

# Respiratory Virus

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Rui da Costa, PhD

Abteilung für Molekulare & Medizinische Virologie

# Structure and Objectives

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- 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

## What do people die from? Causes of death globally in 2019

The size of the entire visualization represents the total number of deaths in 2019: 55 million.  
Each rectangle within it is proportional to the share of deaths due to a particular cause.

Our World  
in Data

74% died from noncommunicable diseases

14% died from infectious diseases

### 33% died from heart diseases

Heart attacks, strokes, and other cardiovascular diseases.

Per year: 18.5 million deaths  
Per average day: 50,850 deaths

### 18% Cancers

Per year: 10 million deaths  
Per average day: 27,600 deaths

7% Chronic respiratory diseases  
COPD, Asthma, and others

4.5% Digestive diseases  
Cirrhosis and others

2.7% Diabetes

3.9% Neurological diseases  
Alzheimer's, Parkinson's, epilepsy,  
and others

5.7% Other noncommunicable diseases

4.4% Pneumonia  
and other lower respiratory diseases

Per year: 2.5 million deaths  
Per average day: 6800 deaths

2.7% Diarrheal diseases

Per year: 1.5 million deaths  
Per average day: 4200 deaths

2% Tuberculosis

1.5% HIV/AIDS

1.1% Malaria

2.1% other infectious diseases

3.3% Neonatal deaths

babies who died within the first 28 days of life

0.4% Maternal deaths

0.4% Nutritional deficiencies

2.3% Transport accidents

Per year: 1.3 million deaths  
Per average day: 3500 deaths

3.1% Other accidents

including falls, drownings, and fires.

1.3% Suicides

Per year: 760,000 deaths  
Per average day: 2080 deaths

0.7% Homicides

Per year: 415,000 deaths  
Per average day: 1140 deaths

0.2% War battle deaths

0.05% Terrorism

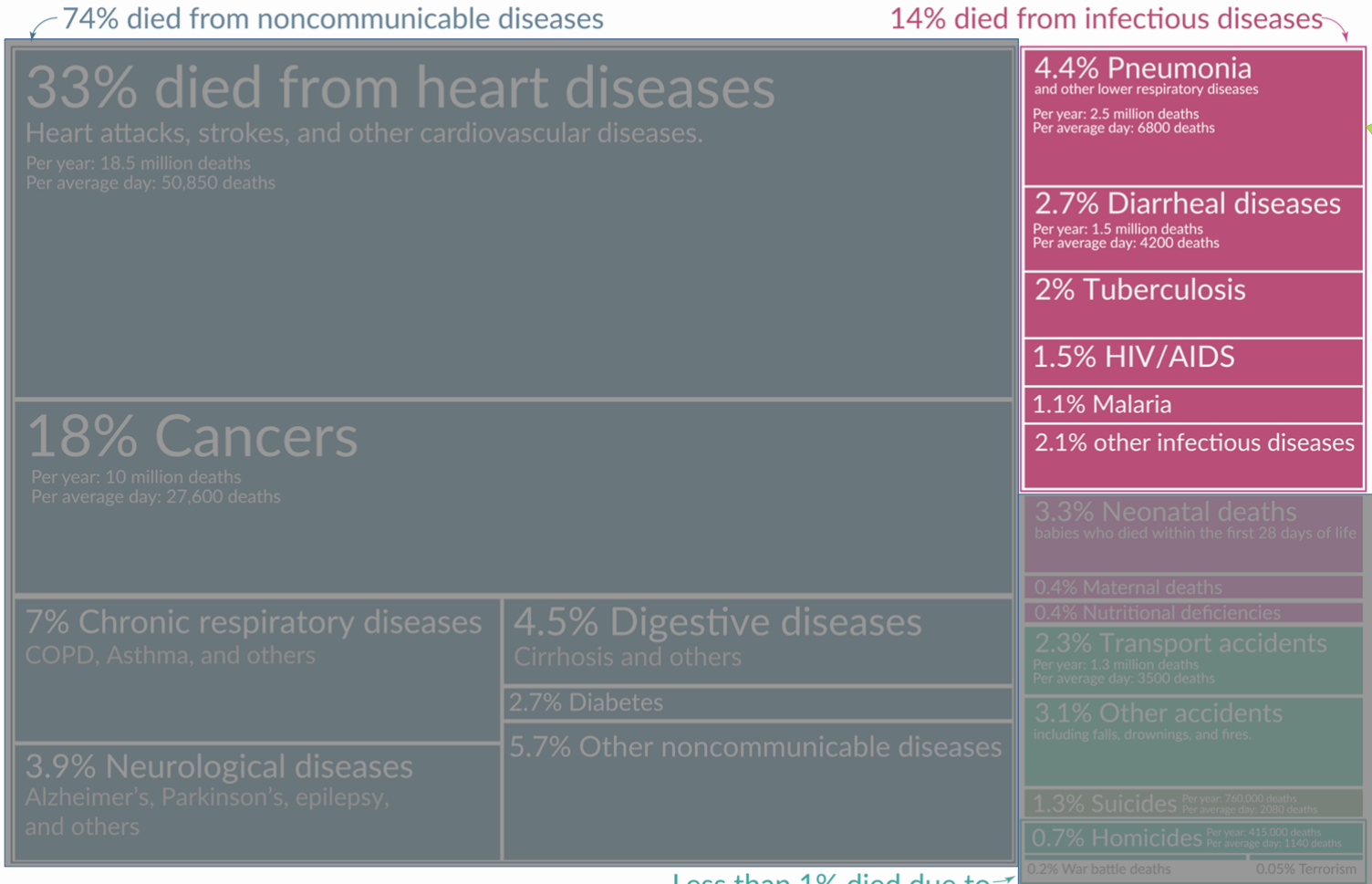
Less than 1% died due to  
interpersonal violence

# Global burden of respiratory virus

## What do people die from? Causes of death globally in 2019

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Our World  
in Data



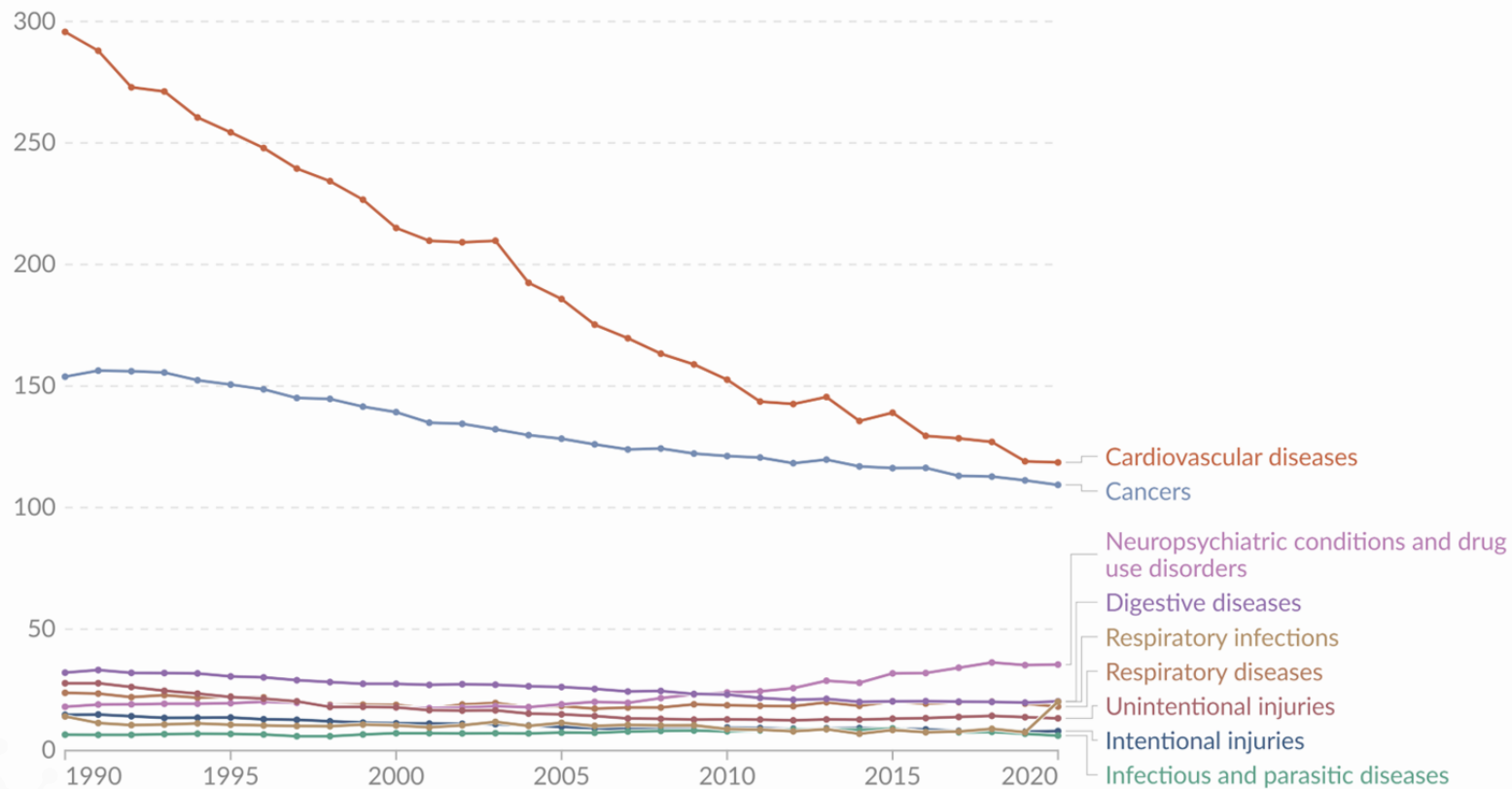


# Global burden of respiratory virus

## Death rates from different causes, Germany

Reported annual death rate from different causes per 100,000 people, based on the underlying cause<sup>1</sup> listed on death certificates. Comparisons may be affected by differences in measurement.

Our World  
in Data



Data source: WHO Mortality Database (2024)

OurWorldinData.org/causes-of-death | CC BY

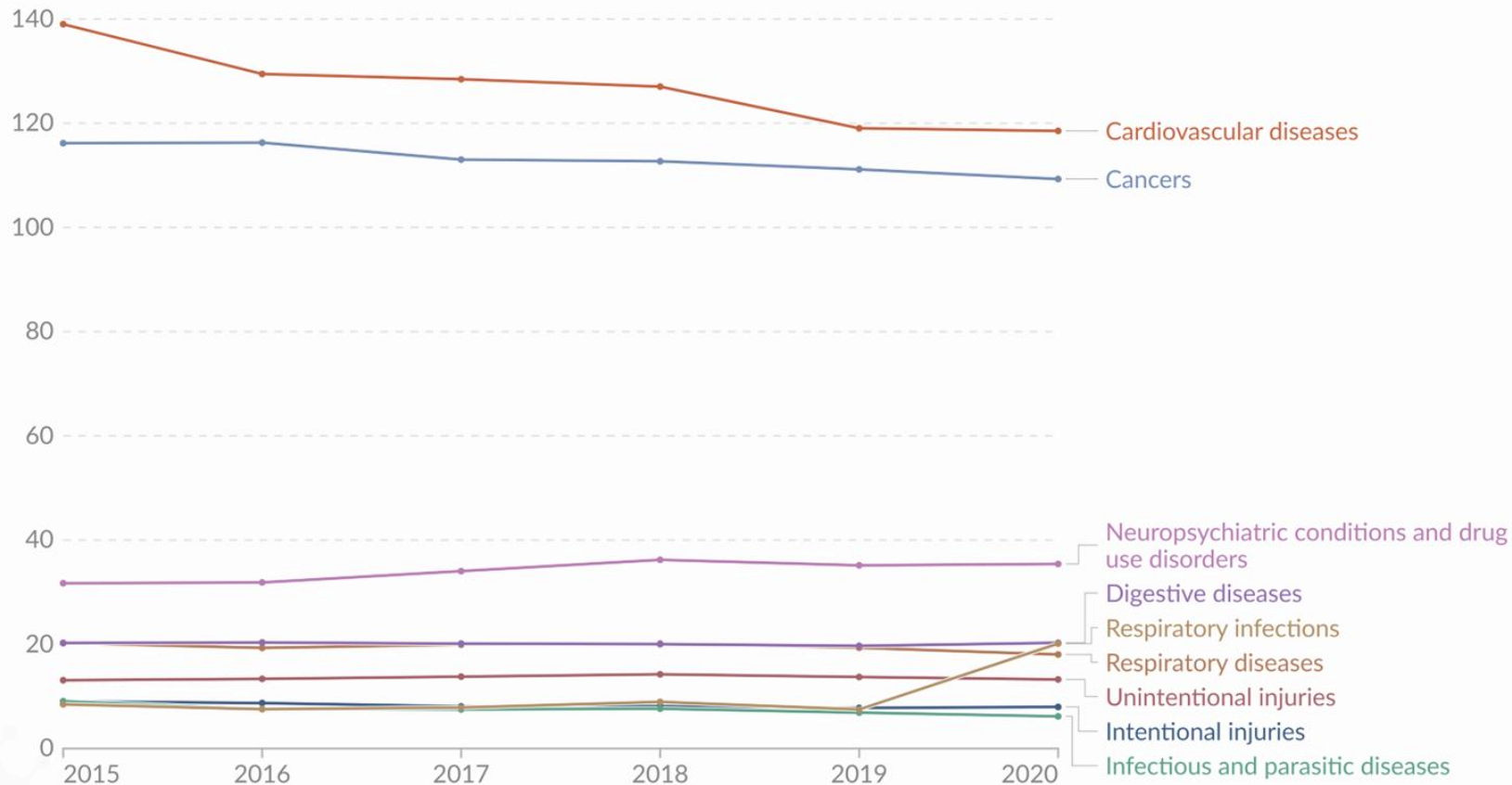
Top 4 cause of death in Germany

# Global burden of respiratory virus

## Death rates from different causes, Germany

Our World in Data

Reported annual death rate from different causes per 100,000 people, based on the underlying cause<sup>1</sup> listed on death certificates. Comparisons may be affected by differences in measurement.



Data source: WHO Mortality Database (2024)

OurWorldinData.org/causes-of-death | CC BY

Main cause of death via communicable diseases

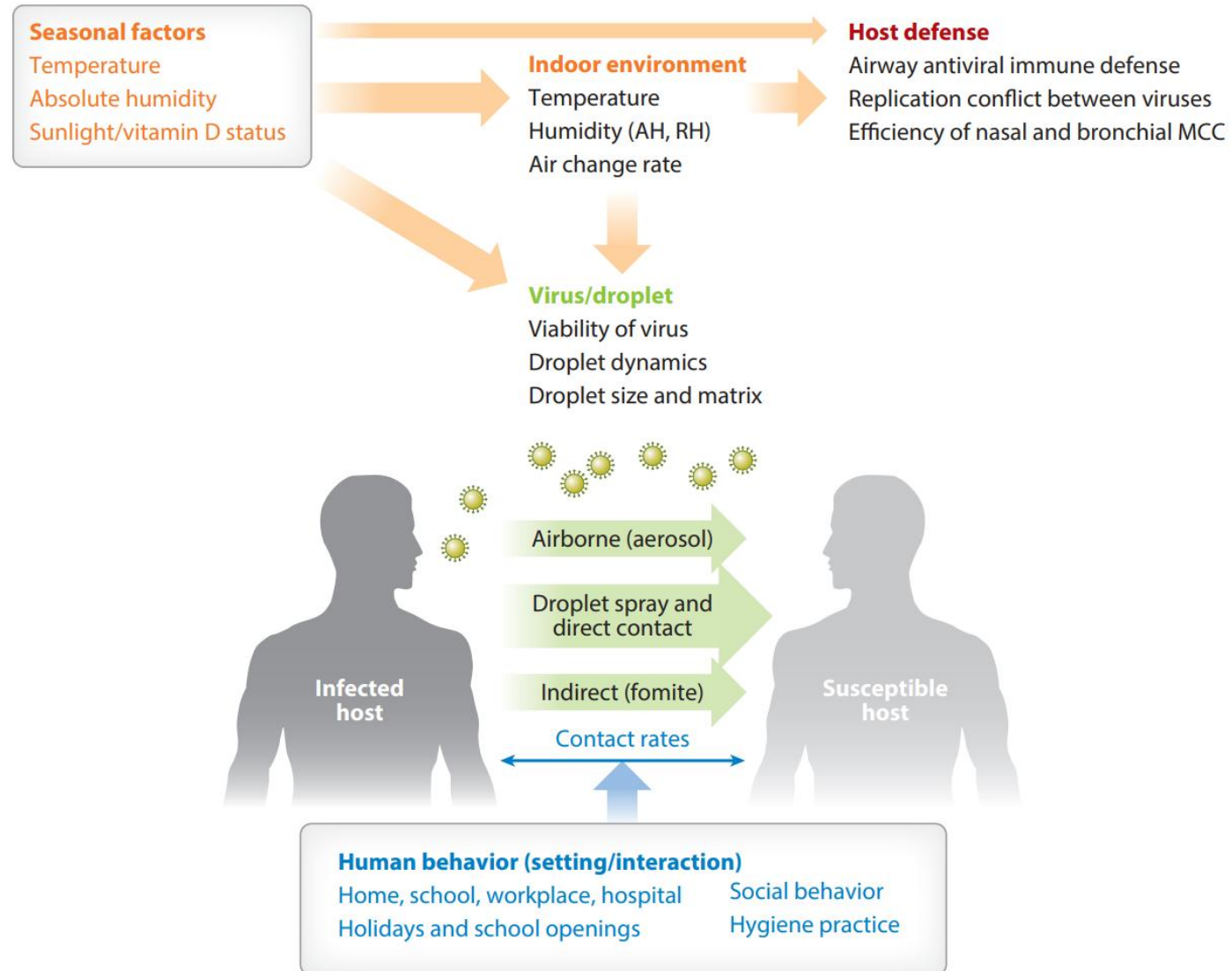
# Seasonality of respiratory virus

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

# Seasonality of respiratory virus

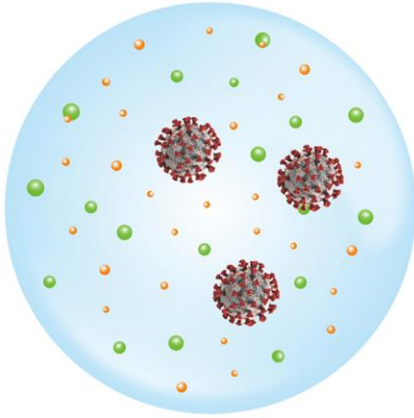
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|----------------|------------------------------|------|------|------|------|-----------------|------|------|------|------|------|-----|
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# Seasonality of respiratory virus

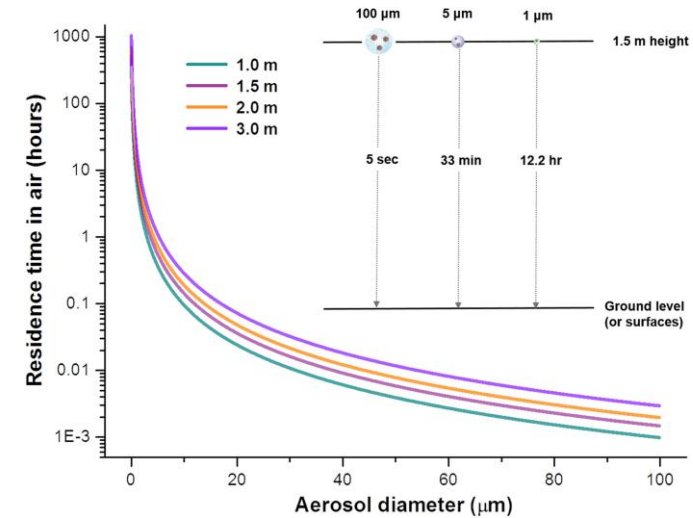


# Seasonality of respiratory virus

## Physicochemical properties of virus-laden aerosols:



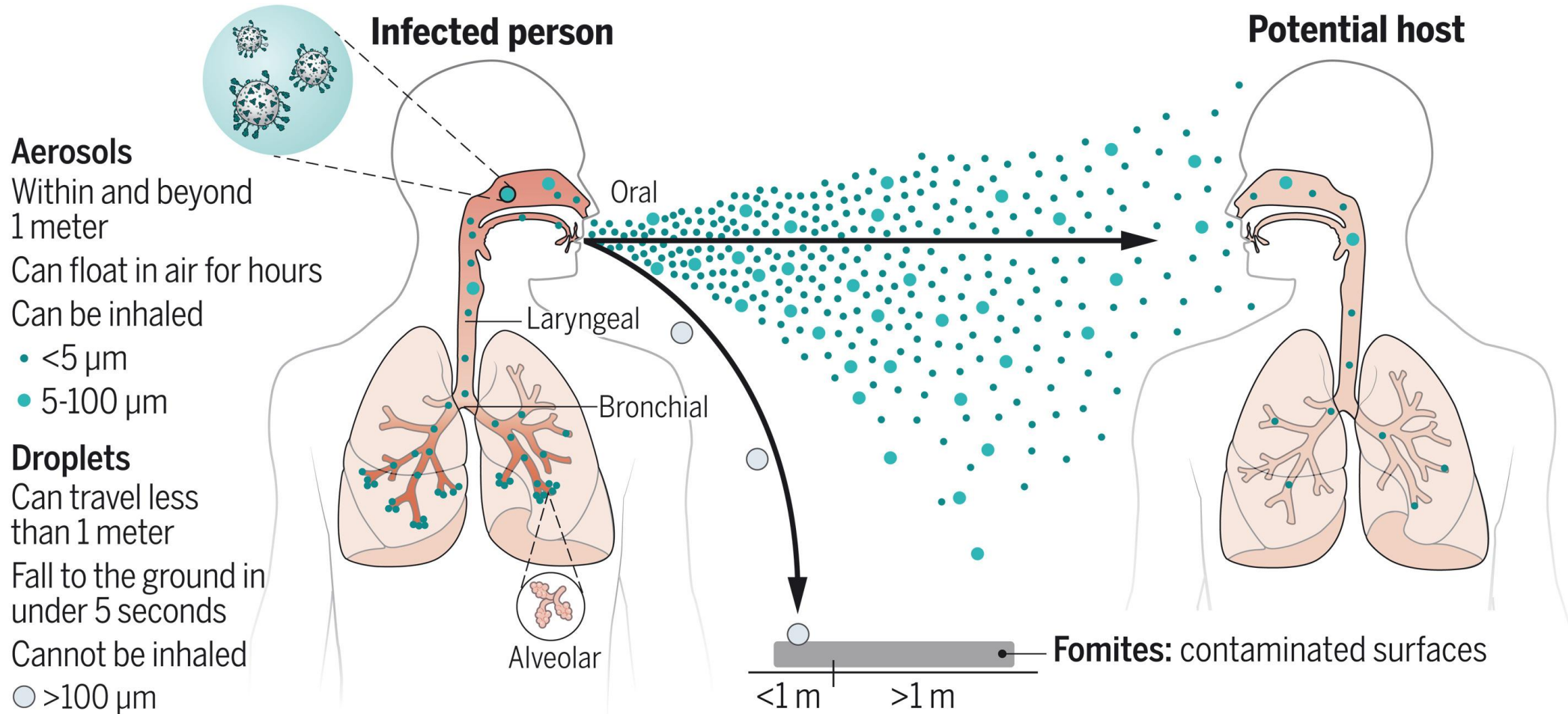
- Size
- Viral load and infectivity
- Other chemical components:  
- electrolytes, proteins, surfactants
- pH value
- Electrical charge
- Air/liquid interfacial properties



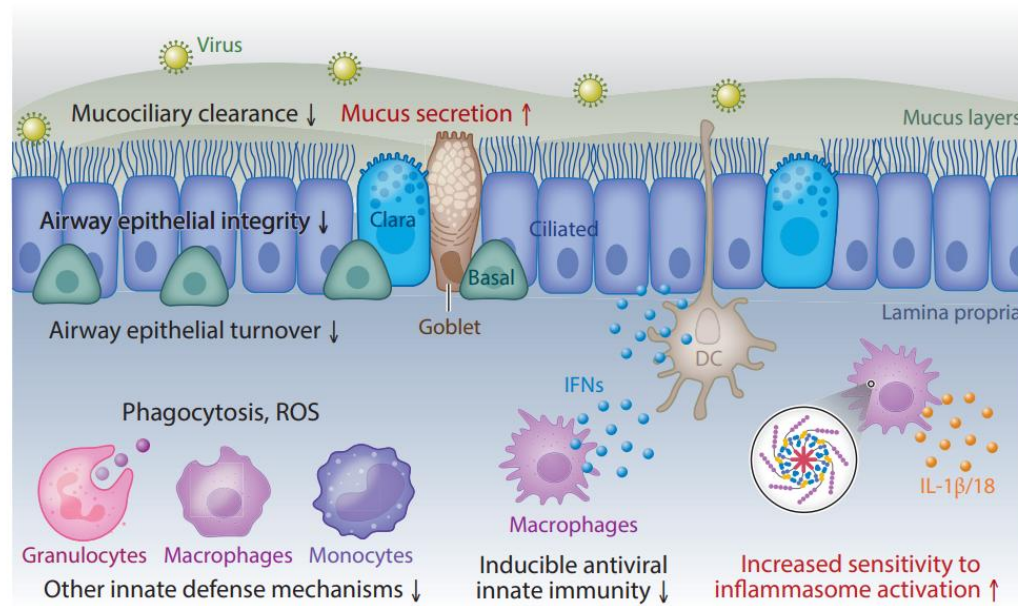
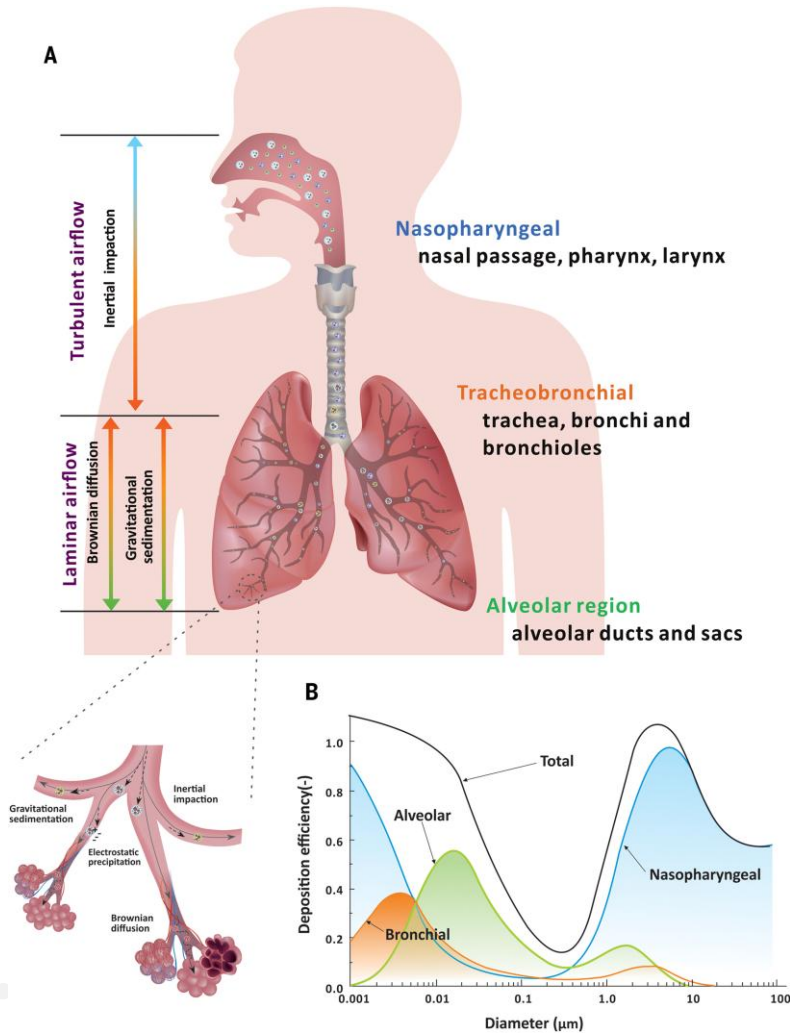
| Climate/season          | Outdoor absolute humidity | Indoor relative humidity (%) | Respiratory virus stability | Proportion of droplet nuclei | Viability of respiratory viruses | Predominant transmission            |
|-------------------------|---------------------------|------------------------------|-----------------------------|------------------------------|----------------------------------|-------------------------------------|
| 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              |



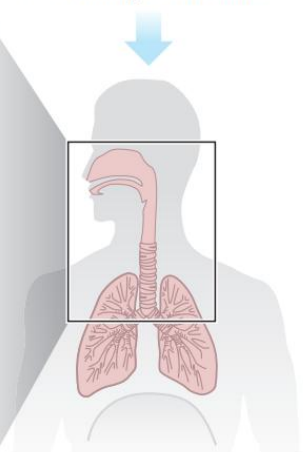
# Seasonality of respiratory virus



# Seasonality of respiratory virus



**Winter features:**  
**Outdoors**  
Dry and cold air  
Less sunlight/vitamin D

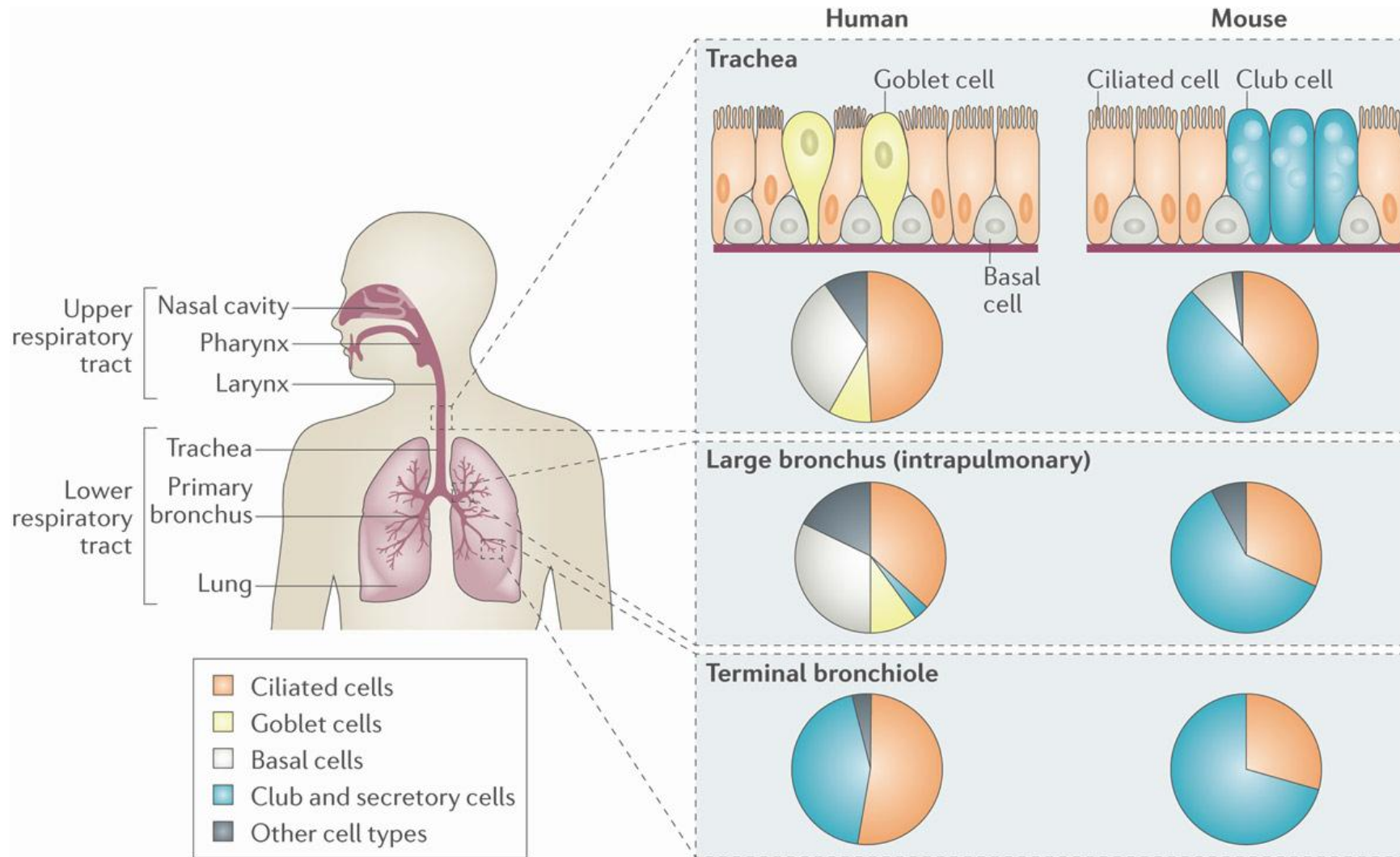


**Winter features:**  
**Indoors**  
Dry air at 20 to 24°C

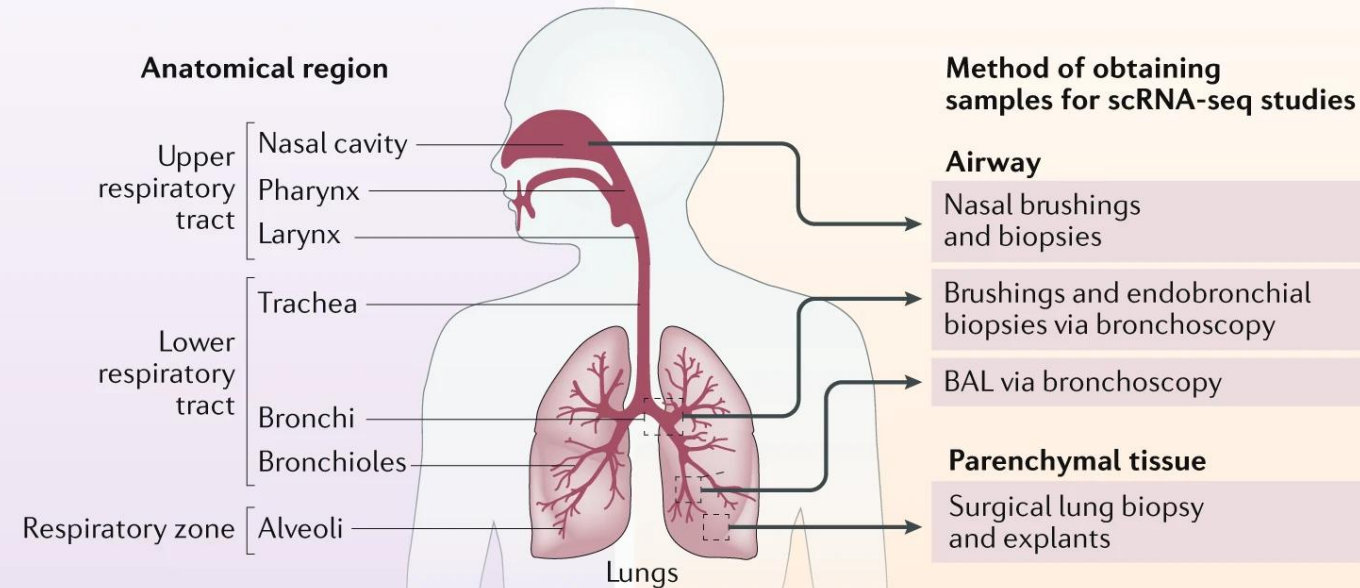
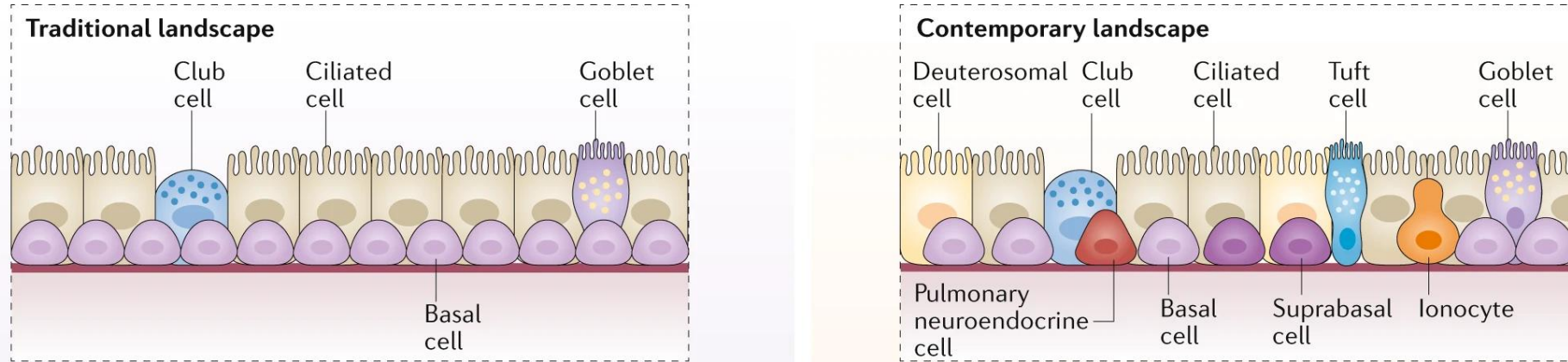


# The human respiratory tract

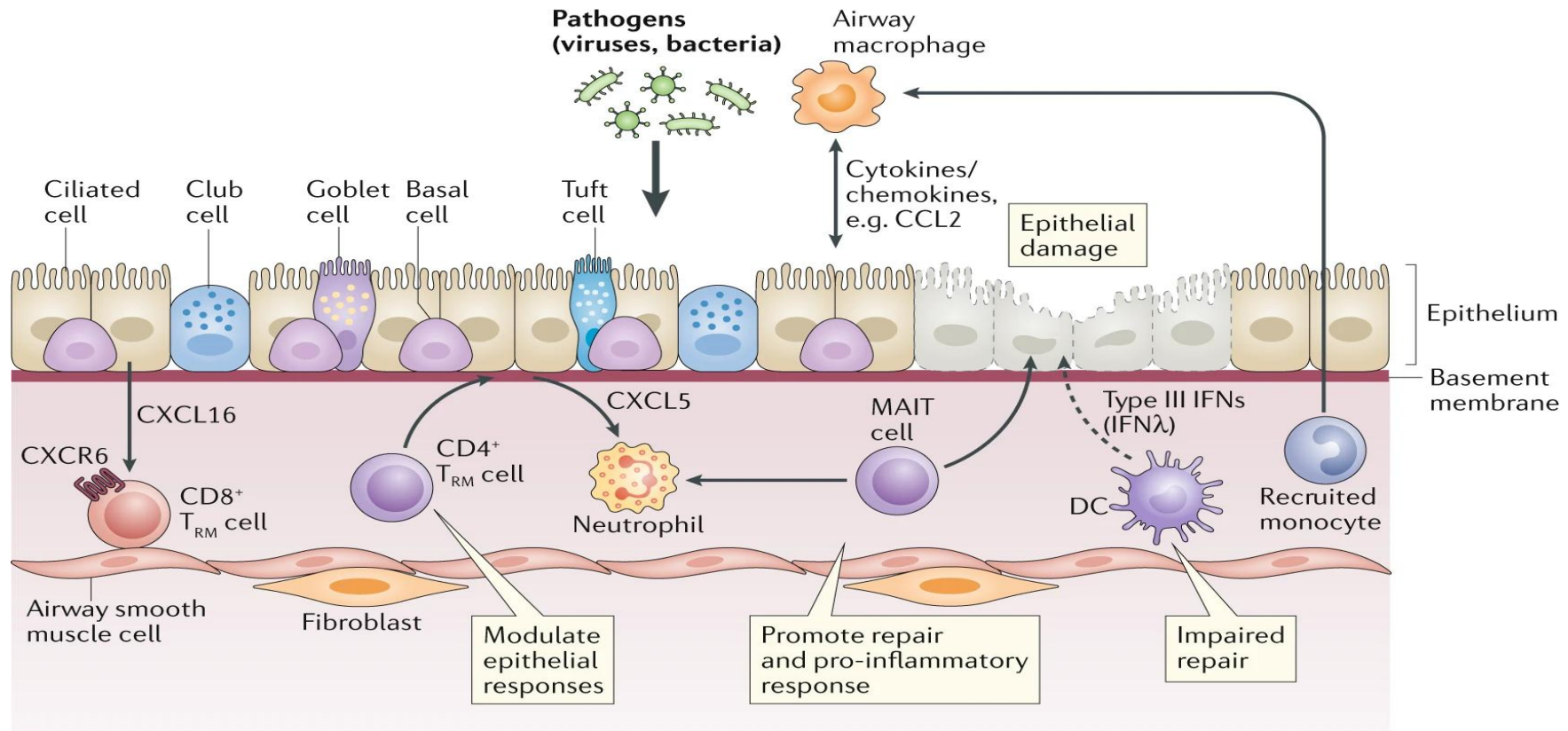
# Respiratory tract

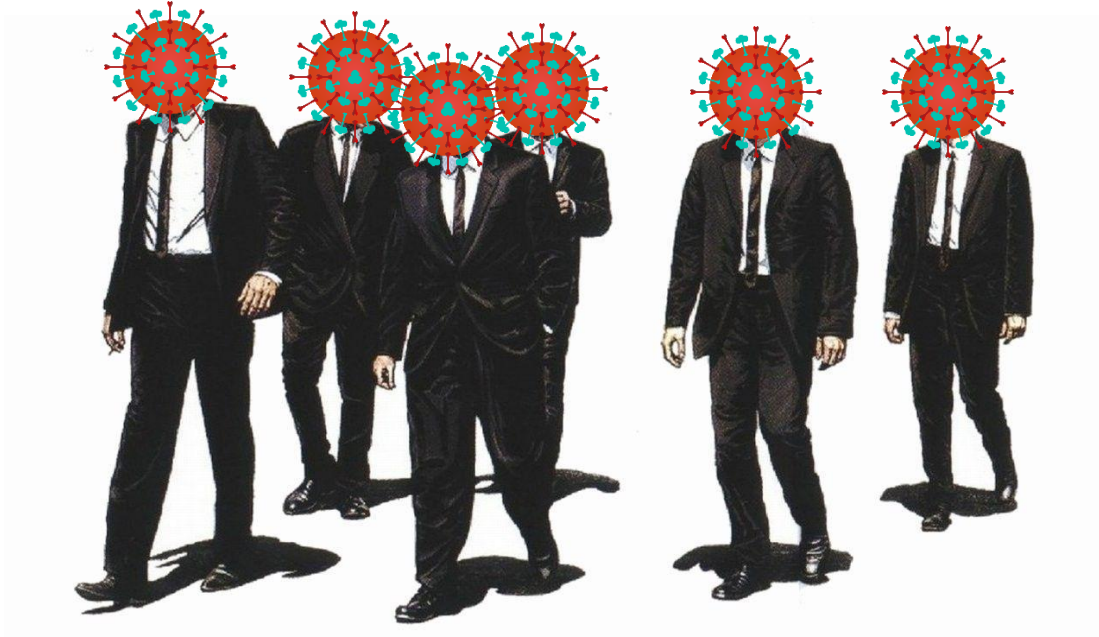


# Respiratory tract



# Respiratory tract





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

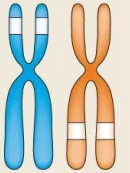
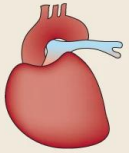
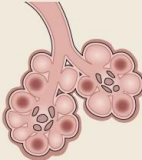
Vaccines are available

## Influenza virus

**a**

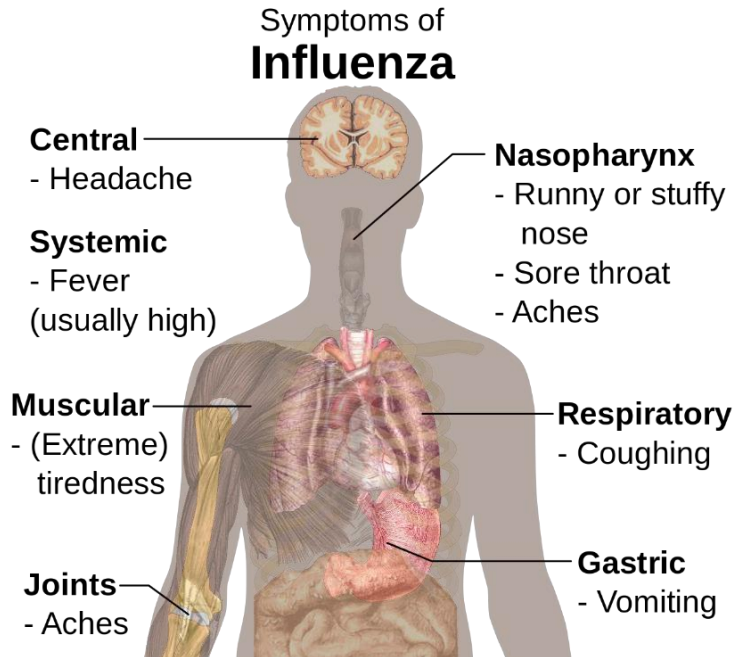
| Global (WHO data)                  |                 |
|------------------------------------|-----------------|
| Severe infections                  | 3–5 million     |
| Estimated deaths                   | 290,000–650,000 |
| United States (2018–2019 CDC data) |                 |
| Infections                         | 35.5 million    |
| Medical visits                     | 16.5 million    |
| Hospitalizations                   | 490,600         |
| Deaths                             | 34,200          |

**b**

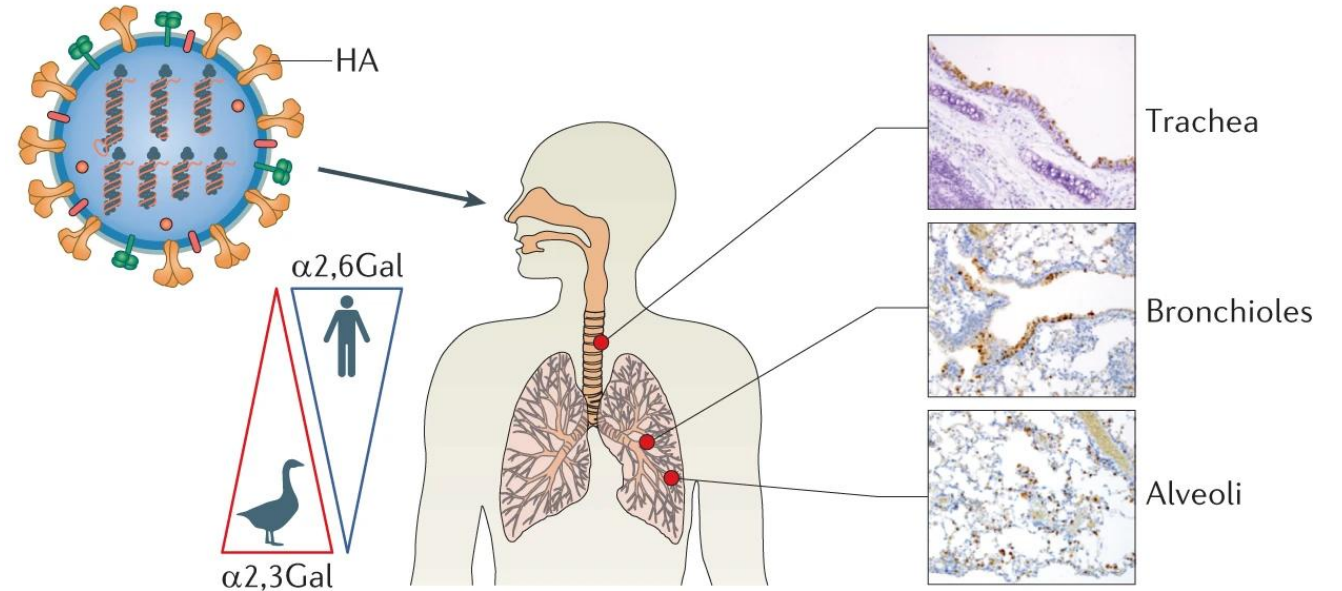
| Patient-related risk factors                                                        |                                                                                     |                                                                                                                              |                                                                                          |                                                                                      |                                                                                     |
|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Smoking                                                                             | Genetics                                                                            | Comorbid conditions                                                                                                          | Pregnancy or sex                                                                         | Obesity                                                                              | Age                                                                                 |
| Impaired epithelial, immune and fibroblast function                                 | Genes associated with viral recognition and interferon signalling                   | Heart disease                                                                                                                | Tolerant immunological state                                                             | Diminished antibody response                                                         | Type 2 bias                                                                         |
|  |  | <br>Chronic obstructive pulmonary disease | Sex steroid influence on immune response                                                 | Immune dysregulation due to adiposity                                                | Lack of prior immunity                                                              |
|                                                                                     |                                                                                     |                                          | <br>♂ | Deficient adaptive responses                                                         | Immuno-senescence                                                                   |
|                                                                                     |                                                                                     |                                                                                                                              |                                                                                          |  |  |



# Influenza: pathophysiology



**a Influenza virus**



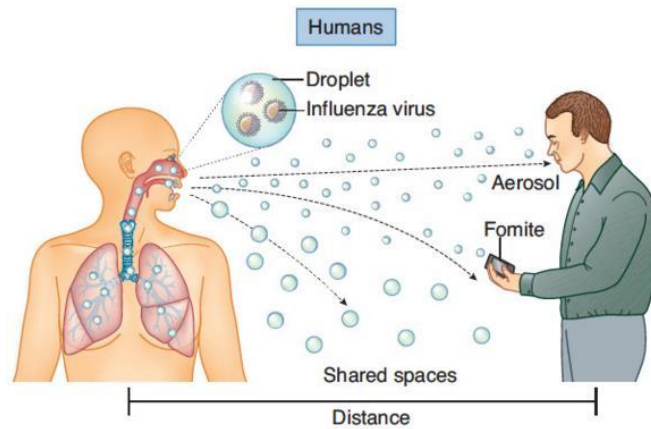
Infests **upper** and **lower** respiratory tract (epithelial cells)

Symptoms arise after 1-2 days after infection

Infected cells produce proinflammatory cytokines (cytokine storm)

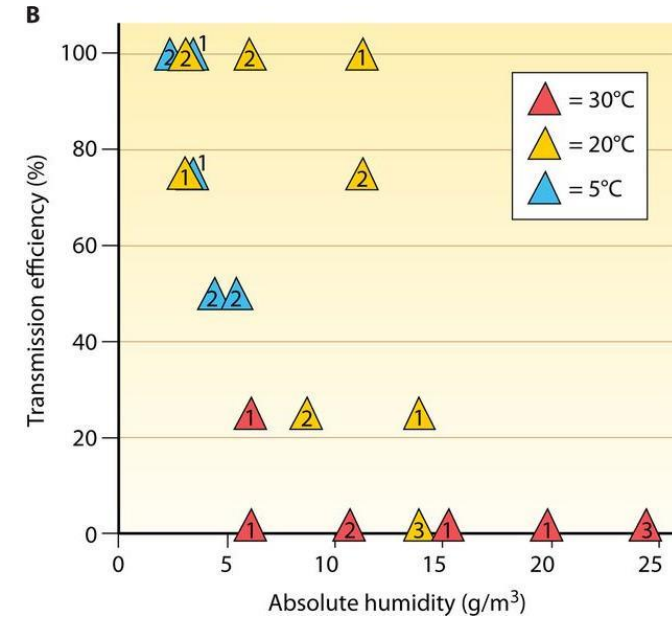
Severity of disease is the result of the interplay between viral virulence, host resistance and infection tissue

# Influenza: transmission



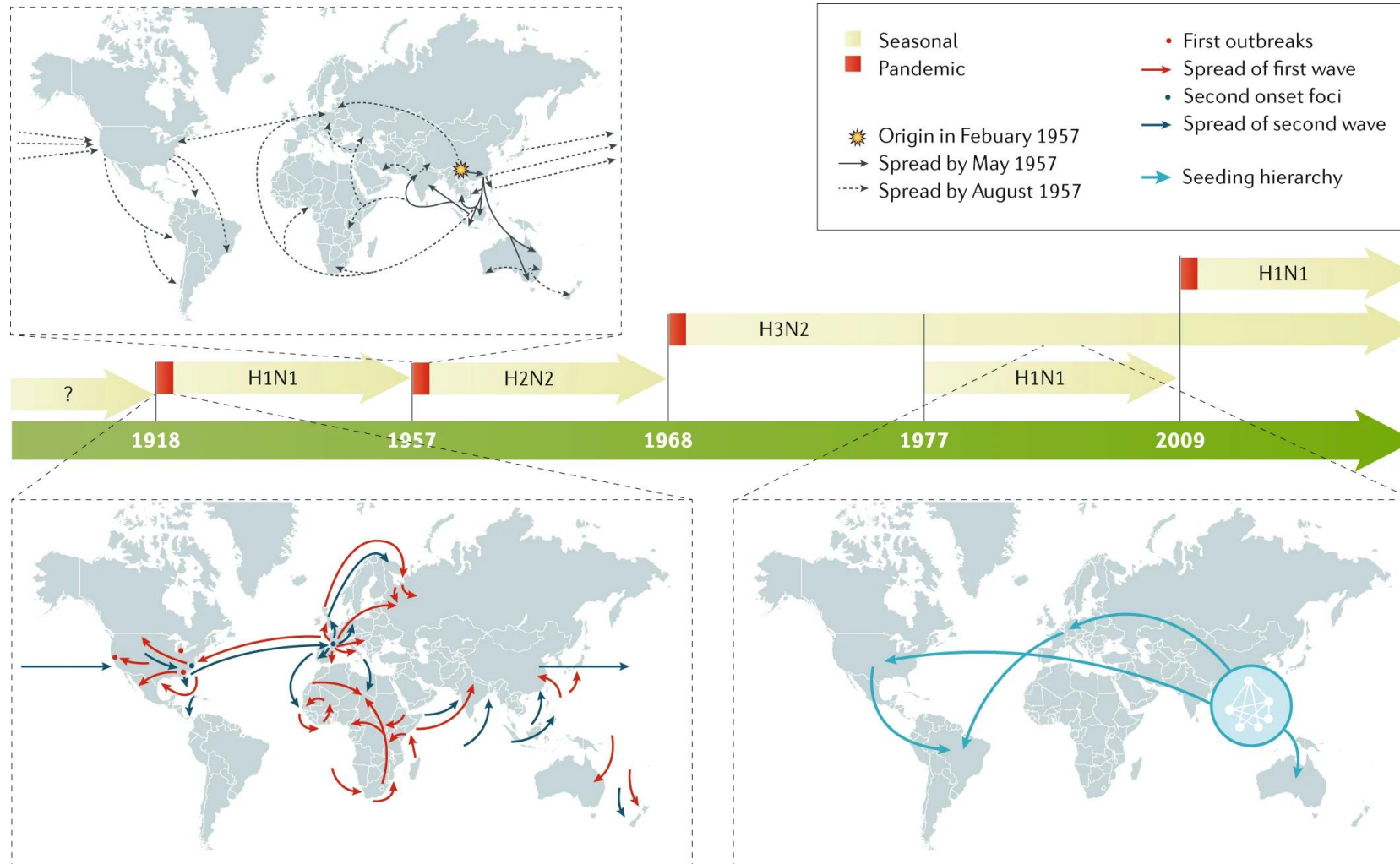
Respiratory droplets (main mechanism)  
Short distance (1m or less)

(In-)Direct contact  
infected individuals  
Fomites

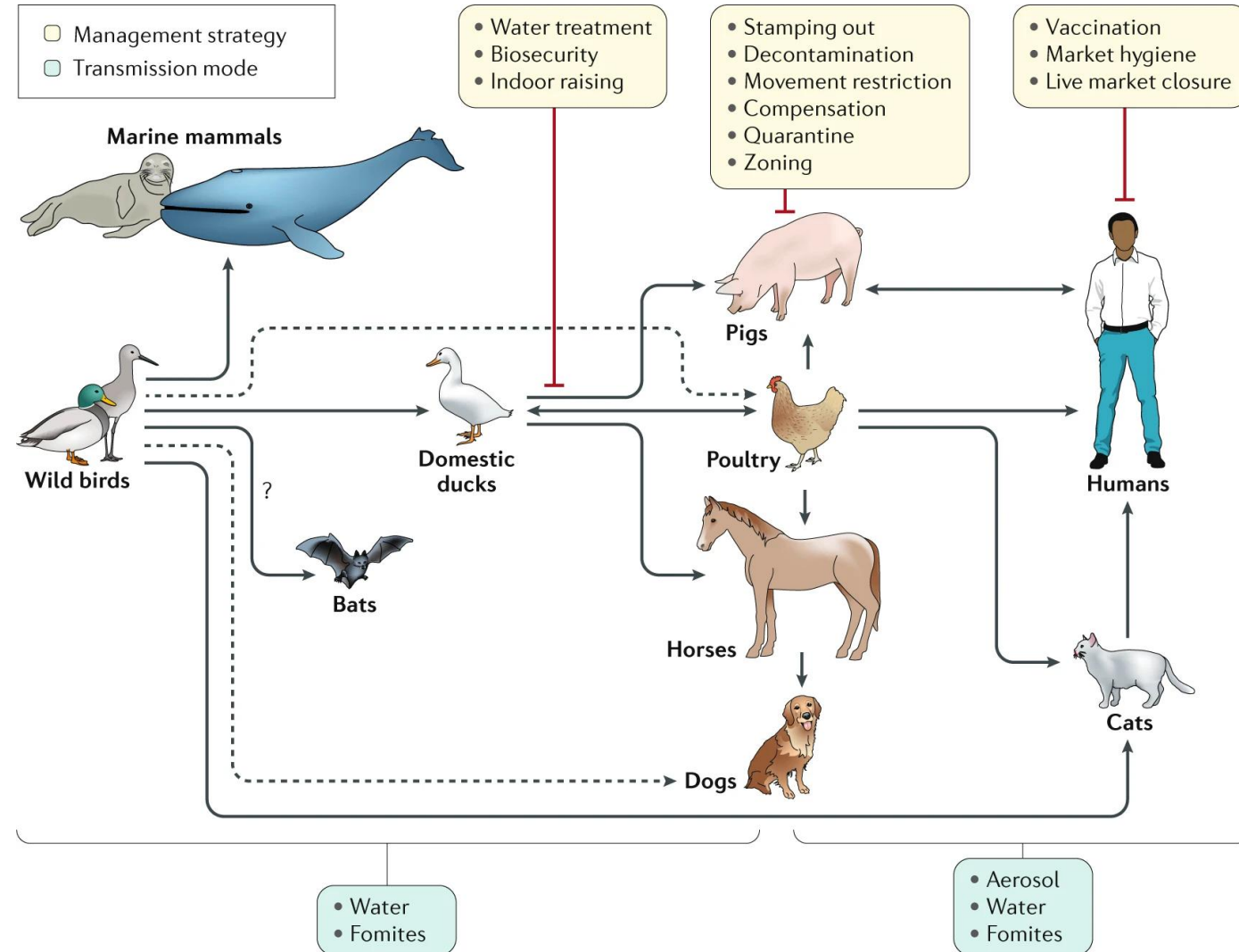
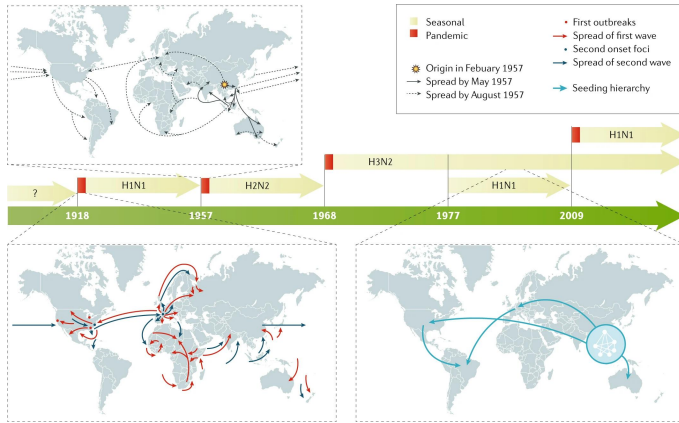


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| Temperate: spring, fall | Intermediate              | 40–60                        | Low                         | Low                          | Low                              | All transmission modes possible     |
| Temperate: winter       | Low                       | 10–40                        | High                        | High                         | High                             | Predominantly airborne              |

# Influenza: Global distribution



# Influenza: Global distribution





# Influenza: Host range

**A**

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

**B**

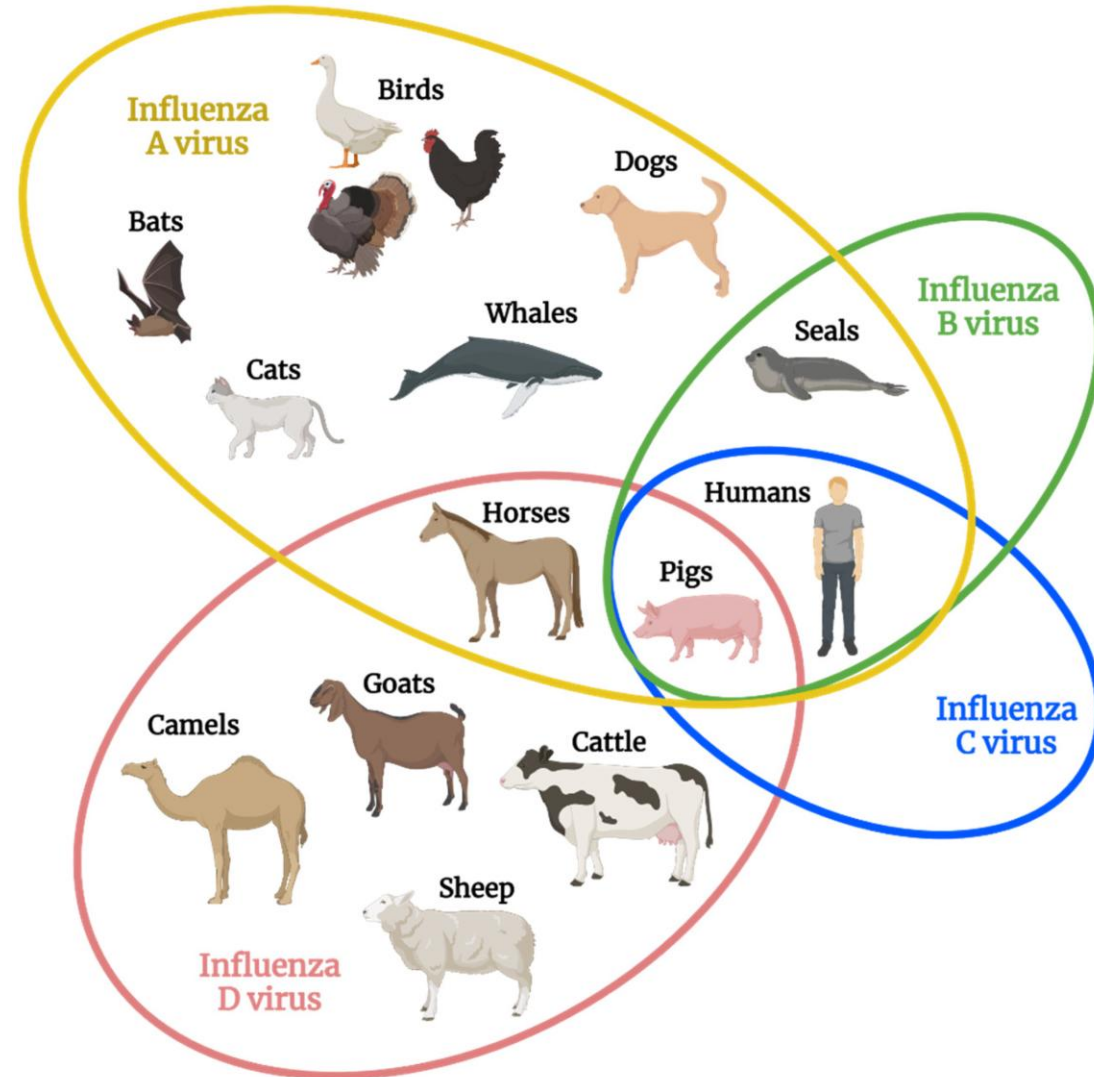
- Infects humans
- 

**C**

- Mostly infects humans
- Causes mild symptoms

**D**

- Identified in 2011 from pigs
- No human infections described



# Influenza: Biology

Order: Articulavirales

Family: Orthomyxoviridae

Genus: Alphainfluenzavirus

Betafluentezavirus

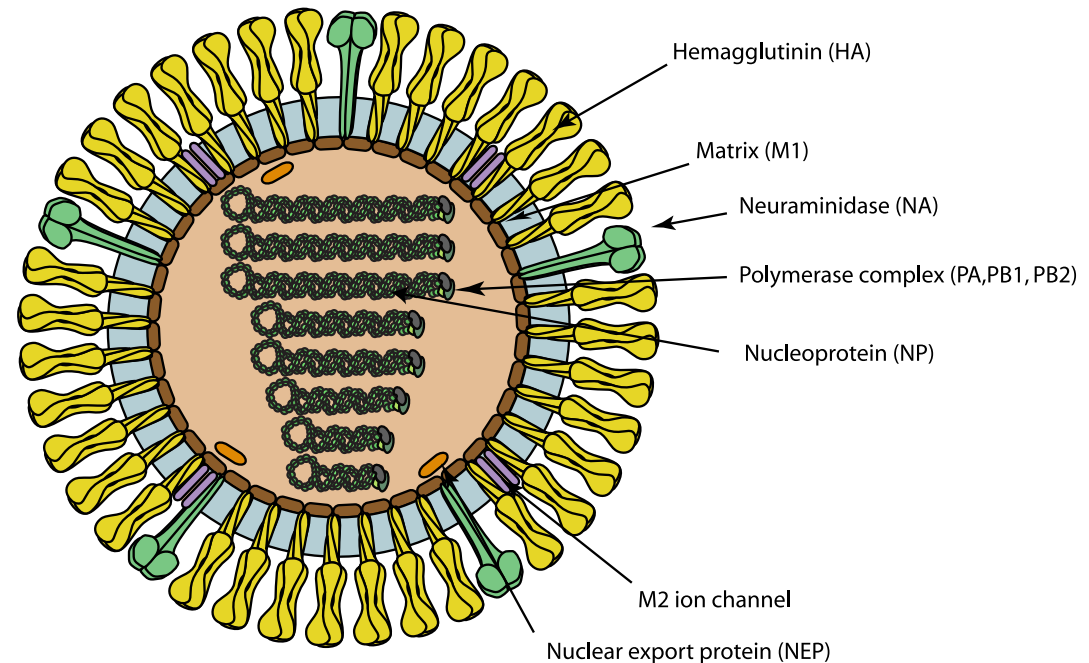
Gammainfluenzavirus

Deltafluentezavirus

Enveloped

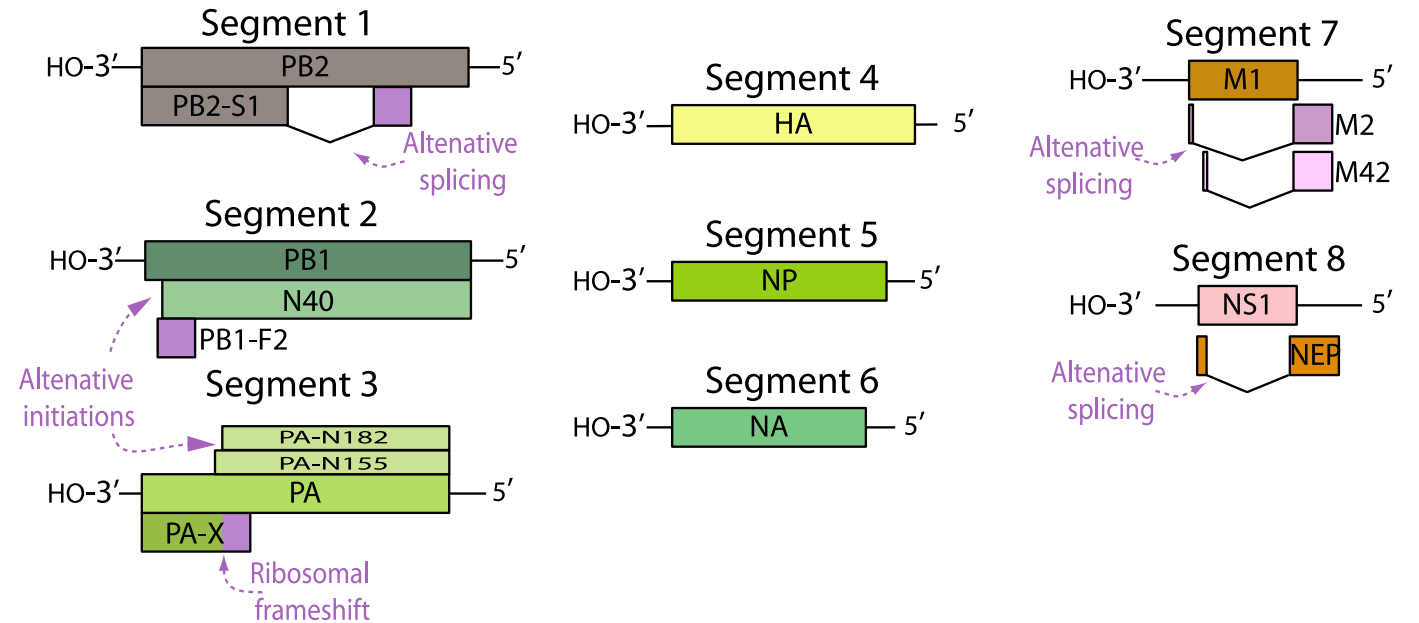
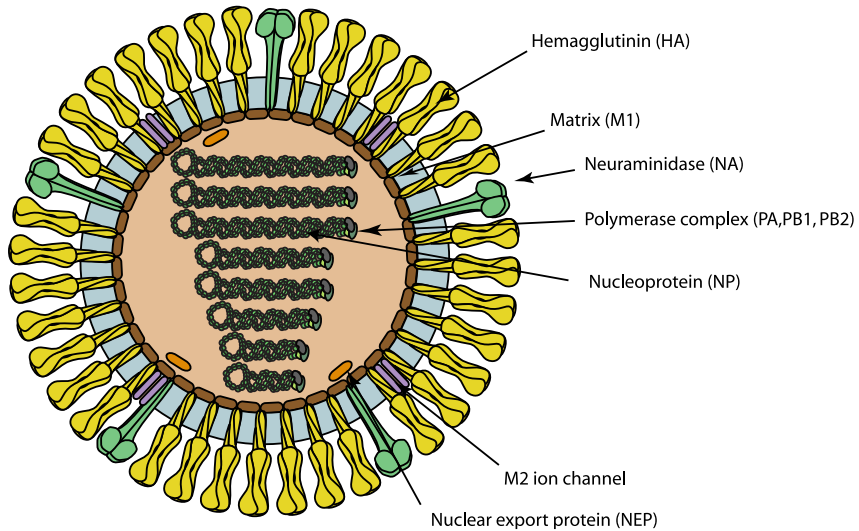
Diameter of 80-120nm

Segmented (8AB – 7CD)

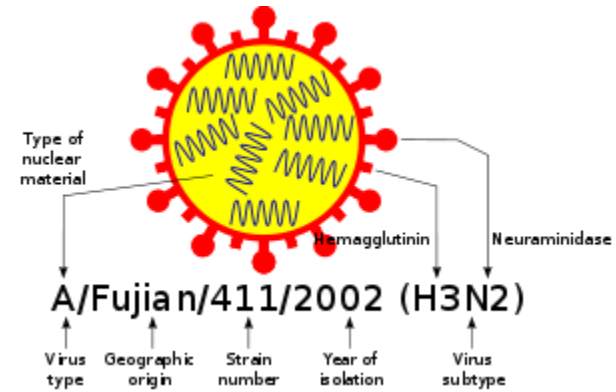
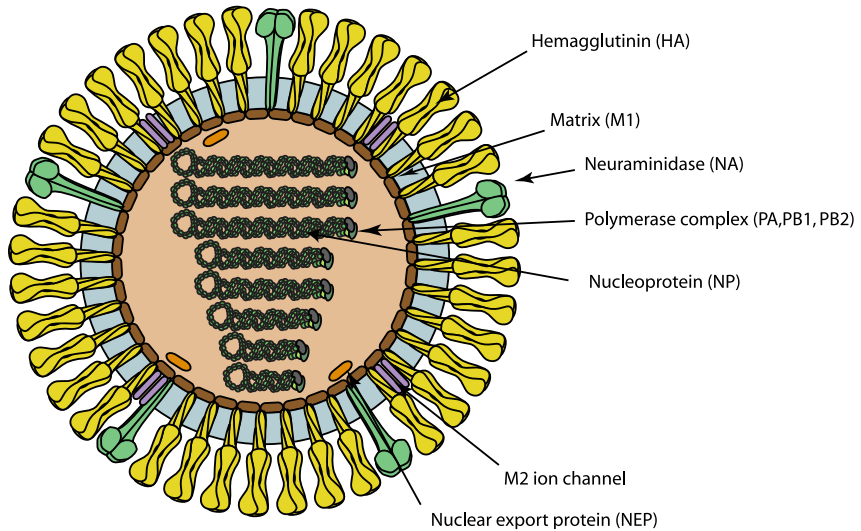




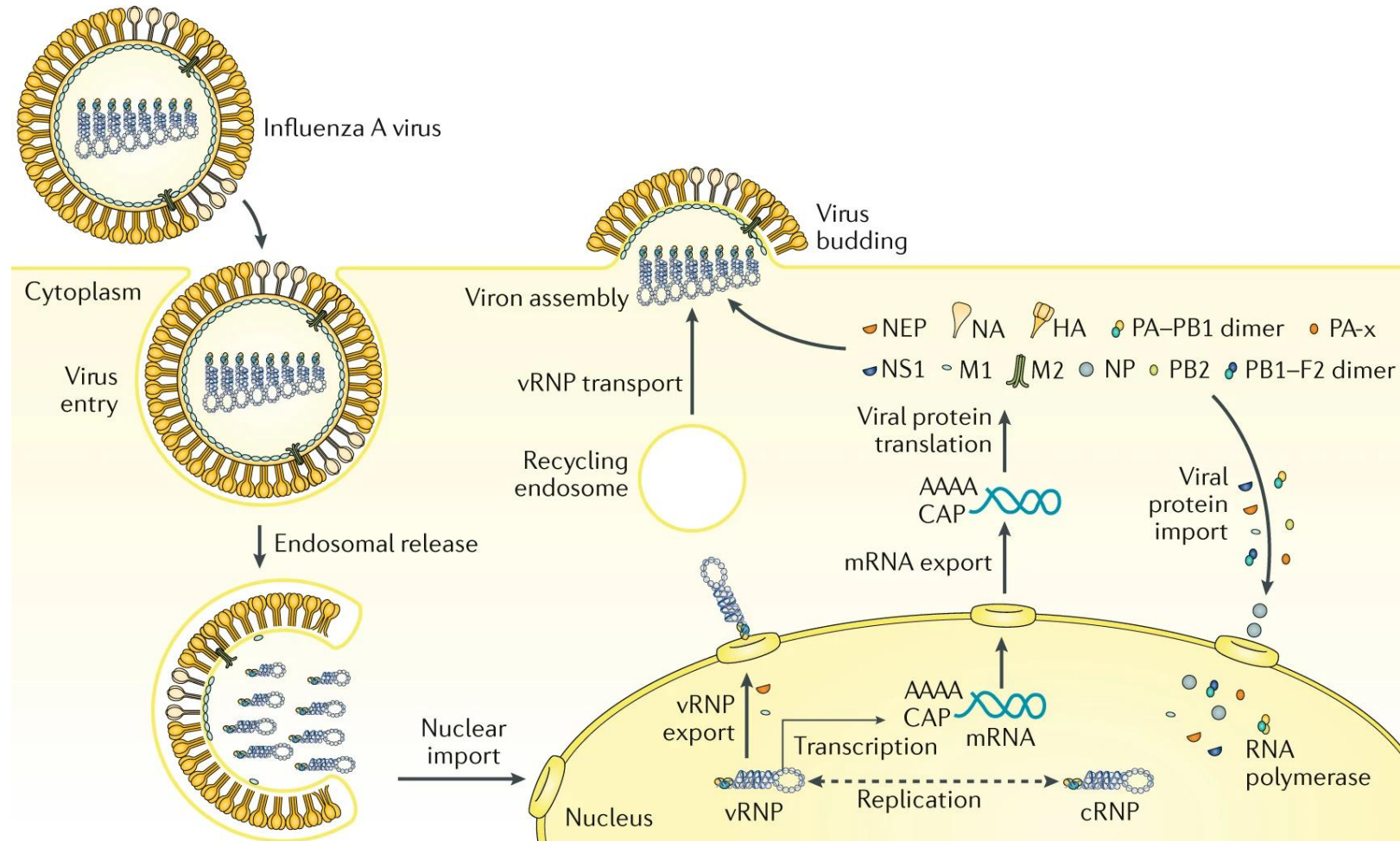
# Influenza: Biology



# Influenza: Nomenclature

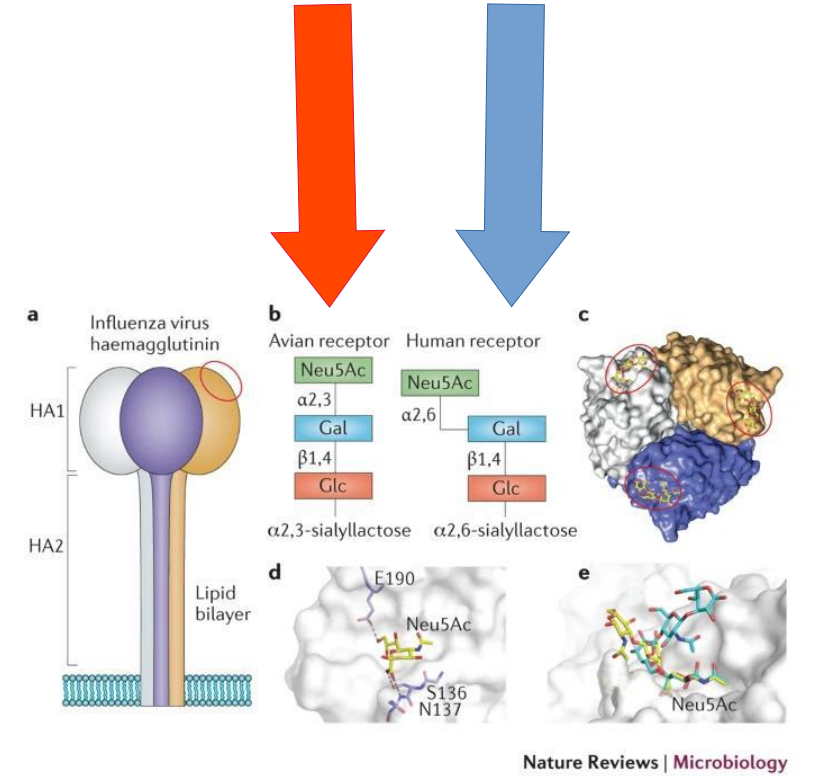
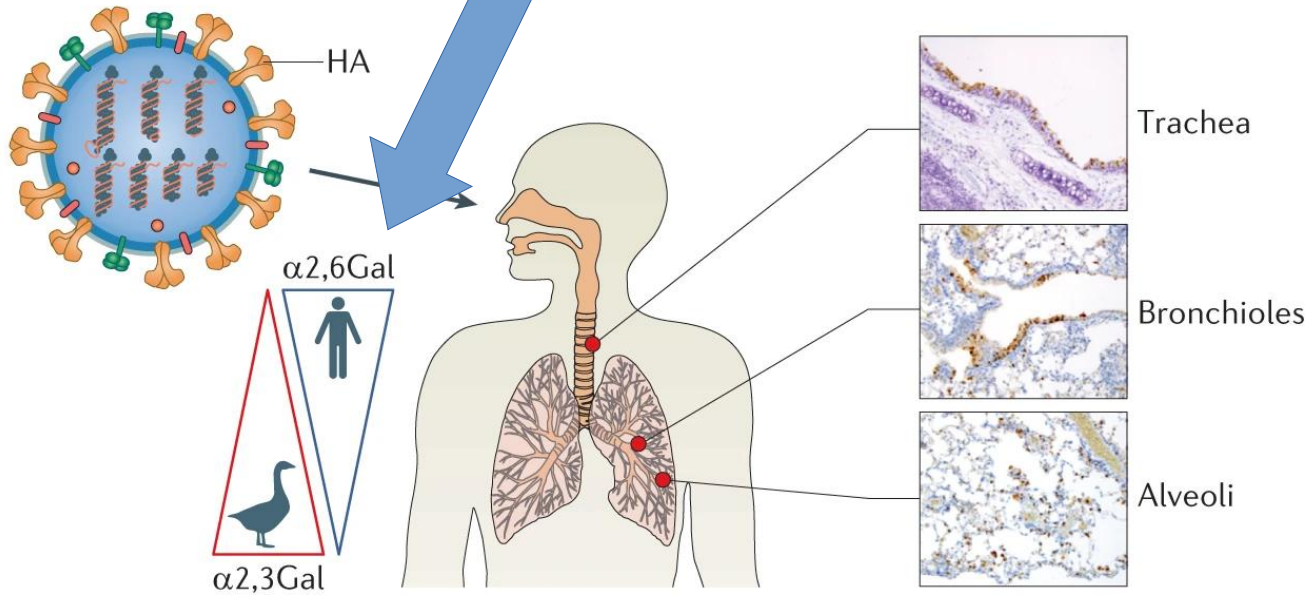


# Influenza: replication



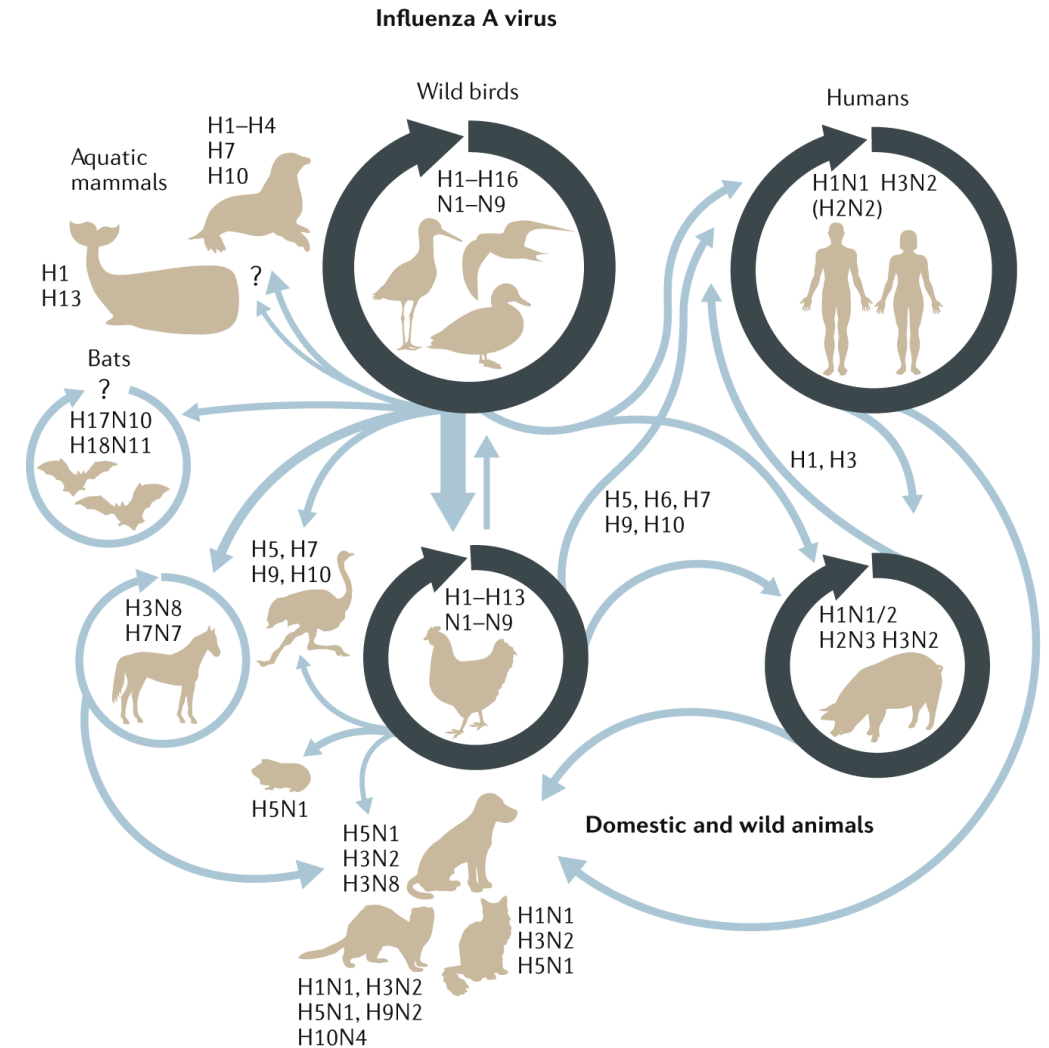
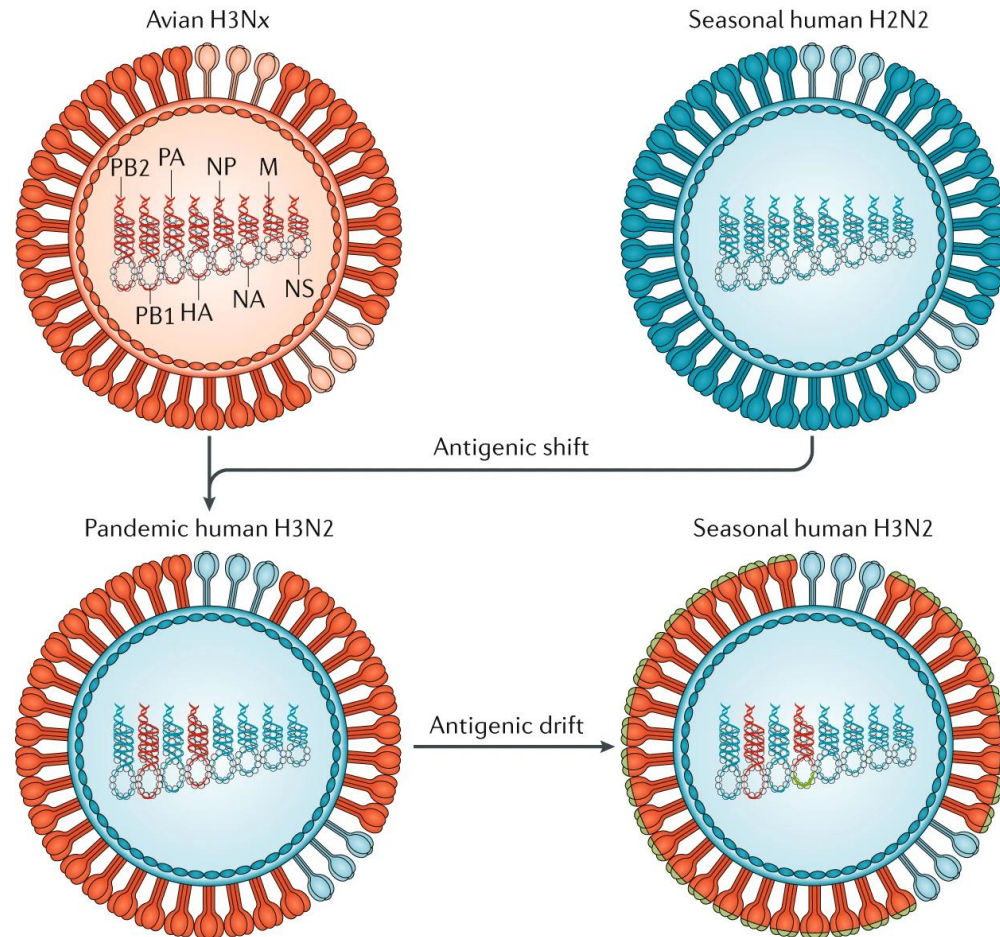
# Influenza: binding

**a Influenza virus**





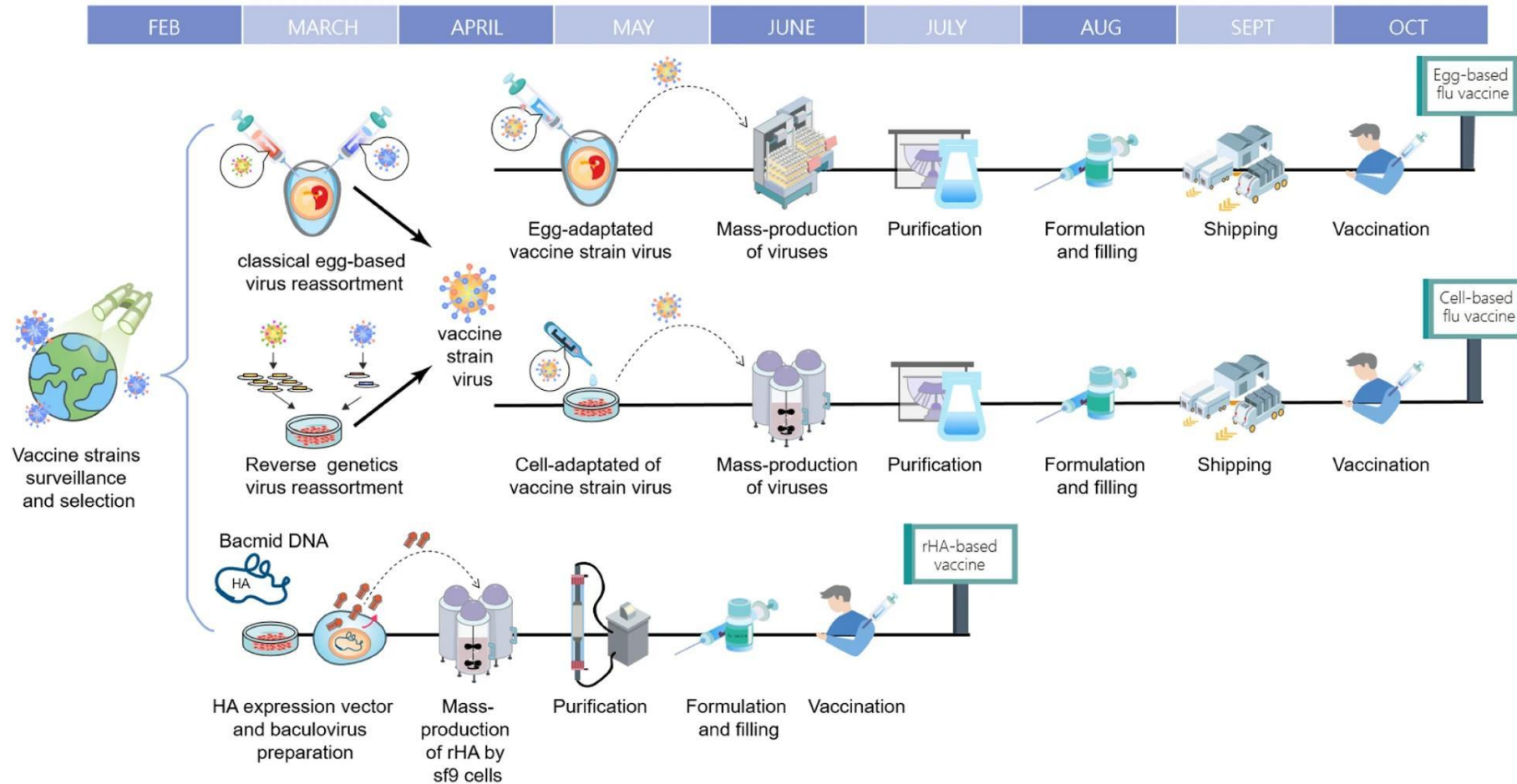
# Influenza: Antigenic „schwifrt“





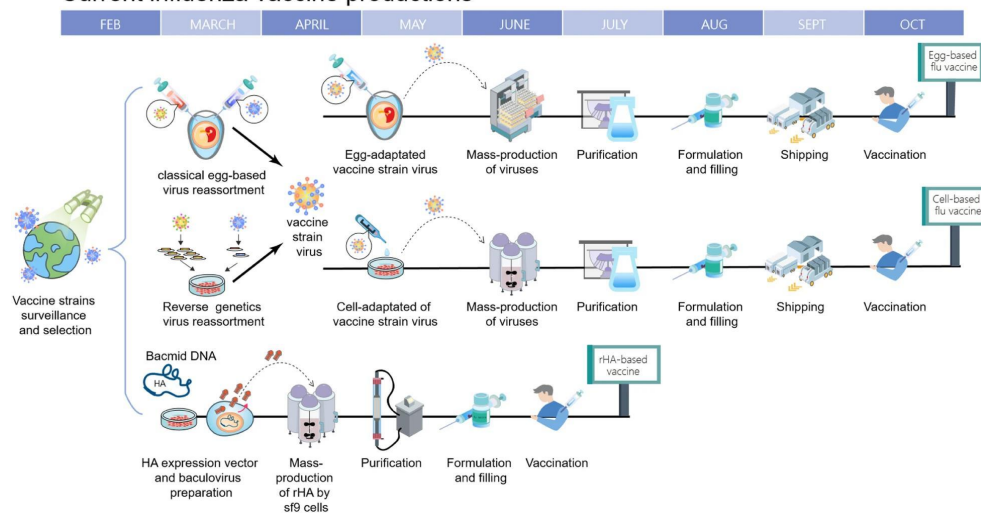
# Influenza: Vaccination

## Current influenza vaccine productions



# Influenza: Vaccination & Drugs

Current influenza vaccine productions



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

# Influenza: Vaccination & Drugs

| <p>Neuraminidase</p> <p>Cap endonuclease activity</p> |  | 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 <sup>[1]</sup> | 40 milligrams (mg) dose for people at least 10 years old, 20 mg for those under 10 <sup>[66]</sup> |
|                                                       |  | Baloxavir marboxil | Oral <sup>[4]</sup>       | At least 12 years old <sup>[46]</sup>                                                              |



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

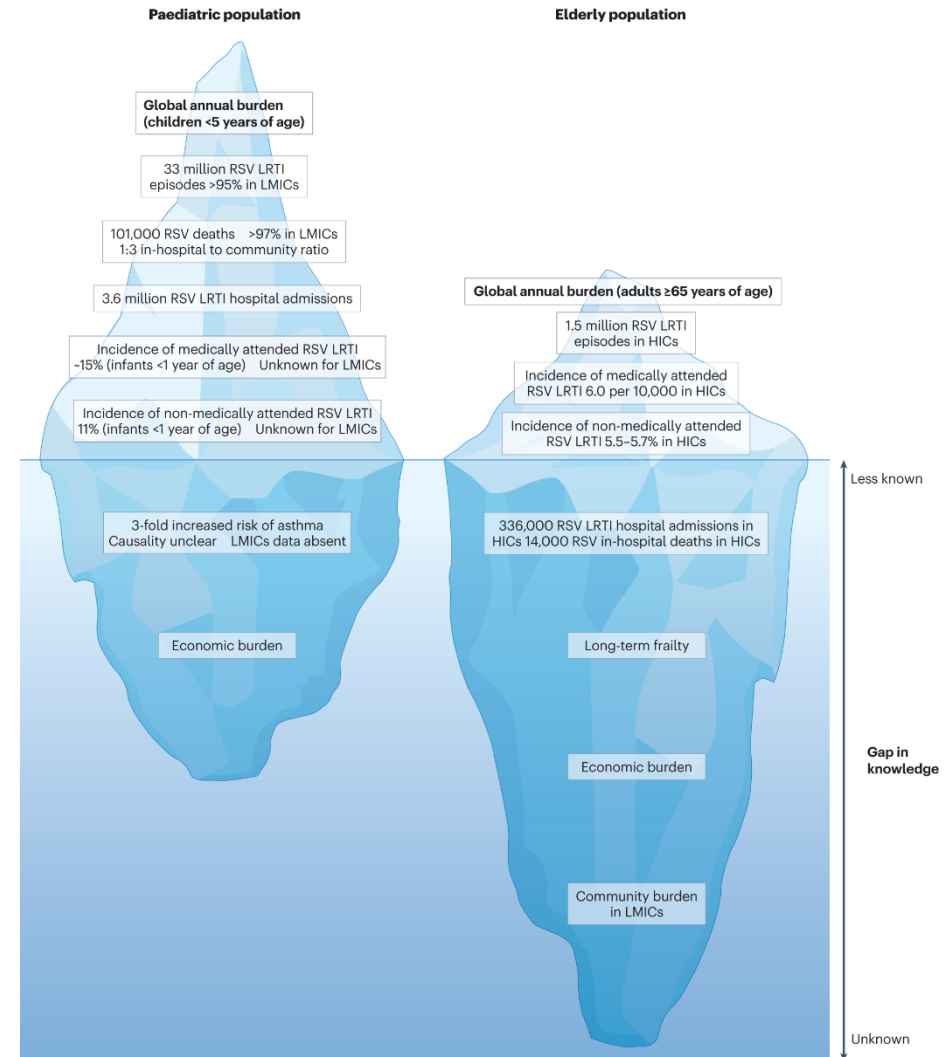
Children up to 5y: 33M annually LMIC

Leading cause of bronchiolitis and pneumonia in young children

Circulates in humans

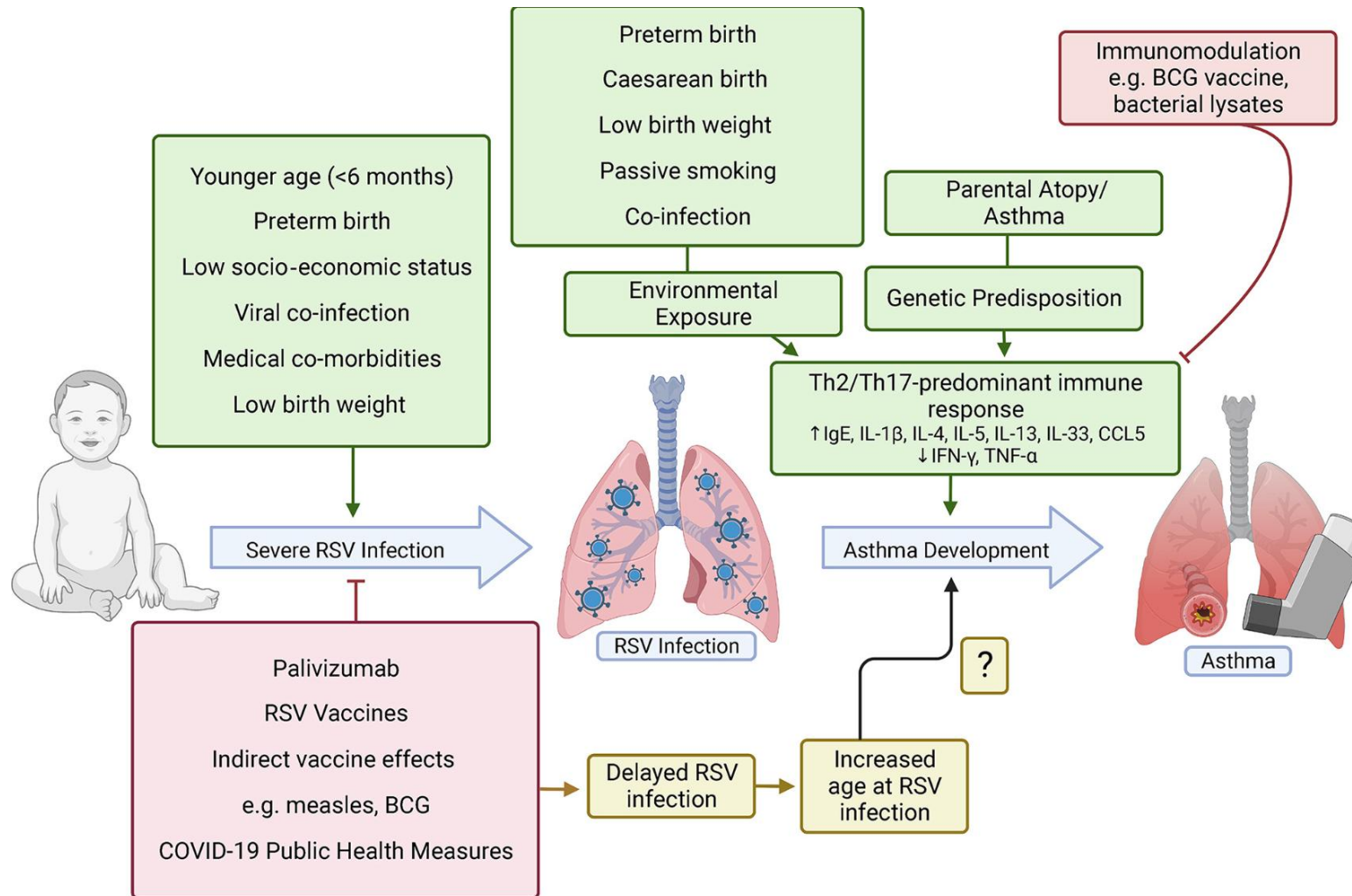
Vaccines: Arexvy (GSK) (EU-US), Abrysvo (Pfizer) (US), and Mresvia (Moderna)(US)

Normally, seasonal

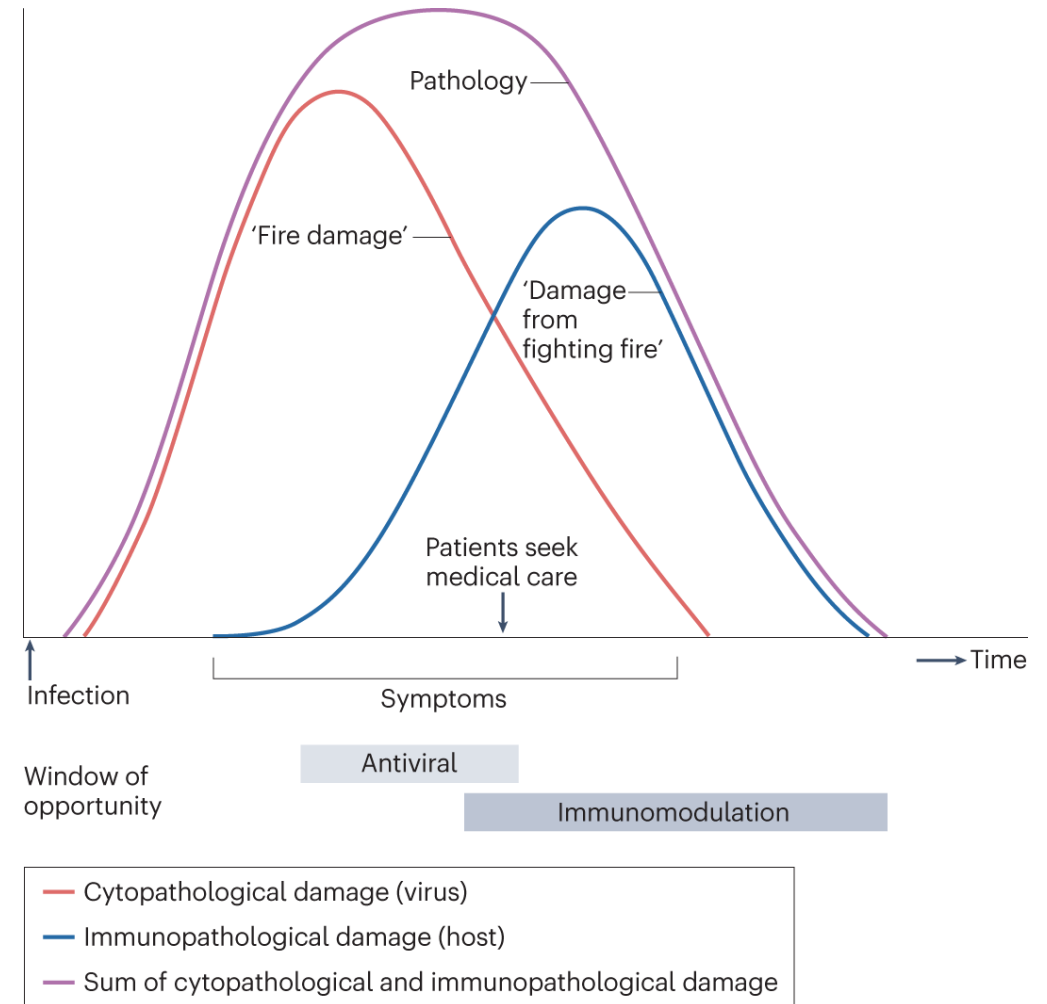
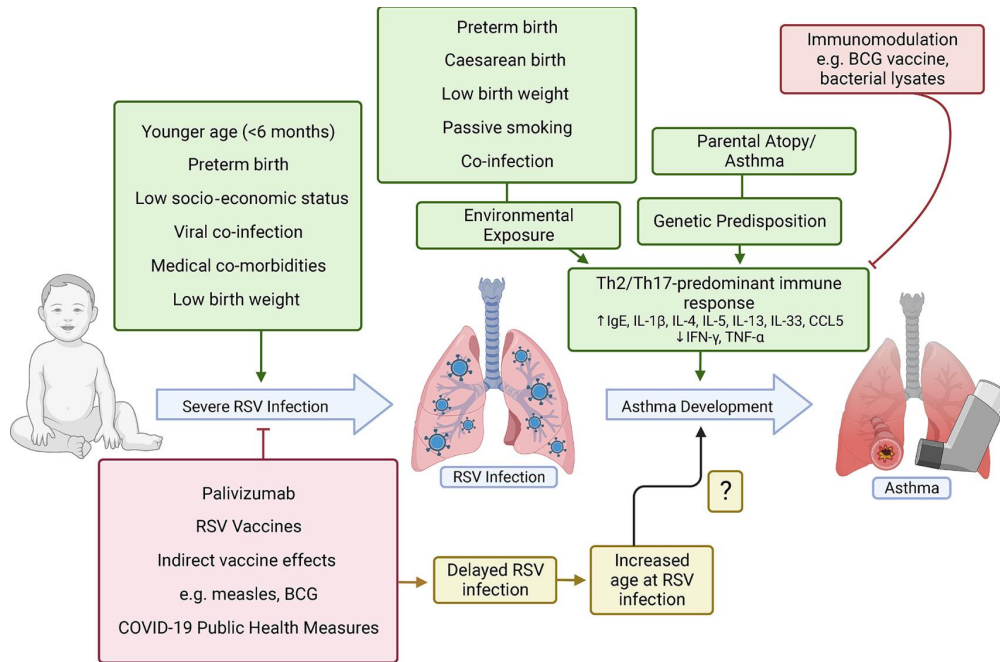




# RSV: Pathophysiology



# RSV: Pathophysiology



# RSV: Biology

Order: Mononegavirales

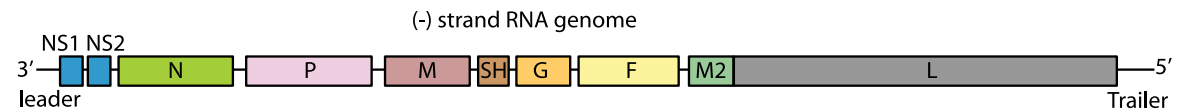
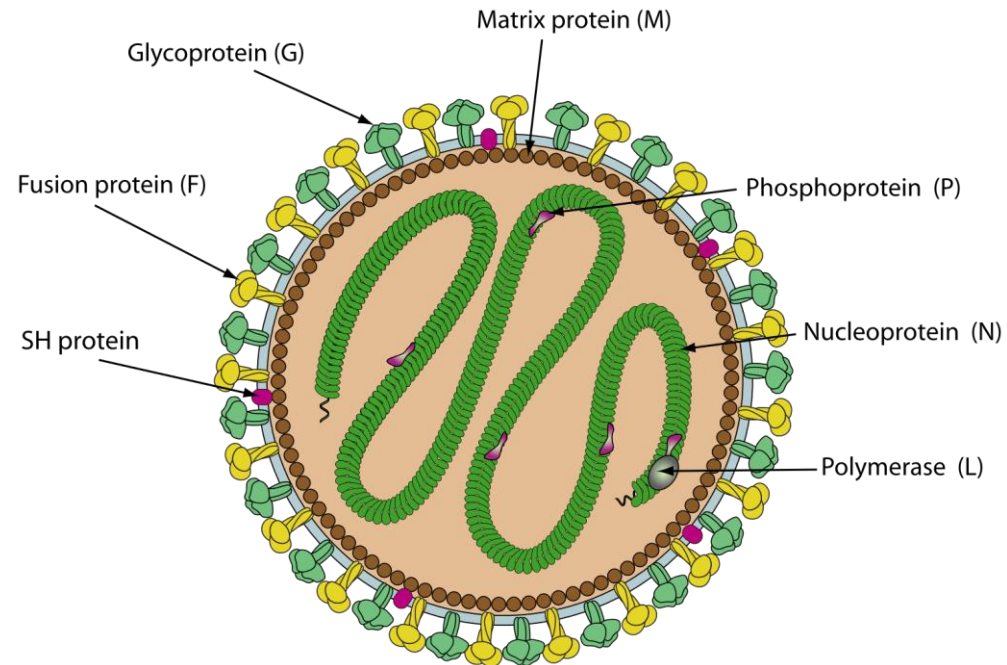
Family: Pneumoviridae

Genus: Orthopneumovirus

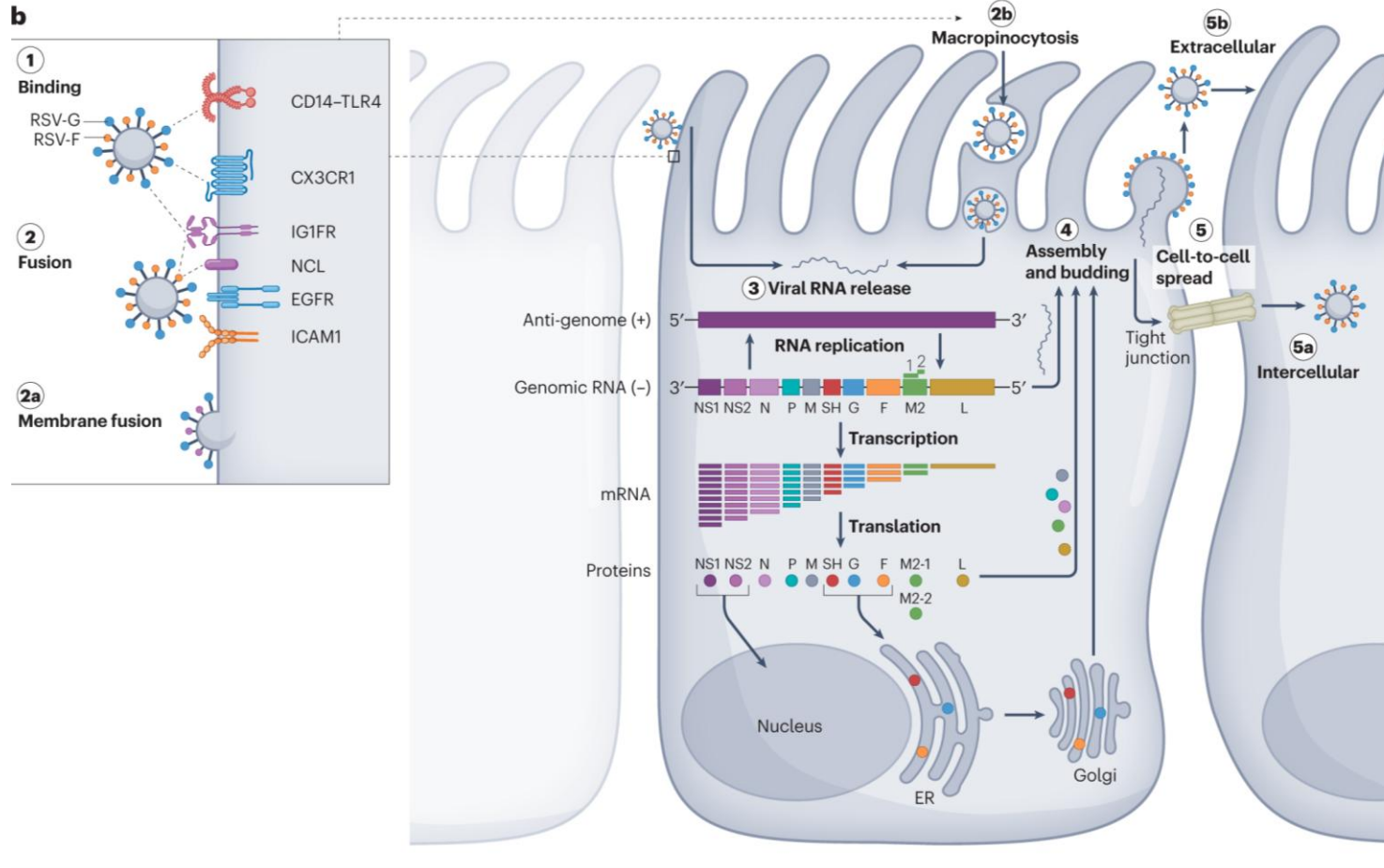
Enveloped, spherical.

Diameter ~ 150nm

Subtypes RSV-A and RSV-B

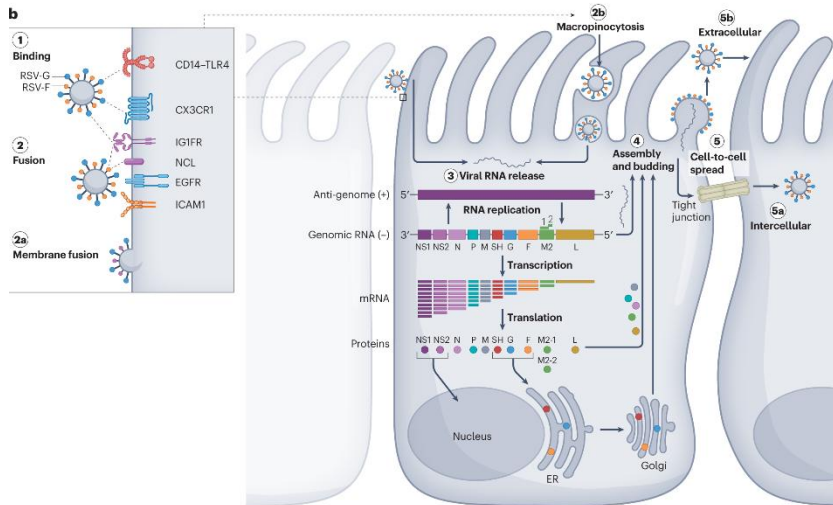


# RSV: Biology

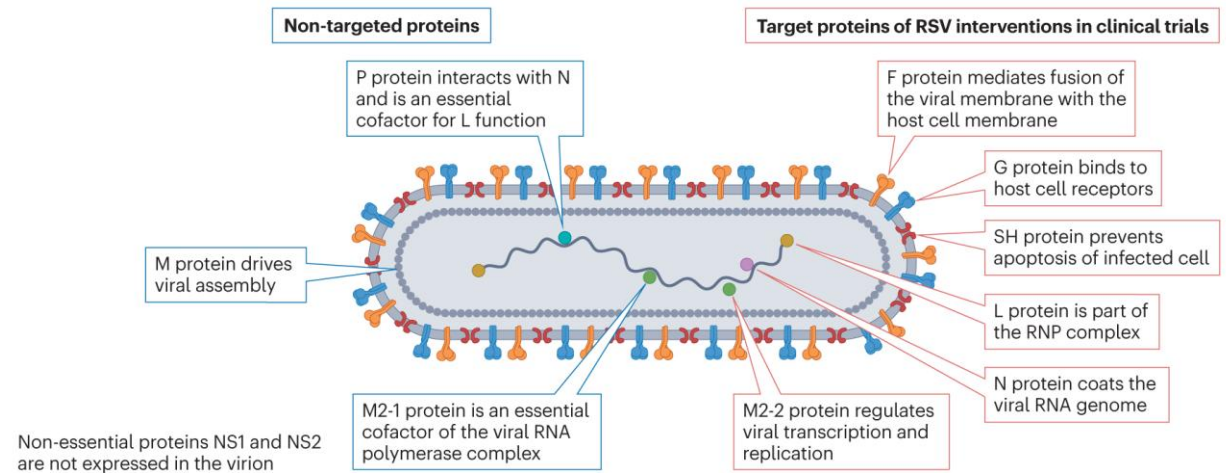


| Location in the Virion                          | Protein | Alternative Name               | Function                                                                      | Additional Information                                                                                                                                                                                                                          |
|-------------------------------------------------|---------|--------------------------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 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 <a href="#">neutralizing antibodies</a> during natural infection. |
|                                                 | F       | <a href="#">Fusion protein</a> | Fusion of viral and host cell membranes; syncytium formation                  |                                                                                                                                                                                                                                                 |
|                                                 | SH      | Small hydrophobic protein      | <a href="#">Viroporin</a> ; <a href="#">ion channel</a>                       | Participates in cell fusion, but no known neutralizing epitope                                                                                                                                                                                  |
| Inner envelope face                             | M       | Matrix protein                 | Assembly                                                                      |                                                                                                                                                                                                                                                 |
| Ribonucleocapsid                                | N       | Nucleoprotein                  | RNA-binding                                                                   | Involved in genome <a href="#">transcription</a> , RNA replication, and particle budding                                                                                                                                                        |
|                                                 | P       | Phosphoprotein                 | <a href="#">Phosphorylation</a>                                               |                                                                                                                                                                                                                                                 |
|                                                 | L       | "Large" protein                | <a href="#">RNA-dependent RNA polymerase</a>                                  |                                                                                                                                                                                                                                                 |
|                                                 | M2-1    | -                              | Transcription processivity factor                                             |                                                                                                                                                                                                                                                 |
| Regulatory                                      | M2-2    | -                              | Regulation of <a href="#">transcription</a> / <a href="#">RNA replication</a> |                                                                                                                                                                                                                                                 |
| Nonstructural                                   | NS-1    | -                              | Involved in evasion of the <a href="#">innate immune system</a>               | Act by inhibiting <a href="#">apoptosis</a> and inhibiting <a href="#">Type I IFN</a> signaling                                                                                                                                                 |
|                                                 | NS-2    | -                              |                                                                               |                                                                                                                                                                                                                                                 |

# RSV: Biology



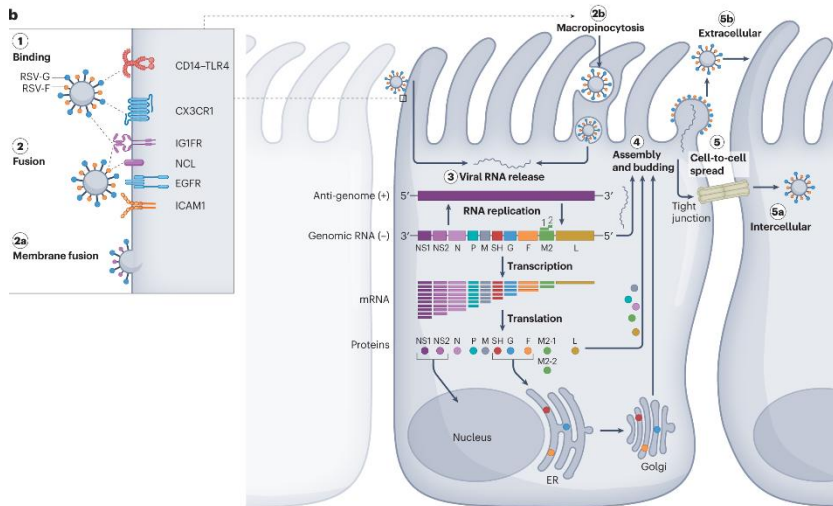
**a**



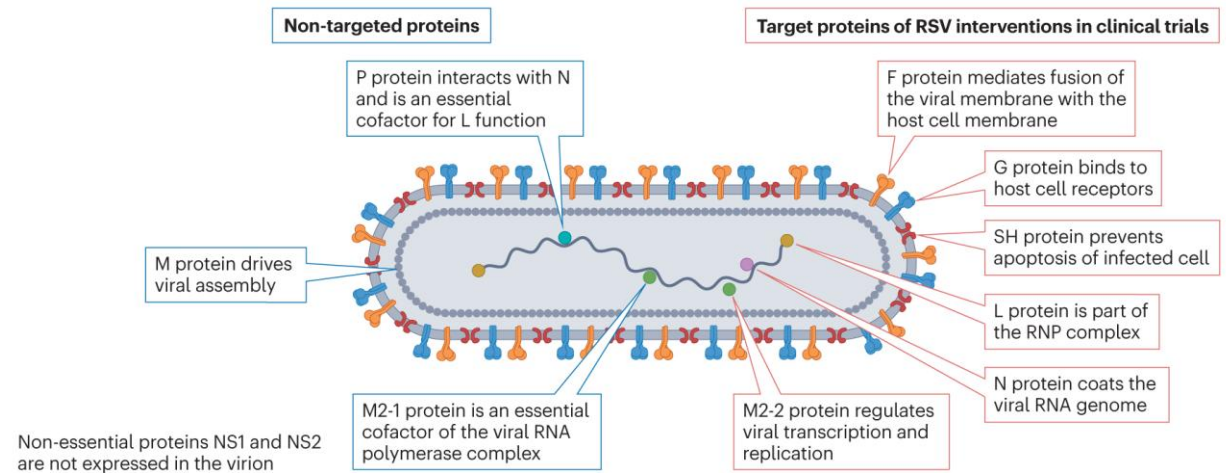
Non-essential proteins NS1 and NS2 are not expressed in the virion



# RSV: Biology



**a**



# RSV: Treatment

| Phase I                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Phase II               | Phase III     | Market-approved |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|---------------|-----------------|
| <b>Live attenuated</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                        |               |                 |
| 6120/ΔNS1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | SP0125 (VAD00001)      |               |                 |
| 6120/ΔNS2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | RSV ΔNS2/Δ1313/ I1314L |               |                 |
| 6120/F1/G2/ΔNS1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | MV-012-968             |               |                 |
| RSV-MinL4.0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                        |               |                 |
| IT-RSV-ΔG                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                        |               |                 |
| LIDΔM2-2 1030s                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                        |               |                 |
| <b>Chimeric</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        |               |                 |
| rBCG-N-hRSV                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                        |               |                 |
| SeV/RSV                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                        |               |                 |
| <b>Particle</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        |               |                 |
| V306 VLP                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                        |               |                 |
| IVX-121                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                        |               |                 |
| <b>Subunit</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                        |               |                 |
| DS-Cav1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | BARS13                 | RSVPreF       | RSVPreF3        |
| DPX-RSV                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                        |               | RSVPreF         |
| VN-0200                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                        |               |                 |
| <b>Vector</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                        |               |                 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        | Ad26.RSV.PreF |                 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        | MVA-BN-RSV    |                 |
| <b>Nucleic acid</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                        |               |                 |
| mRNA-1345                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                        | mRNA-1345     |                 |
| <b>Immunoprophylaxis</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                        |               |                 |
| RSM01                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                        | Clesrovimab   | Palivizumab     |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        |               | Nirsevimab      |
| <b>Viral fusion protein inhibitors</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                        |               |                 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Sisunatovir            | Ziresovir     |                 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | EDP-938                |               |                 |
| <b>Nucleoside analogue</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                        |               |                 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        |               | Ribavirin       |
| <div> <div> <div>Target population</div> <div> P Paediatric<br/>M Maternal<br/>O Older adults<br/>I Immunocompromised </div> </div> <div> <div>Preferred route of administration</div> <div> A Aerosol<br/>ID Intradermal<br/>IM Intramuscular<br/>IN Intranasal<br/>O Oral </div> </div> <div> <div>Target protein</div> <div> F Fusion<br/>FII F protein site II<br/>G Attachment<br/>L L protein<br/>M2-1 M2-1 protein<br/>M2-2 M2-2 protein<br/>N N protein </div> </div> <div> <div>Non-structural protein 1</div> <div> NS1 Non-structural protein 1<br/>NS2 Non-structural protein 2<br/>pol Polymerase<br/>preF Pre-fusion<br/>preFIII Site III of the F protein in the pre-fusion state<br/>preF<sub>0</sub> Site 0 of the F protein in the pre-fusion state<br/>SHe Ectodomain of SH<br/>VAGA VAGA-9001 antigen </div> </div> </div> |                        |               |                 |

# RSV: Treatment & Prophylaxis

| Phase I                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Phase II                                                                                                                    | Phase III                                                                                                                                                   | Market-approved                                                                                                                      |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------|
| <b>Live attenuated</b><br>612Q/ΔNS1 (P, IN, NS1)<br>612Q/ΔNS2 (P, IN, NS2)<br>612Q/F1/G2/ΔNS1 (P, IN, NS1, F, G)<br>RSV-MinL4.0 (P, O, IN, L)<br>IT-RSV-ΔG (P, IN, G)<br>LIDΔM2-2 1030s (P, IN, M2-2, L)<br><b>Chimeric</b><br>rBCG-N-hRSV (P, ID, N)<br>SeV/RSV (P, IN, F)<br><b>Particle</b><br>V306 VLP (M, IM, FII)<br>IVX-121 (O, IM, preF)<br><b>Subunit</b><br>DS-Cav1 (O, IM, preF)<br>DPX-RSV (O, IM, SHe)<br>VN-0200 (O, IM, VAGA)<br><b>Vector</b><br>Ad26.RSV.PreF (O, IM, preF)<br>MVA-BN-RSV (O, IM, F, G, N, M2-1)<br><b>Nucleic acid</b><br>mRNA-1345 (P, IM, preF)<br><b>Immunoprophylaxis</b><br>RSM01 (P, IM, preF)<br><b>Viral fusion protein inhibitors</b><br>Sisunatovir (P, A, F)<br>EDP-938 (P, A, N)<br>Ziresovir (P, O, F)<br><b>Nucleoside analogue</b><br>Ribavirin (P, I, A, pol) | SPO125 (VAD00001) (P, IN)<br>RSV ΔNS2/Δ1313/11314L (P, IN, NS2)<br>MV-012-968 (P, IN, SH, G, NS1, NS2)<br>BARS13 (O, IM, G) | RSVPreF (M, IM, preF)<br>Ad26.RSV.PreF (O, IM, preF)<br>MVA-BN-RSV (O, IM, F, G, N, M2-1)<br>mRNA-1345 (O, IM, preF)<br>Clesovimab (P, IM, F <sub>v</sub> ) | RSVPreF3 (O, IM, preFIII)<br>RSVPreF (O, IM, preF)<br>Palivizumab (P, IM, F <sub>v</sub> )<br>Nirsevimab (P, IM, preF <sub>3</sub> ) |

● Target population  
 P Paediatric  
 M Maternal  
 O Older adults  
 I Immunocompromised

● Preferred route of administration  
 A Aerosol  
 ID Intradermal  
 IM Intramuscular  
 IN Intranasal  
 O Oral

● Target protein  
 F Fusion  
 FII F protein site II  
 G Attachment  
 L L protein  
 M2-1 M2-1 protein  
 M2-2 M2-2 protein  
 N N protein  
 NS1 Non-structural protein 1  
 NS2 Non-structural protein 2  
 pol Polymerase  
 preF Pre-fusion  
 preFIII Site III of the F protein in the pre-fusion state  
 preF<sub>3</sub> Site Ø of the F protein in the pre-fusion state  
 SHe Ectodomain of SH  
 VAGA VAGA-9001 antigen

| 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 SA | 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       |

# RSV: Treatment & Prophylaxis

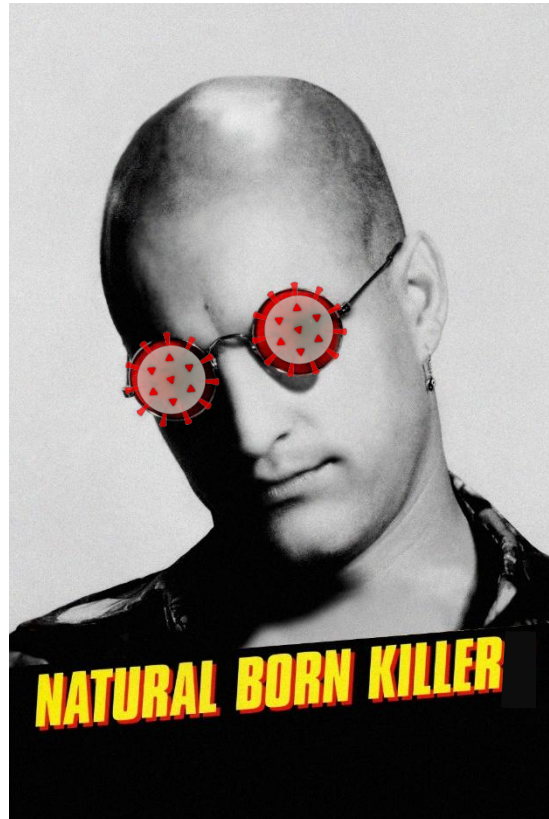
| Phase I                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Phase II                                                                                                                    | Phase III                                                                                                                                                    | Market-approved                                                                                                                      |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------|
| <b>Live attenuated</b><br>612Q/ΔNS1 (P, IN, NS1)<br>612Q/ΔNS2 (P, IN, NS2)<br>612Q/F1/G2/ΔNS1 (P, IN, NS1, F, G)<br>RSV-MinL4.0 (P, O, IN, L)<br>IT-RSV-ΔG (P, IN, G)<br>LIDΔM2-2 1030s (P, IN, M2-2, L)<br><b>Chimeric</b><br>rBCG-N-hRSV (P, ID, N)<br>SeV/RSV (P, IN, F)<br><b>Particle</b><br>V306 VLP (M, IM, FII)<br>IVX-121 (O, IM, preF)<br><b>Subunit</b><br>DS-Cav1 (O, IM, preF)<br>DPX-RSV (O, IM, SHe)<br>VN-0200 (O, IM, VAGA)<br><b>Vector</b><br>Ad26.RSV.PreF (O, IM, preF)<br>MVA-BN-RSV (O, IM, F, G, N, M2-1)<br><b>Nucleic acid</b><br>mRNA-1345 (P, IM, preF)<br><b>Immunoprophylaxis</b><br>RSM01 (P, IM, preF)<br><b>Viral fusion protein inhibitors</b><br>Sisunatovir (P, A, F)<br>EDP-938 (P, A, N)<br>Ziresovir (P, O, F)<br><b>Nucleoside analogue</b><br>Ribavirin (P, I, A, pol) | SP0125 (VAD00001) (P, IN)<br>RSV ΔNS2/Δ1313/11314L (P, IN, NS2)<br>MV-012-968 (P, IN, SH, G, NS1, NS2)<br>BARS13 (O, IM, G) | RSVPreF (M, IM, preF)<br>Ad26.RSV.PreF (O, IM, preF)<br>MVA-BN-RSV (O, IM, F, G, N, M2-1)<br>mRNA-1345 (O, IM, preF)<br>Clesrovimab (P, IM, F <sub>v</sub> ) | RSVPreF3 (O, IM, preFIII)<br>RSVPreF (O, IM, preF)<br>Palivizumab (P, IM, F <sub>v</sub> )<br>Nirsevimab (P, IM, preF <sub>9</sub> ) |

● Target population  
 P Paediatric  
 M Maternal  
 O Older adults  
 I Immunocompromised

● Preferred route of administration  
 A Aerosol  
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| Name    | Description                                                                                                                                                                                                                                                                                                                                       | Marketing Authorisation Holder | Kind of Vaccine | License Number | License Date | Further Information |
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The cast:  
Natural born killer  
Episodes I & II



# SARS Coronavirus: Episode I

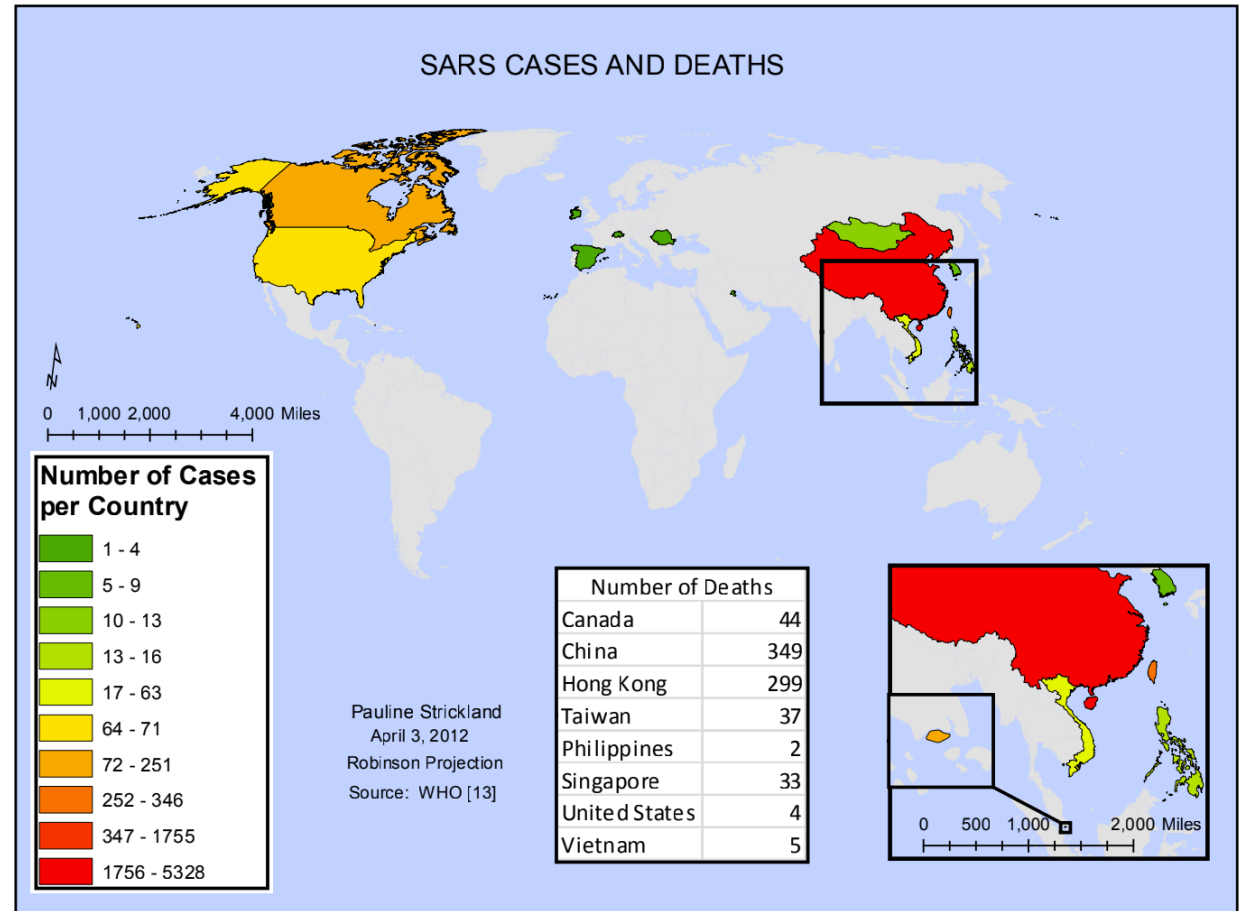
Infectious respiratory disease  
(mild to severe illness)

Dangerous to the population

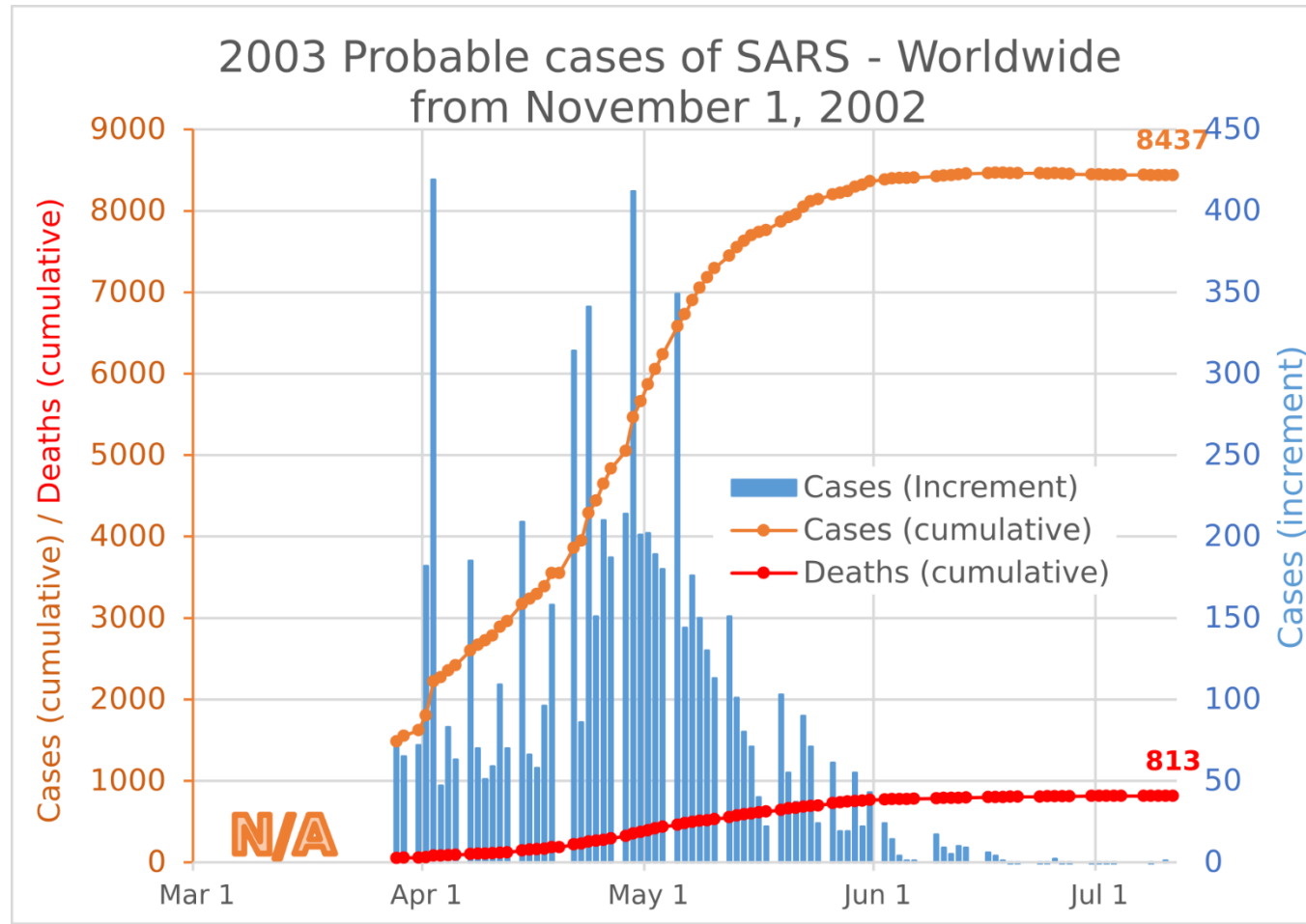
Pangolin natural reservoir

infected over 8,000 people (30 countries)

~800 deaths worldwide



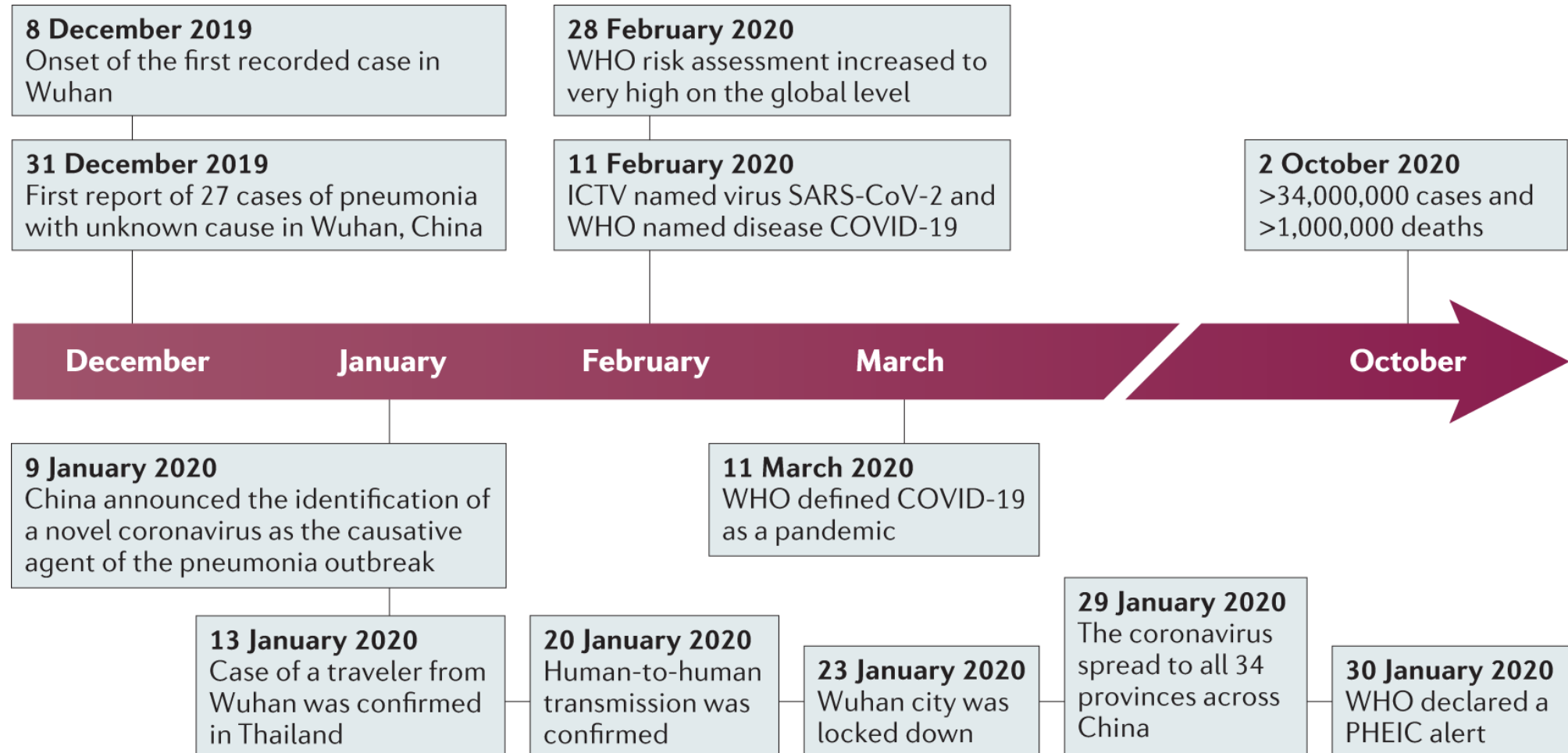
# SARS Coronavirus: Episode I



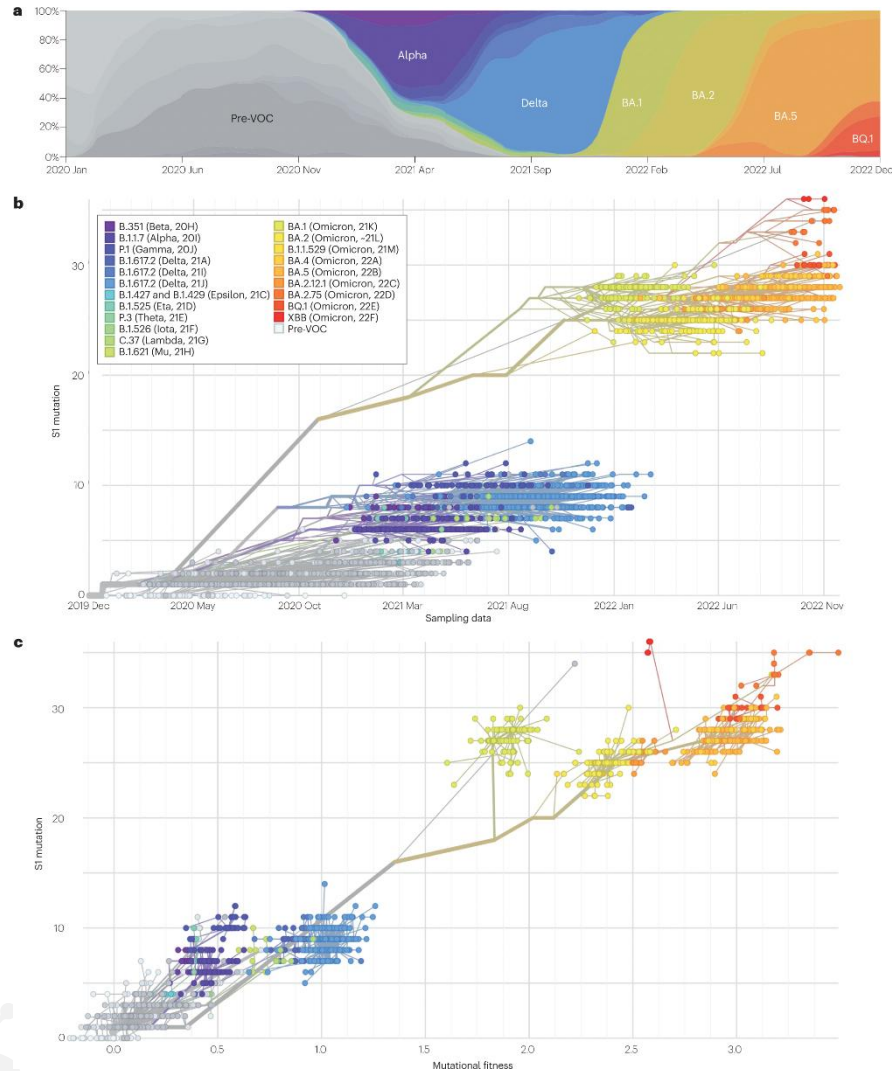
May 2004 last registered case

Well, this will never happen again... EVER!

# SARS Coronavirus 2: Episode II



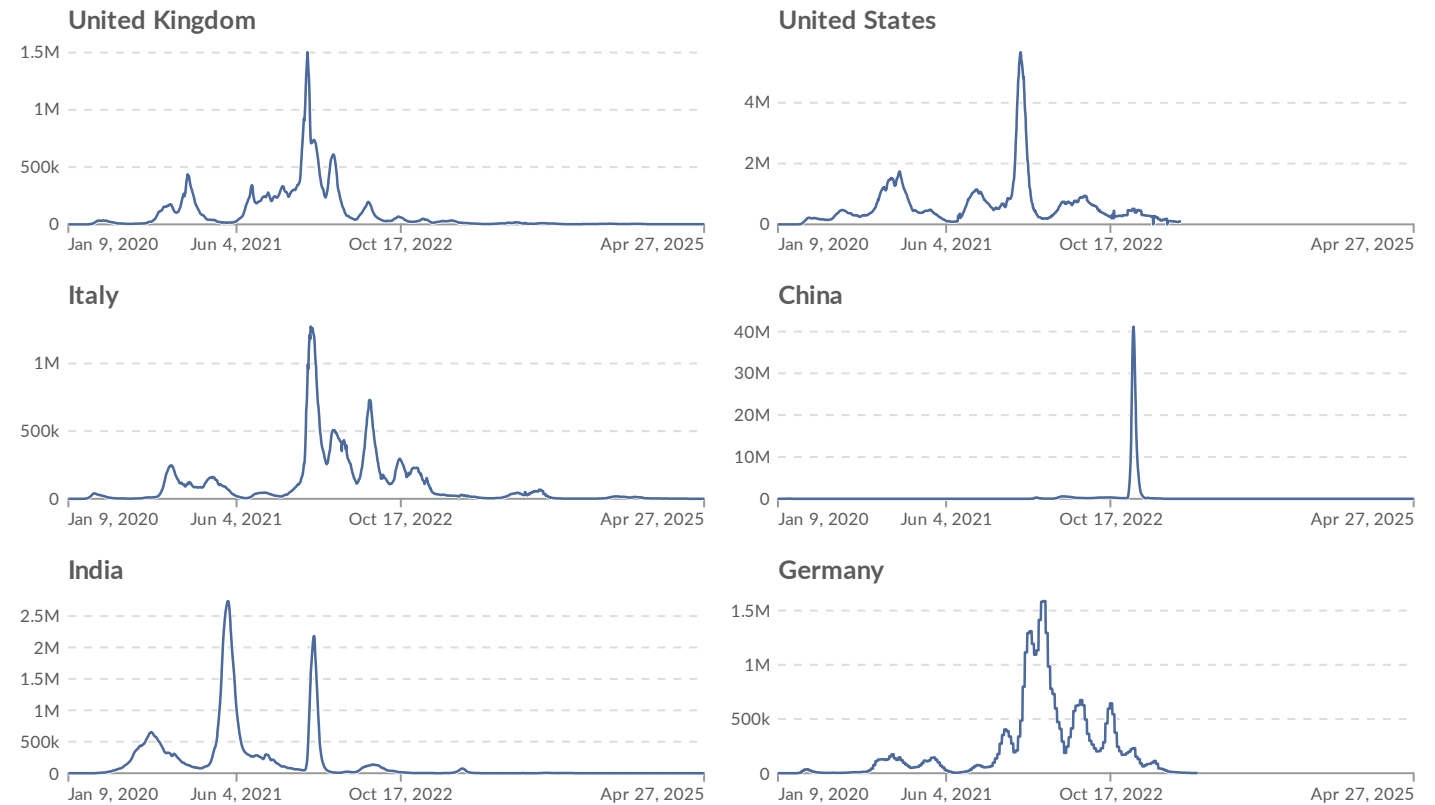
# SARS Coronavirus 2: Episode II



## Weekly confirmed COVID-19 cases

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

Our World  
in Data



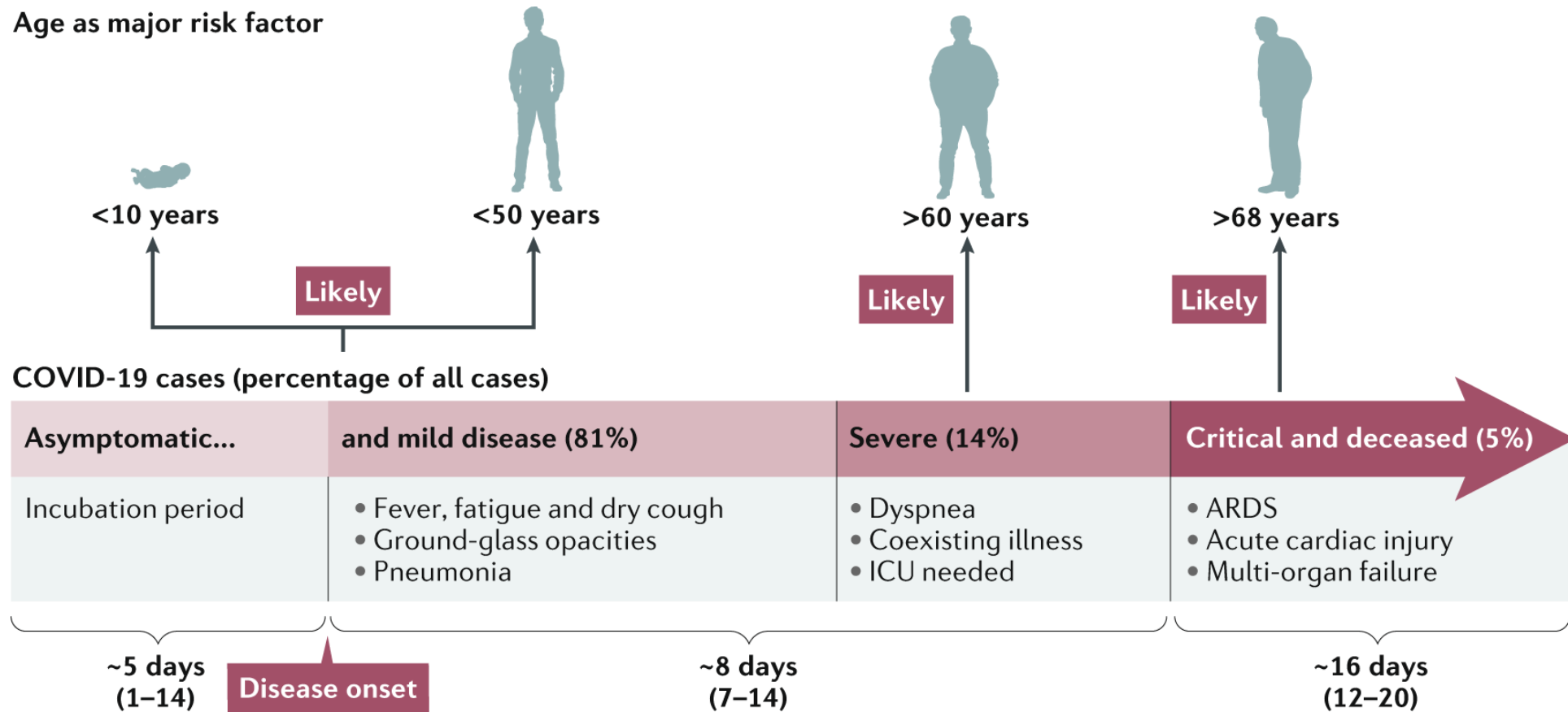
Data source: World Health Organization (2025)

OurWorldinData.org/coronavirus | CC BY



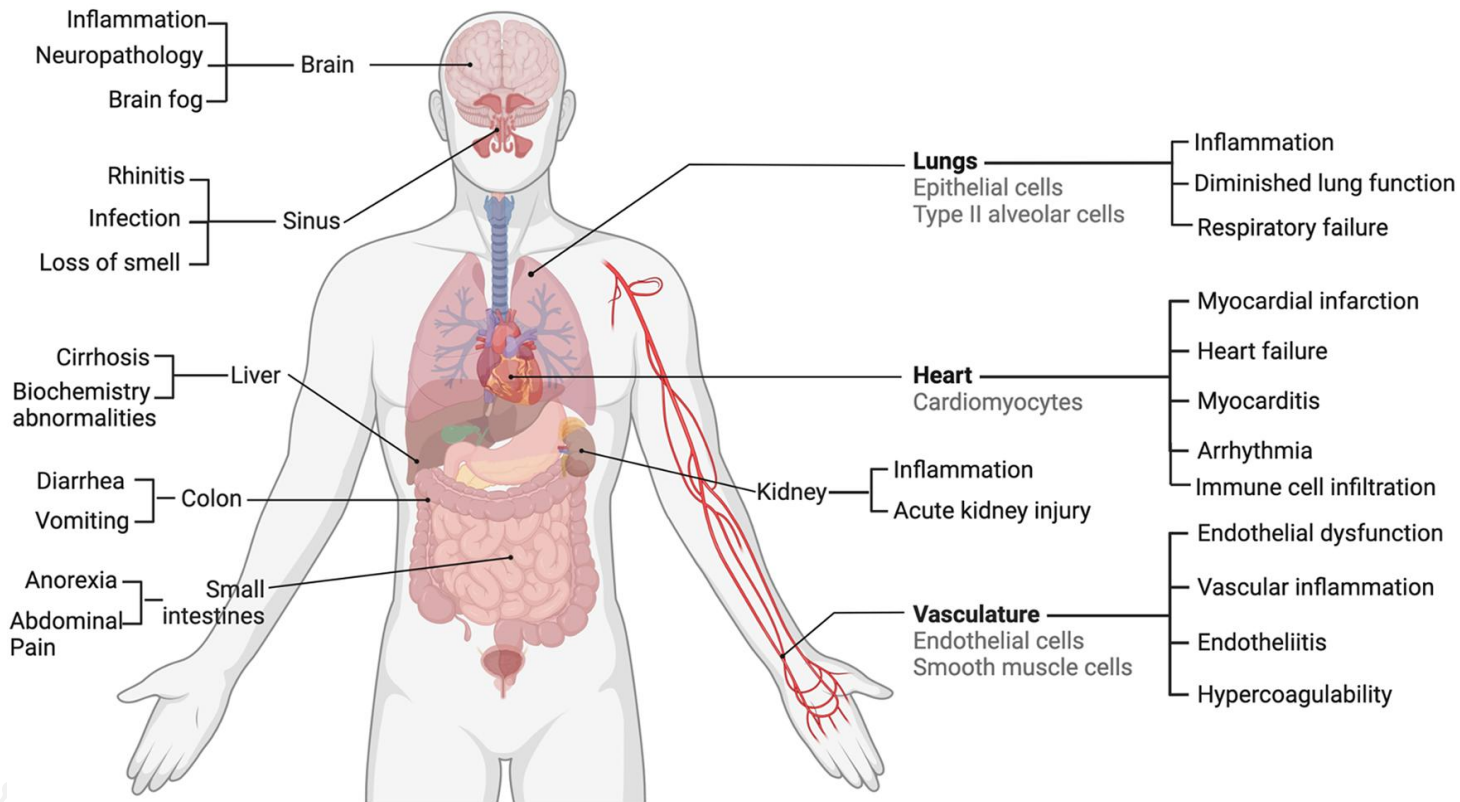
# SARS Coronavirus 2: Pathophysiology

Age as major risk factor

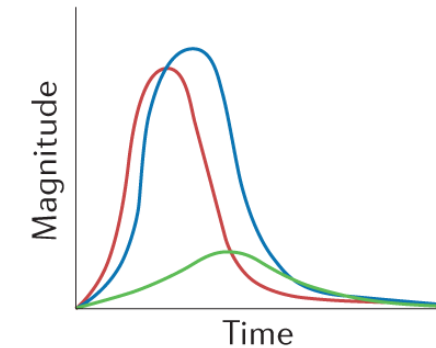


# SARS Coronavirus 2: Pathophysiology

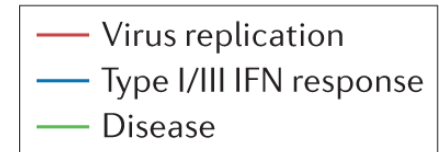
## Organ System Adaptations to COVID19



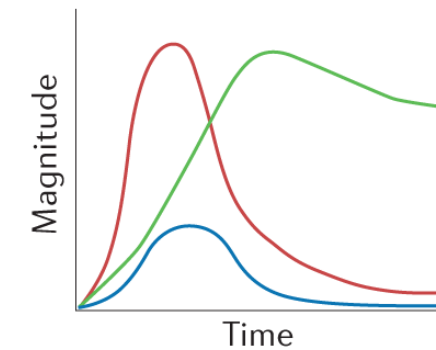
## Mild or symptomatic case



- Rapid IFN response
- Few or no symptoms
- Controlled viral replication

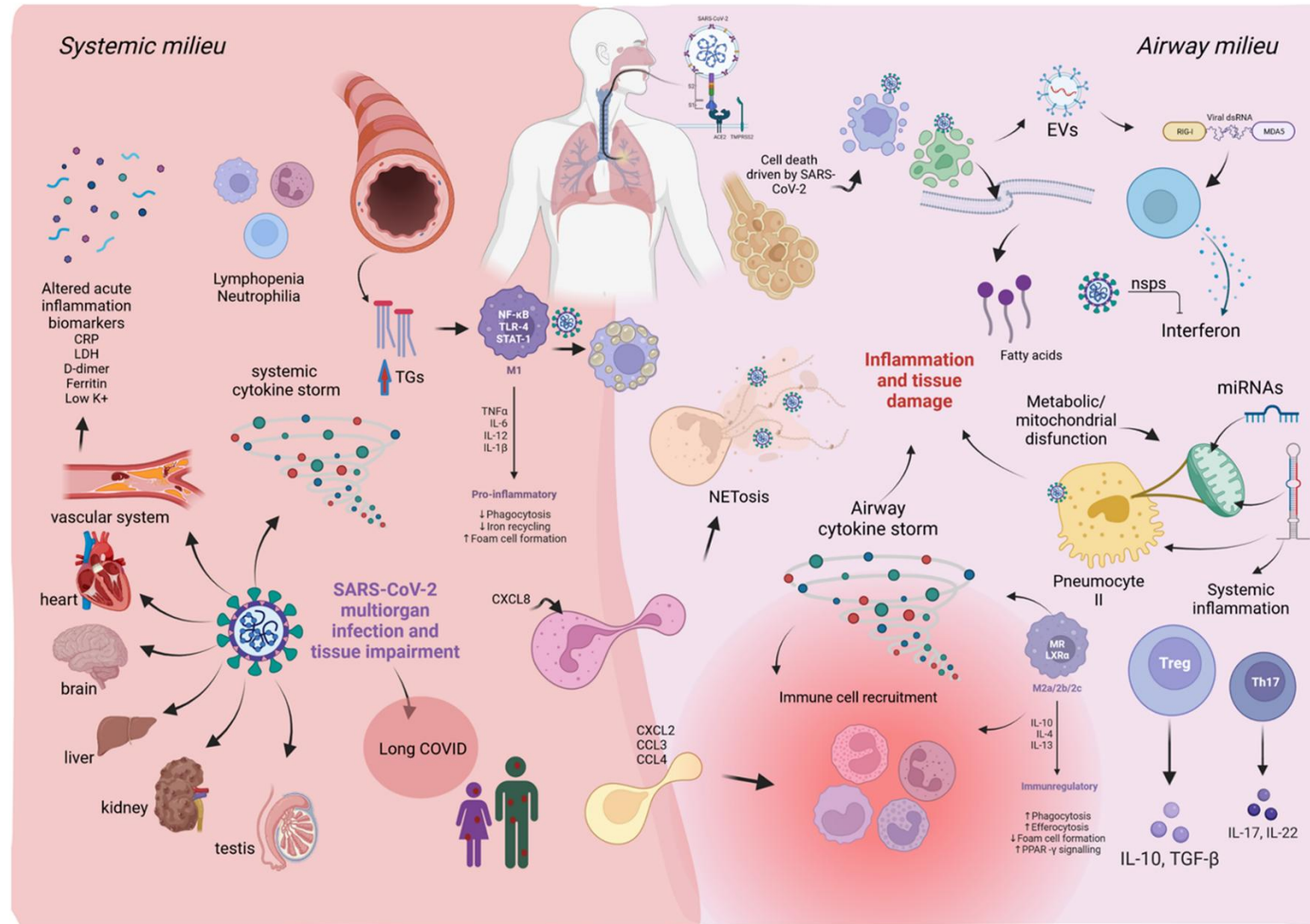


## Severe COVID-19



- Delayed or poor IFN response
- Increased viral replication
- Potentially fatal disease
- Auto-IFN antibodies
- Mutations in IFN or TLR signalling genes
- Poor plasmacytoid DC responses
- Inflammatory monocytes and neutrophils
- Immunothrombosis

# SARS Coronavirus 2: Pathophysiology



# SARS Coronavirus 2: Biology

Realm: Riboviria

Order: Nidovirales

Family: Coronaviridae

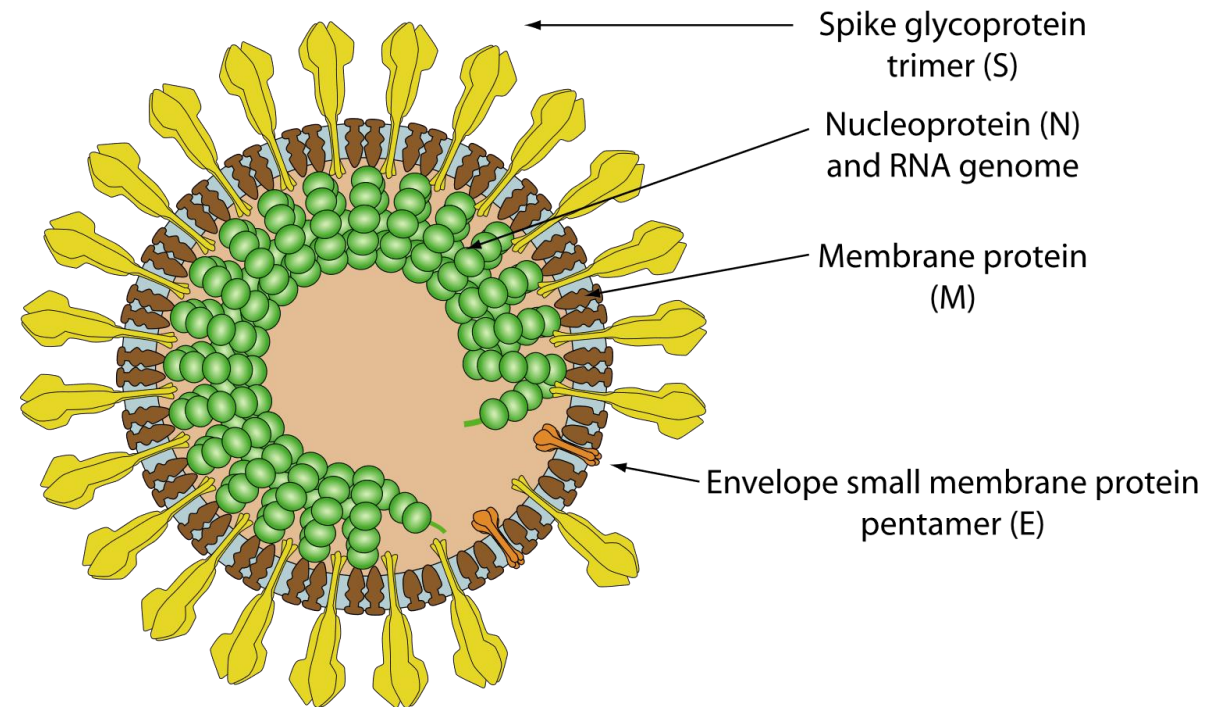
Subfamily: Orthocoronavirinae

Genus: Betacoronavirus

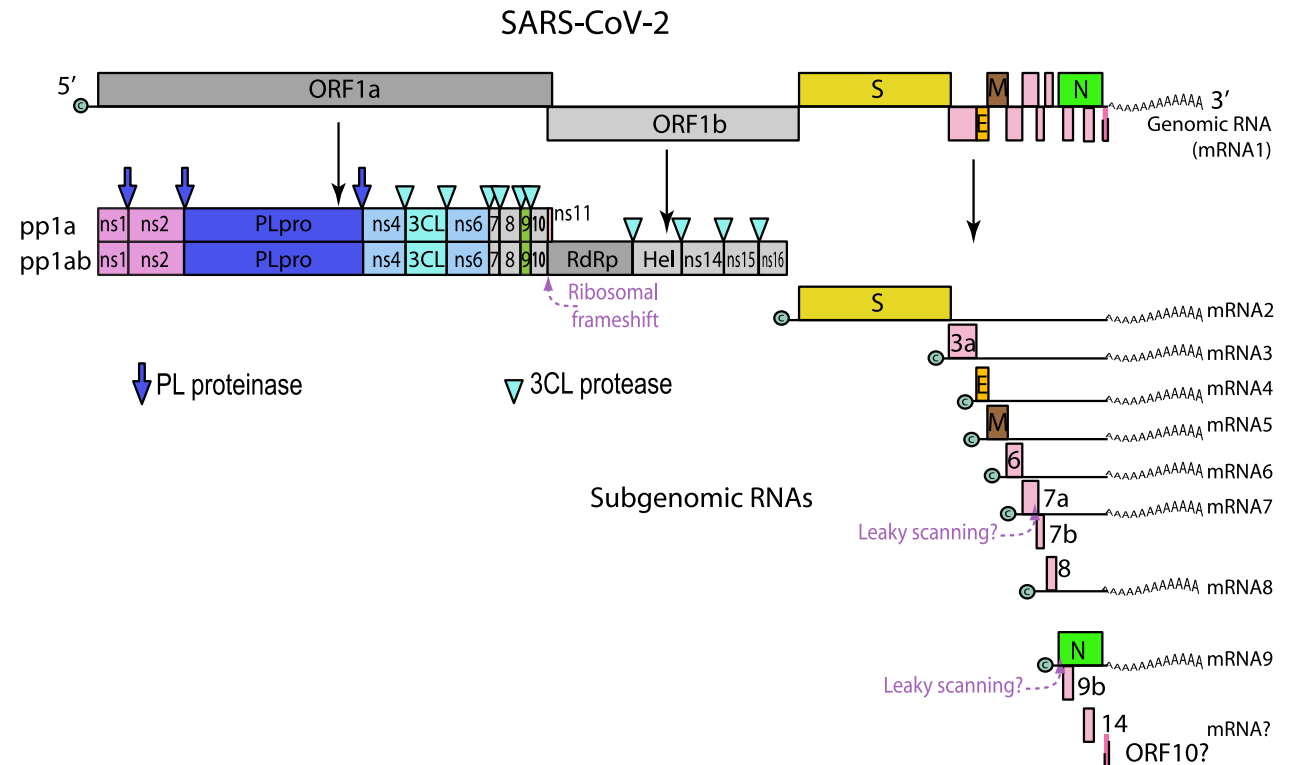
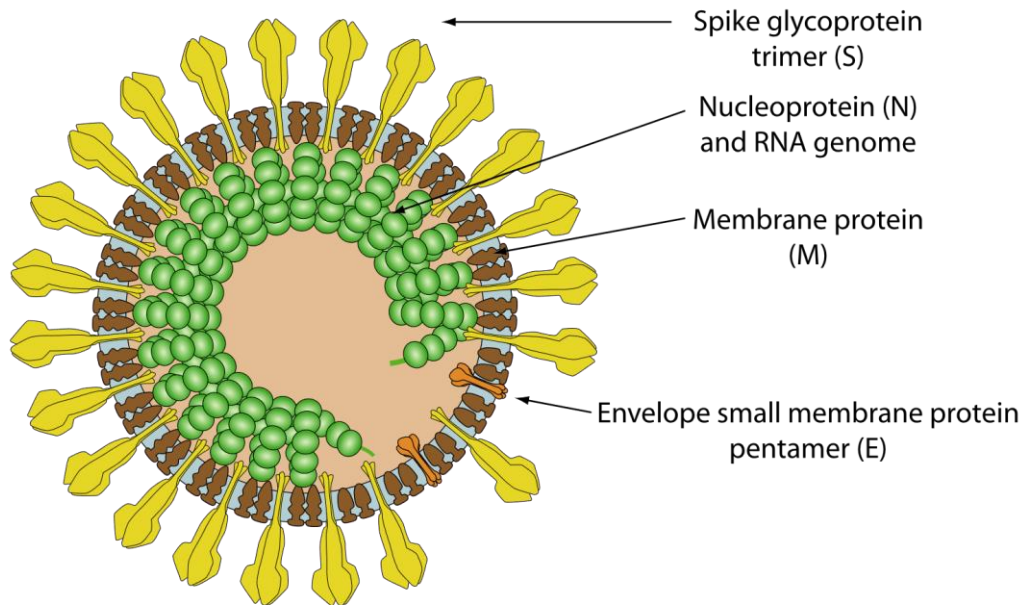
Several human pathogens:

SARS-Cov, SARS-Cov-2, HCoV-

OC43, MERS...



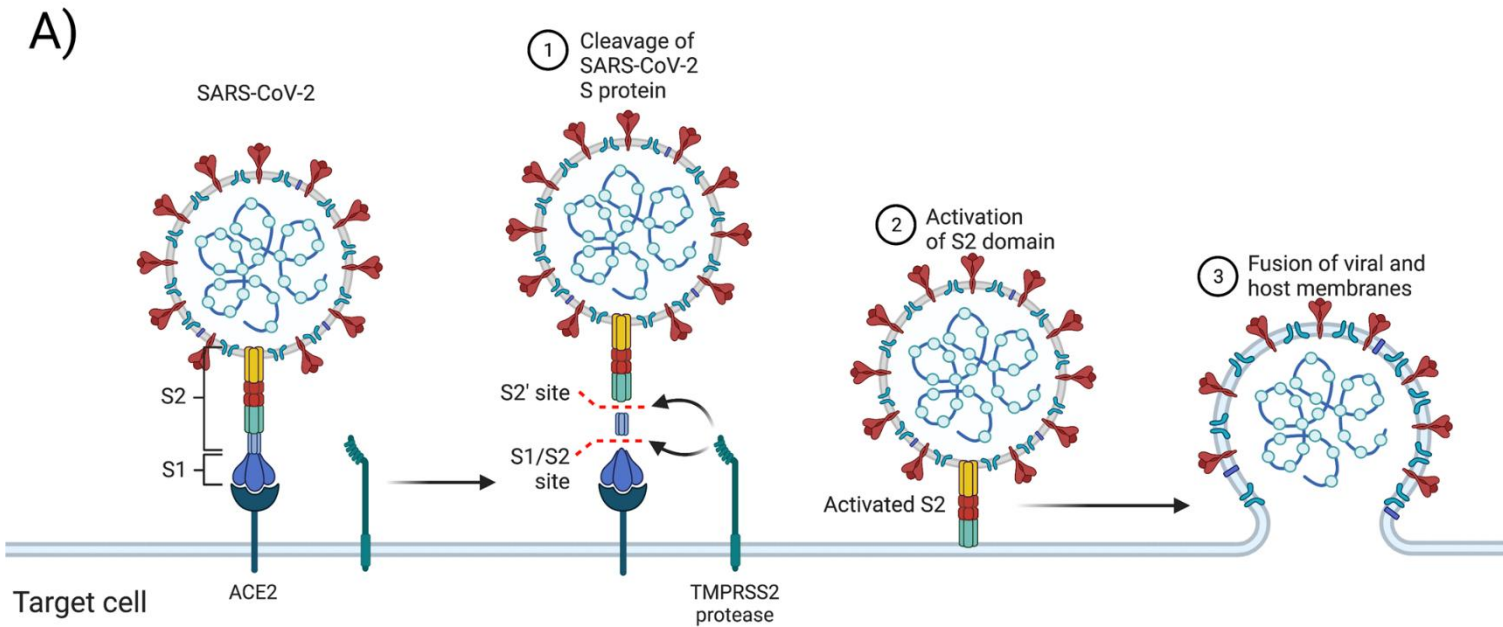
# SARS Coronavirus 2: Biology





# SARS Coronavirus 2: Biology

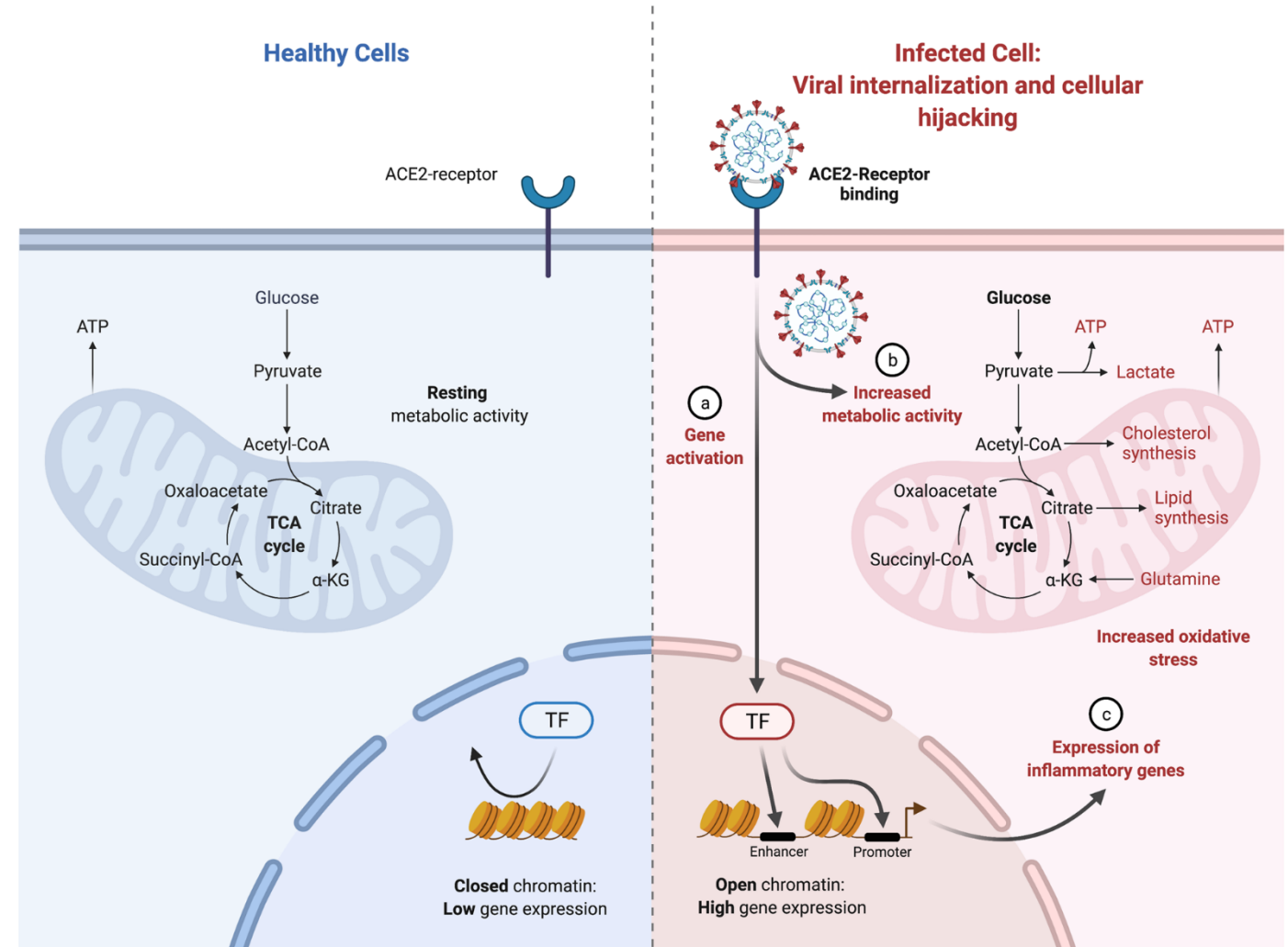
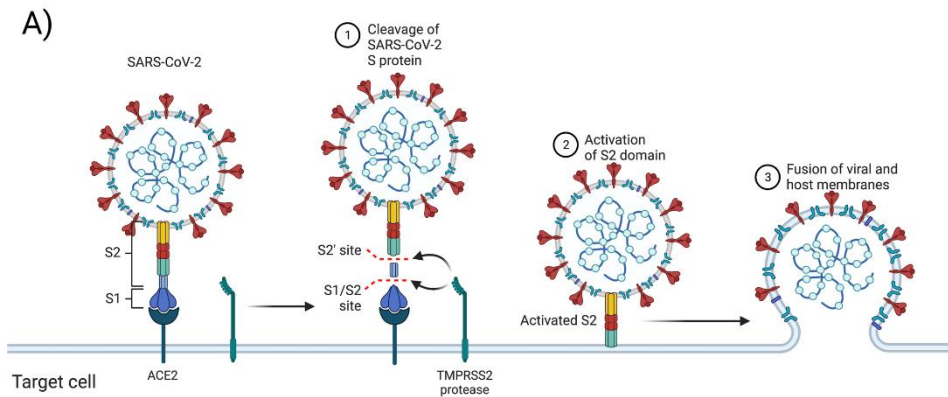
## SARS-CoV-2 Cellular Internalization and Intracellular Processes



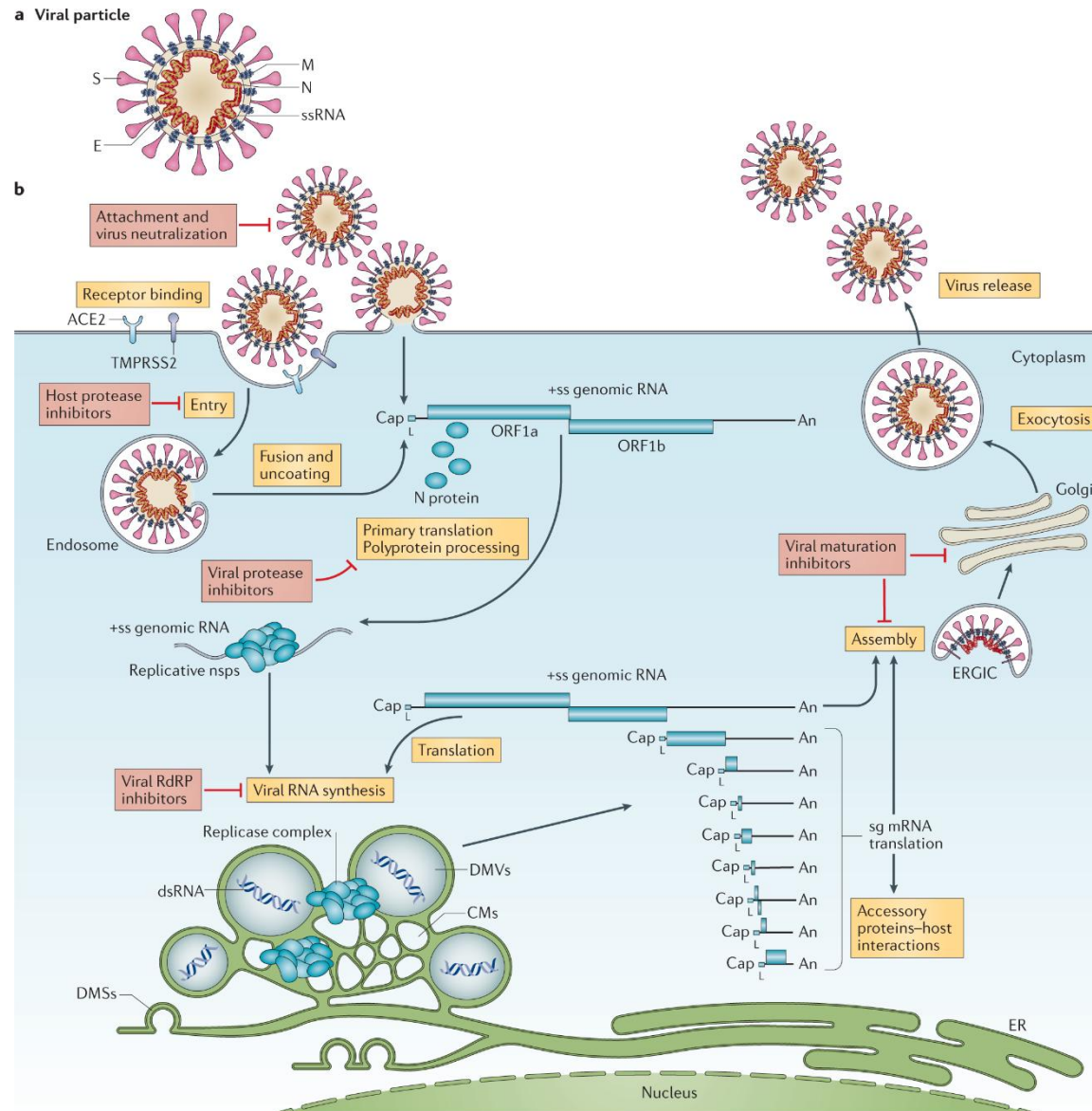


# SARS Coronavirus 2: Biology

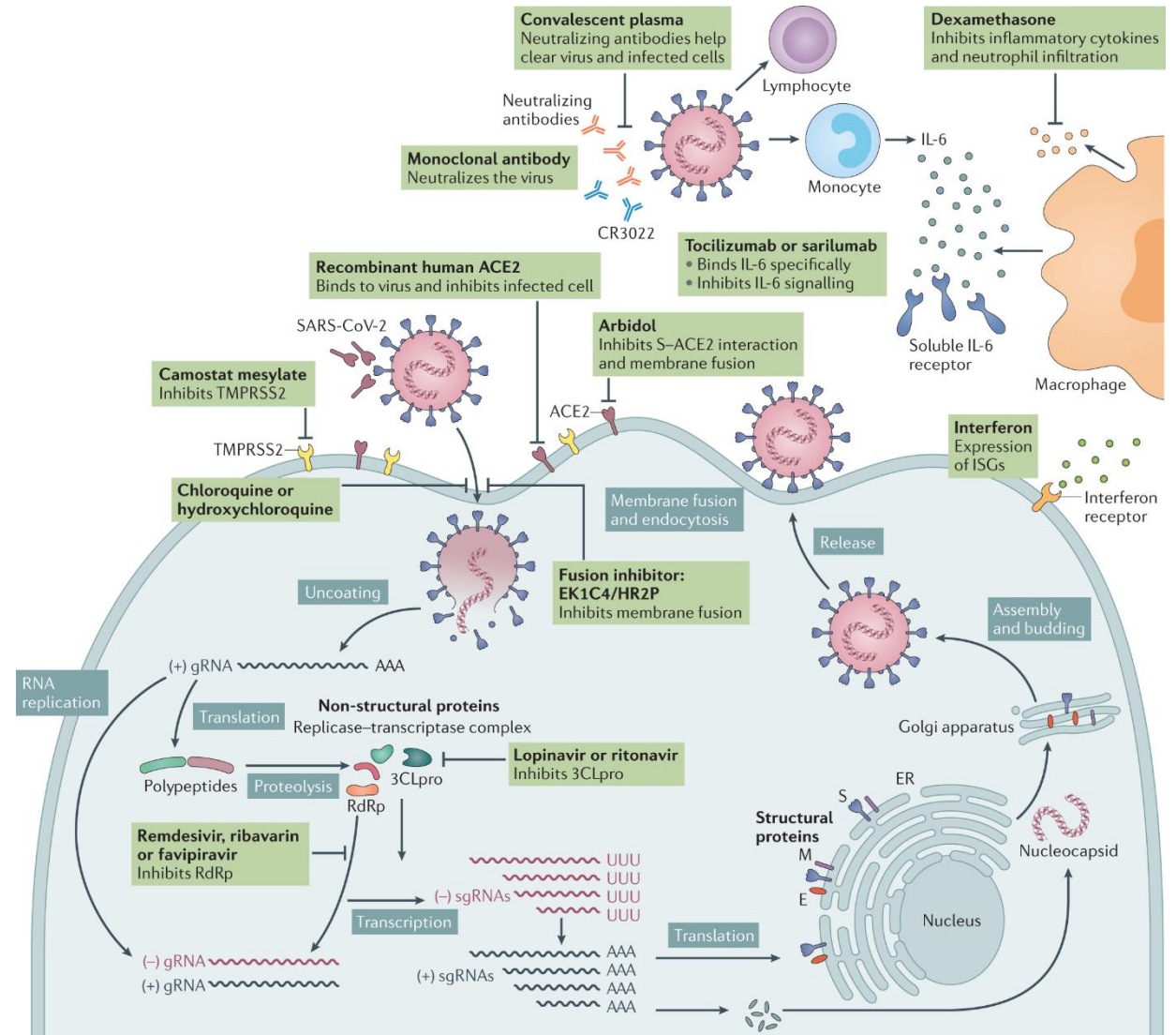
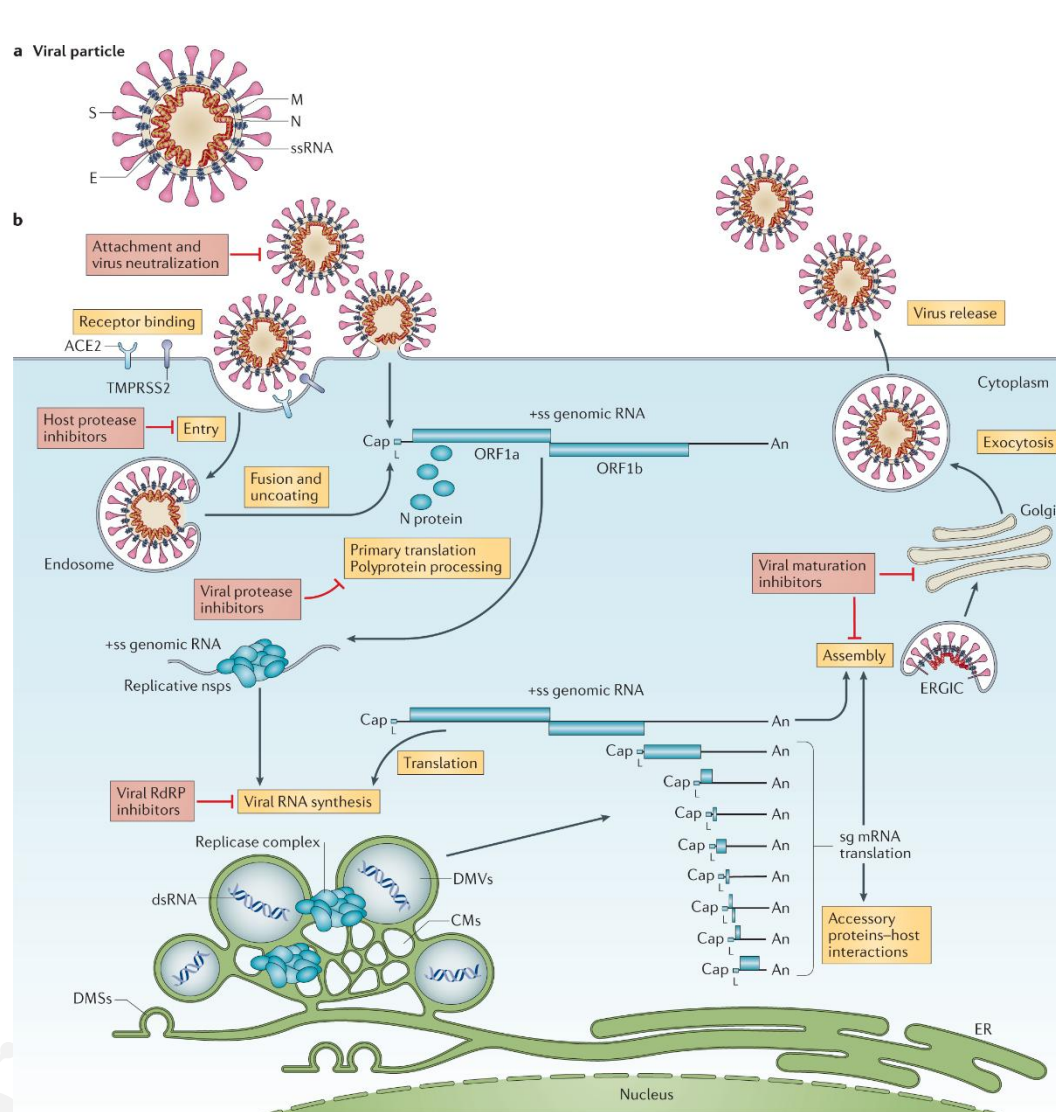
## SARS-CoV-2 Cellular Internalization and Intracellular Processes



# SARS Coronavirus 2: Biology



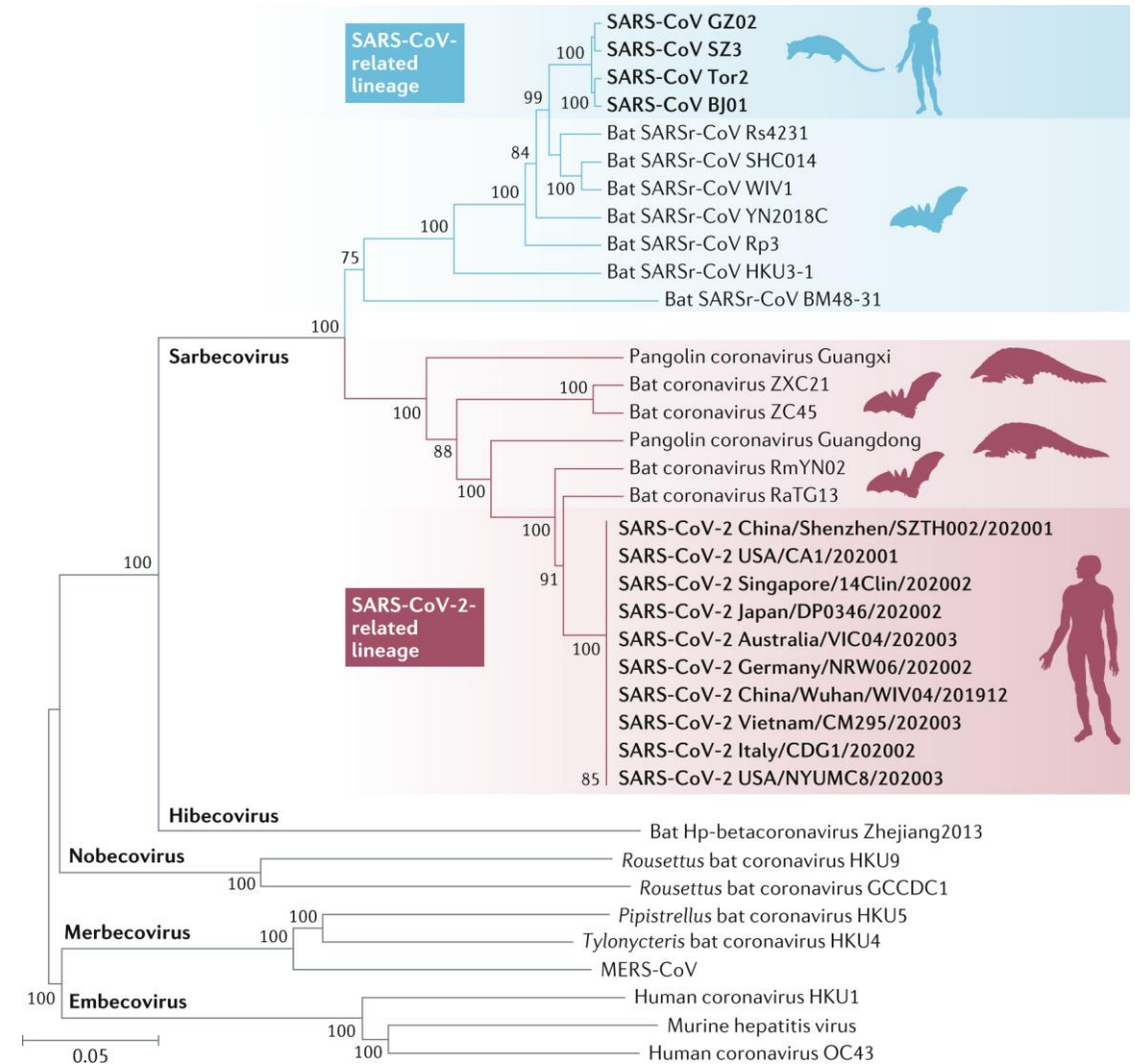
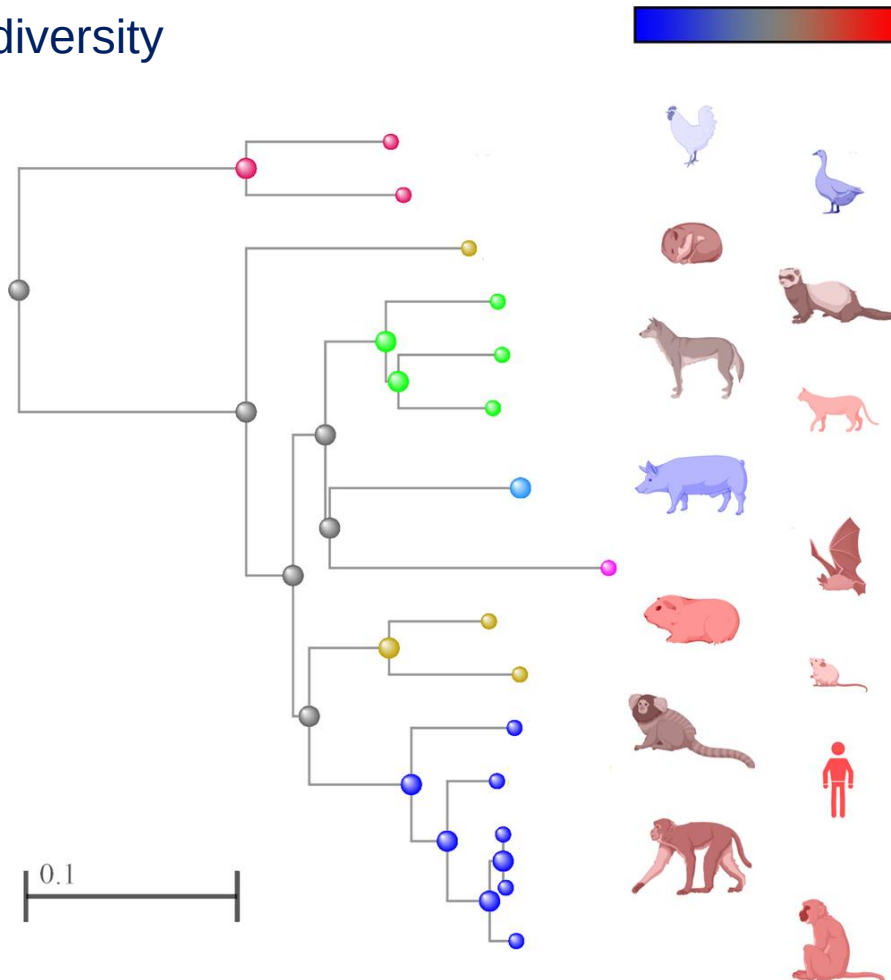
# SARS Coronavirus 2: Biology



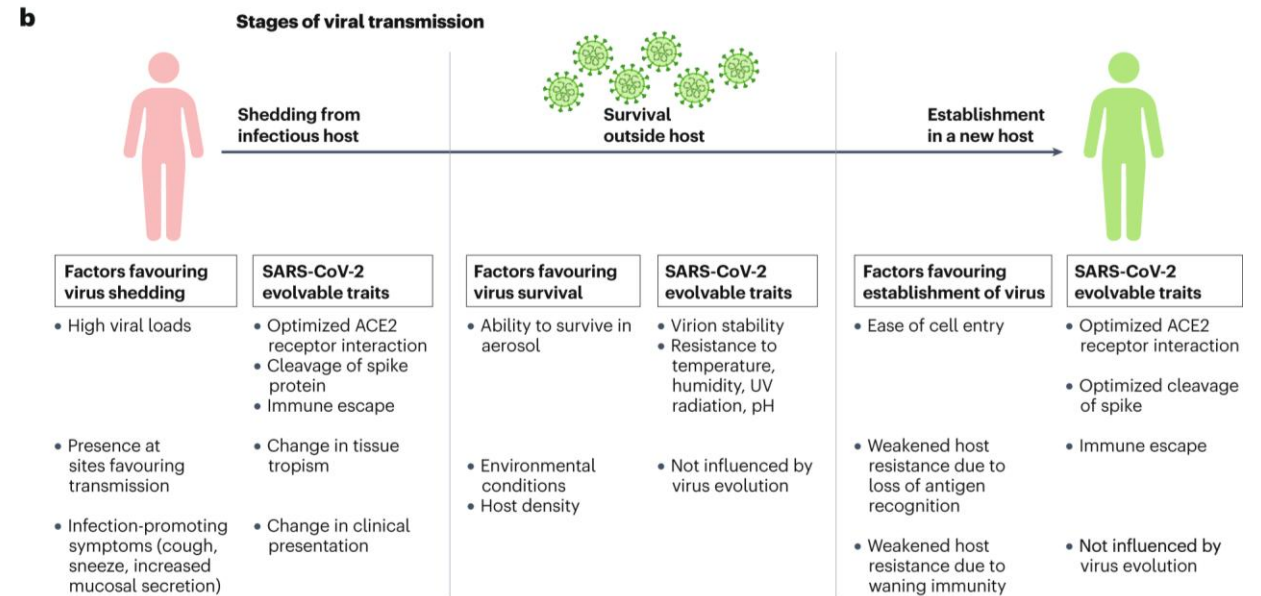
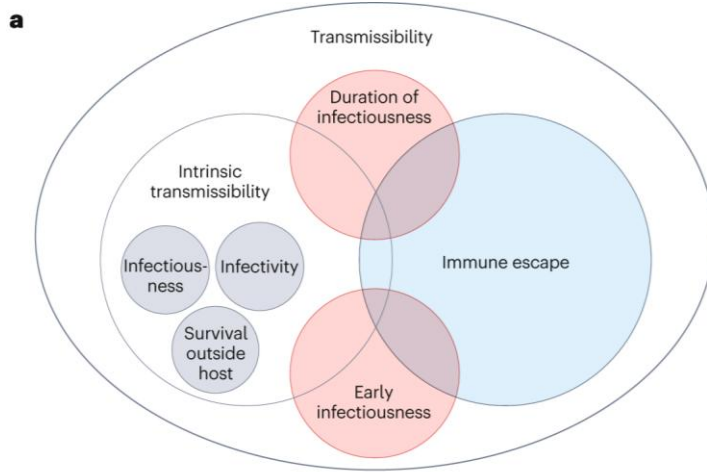


# SARS Coronavirus 2: Distribution

## ACE2 diversity



# SARS Coronavirus 2: Distribution

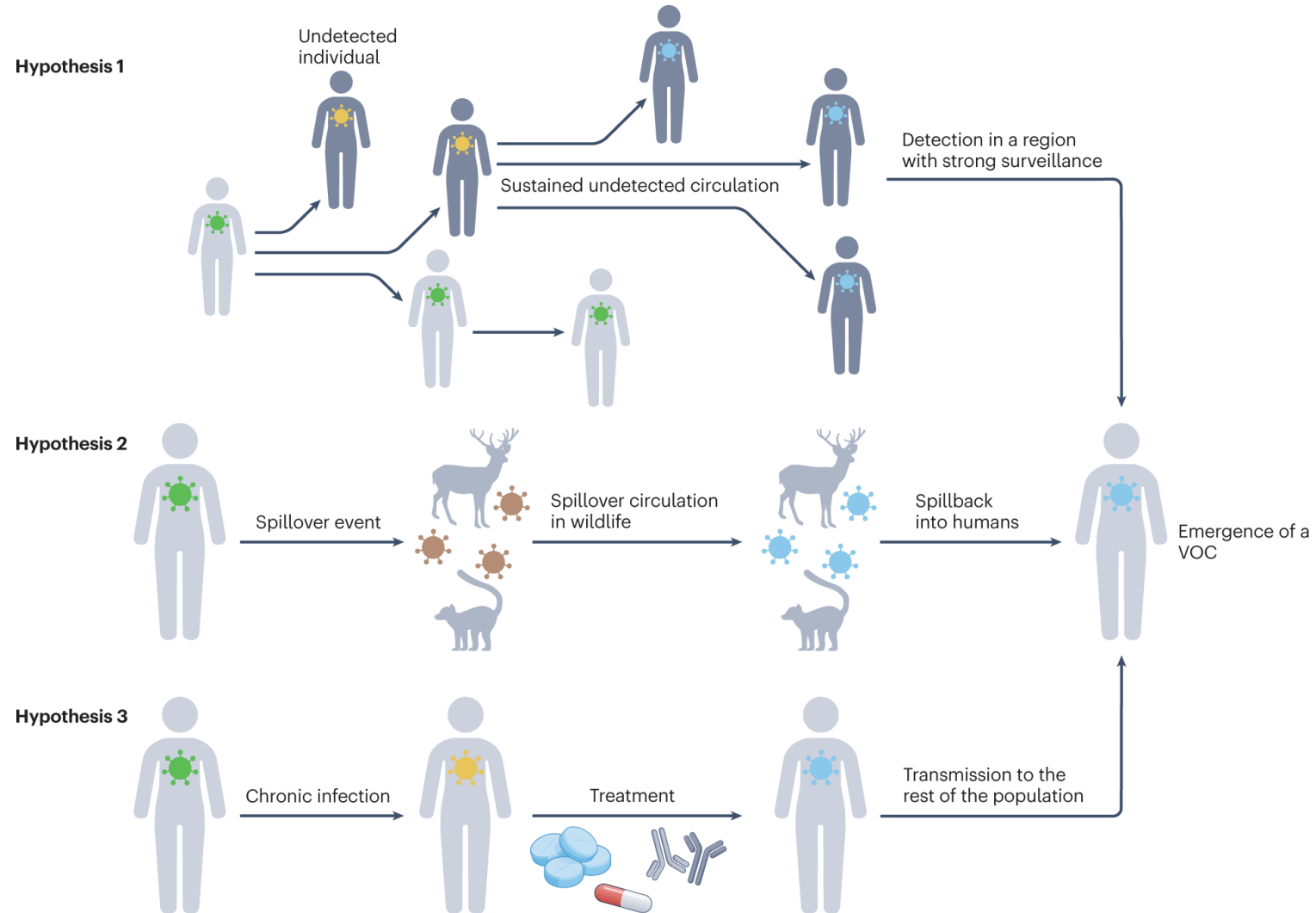


**c**

| 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                               | ✓                                              | ✓     | ✗                   | ✓                      | ✓                       | ✓ <sup>a</sup> /✗ | ✓                    | ✓                 |
| Duration of infectiousness                               | ✓                                              | ✓     | ✗                   | ✓                      | ✓                       | ✓ <sup>a</sup> /✗ | ✓                    | ✓                 |
| Early onset of infectiousness                            | ✗                                              | ✗     | ✓                   | ✓                      | ✓                       | ✓ <sup>a</sup> /✗ | ✓                    | ✓                 |
| Immune escape                                            | ✗                                              | ✓     | ✗                   | ✓                      | ✓                       | ✓                 | ✓                    | ✓                 |

✓ = Effect ✗ = No effect

# SARS Coronavirus 2: Distribution





# 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 |      |      |      |      |      |      |      |      |      |      |     |

# We're forgetting something - 🤔

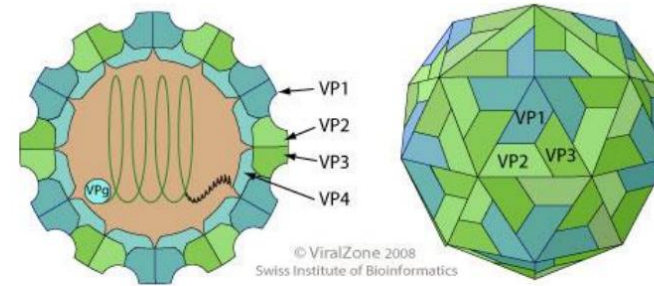
| Pathogen                   | Virus            | Genome     |
|----------------------------|------------------|------------|
| Influenzavirus             | Orthomyxoviruses | ss (-) RNA |
| Respiratory Syncytialvirus | Pneumoviruses    | ss (-) RNA |
| HumanesMetapneumovirus     | Pneumoviruses    |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



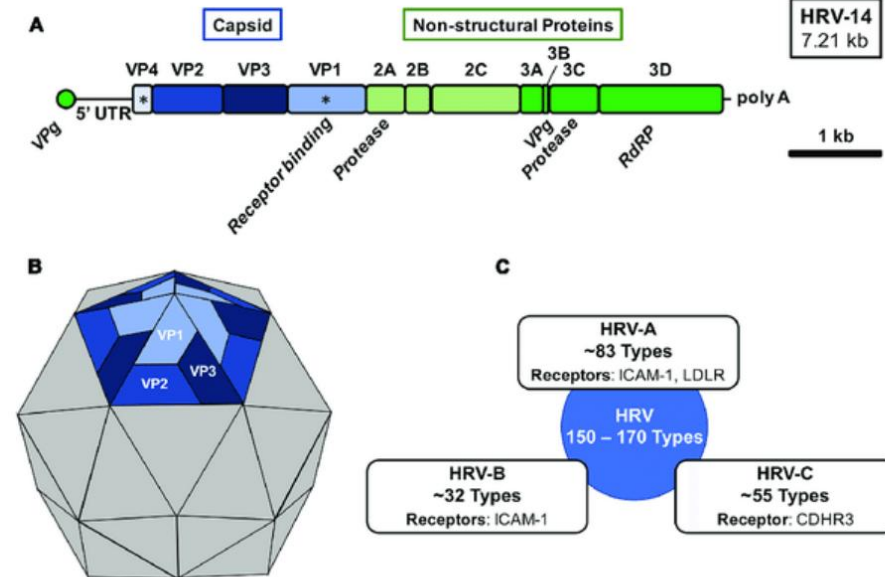
The cast:  
Pulp afflictions  
“we badass too”

# Picornaviridae - Human Rhinovirus (HRV)

|                              |                                                                                                                                                          |
|------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Family</b>                | Picornaviridae                                                                                                                                           |
| <b>Genus</b>                 | Enterovirus                                                                                                                                              |
| <b>Genotypes / Serotypes</b> | 3 Genotypes <ul style="list-style-type: none"> <li>• HRV-A (~83 Serotypes)</li> <li>• HRV-B (~32 Serotypes)</li> <li>• HRV-C (~ 55 Serotypes)</li> </ul> |
| <b>Genome</b>                | 7.2 kb; (+)ssRNA; non-enveloped (icosahedric capsid)                                                                                                     |
| <b>Target cells</b>          | Epithel-, Endothel-, Mucosal cell, Fibroblasts, Lymphocytes, Monocytes / Macrophages                                                                     |



- **Genotype?** Genomic differences
- **Serotype?** Surface antigen

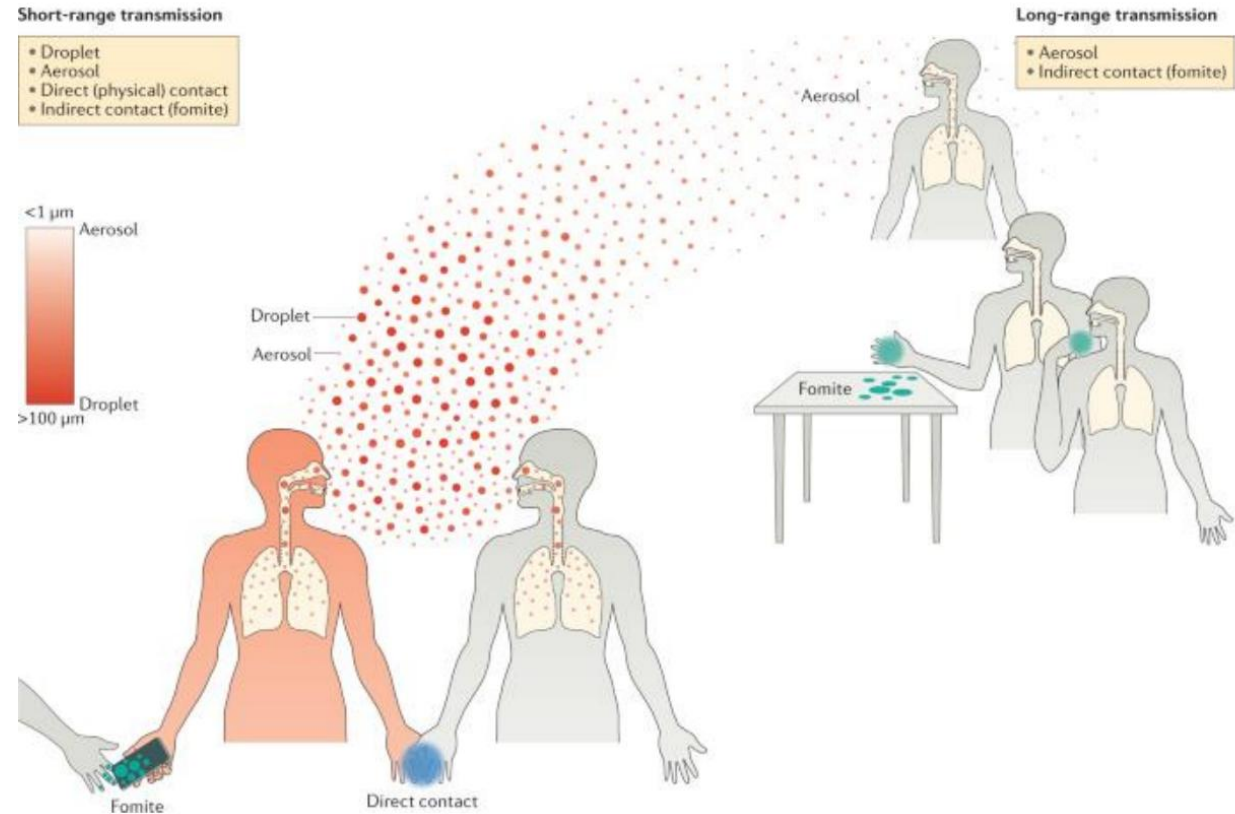
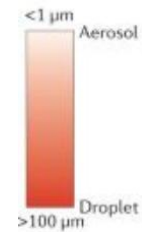


# Picornaviridae - Human Rhinovirus (HRV)

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

## Short-range transmission

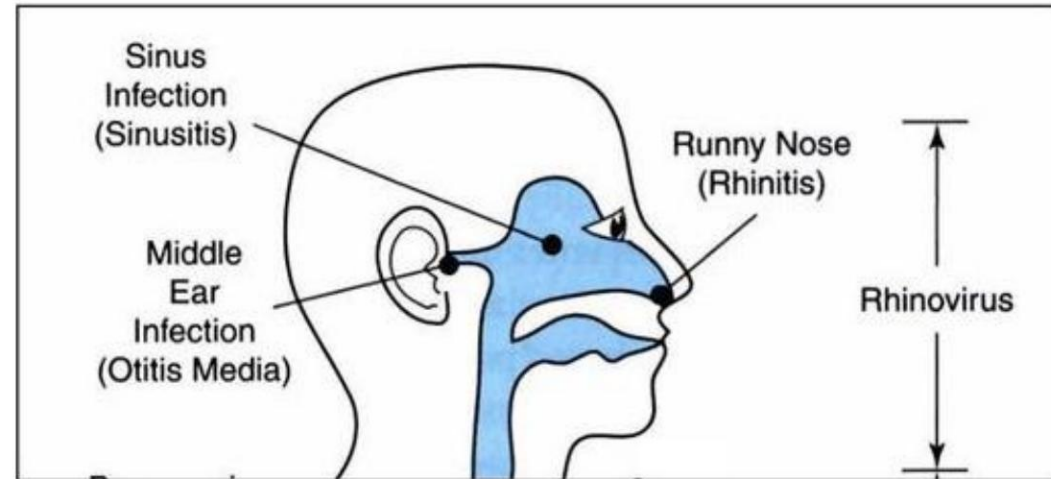
- Droplet
- Aerosol
- Direct (physical) contact
- Indirect contact (fomite)



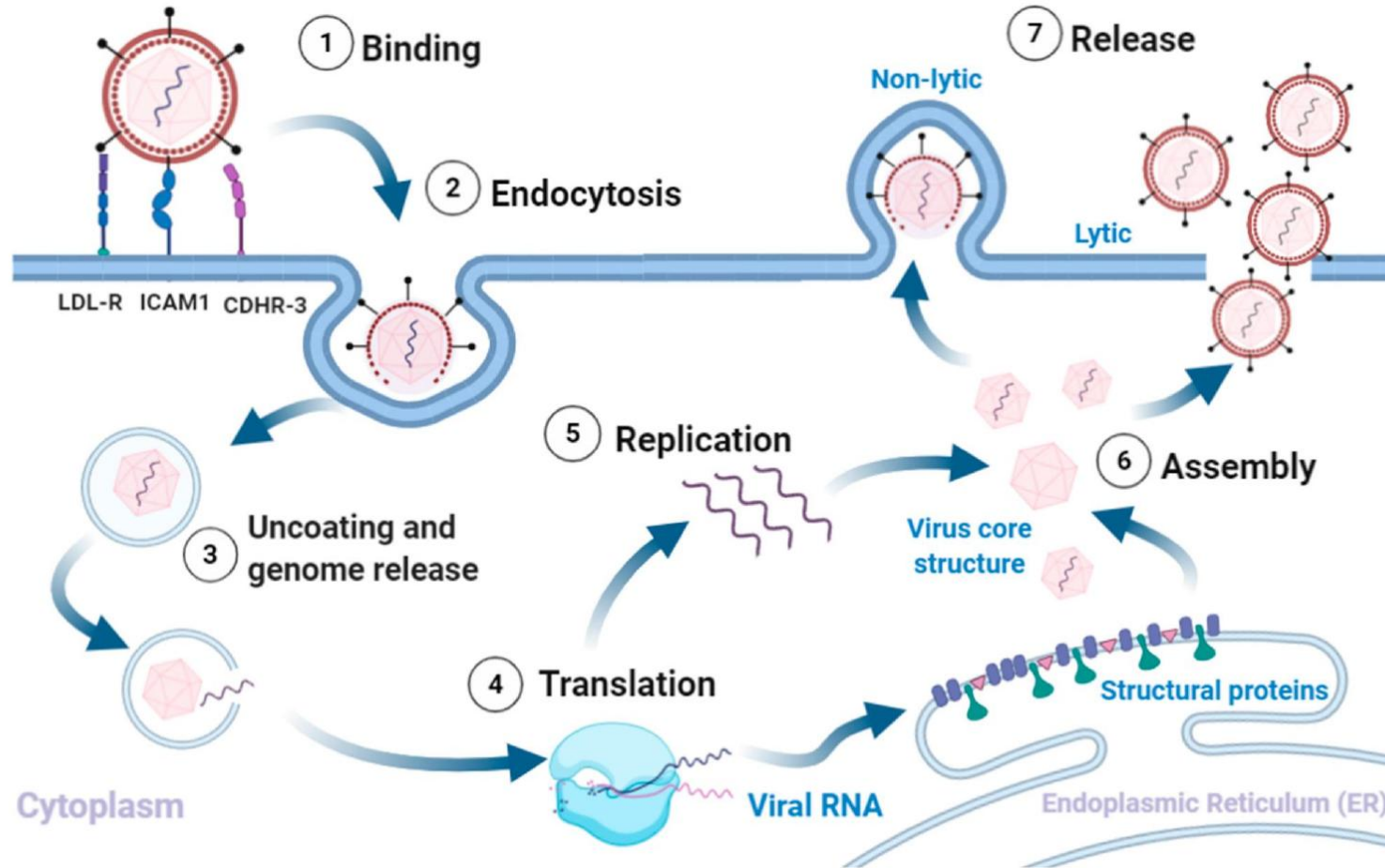


# Picornaviridae - Human Rhinovirus (HRV)

|                     |                                                                                                                                                                                                                                                                                                                                                                           |
|---------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Clinic</b>       | Common cold (e.g. fever, cough, runny nose)                                                                                                                                                                                                                                                                                                                               |
| <b>Pathogenesis</b> | <p>Focal destruction of the epithelium</p> <ul style="list-style-type: none"> <li>• Strictly localized</li> <li>• Inflammatory reaction of nasal mucous membrane</li> <li>• Vessels become permeable, fluid escapes</li> <li>• Nasal mucous membrane swells up</li> <li>• Breathing through the nose restricted</li> <li>• Often secondary bacterial infection</li> </ul> |
| <b>Diagnosis</b>    | Not performed                                                                                                                                                                                                                                                                                                                                                             |
| <b>Therapy</b>      | Symptomatic                                                                                                                                                                                                                                                                                                                                                               |
| <b>Prophylaxis</b>  | Hygienic measures                                                                                                                                                                                                                                                                                                                                                         |

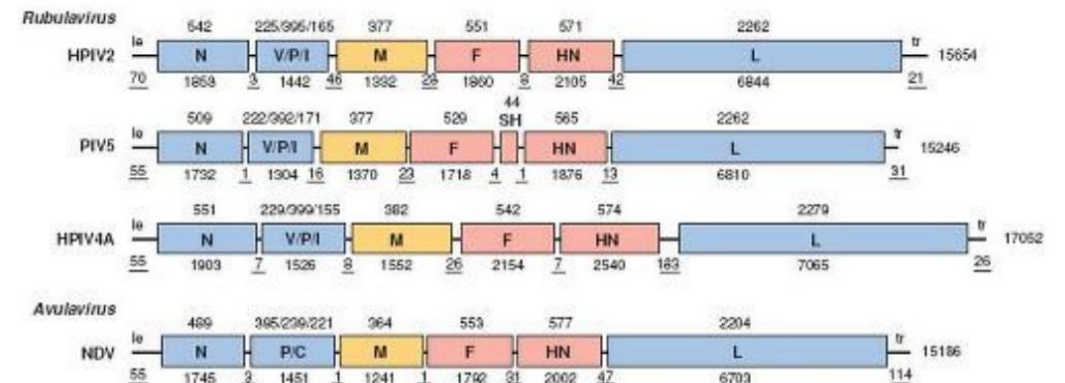
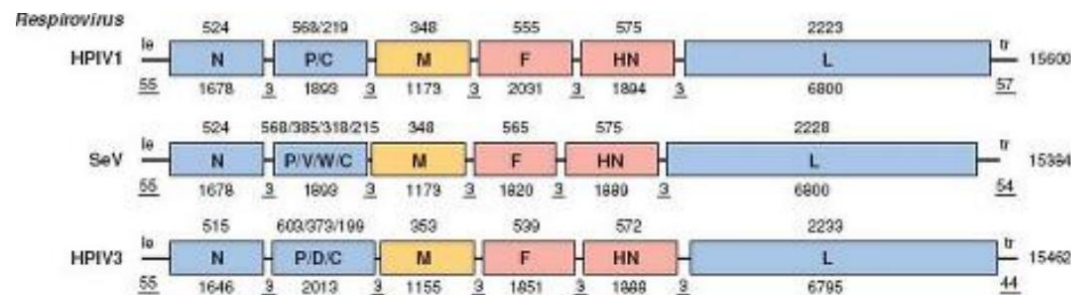
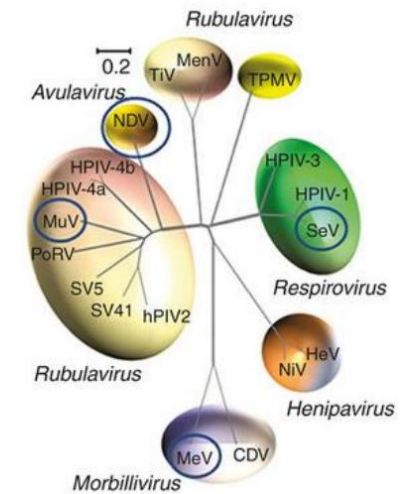


# Picornaviridae - Human Rhinovirus (HRV)



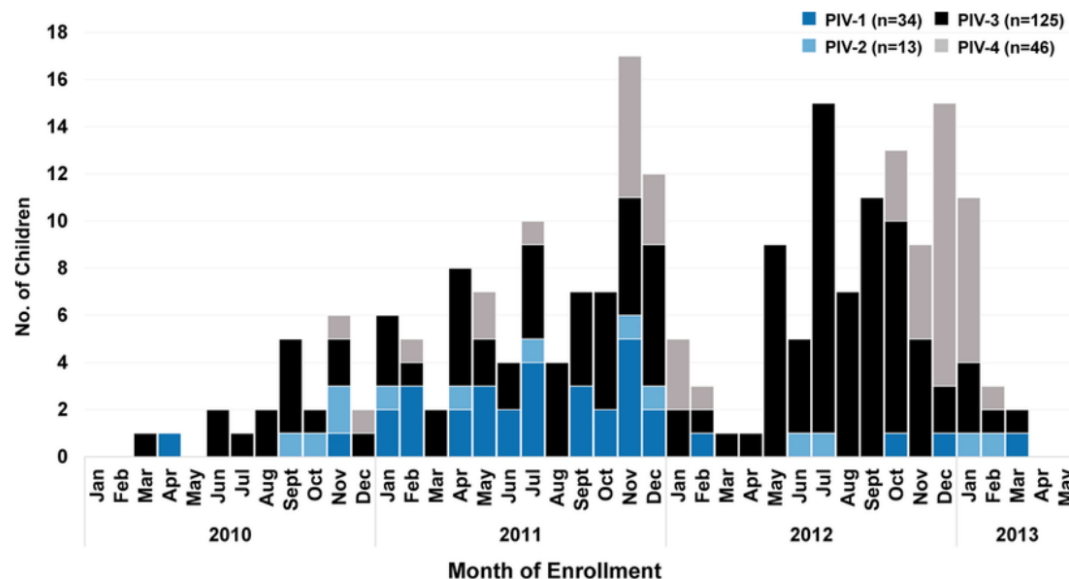
# Paramyxoviridae

|               |                              |                                                |
|---------------|------------------------------|------------------------------------------------|
| <b>Genus</b>  | 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)                        |
| <b>Genome</b> | 15-18kb; (-)ssRNA; enveloped |                                                |



# Paramyxoviridae: Parainfluenza virus

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

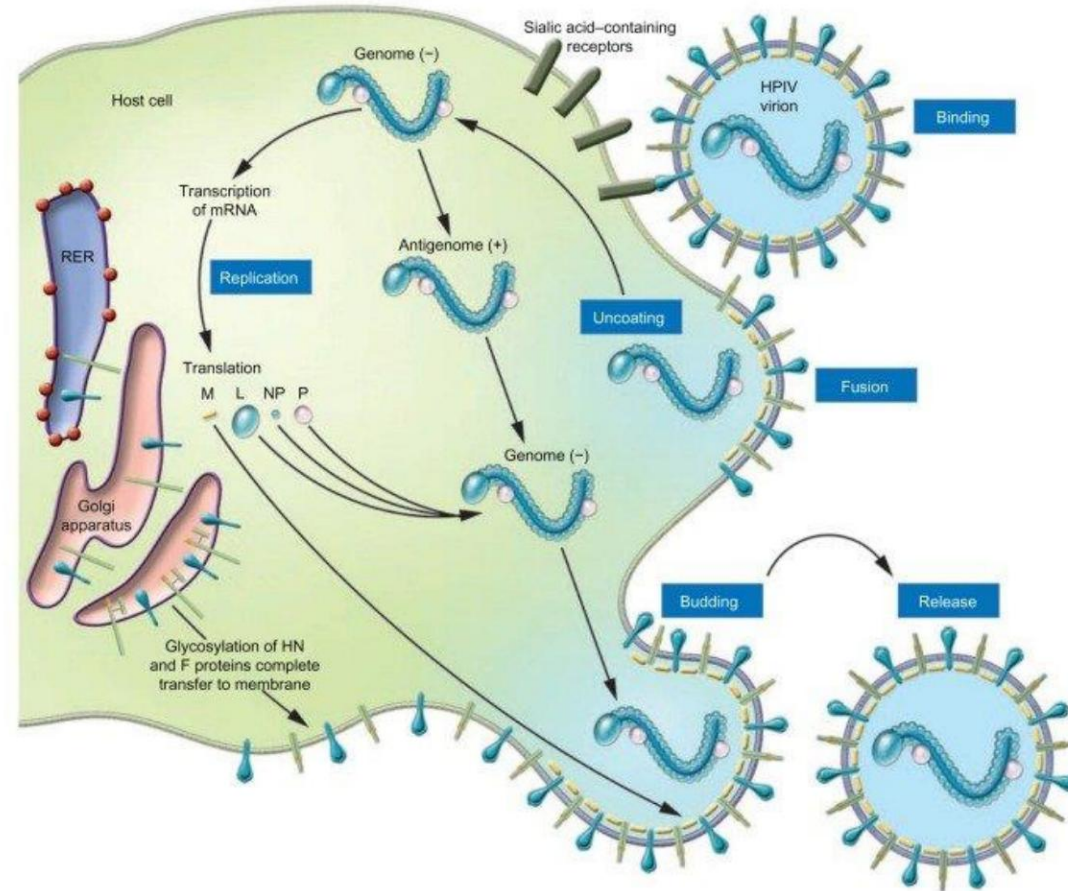
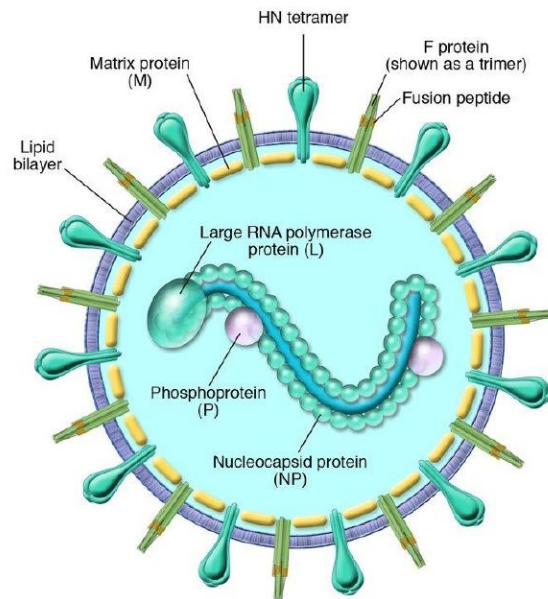
# Paramyxoviridae: Parainfluenza virus

|                           |                                                                                                                                                                                                                                                                                                                                                                                                        |
|---------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Pathogenesis</b>       | <ul style="list-style-type: none"> <li>• Infection of the mucous membranes of the nasopharynx</li> <li>• it can spread to the entire tracheobronchial space.</li> <li>• An infection generally triggers inflammation and releases cytokines such as interferon-gamma and TNF-alpha.</li> <li>• In small children, the build-up of mucus can lead to an obstruction of the airways</li> </ul>           |
| <b>Incubation periode</b> | 2-4 days                                                                                                                                                                                                                                                                                                                                                                                               |
| <b>Klinik</b>             | <ul style="list-style-type: none"> <li>• One of the major causes of lower respiratory tract infections in young children</li> <li>• Respiratory problems in children (rhinitis, cough, fever, laryngitis, tonsillitis and pseudocroup (HPIV-1), more rarely as pneumonia)</li> <li>• Bacterial superinfections are common</li> <li>• Re-infection possible, usually leads to mild illnesses</li> </ul> |
| <b>Diagnosis</b>          | Mostly clinically<br>Direct detection possible                                                                                                                                                                                                                                                                                                                                                         |
| <b>Therapy</b>            | Symptomatic, severe courses Ribavirin                                                                                                                                                                                                                                                                                                                                                                  |
| <b>Prophylaxis</b>        | Hygienic measures                                                                                                                                                                                                                                                                                                                                                                                      |





# Paramyxoviridae: Parainfluenza virus

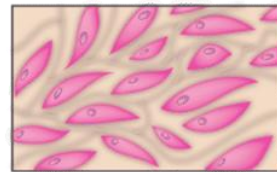
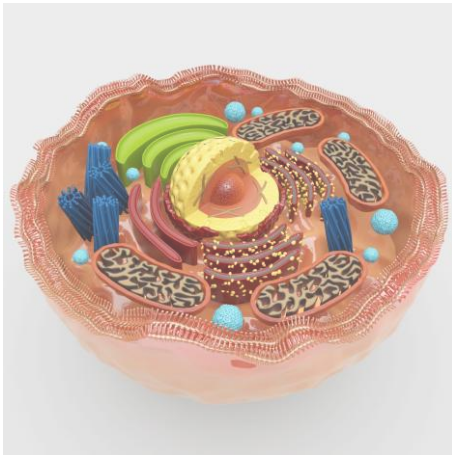


# Thank you for your attention



# What is viral tropism

- Capability of an infectious virus to infect:



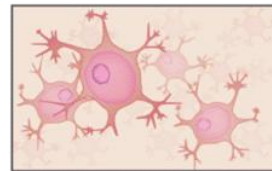
Connective tissue



Epithelial tissue



Muscle tissue



Nervous tissue

