What factors can affect the severity of side effects of the COVID-19 vaccine?

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With the administration of COVID-19 vaccines, concerns have arisen about the side effects that tend to come along with receiving the vaccine. Scientists have identified patterns about the severity of side effects that are based on factors such as age, sex, and health. Previous studies do show support for this; for example, one study found that women tend to have stronger immune reactions to pathogens (Mauvais-Jarvis, Klein, and Levin 2020). Another preprint study, which is loosely related, investigated whether or not seropositive (meaning the individual already has the COVID-19 antibodies) individuals need a second vaccine dose, or if they were adequately protected against COVID-19 after the first vaccination (Krammer, Srivastava, and Simon 2021). The preprint article led to an interest in whether seropositivity is associated with severity of side effects of the vaccine. The most widely administered vaccines, and the ones that require two doses, are made by Pfizer and Moderna. The Pfizer and Moderna vaccines are mRNA vaccines, meaning that they inject mRNA from the COVID-19 virus. This mRNA contains the code to make spike proteins, or S proteins, that are located on all coronaviruses. After injection, the human cells will use this mRNA to create a harmless S protein that the immune system will then respond to. This allows the immune system to create antibodies *before* a "real" COVID-19 infection. This mechanism is what makes vaccines effective; they preemptively introduce the pathogen so that the body is ready to defend itself once the virus actually infects the host. Despite this rather consistent cellular response to vaccines, there have still been some observed discrepancies in the side effects. In this observational study, I set out to investigate whether or not sex, age, and previously having COVID-19 affect the severity of side effects after receiving the vaccine.

Method

This is a purely observational study, meaning that I attempted to "observe" the side effects of a large sample of individuals without using control variables or treatments. To carry out the goal of the project, I created a survey that asked the responder their sex, age, the vaccine they received, what side effects they felt, the severity of their side effects (on a scale from 1-10, 10 being the worst), and whether or not they had contracted COVID-19 in the past. I received over 300 responses, 76.9% of which were female.

In analyzing the data, I focused on the difference in average severity ratings after the first and second dose between males and females, between younger responders (ages 17-24) and older responders (50-54), and between people who have had COVID-19 in the past and people who haven't.

Using Python, I created box plots and histograms of all the different severity ratings by sorting the data by the groups I mentioned previously. I also used Python to get summary statistics, such as the sample size of each particular group, mean, median, and standard deviation. I performed hypothesis tests (specifically independent samples t-tests) between the different groups. These groups are: average severity rating after the first dose between males and females, average

severity rating after the second dose between males and females, average severity rating after the first dose between younger individuals and older individuals, and average severity rating after the second dose between younger and older individuals. I was unable to perform hypothesis testing on the group that included people who have or haven't had COVID-19 in the past because the sample sizes were too small. For all of the tests, I used a significance level of 0.05.

Results

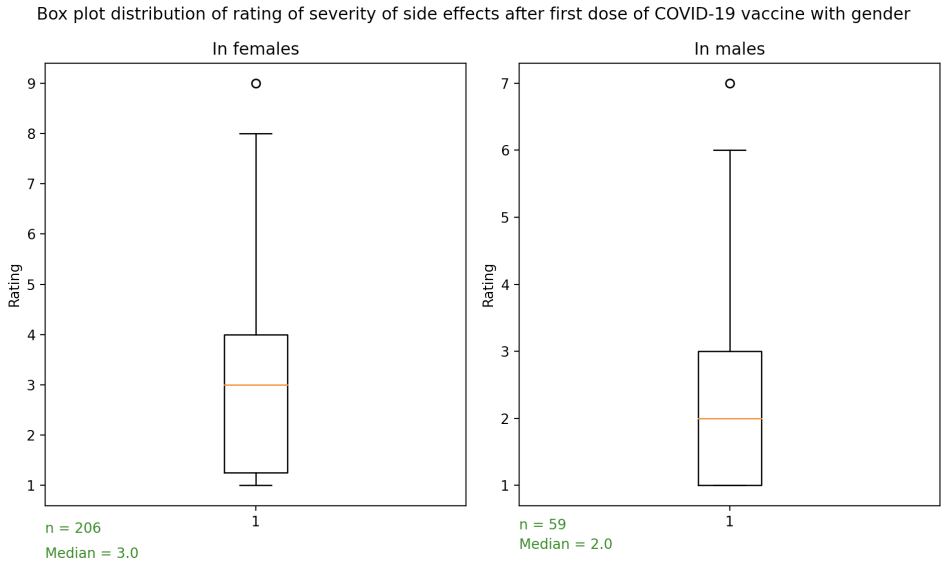

Figure 1. Box plot of severity rating of side effects after the *first* dose, between males and females. Medians and sample sizes are shown.

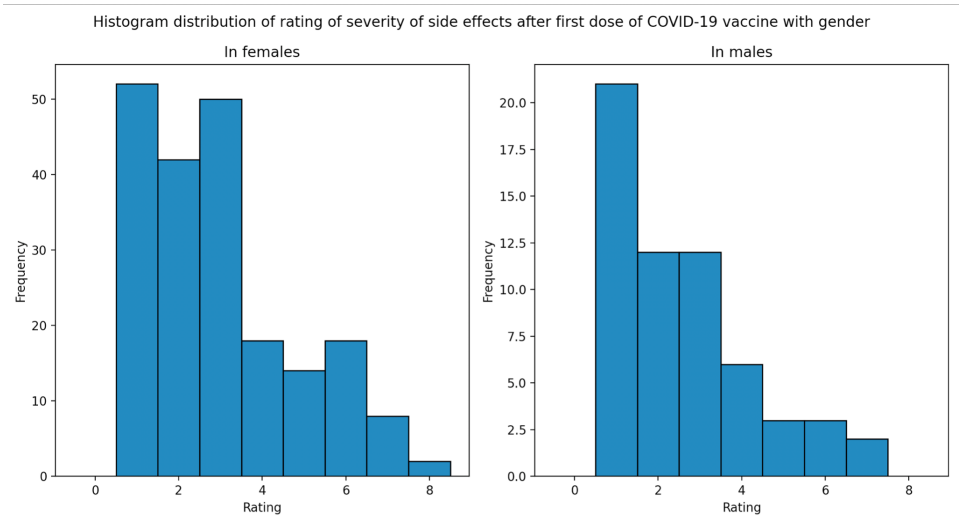

Figure 2. Histogram of severity rating of side effects after the *first* dose, between males and females. Both distributions are skewed right.

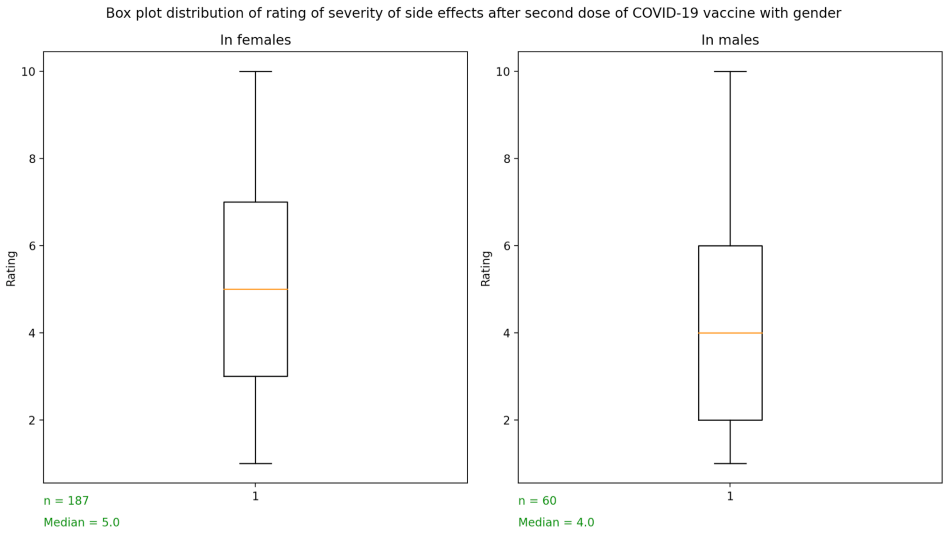

Figure 3. Box plot of severity rating of side effects after the *second* dose, between males and females. Medians and sample sizes are shown.

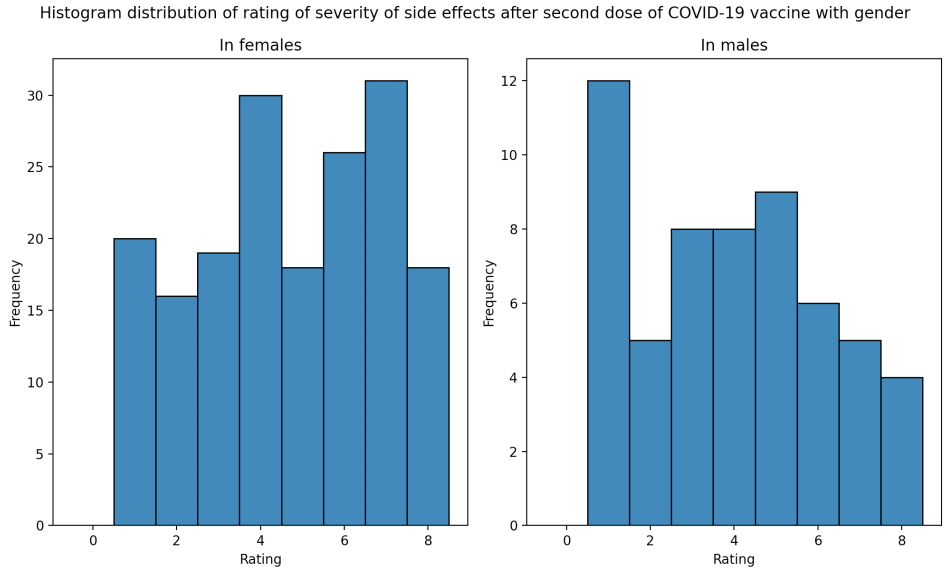

Figure 4. Histogram of severity rating of side effects after the *second* dose, between males and females. The distributions are slightly more uniform than in Figure 2.

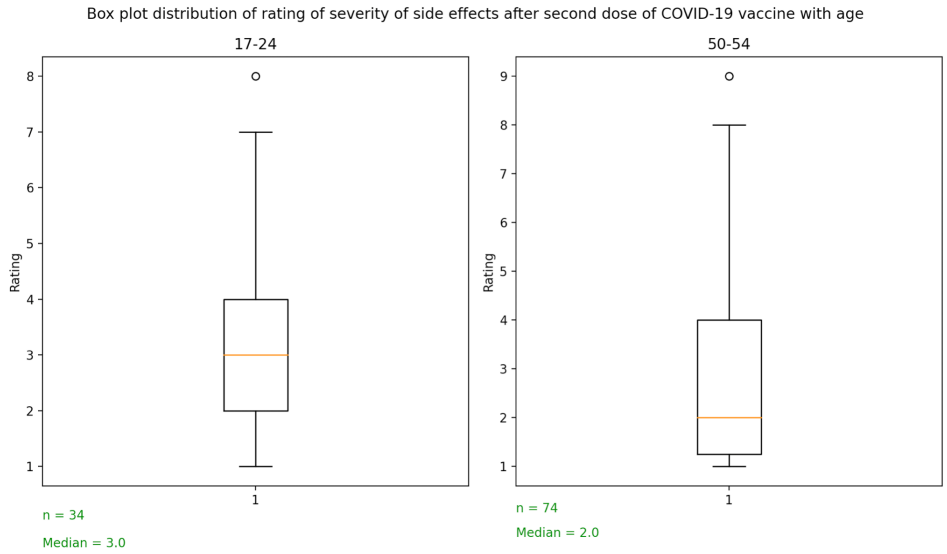

Figure 5. Box plot of severity rating of side effects after *first* dose (disregard the title saying "second dose"), between two age groups, 17-24 and 50-54. Medians and sample sizes are shown.

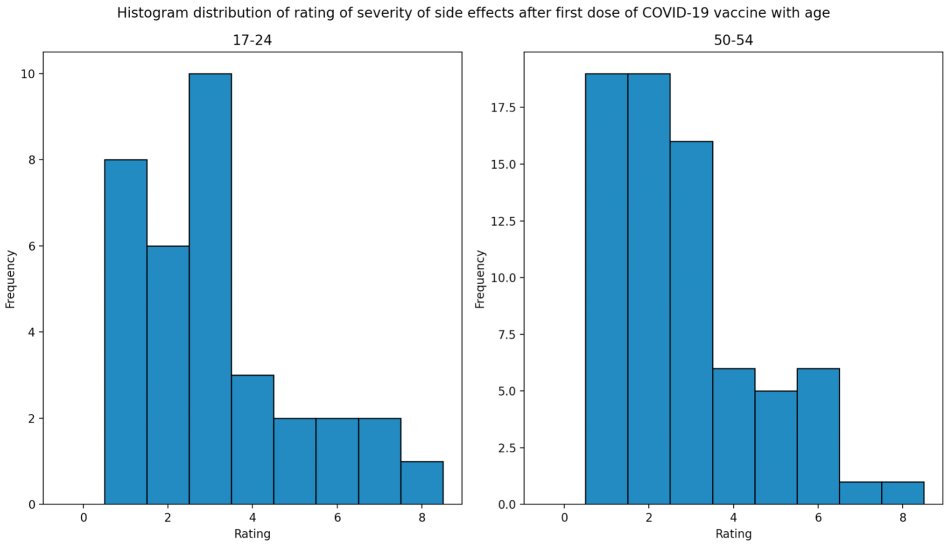

Figure 6. Histogram of severity rating after *first* dose of, between two age groups, 17-24 and 50-54. Both distributions are skewed right.

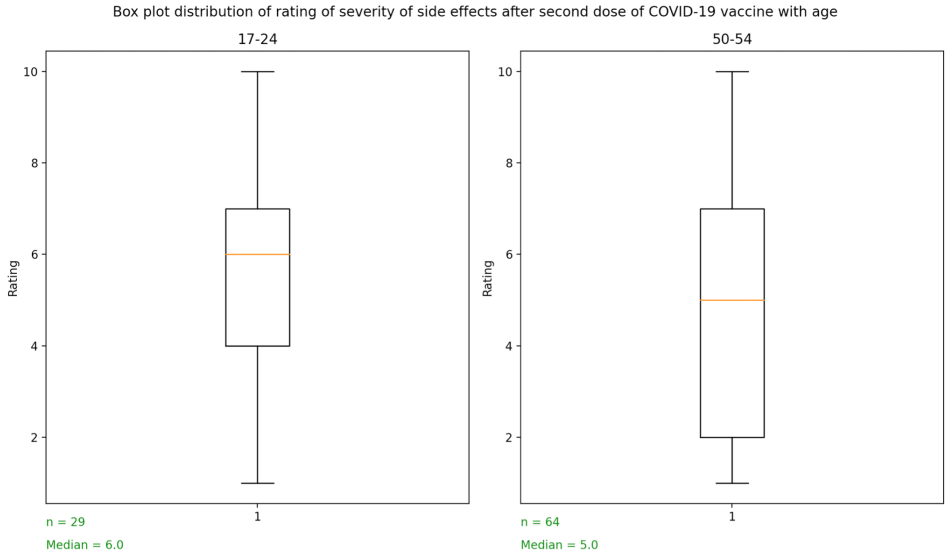

Figure 7. Box plot of severity rating of side effects after *second* dose, between two age groups, 17-24 and 50-54. Medians and sample sizes are shown.

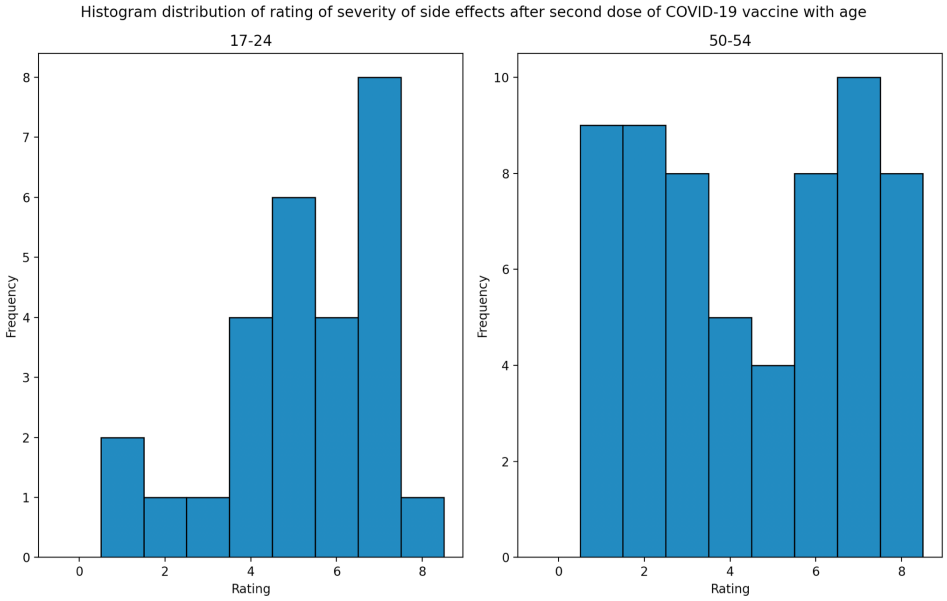

Figure 8. Histogram of severity rating of side effects after *second* dose, between two age groups, 17-24 and 50-54. The 17-24 distribution is slightly skewed left, while the 50-54 distribution is approximately bimodal.

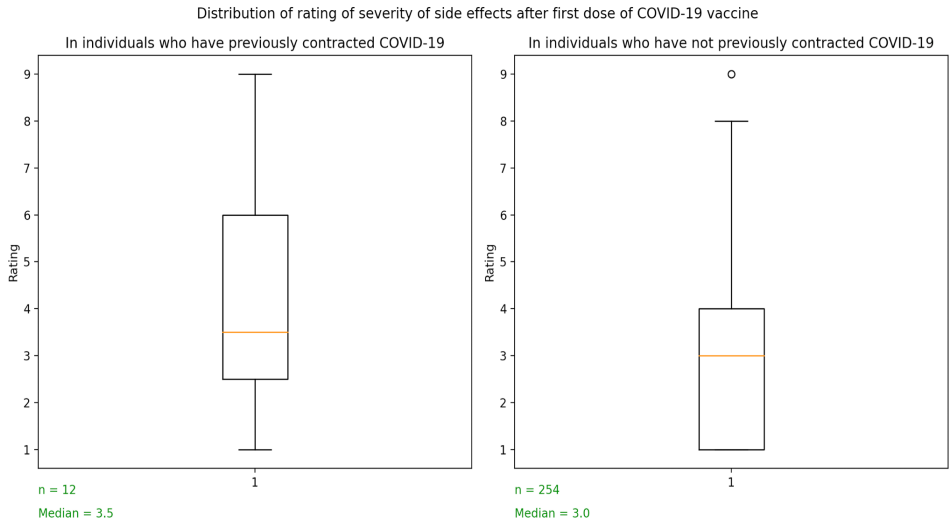

Figure 9. Box plot of severity rating of side effects after the *first* dose between individuals who have and have not previously contracted COVID-19. Medians and sample sizes are shown.

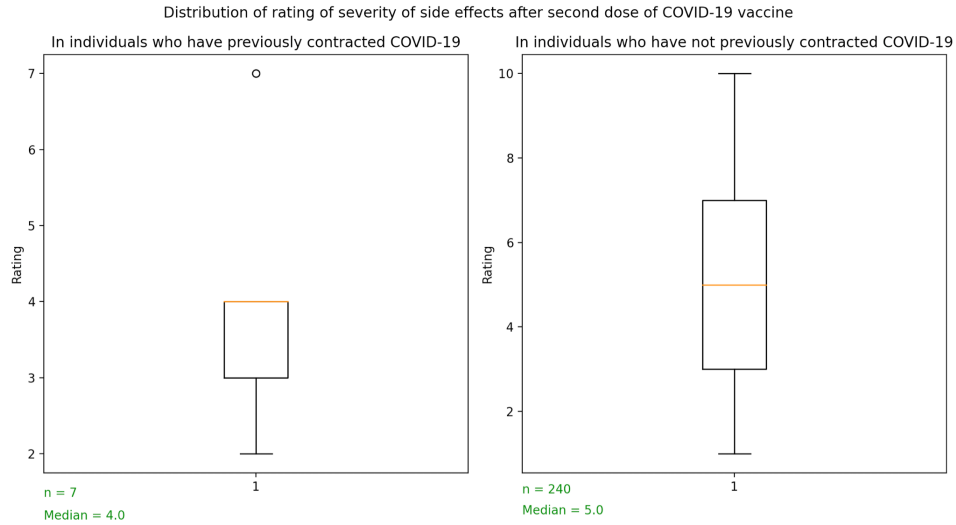

Figure 10. Box plot of severity rating of side effects after the *second* dose between individuals who have and have not previously contracted COVID-19. Medians and sample sizes are shown.

Conclusion

I carried out significance testing using a one-sided two-sample T-tests between each two observed groups for each dose. For both doses given to males and females, I found that the difference between their mean severity ratings was significant. For the first dose, the p-value was 0.0456, and for the second dose, the p-value was 0.02813. Both p-values are significant at the significance level of 0.05 that I used.

For both doses given to the younger and older age groups, I found that the difference between their means was not significant. For the first dose, the p-value was 0.2817, and for the second dose, the p-value was 0.073. Neither of the p-values are significant and we cannot conclude that age has an effect on the severity of side effects after each dose.

For whether or not an individual has had COVID-19 in the past, I was unable to perform significance testing due to the very small sample size I obtained for those who had COVID-19 in the past (see Figures 9 and 10). To give a visual analysis, in the first dose, there did not seem to be much of a difference between the range of side effects experienced. In the second dose, it seems like people with COVID-19 before had a better reaction and reduced side effects; however, it is impossible to know for sure from this study alone.

Although I obtained significant results for the data between males and females, I want to address some limitations of the study. First, it was an observational study, meaning that I simply observed (through a survey) and the study did not include treatment groups or control groups. Furthermore, a survey could have potentially introduced response bias, with only people who felt strongly about their side effects to respond to the survey. The rating of severity could have also been inconsistent, with each person interpreting the number differently, leading to an inaccurate measurement of how strong one's side effects were. Future studies should include larger sample sizes and attempt to get more male responses. Furthermore, it would be interesting to specifically investigate women's immune reactions to vaccines and confirm whether or not the magnitude of a reaction to a vaccine is really stronger in women. Finally, future studies should test if the second dose comes with more severe side effects compared to the first dose.

References

Chang, W. (2020 September). A review of vaccine effects on women in light of the COVID-19 pandemic. Taiwan J Obstet Gynecol. Volume 59 (Issue 6), 812-820.

Krammer, F., Srivastava, K., the PARIS team, and Simon, V. (2021 February). Robust spike antibody responses and increased reactogenicity in seropositive individuals after a single dose of SARS-CoV-2 mRNA vaccine. medRxiv

Mauvais-Jarvis, F., Klein, S., and Levin, E. (2020 September). Estradiol, progesterone, Immunomodulation, and COVID-19 outcomes. Endocrinology Volume 161 (Issue 9).