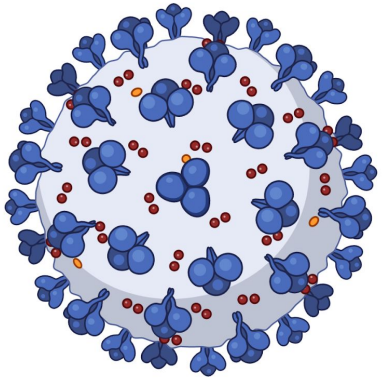
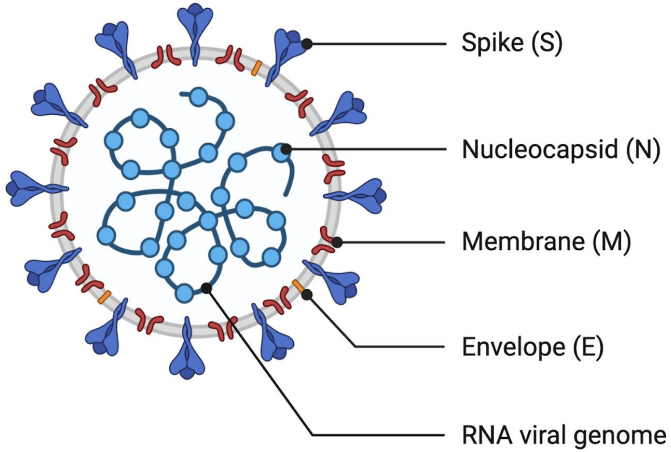
Pathogenesis and Transmission of SARS-CoV-2

Kyle Cordeiro, Karol Derech, Cailyn Eley, Shahithra Kirubalingam, Abigail Oladesu

SARS-CoV-2



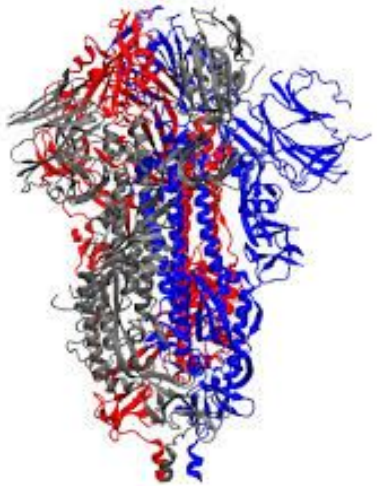


Characteristics

- Betacoronavirus
- Zoonotic
- Made of structural & non-structural proteins

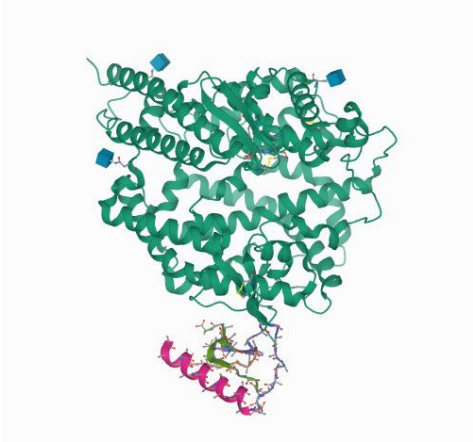
The Protein Data Bank H.M. Berman, J. Westbrook, Z. Feng, G. Gilliland, T.N. Bhat, H. Weissig, I.N. Shindyalov, P.E. Bourne (2000)
Nucleic Acids Research, **28**: 235-242. doi:10.1093/nar/28.1.235

SARS-CoV-2 Spike Protein



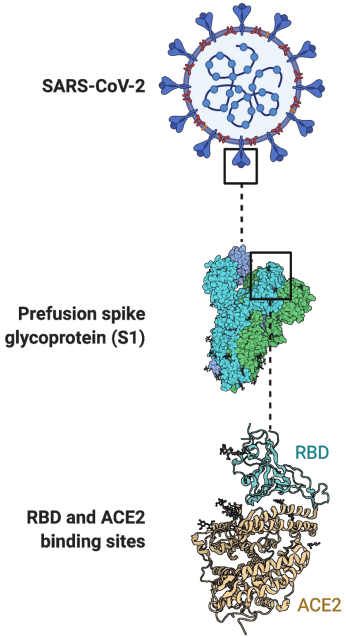
- N-terminal S1 domain binding subunit
- T-terminal S2 membrane fusion subunit
- Trimer of S1/S2 subunits
- Cleavage by ACE2 causes conformational change

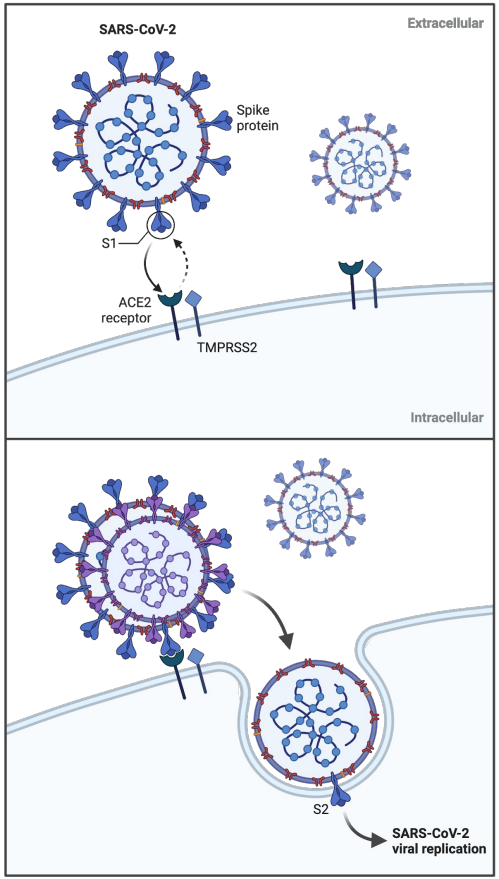
Angiotensin Converting Enzyme 2 (ACE2)



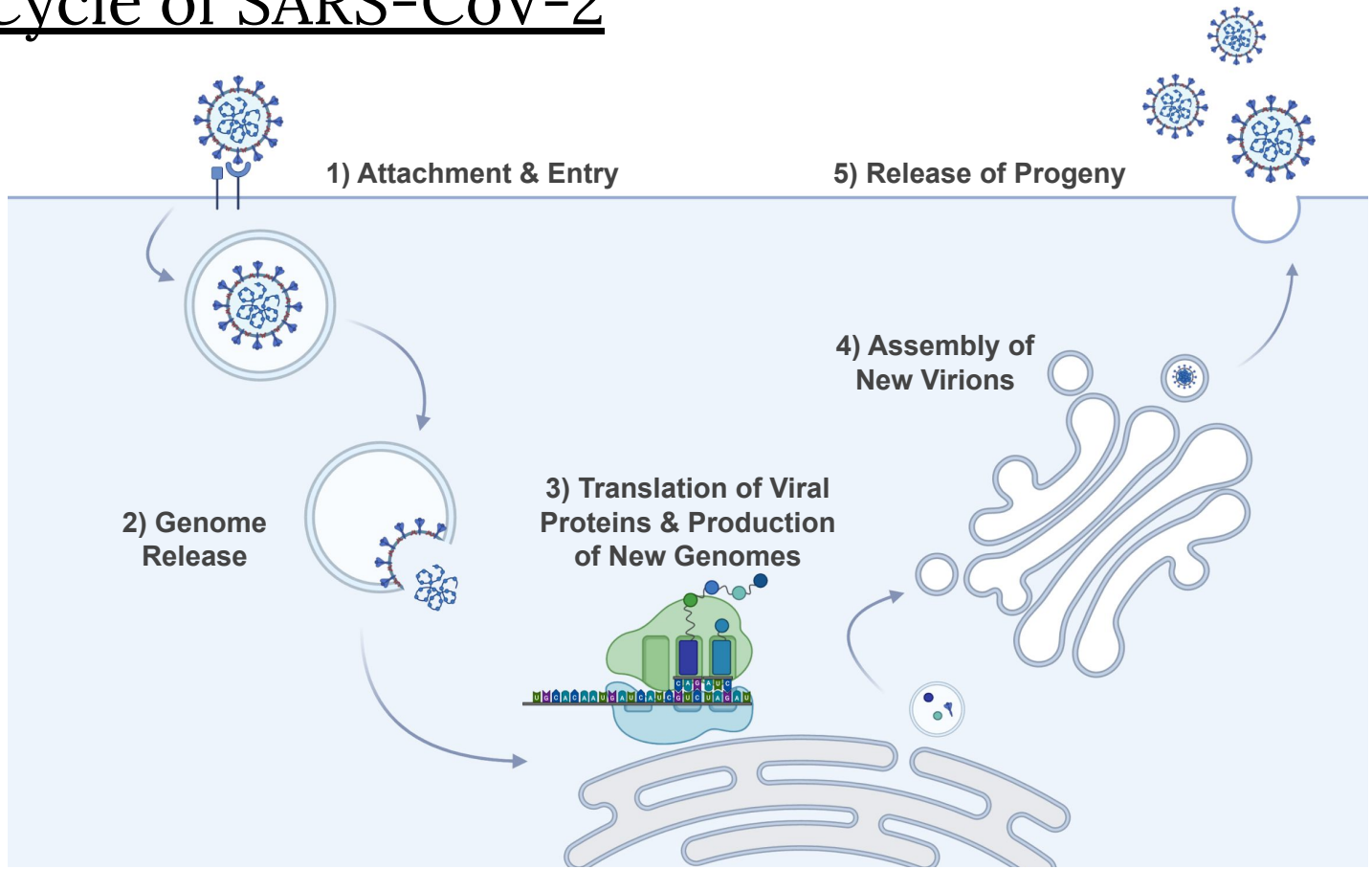
- Functional receptor of SARS-CoV-2
- Found on epithelial of lung and small intestine
- Functions as RAS attenuator
  - Cleaves one AA from angiotensin II
- Required for SARS-CoV-2 entry

Lock and Key Mechanism



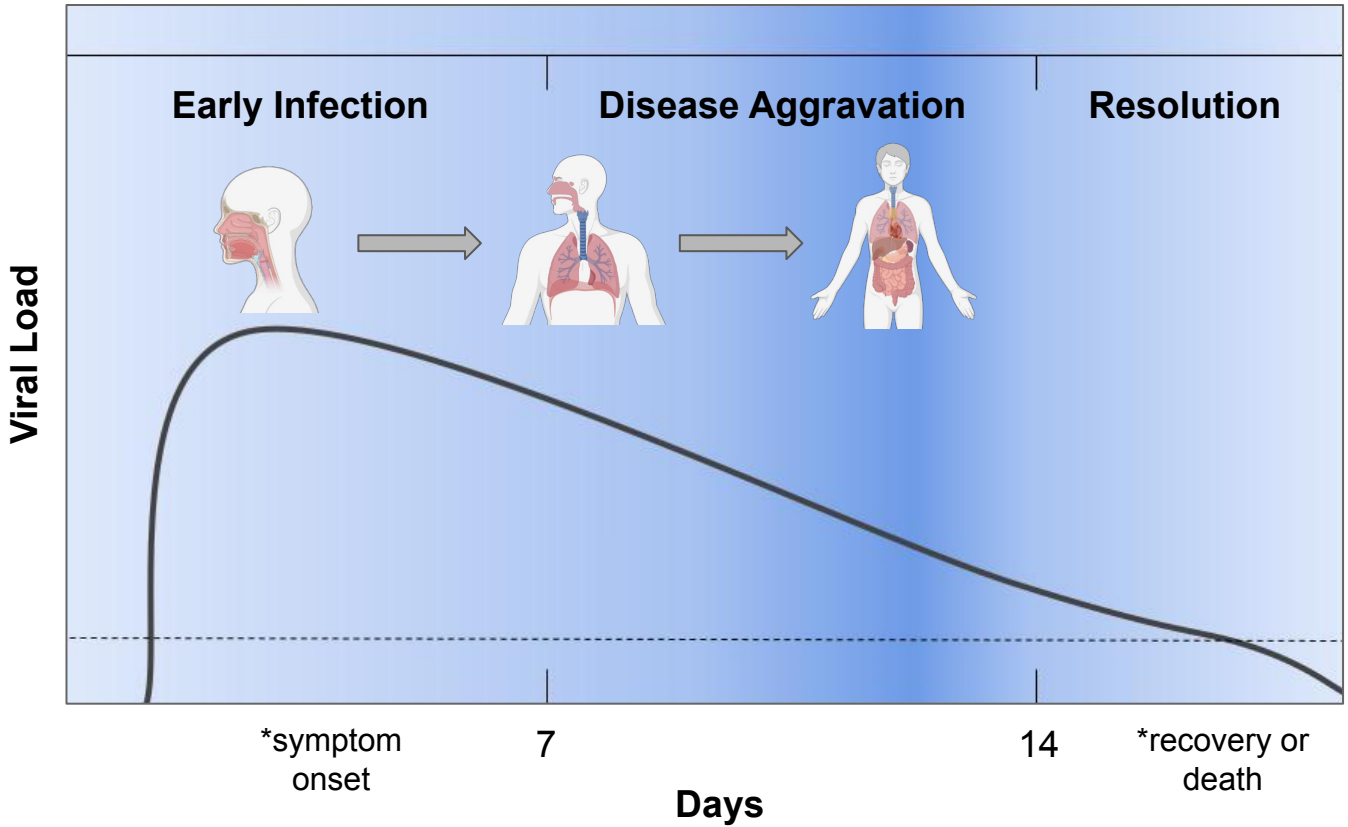


Life Cycle of SARS-CoV-2

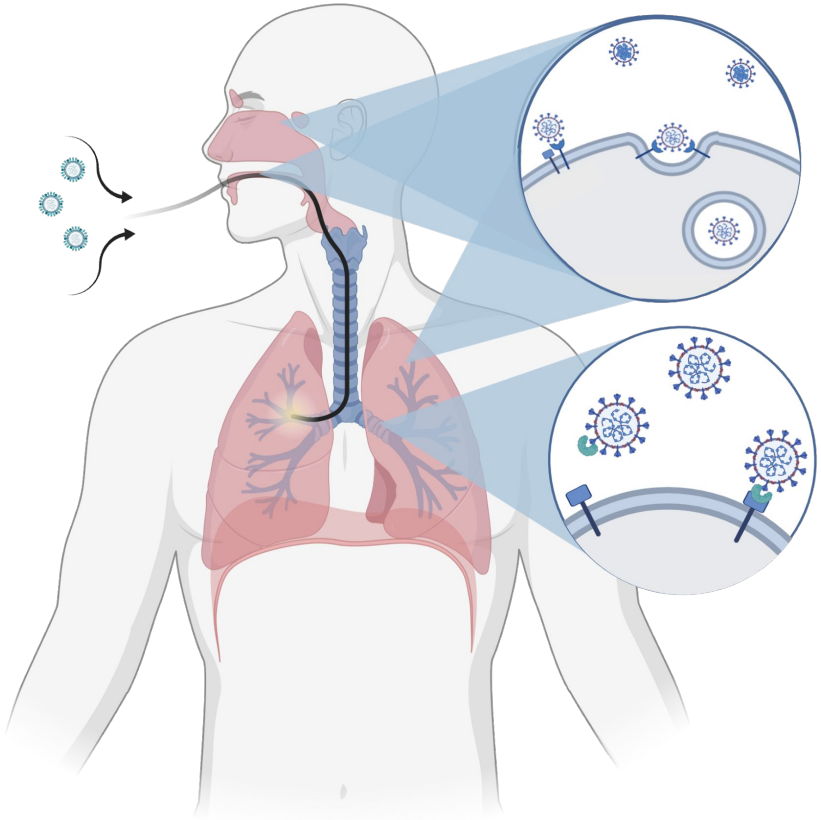


Adapted from: Acosta, M. A. T., & Singer, B. D. (2020). Pathogenesis of COVID-19-induced ARDS: implications for an aging population. *European Respiratory Journal*. https://doi.org/DOI: 10.1183/13993003.02049-2020
Image Created with BiorRender.com

SARS-CoV-2 Pathogenesis: Overview



Progression of COVID-19: Early Infection



DAYS 0-7

First Cells Attacked

- Oral and Nasal
- Alveolar
- Bronchial

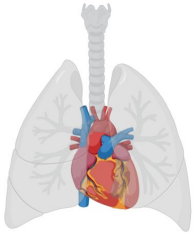
Onset of Symptoms (5-7 days)

- Loss of Taste and Smell
- Cough
- “Flu-like”

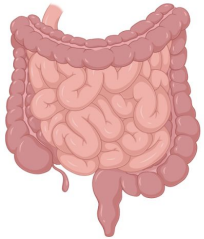
Progression of COVID-19: Disease Aggravation

DAYS 7-14

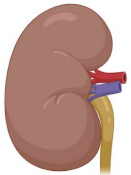
Viremia
SARS-CoV-2 enters the circulation



Cardiac & Pulmonary
- Myocardial injury
- Hypoxemia
- Lung infiltrates



Gastrointestinal
- Nausea
- Anorexia



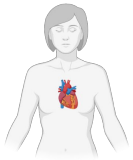
Renal
- Kidney injury
- Proteinuria

Progression of COVID-19: Resolution

DAYS 14+

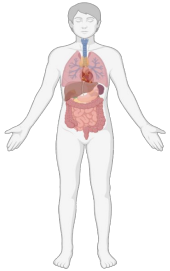
	Recover	Succumb
Inflammation	↓	↑
Tissue Repair	↑	↓

Potentially Fatal Complications



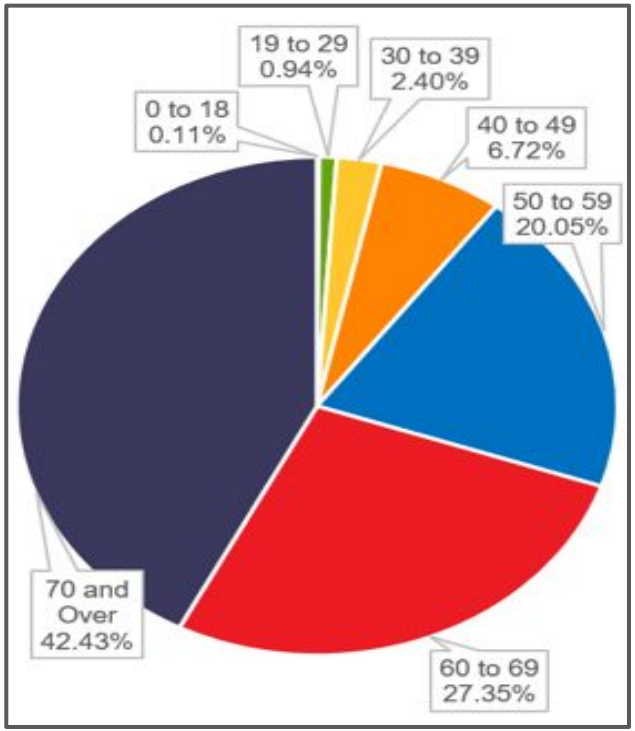
Cardiac Arrest

Acute Respiratory Distress Syndrome (ARDS)

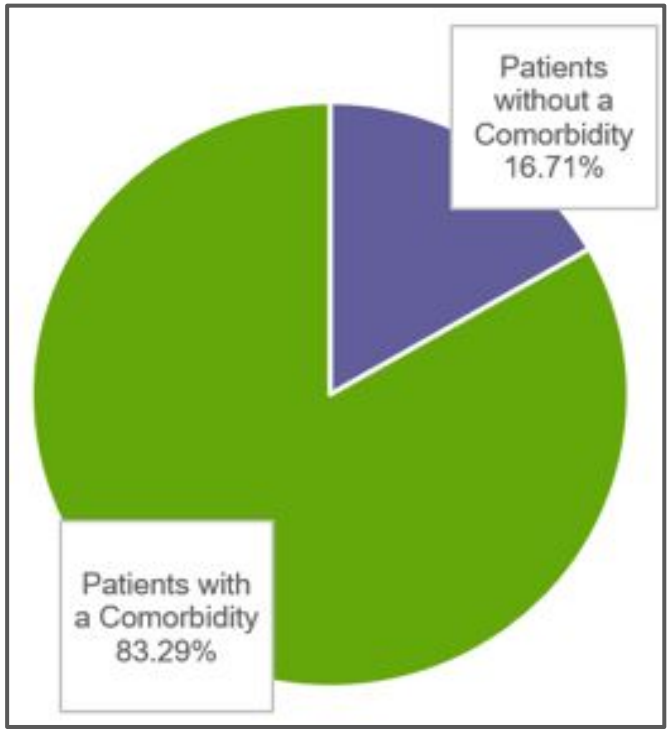


Multiple-Organ Failure

What Factors Contribute to a Fatal Outcome?

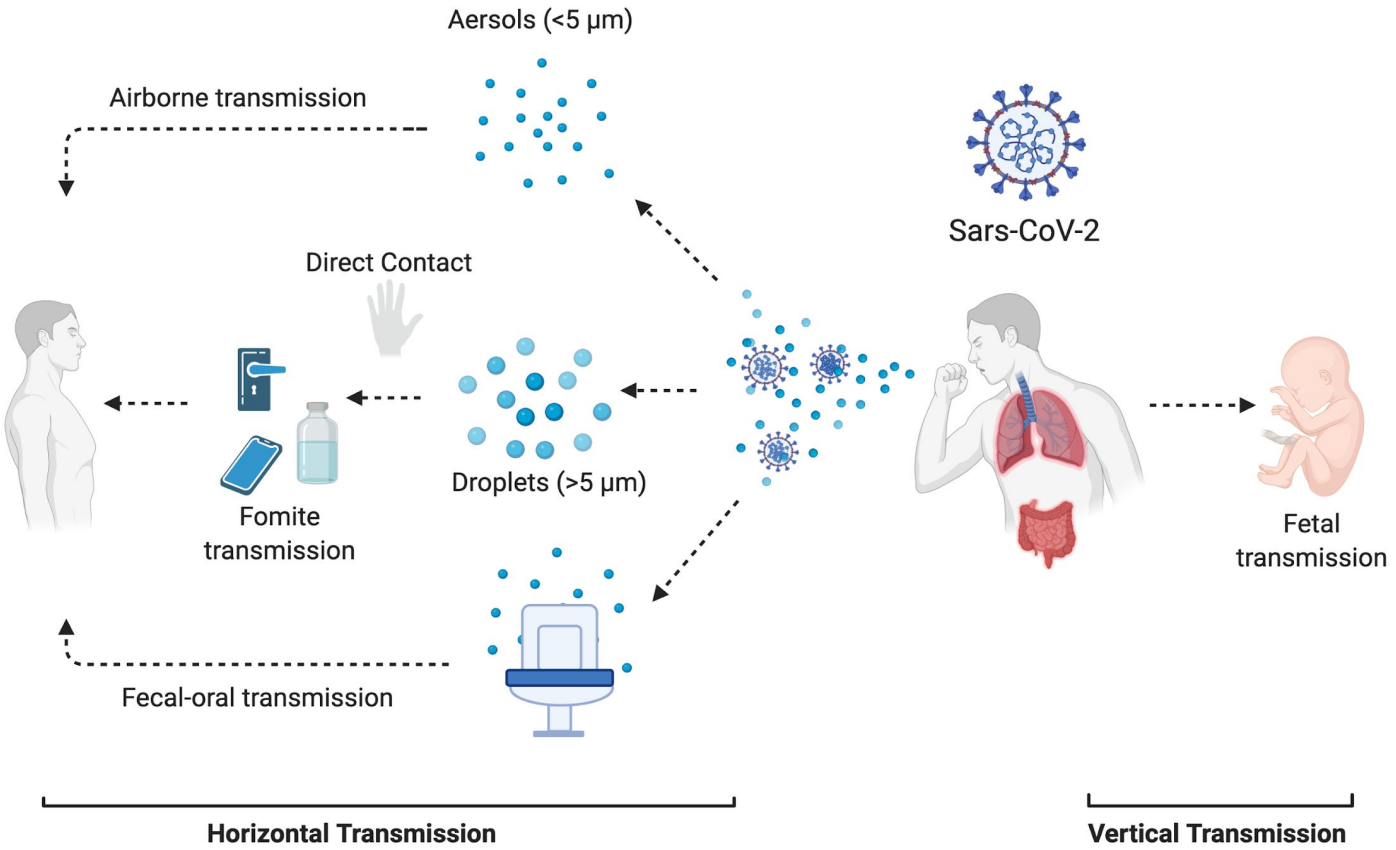


COVID-19 Death Toll by Age

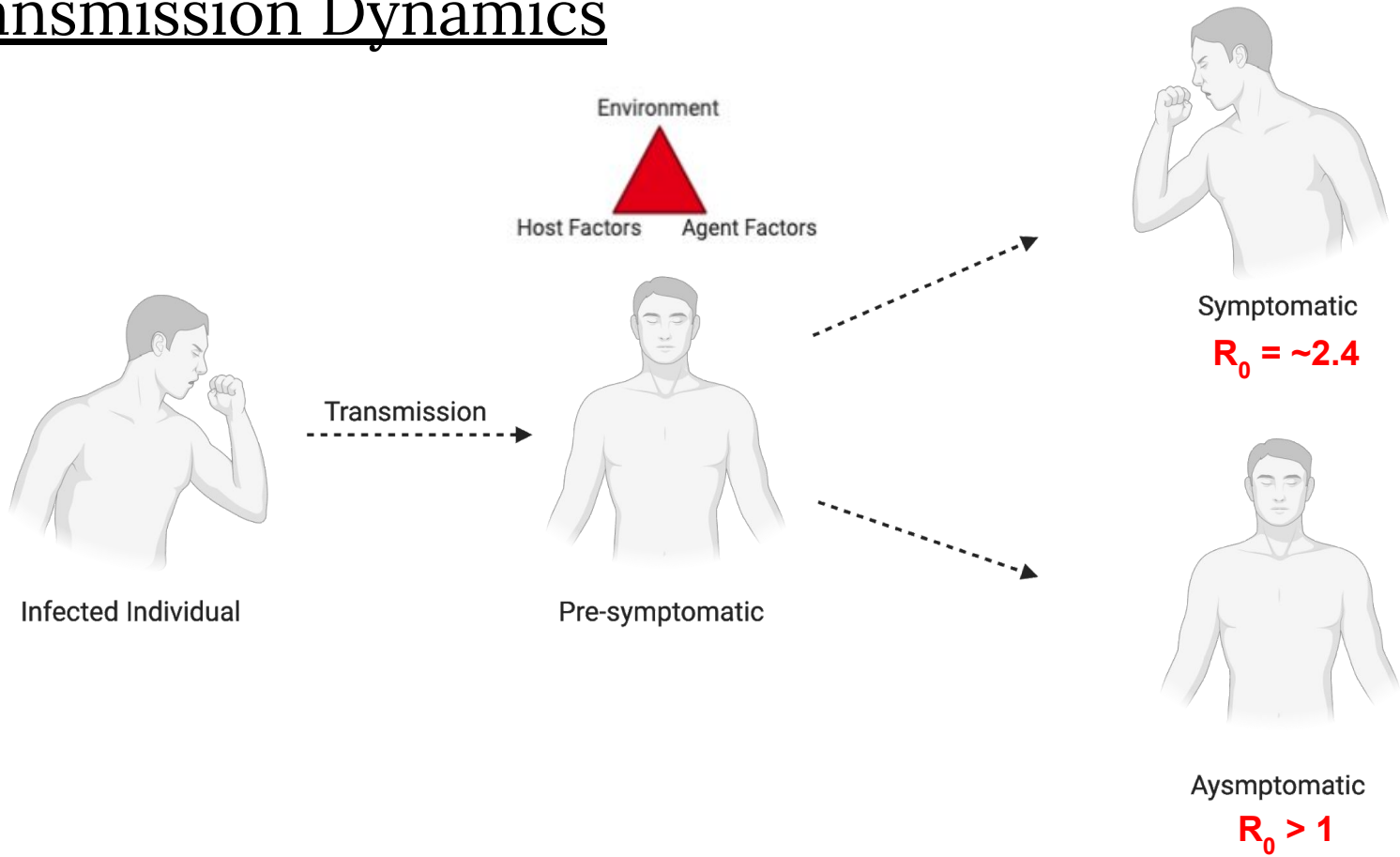


COVID-19 Deaths by Comorbidity Presence

Modes of Transmission

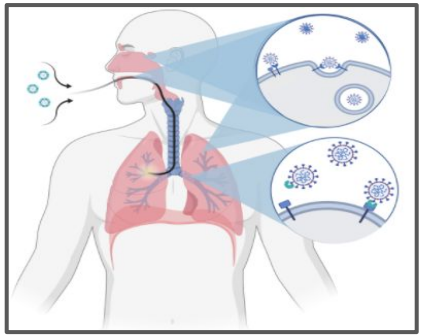


Transmission Dynamics

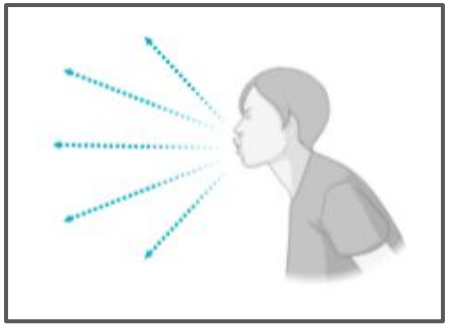


Challenges and Future Implications

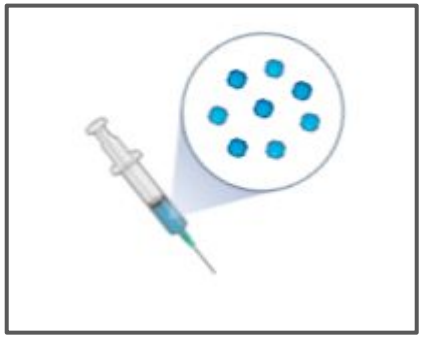
Discovering Viral Mechanism of Pathogenesis



Understanding Transmission Dynamics



Identifying Therapeutic Targets



Testing Preventative Measures

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Transgenic hACE2 Mouse Model

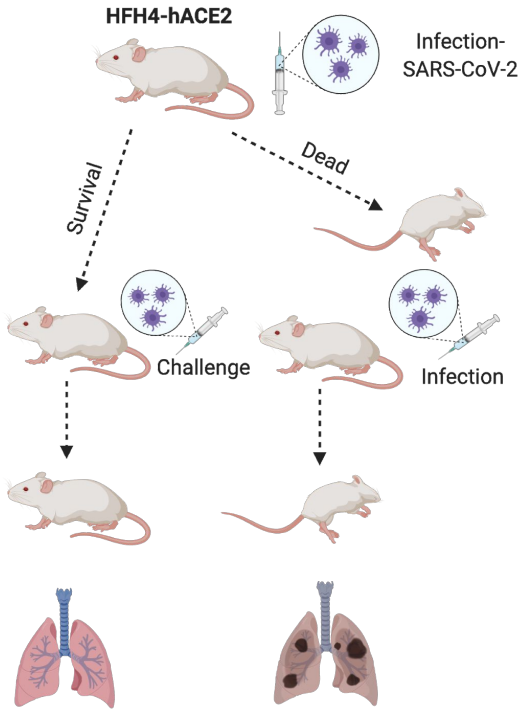
Cell

Volume 182, Issue 1, 9 July 2020, Pages 50-58.e8

Article

Pathogenesis of SARS-CoV-2 in Transgenic Mice Expressing Human Angiotensin-Converting Enzyme 2

Ren-Di Jiang [1, 2, 5], Mei-Qin Liu [1, 2, 5], Ying Chen [1, 2, 5], Chao Shan [1], Yi-Wu Zhou [3], Xu-Rui Shen [1, 2], Qian Li [1, 2], Lei Zhang [1], Yan Zhu [1], Hao-Rui Si [1, 2], Qi Wang [1], Juan Min [1], Xi Wang [1, 2], Wei Zhang [1], Bei Li [1], Hua-Jun Zhang [1], Ralph S. Baric [4], Peng Zhou [1] ... Zheng-Li Shi [1, 6]



Thank you for listening

Now we will be taking questions

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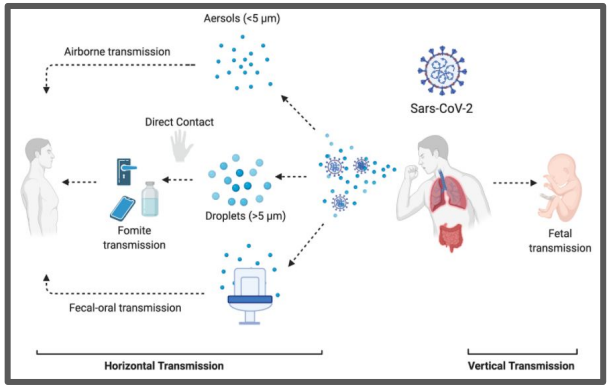
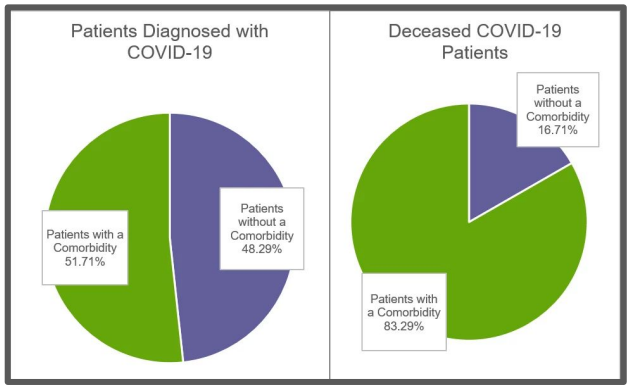
Supplemental Slides

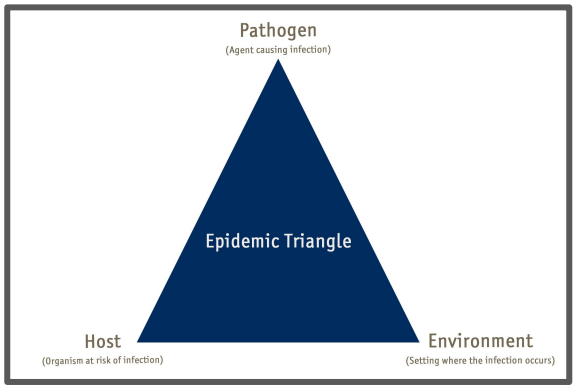
Challenges



Identify and Research Routes of Transmission

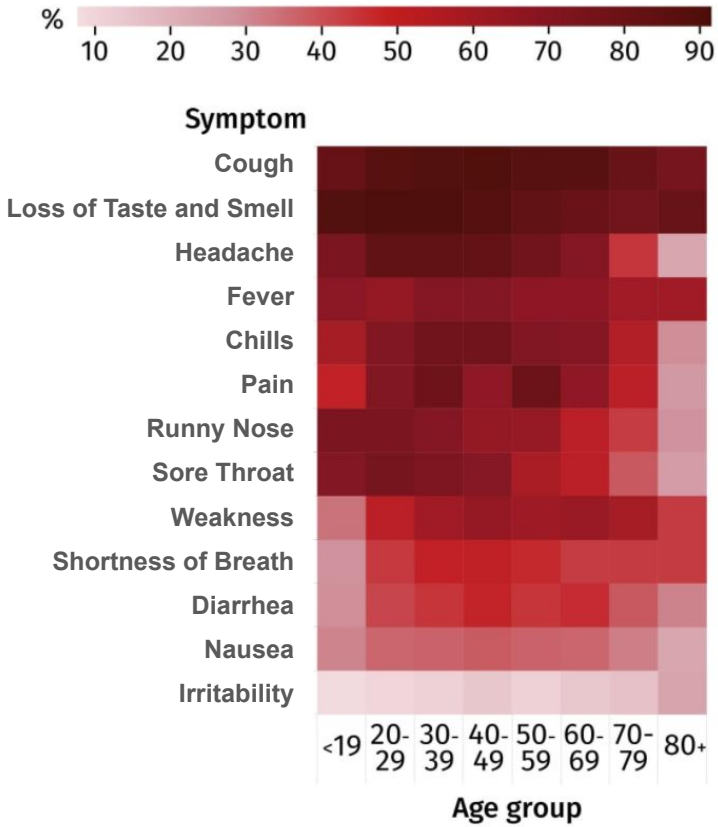


Gain insight on comorbidity effect



Epidemiologic triad

Differences Amongst Age Groups



COVID-19 Transmission