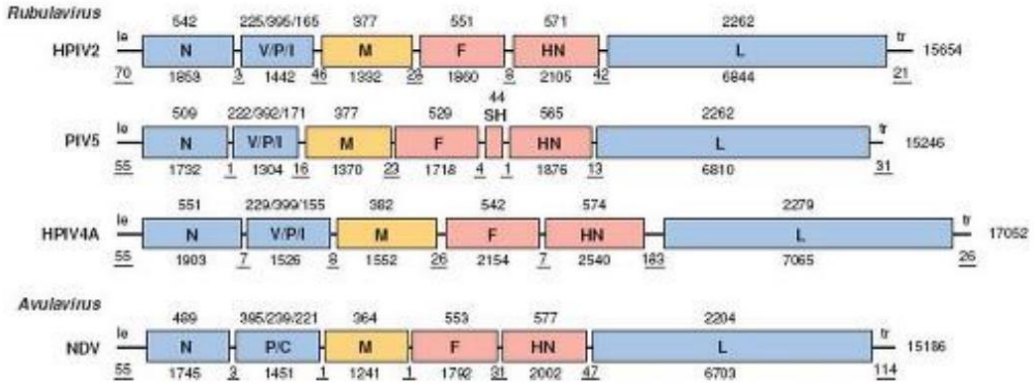


# Paramyxoviridae

| | | |
|---|---|---|
| **Genus** | Rubulavirus | (Mumpsvirus; Parainfluenzaviren Typ 2, 4a, 4b) |
| | Avulavirus | (Newcastle-Disease-Virus) |
| | Respirovirus | (Parainfluenzaviren Typ 1, 3) |
| | Henipavirus | (Nipahvirus) |
| | Morbillivirus | (Measles virus) |
| | Orthopneumovirus | (Respiratory Syncytial virus) |
| | Metapneumovirus | (Human Metapneumovirus) |
| **Genome** | 15-18kb; (-)ssRNA; enveloped | |

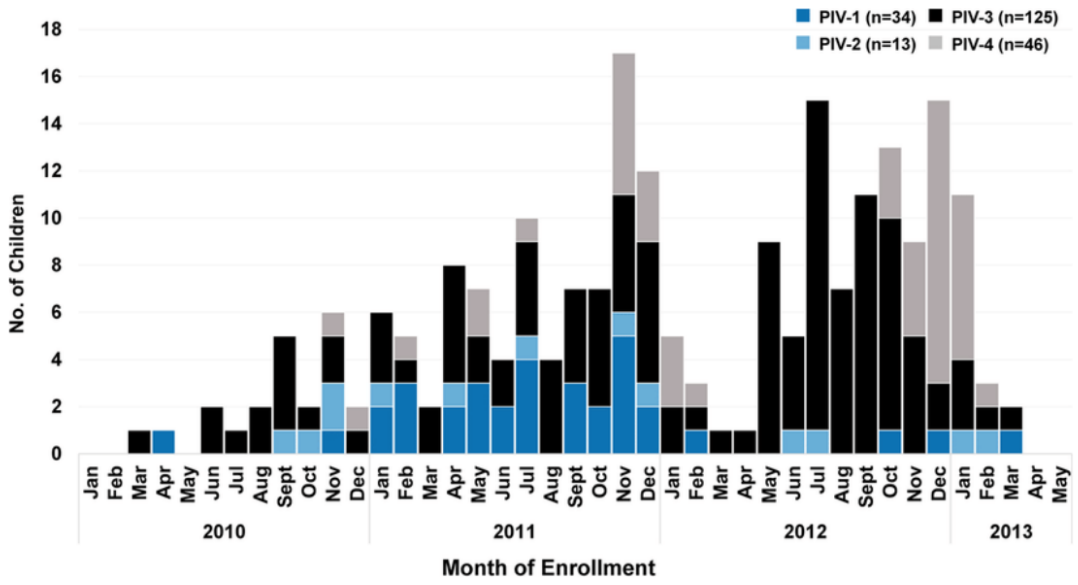


# Paramyxoviridae: Parainfluenza virus

| | |
|---|---|
| **Family** | Paramyxoviridae |
| **Genus** | Respirovirus (Serotype 1 und 3) and Rubulavirus (Serotype 2 und 4) |
| **Epidemiology** | 5-30% all acute respiratory infections, causes **upper and lower** respiratory illness |
| **Transmission** | Droplet infection |
| **Target cells** | Epithelial cells |

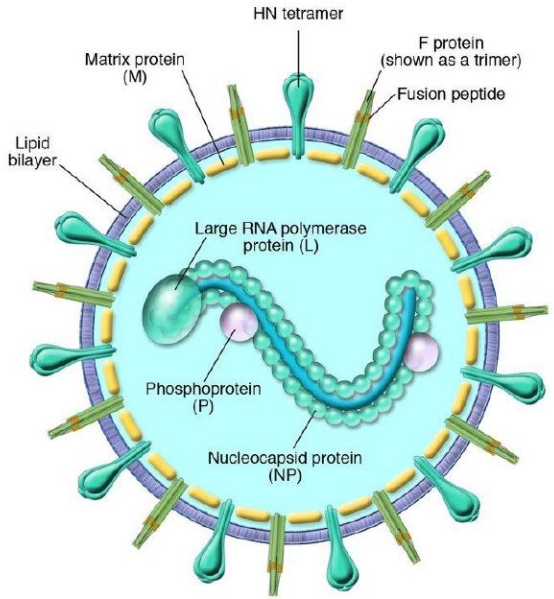


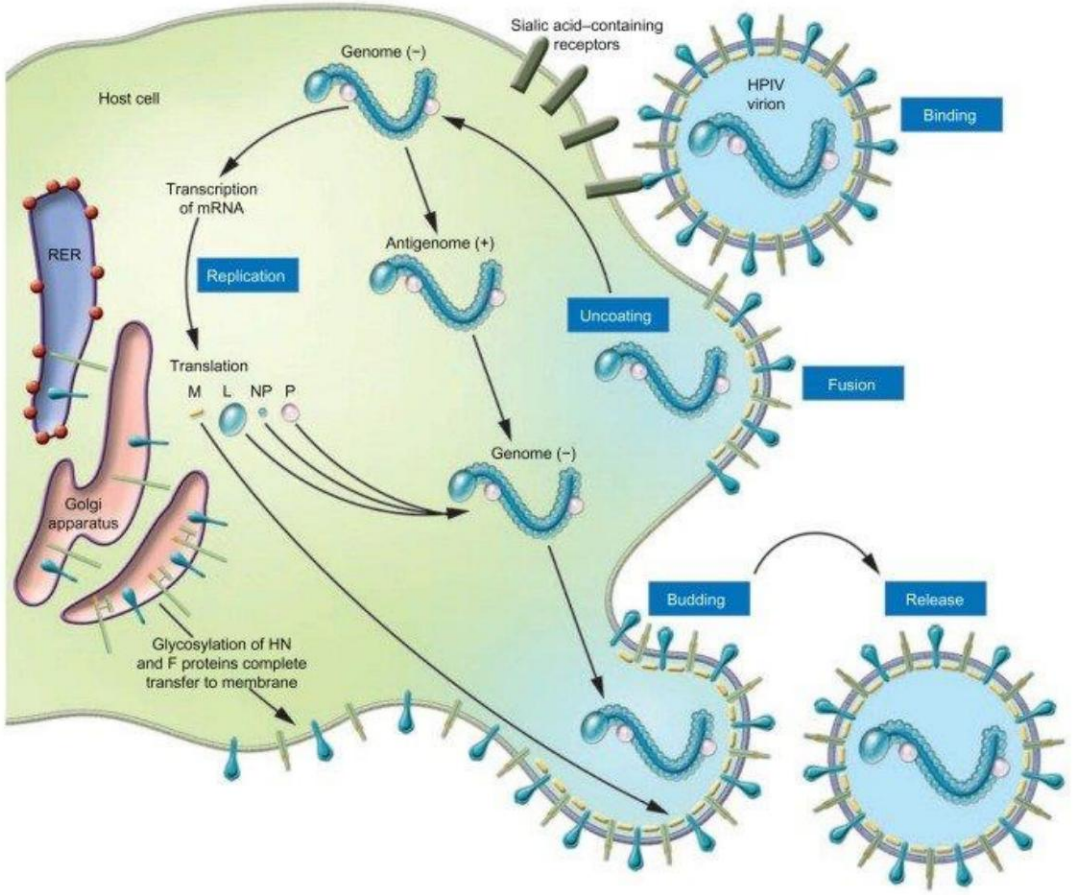

- HPIV-1 and HPIV-2: the main causes of laryngotracheobronchitis in young children
- HPIV-3: causes bronchiolitis and pneumonia and affects mainly infants
- HPIV-4: likely to cause mild progressions.

# Paramyxoviridae: Parainfluenza virus

| | |
|---|---|
| **Pathogenesis** | • Infection of the mucous membranes of the nasopharynx<br>• it can spread to the entire tracheobronchial space.<br>• An infection generally triggers inflammation and releases cytokines such as interferon-gamma and TNF-alpha.<br>• In small children, the build-up of mucus can lead to an obstruction of the airways |
| **Incubation periode** | 2-4 days |
| **Klinik** | • One of the major causes of lower respiratory tract infections in young childern<br>• Respiratory problems in children (rhinitis, cough, fever, laryngitis, tonsillitis and pseudocroup (HPIV-1), more rarely as pneumonia)<br>• Bacterial superinfections are common<br>• Re-infection possible, usually leads to mild illnesses |
| **Diagnosis** | Mostly clinically<br>Direct detection possible |
| **Therapy** | Symptomatic, severe courses Ribavirin |
| **Prophylaxis** | Hygienic measures |

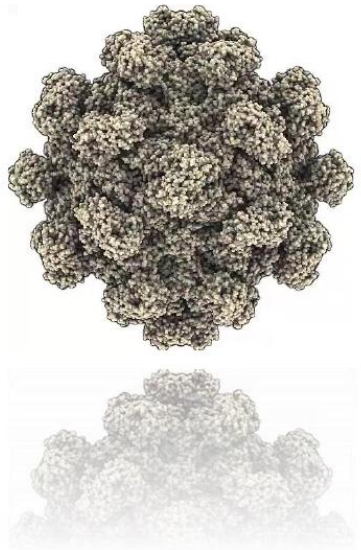
# Paramyxoviridae: Parainfluenza virus



# Thank you for your attention

Molecular & Medical Virology



# What is viral tropism

- Capability of an infectious virus to infect: