



Determinants of Life-Threatening COVID-19



Alyssa Evangelista

College Park Scholars – Science & Global Change Program

Physiology and Neurobiology

aevangel@umd.edu

College Park Scholars Academic Showcase, April 30, 2021

1. Introduction

Since the early days of the COVID-19 pandemic, it has been well known that certain comorbidities, such as diabetes, obesity, and being of old age, increase the likelihood of contracting life-threatening COVID-19. However, reports of young, healthy people being hospitalized and dying were unexpected and terrifying. Thus, the focus of this project is to determine what leads to this outcome for people who do not seem to be high-risk, as well as propose potential screening methods for identifying these individuals.

2. Research Topic

- The main idea of this research: The genetic and environmental factors that influence the severity of COVID-19
- The question to be answered: How do the genetic and environmental factors interact and affect the immune system's response to SARS-CoV-2?
- The significance of this research: Information on what causes severe COVID-19 can be used to determine who is more vulnerable and assess the risk of a patient contracting severe COVID-19.

3. Research Method

My research method has been to gather relevant sources on this topic and analyze their findings. Most of these sources are either clinical studies or literature reviews that analyze trends. In order to better understand these sources, I have also gathered background information on cellular signaling in the immune system.

4. Discussion of Findings

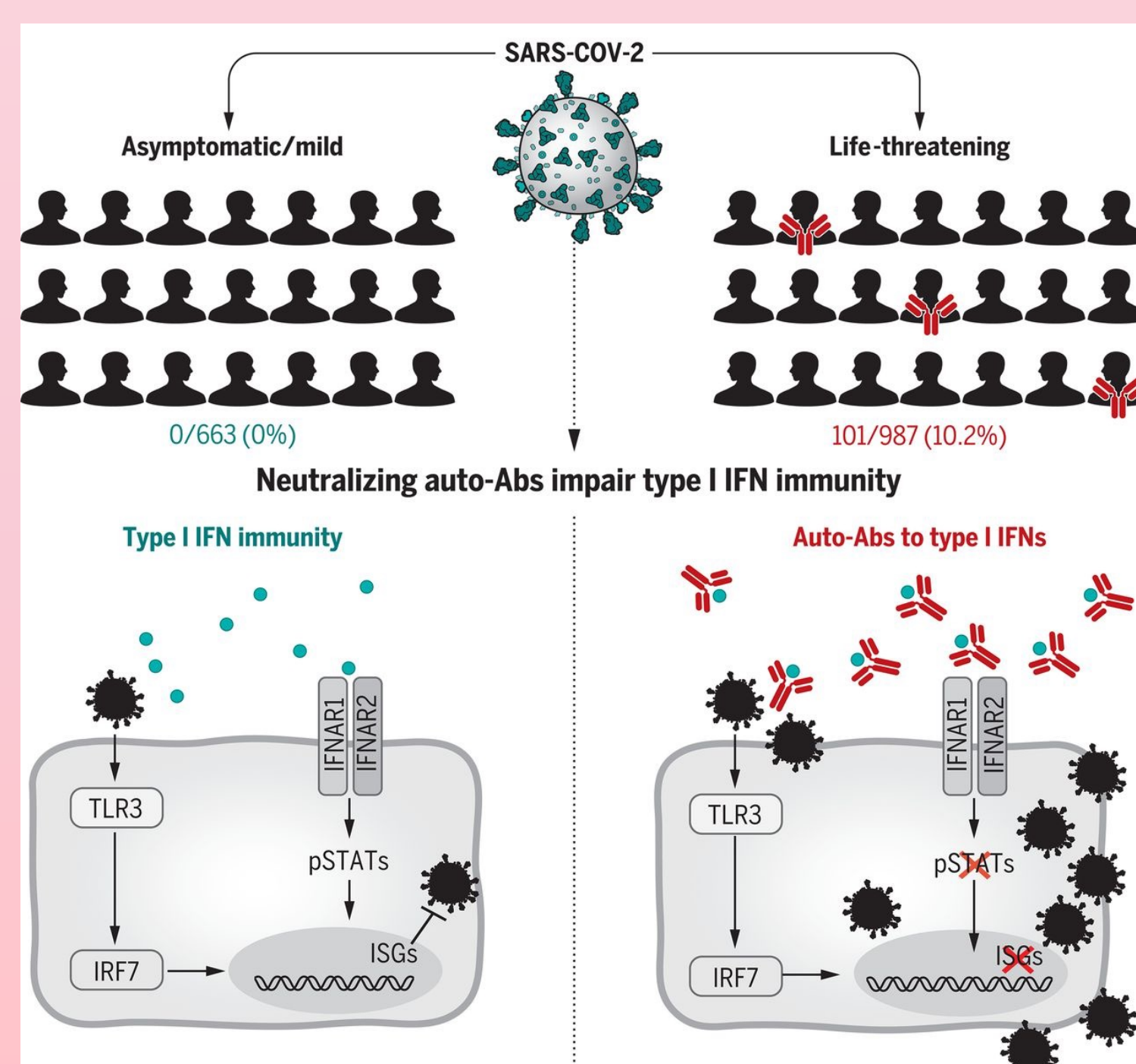


Figure 1. Graphic showing the intracellular signaling pathway in a normal immune response to SARS-CoV-2 (left) and how it is inhibited by auto-antibodies (right). Adapted from "Autoantibodies against type I IFNs in patients with life-threatening COVID-19," by Bastard et. al., 2020.

4. Discussion of Findings – cont.

- Genetic Factors
 - Some patients have auto-antibodies (auto-Abs) against type-I interferons (IFNs), which are crucial for fighting SARS-CoV-2 (Bastard et. al, 2020)
 - Auto-Abs also limit the expression of interferon-stimulated genes (ISGs), which are essential for mobilizing immune cells (Combes et. al., 2021)
- Environmental Factors
 - Higher COVID mortality rates and lower vitamin D levels in people living in higher latitudes (Rhodes et. al., 2020)
 - Higher exposure to SARS-CoV-2 increases the strength of the immune response and the chance of dangerous inflammatory responses (Wang et. al., 2020)
 - Vaccine hesitancy varies by community due to beliefs, income, past experiences, etc., and the chance of contracting severe COVID-19 increases in areas with more hesitancy (Khubchandani et. al., 2021)

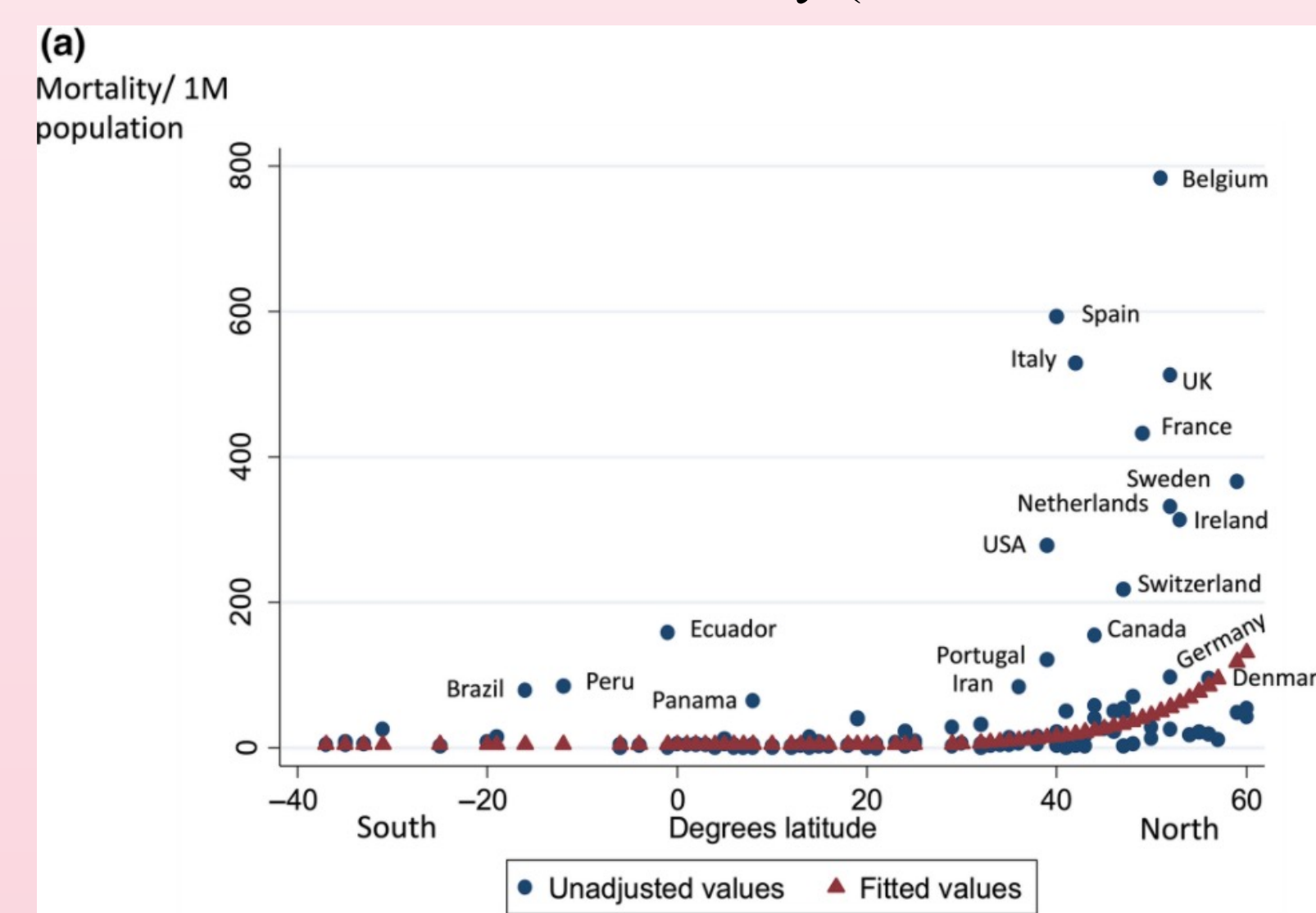
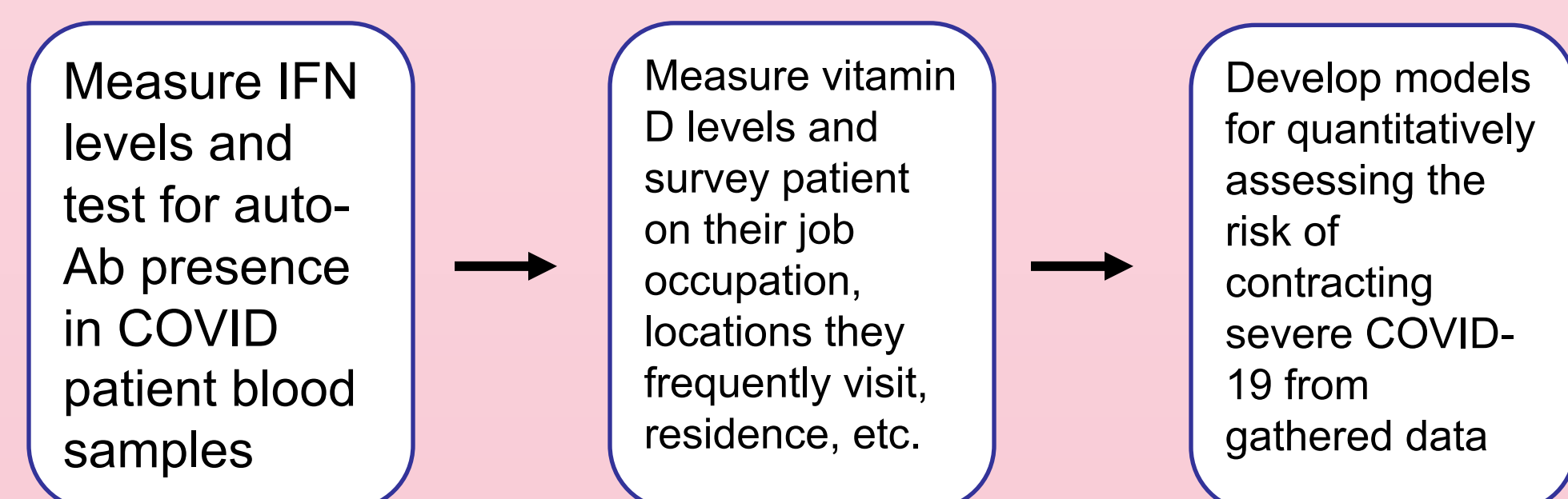


Figure 2. Graph plotting the COVID-19 mortality rates of several countries versus their latitudes. Mortality rate tends to increase with latitude. Adapted from "Vitamin D deficiency and COVID-19 severity – plausibly linked by latitude, ethnicity, impact on cytokines, ACE2 and thrombosis," Rhodes et. al., 2020.

5. Recommendations for Assessing Risks



6. Limitations and Future Work

Some limitations include not being able to conduct lab research and work with a team. Since there is also an abundant amount of information, as well as new information being released at a fast pace, it was difficult to narrow this topic down and focus on specific factors. Despite this, being able to conduct research on COVID-19 has helped me expand on prior knowledge from my coursework and educate myself and others about the pandemic. I have also become more interested in conducting lab research, which I hope to be able to do with other people to expand this project and develop a functional risk assessment.

References

Bastard, P., L.B. Rosen, Q. Zhang, et. al. 2020. [Autoantibodies against type I IFNs in patients with life-threatening COVID-19](#). *Science* 370(6515): eabd4584. doi: 10.1126/science.abd4584

Combes, A. J., T. Courau, N.F Kuhn, et. al. 2021. [Global absence and targeting of protective immune states in severe COVID-19](#). *Nature* 591: 124-130. doi 10.1038/s41586-021-03234-7

Khubchandani, J., S. Sharma, J.H Price, M.J. Wiblehauser, M. Sharma, and F.J. Webb. 2021. [COVID-19 Vaccine Hesitancy in the United States: A Rapid National Assessment](#). *Journal of Community Health* 46(2): 270-277. doi: 10.1007/s10900-020-00958-x

Rhodes, J. M., S. Subramanian, E. Laird, G. Griffin, and R.A. Kenny. 2020. [Vitamin D deficiency and COVID-19 severity – plausibly linked by latitude, ethnicity, impact on cytokines, ACE2 and thrombosis](#). *Journal of Internal Medicine* 289(1): 97-115. doi: 10.1111/joim.13149

Wang, Y., L. Zhang, L. Sang, et. al. 2020. [Kinetics of viral load and antibody response in relation to COVID-19 severity](#). *The Journal of Clinical Investigation* 130(10): 5235-5244. doi: 10.1172/JCI138759

Acknowledgements and Class Information

Research was conducted through CPSP359S: Discovery Research. The goal of this class is to introduce students to the process of starting research in a topic of interest. This class was taught by Dr. Marilee Lindemann.

I would like to thank Drs. Thomas Holtz and John Merck for providing me with the opportunity to conduct this research. I would also like to thank Dr. Lindemann and my classmates in CPSP359S for providing guidance in my research.

