ABSTRACT

Relationship Between Sex and Symptom Status in University Students Who Tested Positive for COVID-19

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Due to the novelty of research involving differences in sex for COVID-19, more studies covering this topic are required. This study examines if there is a statistically significant difference between males and females in COVID-19 symptom rates. Data was collected during regular COVID-19 contact tracing, where upon positively tested students were contacted and asked to answer their sex and if they had symptoms present or not. Afterwards, a Chi-Square test was performed. The results designate that there is no statistically significant difference between the sexes (p=0.703). However, females exhibited higher incidence for COVID-19 symptomatic status (62.59%) than males (58.20%). In conclusion, there is no statistically significant relationship between sex and symptom rate; however, more studies in this topic would be appreciated due to its importance.

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RELATIONSHIP BETWEEN SEX AND SYMPTOM STATUS IN UNIVERSITY STUDENTS WHO TESTED POSITIVE FOR COVID-19

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CHAPTER ONE

Introduction

The coronavirus (also known as COVID-19) has impacted the world on a global scale. This virus has changed the ways we interact with others and disrupted daily life. In December of 2019, an unknown illness, later known as COVID-19, was discovered in Wuhan, Hubei Province with the World Health Organization declaring COVID-19 a pandemic in March 2020 (CDC, 2022). It wasn’t until December 11, 2020, that the first COVID-19 vaccine became available in the form of the Pfizer-BioNTech vaccine. This breakthrough in the creation of the first COVID-19 vaccine was followed by the authorization of the Moderna COVID-19 vaccine on December 18, 2020 and the authorization of the Johnson and Johnson COVID-19 vaccine on February 27, 2021 (CDC, 2022). In the months leading up to the release of the three COVID-19 vaccines, multiple studies were conducted on the effects of patients’ sex differences on the presentation and severity of COVID-19 symptoms. However, due to the novelty of the topic, more research needs to be performed to see any differences that arise. In this chapter, we will examine COVID-19 symptoms, studies that have looked into gender differences for symptoms, why it is important to research COVID-19 symptom differences by gender in a university setting, and background information about COVID-19 on Baylor University campus.

The virus that causes COVID-19 results in two outcomes for those infected: either the individual experiences symptoms or is asymptomatic. The most common symptoms patients diagnosed with COVID-19 are fevers, coughs, fatigue, dyspnea, and sputum (Alimohamadi et al., 2020). Other symptoms common in patients include difficulty breathing, headache, loss of taste or smell, diarrhea, nausea, and sore throat (CDC, 2022).

Interestingly, some individuals infected with the virus are asymptomatic- do not show symptoms at all. In a meta-analysis conducted in 2021 and covering over 95 separate studies, this asymptomatic population of those with a confirmed COVID-19 diagnosis came out to be 40.50% (Ma et al., 2021). This is a significantly large percentage of the infected population. This large group of asymptomatic patients is especially important to study. Reasons for the necessity of a study on COVID-19 asymptomatic patients are that this large population could result in the undetected and rapid spread of COVID-19. Additionally, an increased chance of COVID-19 reinfection occurs with increased time after recovery from initial infection and possible variants arising (CDC, 2022). One study found that asymptomatic cases were the cause of 24% of all transmissions of the SARS-CoV-2 virus (Johansson et al., 2021).

During the duration of this study's data collection period, Baylor University defined isolation periods, abiding to CDC policies. Baylor University defines an isolation period for those who tested positive to be 10 days since symptoms began or if asymptomatic, 10 days since testing positive. The university also defines infectious periods as 48 hours before exhibiting symptoms for symptomatic students or 48 hours before getting tested for asymptomatic students. Symptomatic students who did not exhibit COVID symptoms and got tested on the same date, would count their isolation period 48 hours before the earliest event (whether it be the presence of symptoms or getting a test). This is reaffirmed by the CDC policy stating that individuals with mild cases should isolate for at least 10 days and up to 20 days if symptoms are severe or do not go away (CDC, 2022). During this time of asymptomatic infection, an individual, unaware that they carry the virus, could spread the virus to many they come into contact with. This could lead to an uncontrollable spread of COVID-19 virus and cause disastrous results in society from economic shutdowns to longer extensions of mandatory lockdowns.

The CDC's guidance on isolation for COVID-19 states that more data information is needed regarding the length of time and frequency of SARS-CoV-2 infections of both asymptomatic and symptomatic people (CDC, 2022).

Differences in sex arise quite often in biological research and is a reason why it is important to study the differences in sex for many research topics. Sex differences can influence behavior, lifestyle, biology, and societal determinants of health like access to healthcare. For example, women are more likely to work inside the home than men (Regitz-Zagrosek, 2012). Therefore, women are more likely to be injured or perish from home fire related accidents than their male counterparts (Regitz-Zagrosek, 2012). While men are more likely to work outside the home or in more dangerous jobs and are more likely to be injured or perish from occupation related accidents (Regitz-Zagrosek, 2012). These differences can affect medical care in preventing a more individualized care and consideration of the differences of each sex. For example, one treatment might be more effective for males than females based on trends and data. The same is true for the reverse scenario. To exemplify this, it is common knowledge that women are prone to osteoporosis and men are more well-researched in heart disease signs and treatments. Therefore, more data is required to study trends in female cardiovascular health and in men for osteoporosis (Regitz-Zagrosek, 2012).

As the COVID-19 pandemic has occurred within the past few years, there have been some studies looking into the medical differences in COVID-19 status, symptoms, and severity. However, more research needs to be done, due to the novelty of the topic. Males and females differed in their bodily responses to pathogens with females demonstrating a stronger immune response due to biological differences such as having more immune genes on their sex chromosomes and higher estrogen levels in females which can help in immune enhancement (Pradhan & Olsson, 2020). These differences are possible contributors to the rate of males around the world possessing a higher severity and mortality rate than females for COVID-19; however, this observed difference could be caused by numerous other factors and is not completely understood (Pradhan & Olsson, 2020).

A separate study of Chinese individuals found with a sample independent of age differences that men infected with COVID-19 and men infected with SARS (2003) exhibited greater severity of symptoms than women abiding to the clinical classification of severity (Jin et al., 2020). This study also found that although males were more susceptible to dying from COVID-19 infection, there were no differences in infection between males and females for COVID-19 with rates found at 56%, 50.7%, 50.0%, and 51.2% of the observed samples being male across four studies of different patient populations (Jin et al., 2020).

On the other hand, another study showed that an individual's age, not their gender, was the main risk factor for SARS-CoV-2 infection with males having 57.69% and females having 56.29% positive rates; however, this study analyzed gathered only from data from Fever Clinics (Liu et al., 2020). This particular study realized this possible source of error and expanded their subject population group to include data collected from a general hospital located in Wuhan. This study found that the positive rate was significantly higher for males (40.43%) than females (36.71%). This means that of the populations who got tested, males were more likely to receive a positive test result (Liu et al., 2020).

Looking at theses previous studies is it clear that there is a difference between infection rates and severity of symptoms between males and females. However, our study will be looking at the presence of COVID symptoms differences between the sexes.

COVID-19 has been heavily studied on older populations with good reason. The positive rate of elderly individuals (aged 70 or older) is 61.81% as opposed to 24.90 % of younger people (age 18-30) in a study of COVID-19 infection in a Wuhan hospital during the early months leading into the pandemic (Liu et al., 2020). In addition, the CDC states that elderly adults have an increased chance of displaying symptoms once they are infected with COVID-19 infection. This makes them more likely to require hospitalization or intensive care in their treatment plans (CDC, 2021). However, Coronavirus (COVID-19) does affect young adults as well. Although elderly are more at risk for death due to COVID-19, it is important to not neglect the youth for thier high rates of infection. One study found that infection rates are highest in the young adult population with men and women having 17.2 and 15.3 active infections for COVID-19 per 1,000 people compared to men (5.0) and women (4.1) in their sixties (Doerre & Doblhammer, 2022). Some issues young adults have as a result of the pandemic include symptoms, mental, social, and emotional well-being caused by employment challenges and changes in routine (CDC, 2022). Trauma caused by the pandemic could lead to critical long-term consequences for life during this important developmental stage of adulthood (CDC, 2022). Furthermore, the misconception that young, college aged adults cannot have COVID-19 or at least will experience COVID symptoms to a lesser extent is false. Although it is true that elderly have higher rates of hospitalization and are at greater risk, (CDC, 2021) it is still important to study the effects it has on the younger population. Providing for the needs of this younger population is necessary as they are the future workforce and understanding COVID's effects on younger subjects has the potential to lessen the spread of COVID-19 to the entire population.

From the 2020 summer months when the pandemic occurred, over 20% of all COVID-19 cases were from people aged 20-29 years; this was a higher incidence- occurrence of a disease- than all other age groups (Boehmer et al., 2020). The CDC recommends that young adults need to adhere to preventative behaviors to help reduce the spread and transmission of COVID-19 to higher risk individuals (Boehmer et al., 2020). Additionally, The CDC recommends college students help prevent and take steps to prevent COVID spread as this could potentially lead to greater transmission within communities (Salvatore et al., 2020).

This demonstrates the importance of young adults' health affecting behaviors during the pandemic. College students nearing graduation during the pandemic in particular had high rates of anxiety (60.8%), loneliness (54.1%) and depression (59.8%) (Lee et al., 2021). A study of 195 students found that 71% experienced increased stress and anxiety as a result of the COVID-19 pandemic (Son et al., 2020). Multiple stressors such as worrying over health are believed to have led to this increase in negative mental health measurements (Son et al., 2020). Studying the symptomatic rates of students can help to see how dire of a situation it is for students and why it is important to study the college student population. In a survey prior to COVID, Young adults aged 18-25 have the highest rate of serious mental illness when compared to all adults (9.7%) and females (7.0%) had a higher rate than males (4.2%) (NIMH, 2022). This highlights the importance of studying the young college student population, as health problems experienced by them due to COVID-19 could worsen their mental health.

Furthermore, the different incidence of serious mental illness highlights the importance of studying sex differences as health differences exist between males and females. For example, if it is found that females have a higher rate of symptoms for COVID-19 than males then it could cause females to present with more incidences or higher severity of mental health issues than their male counterparts.

There are many reasons to study sex differences in COVID-19 symptoms for college students. First, there are not many studies researching college student symptoms and health for COVID-19 due to the tendency to overlook this population for the more severely impacted older adults. Second, studying college student symptomatic rates could give a better picture into how to take care of students during the COVID-19 pandemic or in future pandemics when they arise. This could include which sex might need more resources allocated to them if one sex requires more assistance than another. Lastly college students also commonly live together in dorm or apartment style housing. This similarly models the living situations of other vulnerable populations that may be are underrepresented in research like the poverty stricken who live in public affordable housing living in close quarters with their neighbors.

A group of symptoms called post-COVID conditions, also known as long COVID, can disrupt life for many diagnosed with COVID-19 (CDC, 2022). These conditions can last in varying lengths from weeks, months to years after a positive test result (CDC, 2022). Long COVID is more common in individuals who had severe COVID-19 symptoms. This fact makes it important to see symptom levels in populations due to a higher symptomatic level indicates a higher percentage of those with post-COVID conditions (CDC, 2022). Brain fog is one of these symptoms present after COVID-19 diagnosis in a number of individuals. This symptom causes difficulty in concentrating and thinking (CDC, 2022). In a study, it was observed that 62.3% of patients in Fars province of south Iran had long COVID syndrome with 7.2% of all patients having brain fog (Asadi-Pooya et al., 2021). Females were also more likely to report brain fog (Asadi-Pooya et al., 2021). These symptoms such as brain fog can last in students which can affect their academic performance or job seeking capability in the workforce thus affecting all of society in the long run.

One reason for studying this is if it is found that there are high symptomatic rates even in the young adult population - one of the strongest, healthiest age groups most resistant to COVID-19 - it could be assumed that there are far larger rates of Long COVID symptoms in older more vulnerable age groups.

Furthermore, as stated before, this age group is the workforce of the future and experiences and health they have now could have dire effects on society once they start taking up jobs. Brain fog, and other Long COVID syndrome could have dire effects on their work efficiency and slow the economy. This could also have consequences on their relationships and their motivation.

Lastly, data gathered for this study occurred during the peak of the COVID-19 pandemic which makes this study significant and unique from others which might have conducted their studies during the beginning stages of the pandemic. Having studies highlighting peak pandemic times can reveal correlations that might not have been seen in the other earlier studies. Furthermore, having studies looking into peak pandemic times can be especially useful for making wise decisions of isolating positive cases in a future pandemic.

At Baylor University, located in Waco, Texas, the COVID-19 pandemic forced the school to shut down in early March 2020 and transition into a virtual format. In this virtual format students attended classes virtually and there was little to in-person contact between students and or faculty. In Fall 2020, the university tried reopening with the addition of a contact tracing team. This team reached out through various methods to contact and instruct students, staff, and faculty on how to isolate or quarantine for a set number of days to prevent the spread of COVID-19 around campus and in the Waco area.

Baylor University defines a positive case as a student, staff, or faculty who has tested positive for COVID-19. These cases must abide by rules of the campus based on CDC guidelines which states that they cannot leave their room for 10 days after symptom onset or after getting tested. The delivery of contact tracing was done either through text, phone call, or email to increase response rate. During contact tracing, tracers were required to ask the respondent if they had any symptoms present and if so, what they were. Some respondents stated they did not have any symptoms present; these were defined as asymptomatic cases. Respondents who did have symptoms present regardless of the severity were classified as symptomatic cases.

The purpose of this study is to examine the relationship between sex and COVID-19 symptom rates in college aged students. We hypothesize that sex has an effect on symptomatic rates

CHAPTER TWO

Methods

Data was collected from August 5, 2021 to November 23, 2021 as a regular routine of the contact tracing job I was hired for. This contact tracing job required that I be HIPPA certified and certified for Contact tracing after completing a contact tracing course. A total of 496 students were contacted and included for analysis in this study. For the data collection, this came from the contact tracing data we tracers collected. During regular contact tracing most of the cases were students; however, there would be occasional faculty or staff. These cases were ignored and not included in the analysis as our study is only focusing on college students. During a typical contact trace, I would be provided a daily list of students to contact. All contact tracers claimed their cases on an availability basis. I utilized data from the contact tracing team with their permission. During each case, each survey response was completely voluntary. Abiding by HIPAA standards, we would never reveal any data to the public without first removing identifiable information from each case. Each case typically knows of their positive case status via email from Baylor's health portal. During a trace, I would first ask the student their identity to confirm I was working with the right person. I would then ask them a list of questions required by Baylor's Contact tracing team unrelated to this study. Next, I asked students what their sex was and recorded the information. Afterward, I asked them if they had symptoms. If the positive case answered that they had symptoms, I asked them when the symptoms began appearing and what the symptoms were. I wrote down all the symptoms the student listed. If the student answered that they did not have any symptoms, I would write that they were asymptomatic.

In total 523 students were contacted for this study; however, some students never responded despite our best efforts to get their response. 27 students in total did not respond to our emails, texts, or phone calls and were not included in the analysis of this study.

Based on if the student had symptoms or not, a number of possible results could occur. If a student reported that they had symptoms, I would ask them for the date of their first symptoms. This date would be used to calculate the student's last date of isolation, that being 10 days after the date of first symptoms. If a student was asymptomatic, the last date of isolation will fall 10 days after the date they completed their COVID-19 test. An overall survey response rate was calculated.

Analysis of the data began first with splitting the data into their respective groups: male and female sex, then further separated by symptomatic status. All identifiable information was removed from this analysis portion to protect students' personal information. The variables considered were male vs female sex and symptomatic rates. Sex was the independent variable whereas the symptomatic rate was the dependent variable.

A chi-square test was conducted for the analysis of the data. This test was performed using the Microsoft excel program and performed to find the relationship between male and female sex and the status of being symptomatic or asymptomatic. To perform this test, the totals for male, female, symptomatic, and asymptomatic were calculated. The expected value was calculated by multiplying the row total and column total for each group and then dividing by the total number of the sample size. For example, the expected value for symptomatic males was calculated by finding the total number of males (e.g. 189) times the total number of symptomatic (e.g. 294) and then dividing the number by the overall total number of students (e.g. 496). This was performed for all four groups: symptomatic males, asymptomatic males, symptomatic females, and asymptomatic females. Lastly, the p-value was calculated in excel using the CHITEST function. In this, I took the range from the observed column and the range from the expected values column to calculate the p-value. The null hypothesis states that there is no significant difference between the expected values and the observed values from this study. The alternate hypothesis states that there is a significant difference between the observed and expected values. If a p-value was greater than 0.05, then we would fail to reject the null hypothesis which assumes no significant difference between the observed and expected values. If a p-value was less than or equal to 0.05, then we would reject the null hypothesis. Finally, a bar graph depicting the total number of observed students in each subcategory was created with calculated percentages of symptomatic and asymptomatic for each sex included in the graph.

CHAPTER THREE

Results

The survey response rate was 94.84%. The observed values for each subcategory were 110 symptomatic males, 79 asymptomatic males, 184 symptomatic females, and 123 asymptomatic females (**Table 1**). The total observed values were 294 symptomatic students, 202 asymptomatic students, 189 males, and 307 females (**Table 1**). 27 no responses were observed during this study but were not included in the analysis of the data using a chi test (**Table 1**).

Table 1: The observed values for the study. The observed values include the symptomatic male, asymptomatic male, symptomatic female, and asymptomatic female totals, along with the no response total.

Observed Values			
	Symptomatic	**Asymptomatic**	**Totals**
Male	110	79	189
Female	184	123	307
Totals	294	202	496
No Response	27		

The expected values from this study were 112.0282 symptomatic males, 76.97177 asymptomatic males, 181.9718 symptomatic females, and 125.0282 asymptomatic females (**Table 2**).

Table 2: The Expected values determined for this study. These are the calculated values expected from the sample studied. Any difference between the expected and the observed values, if significant, could indicate a correlation between sex and symptomatic rate. Expected values were determined for symptomatic male, asymptomatic male, symptomatic female, and asymptomatic female totals.

Expected (E) Values			
	Symptomatic	**Asymptomatic**	**Totals**
Male	112.0282	76.97177	189
Female	181.9718	125.0282	307
Totals	294	202	496

The p-value of this study came out to be 0.702705 much greater than the 0.05 value for significance (**Table 3**).

Table 3: The p-value determined from the CHITEST using Microsoft Word Program. The p-value is 0.702705.

P-value	0.702705

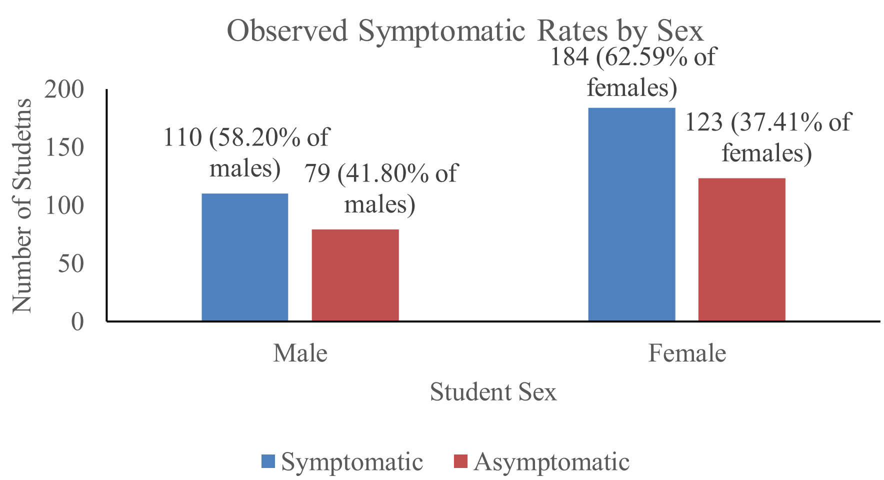

Figure 1: The number of observed symptomatic males (n = 110), asymptomatic males (n=79), symptomatic females (n=184), and asymptomatic females (n=123). The

percentage of symptomatic and asymptomatic for each sex is depicted above each colored bar. These percentages for male students are 58.20% symptomatic and 41.80% asymptomatic. The percentages for female students are 62.59% symptomatic and 37.41% asymptomatic.

CHAPTER FOUR

Discussion

In this study, I hypothesized that a student's sex affected symptomatic rates. However, after performing a chi-square test following data collection, the calculated p-value came out to be 0.702705 (**Table 3**) and is, therefore, greater than 0.05. From this study, we find there is no statistically significant relationship between sex and symptomatic rate.

Despite the observed data being not statistically significant, the results demonstrate that females had a higher rate of symptomatic cases at 62.59% than the male symptomatic rate at 58.20% (**Figure 1**). This is supported by studies as well. One study conducted in Germany, found that although older men had higher rates of COVID-19 infection, at working ages (15-59), women demonstrated higher COVID-19 infection rates (Doerre & Doblhammer, 2022). This higher COVID infection rate in females is supported by my study as I studied college aged adults which is comparable to the working age studied in this journal; however, it is important to note that the study conducted in Germany investigated infection rates whereas my study looks into symptomatic rates. According to the German study, the higher trend of female infection rate was correlated with the higher rates of female close contacts which peaked more at ages 20-29 (Doerre & Doblhammer, 2022). This age group is similar to the ages I studied. Furthermore, I found that my data supported this observation that females in the younger age groups experienced higher infection incidence rates than males. In my analysis, there were more female cases (307) than male cases (189) tested positive for

COVID-19 (**Table 1**) which amounts to almost one third more. This could be due to the higher sensibility and care for health in women and also the higher rates of women in care and health professions resulting in higher rates of COVID-19 test taking (Doerre & Doblhammer, 2022).

As mentioned in the introduction, one study showed that age, not gender of the individual, was the main risk factor for SARS-CoV-2 infection after completing a binary logistic regression analysis implying the results. I found in my analysis that sex might not have as much of a significant impact as previously thought (Liu et al., 2020). A separate study found that no differences were found between sex in COVID symptom onset during the times for hospital admission (Fernandez-de-las-Penas et al., 2022). My results could support the data found here.

There are some possible reasons why I observed this higher incidence of symptoms in females than males. According to a study of 1,000 patients, after adjusting for characteristics such as race, age, and education, physical symptoms were reported at least 50% more often by women than men (Kroenke & Spitzer, 1998). In fact, of all the characteristics, gender was determined to be the most important demographic factor for reporting symptoms (Kroenke & Spitzer, 1998). Of the 13 symptoms reported, 10 of them were statistically significant with all except 1 symptom being more commonly reported by women (Kroenke & Spitzer, 1998). The higher likelihood for women to report symptoms is a possible reason as to the higher, albeit slight, symptom rate observed in my analysis of the data.

There are some possible sources of error in this report which might have skewed the data and resulted in errors in the analysis and results portion of the data. It is recommended that if future studies are conducted, that they keep these sources of error in mind and take precautions to avoid repeating them to get more accurate results.

The first source of error is that I did not look into the severity of symptoms, just symptomatic status. Although my project is not looking into severity as its main focus, severity of symptoms could reveal more underlying factors in the differences felt across sex. If one sex experienced more severe symptoms than another despite having the same symptomatic rate, then this would indicate that more attention and resources should be allocated to that sex. Recommendations for measuring severity of symptoms should be abiding to the clinical classification of severity discussed in an earlier report above in order to avoid measurement by subjective opinions of each subject (Jin et al., 2020).

Another possible source of error was the different vaccines students took. The three vaccines available at the time of the study were Johnson and Johnson, Moderna, and Pfizer. All three of the vaccines are different and unique and students took different vaccines depending on availability or preference. It has been shown that receiving a COVID-19 vaccine can help to lessen symptoms such as severe illness and death during the infectious period (CDC, 2022). It can also do so after, one study found that previously infected individuals who received two doses of COVID-19 vaccines were less likely to report Long COVID symptoms than infected individuals who had not received any COVID-19 vaccine (Kuodi et al., 2022). Furthermore, not all students took the vaccine further complicating the symptomatic rates of students without considering the vaccination rate of the campus. I would recommend that the next time a similar study is done to have a separate group for the vaccinated and nonvaccinated and if possible, to also separate the groups based on which types of vaccine the subject received.

Another source of error was the 27 no responses received during the survey period (**Table 1**). These no responses had unknown sex and it was unknown if they had symptoms or not as these two details were part of the survey. This no response sample might have skewed the data, representing and underrepresenting one subcategory more than another and providing me with inaccurate data. This would result in an inaccurate analysis for the results of this study. Conducting a study with a longer wait time for response or contact through more methods of communication would increase the survey response rate and make the results more accurate.

These results of this study are useful for the world especially for future pandemics that may arise. This study provides insight into the differences in sex for disease symptom rates, a topic that not much research has been done. Firstly, youth have high infection rate with almost three times the rate that elderly have (Doerre & Doblhammer, 2022). Studying this population can lessen the rate of transmission. The information found in this study could help campuses organize against future outbreaks by allocating resources to subgroups who need it more. Furthermore, it is also important to continue research in sex differences in COVID-19 symptom rates as there have been many studies showings that men consistently have higher rates of severity of symptoms and mortality (Pradhan & Olsson, 2020); however, this is not the same metric as symptom rate.

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