

COMORBIDITIES ASSOCIATED WITH RESPONSES TO COVID-19 VACCINATIONS

A Report of a Senior Study

by

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ABSTRACT

SARS-COV-2 is a beta coronavirus which consists of single-stranded sequences of nucleotides called RNA. Comorbidities such as hypertension, diabetes and other cardiovascular disease have been associated with a higher risk of mortality amongst COVID-19 patients. Studies have shown that side effects after vaccination include cough, fever, fatigue, headache, shortness of breath, chills, muscle pain, sore throat, diarrhea, or vomiting. Therefore, our objectives were to: 1) determine the influence of comorbidities on responses to the COVID-19 vaccinations and 2) determine if there is a correlation between comorbidities and the type of vaccine received. A voluntary survey with guaranteed anonymity for participants was emailed to the Maryville College Campus to students, staff, and faculty on 31st of August-2nd September. Data for this study was collected using a blank quiz survey and this research project was approved by the IRB of Maryville College. The total percent of symptoms in participants were compared in all 3 vaccines, with sore arms being the most common symptom in participants (over 40% for all vaccines). Results from data shows that participants who received Moderna reported more sore arms (48%) than those who received Pfizer (46%) and Johnson and Johnson (42%) vaccines. Body mass index (BMI) appeared to significantly impact symptoms after vaccination, with higher BMIs associated with more symptoms. In addition, our data shows that people with comorbidities experienced more side effects than those with no comorbidities. One of the major limitations

in this study was the limited sample size ($n=68$). Thus, future studies should be conducted with a larger sample size and a more representative population.

ACKNOWLEDGEMENTS

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(Underweight = below 18.5 BMI, Normal weight= 18.5-24.9 BMI, Obesity= 25.0-above).

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CHAPTER I

INTRODUCTION

ORIGIN AND FAMILY OF COVID-19:

The severe Acute Respiratory Syndrome, Coronavirus 2 (SARS-CoV-2) virus, also known as Covid-19, was first identified in a patient with pneumonia in Wuhan, capital city of Hubei province, China in December 2019 (Nawaz et al. 2021). SARS-COV-2 is a beta coronavirus which consists of single-stranded sequences of nucleotides called RNA (Nawaz et al. 2021). Up until December 2019, there was little knowledge on Coronavirus despite the virus affecting many species including humans (Junejo et al. 2020). The family of CoVs were thought to have infected only animals until the world witnessed a major global SARS outbreak caused by SARS-CoV in 2002 (Shereen et al. 2020).

A member of the *Coronaviridae*, is a monophyletic cluster in the order *Nidovirales*, are enveloped with positive stranded RNA viruses of three class vertebrates: mammals (corona- and toro-viruses), birds (coronaviruses) and fish (bafiniviruses) (Enjuanes et al. 2008). Based on findings from the International Committee on Taxonomy of viruses, the *Coronaviridae* family is subdivided into two classes namely; *Letoviridae* and *Orthocoronaviridae* (Gorbalenya et al. 2020). According to the International classification of diseases, the coronavirus caused two major infectious respiratory diseases namely, SARS (Severe acute respiratory syndrome) and MERS (Middle respiratory syndrome) (see Figure 1; Gorbalenya et al. 2020).

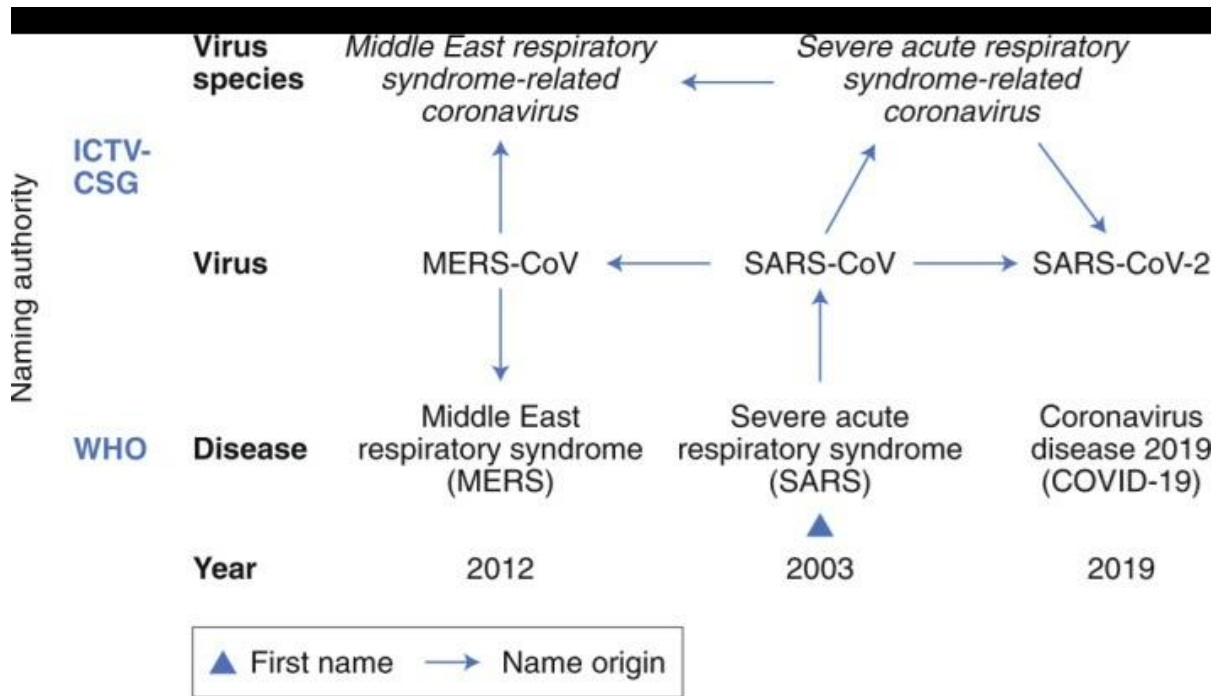


Figure 1: History of coronavirus naming during the three zoonotic outbreaks in relation to virus and disease caused by these viruses (Gorbalenya et al. 2020, pg. 537).

Morphology of SARS-CoV-2:

SARS-CoV-2 contains four structural proteins; 1) spike (s), 2) envelope (E), 3) membrane (M), and 4) nucleocapsid (N) (See Figure 2; Nawaz et al. 2021). The spike is a major definition of the virion as it appears as a solar corona (Agrahari et al. 2021). The envelope of the virus is made up of protein S, M and E (Nawaz et al. 2021). The S and M protein plays an important role in the attachment of the virus during replication while the N protein is mainly associated with the formation of nucleocapsid inside the envelope (Nawaz et al. 2021).

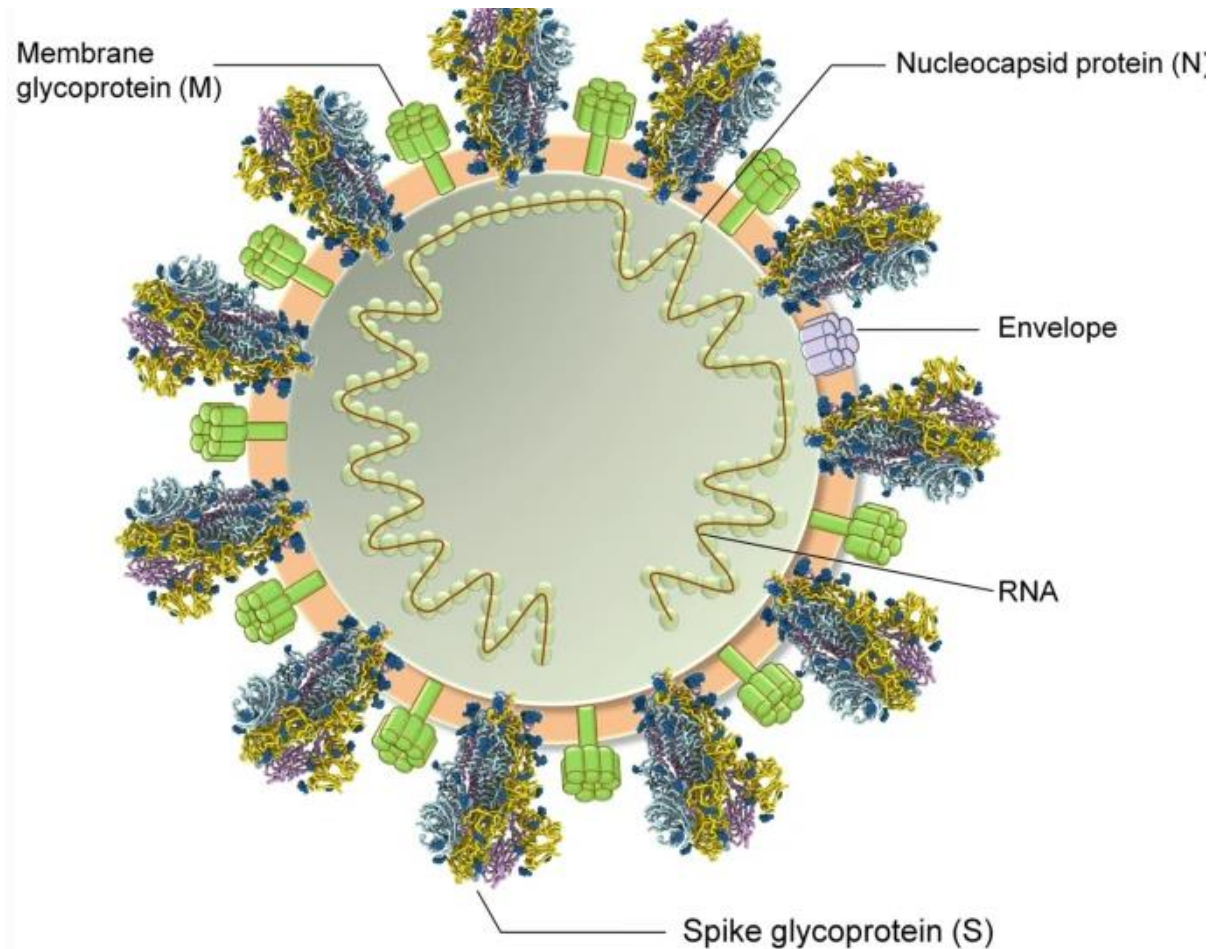


Figure 2: Structure of SARS-CoV-2 (Kumar et al. 2020, pg. 25).

The presence of angiotensin converting enzyme 2 (ACE2) in various organs of the body such as lungs, heart, kidneys, and gastrointestinal tract allows the virus to enter the human body (Nawas et al. 2021). The process of CoV entering into the host cell begins with the S protein that comprises S1 and S2 subunits binding to the ACE2 receptor in the host cell (See Figure 3; Agrahari et al 2021). Viral infections such as SARS-CoV-2 use the cellular machinery of the host to replicate multiple viral copies which are subsequently shed by the

host cell (South et al. 2020). In addition, the majority of protein in ACE2 comprise the NH₂-terminal peptide domain including the catalytic site oriented extracellularly (South et al. 2020).

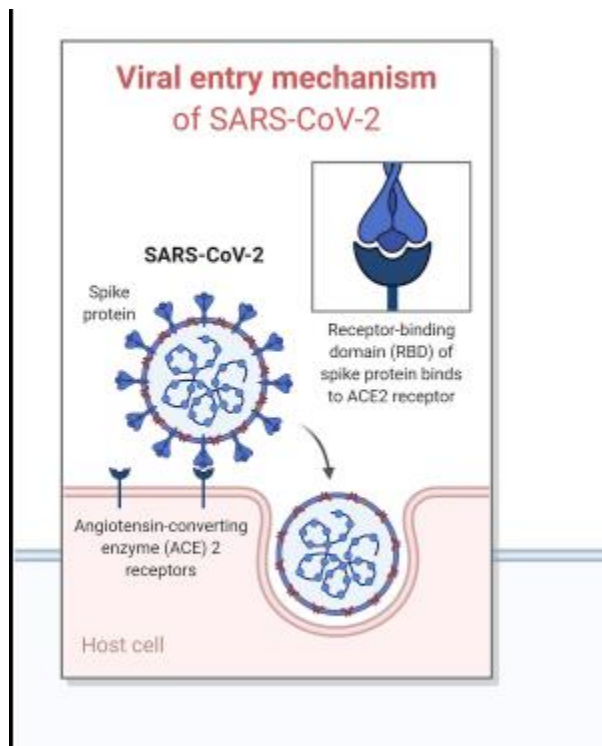


Figure 3: ACE2 in the Entry of SARS-COV-2 into the host cell (Bosso et al. 2020, pg. 322).

Apart from ACE's role as a receptor for SARS-COV 2, ACE2 is well known for its role in hypertension (Bosso et al. 2020). Consensus of evidence from various studies favors a primary role of ACE2 is to efficiently degrade ANG II to ANG-(1-7) (South et al. 2020). Thus, the loss of ACE2 may shift the system to an overall higher ANG II and lower ANG-(1-7) (Krishnamurthy et al. 2021). ANG-(1-7) is an antagonist of ANG II, with vasodilatory, antiangiogenic, antifibrotic, and anti-inflammatory properties (Krishnamurthy et al. 2021).

The ACE2 peptidase pathway constitutes a key inflexion point in the processing pathway of RAAS (South et al. 2020). ACE2 high expression is confined to the endothelial cells of the arteries, arterioles, and venules of the lungs and heart where it modulates blood pressure and maintains blood pressure homeostasis through negatively regulating the renin-angiotensin system (Bosso et al. 2020).

Comorbidities such as hypertension, diabetes and other cardiovascular disease have been associated with a higher risk of mortality amongst COVID-19 patients (See table 1; de Lucena et al. 2020). Studies have shown that these commodities result in a high rate of CFR, thus leading to a higher rate of susceptibility to COVID-19 (de Lucena et al. 2020).

Table 1: This table shows the comorbidities, symptoms and targets concerning SARS-CoV-2 (Ejaz et al. 2020, pg. 1836).

S. No.	Disease	SARS-CoV-2 targets	Symptoms
1	Hypertension	Upregulate ACE-2 expression	Increased blood pressure with pneumonia
2	COPD	Upregulate ACE-2 expression	Severe hypoxemia
3	CVD	Impaired immune system	Myocardial injury, heart attack
4	Liver diseases	ACE-2 expression in liver cells, i.e., cholangiocytes, endothelial cells hepatocytes, and Kupffer cells	Elevated serum aminotransferases
5	Malignancy	Impaired immune system	Adult respiratory distress syndrome
6	Asthma	Delayed innate antiviral immune response and delayed secretion of IFN- λ	Chronic respiratory diseases along with pneumonia-like symptoms
7	Renal diseases	Increase secretion of enzymes, dipeptidyl peptidase-4 and angiotensin-converting enzyme (ACE-2)	Acute kidney injury (AKI)
8	HIV	Antiretroviral therapy (ART) with the impaired immune system and ACE-2 receptor in the lungs	Pneumonia like symptoms with jaundice
9	Obesity	The abnormal secretions of cytokines, adipokines, and interferons	Chronic low-grade inflammation of abdominal obesity with effect on bronchi and lung parenchyma
10	Diabetes	ACE-2 expression, impaired T-cell function and increased interleukin-6 (IL-6)	Pneumonia like symptoms

Comorbidities associated with SARS-CoV-2:

A study conducted by Wang et al reported that patients admitted to intensive care unit had a higher number of comorbidities (72.2%) than those not admitted to the intensive care unit (37.3%) (The use of meta-analysis has been used to broaden our knowledge on other comorbidities such as chronic kidney disease, chronic obstructive pulmonary disease, HTN, DN, sickle cell, and neurological conditions which have been suggested to be major risk factors for predicting the severity in COVID-19 patients (Thakur et al. 2021). These comorbidities are associated with either COVID-19 severity or mortality amongst patients (Thakur et al. 2021). However, the influence (severity or mortality) of COVID-19 comorbidities is determined by factors such as population size, prevalence of comorbidities amongst patients, age and gender distribution, diagnostic testing, COVID-19 management strategies, and reporting accuracy (Thakur et al. 2021).

Obesity and COVID-19:

Obesity is a common COVID-19 comorbidity that occurs as a result in the inflammation of the adipose tissue which generates a systemic and chronic alteration in the lung parenchyma and bronchi (de Lucena et al. 2020). The inflammation of the adipose tissue due to obesity increases vulnerability to infections in the human body (de Lucena et al. 2020). This inflammation is majorly associated with the abnormal secretion of cytokines, adipokines and interferons by the adipocytes which can cause comorbidities such as dyslipidemia, hypertension, cardiovascular diseases and diabetes, thus increasing the risk of infection by SARS-CoV-2 (de Lucena et al. 2020). An overexpression of inflammatory

adipokines from deposits of visceral fat tends to affect immune response as well as alter the differentiation of macrophages (de Lucena et al. 2020). Furthermore, results have shown that patients with severe SARS-CoV-2 tend to experience cytokine storms which occurs as a result of an imbalance between secretion of anti- and pro- inflammatory adipokines from visceral fat deposits (See Figure 4; de Lucena et al. 2020). Finally, the adipose tissue is regarded as a reservoir for several viruses, such as influenza, HIV and cytomegalovirus, and may also be infected by COVID-19 virus, for being an important source of IL-6 and IL-6R receptor (de Lucena et al. 2020).

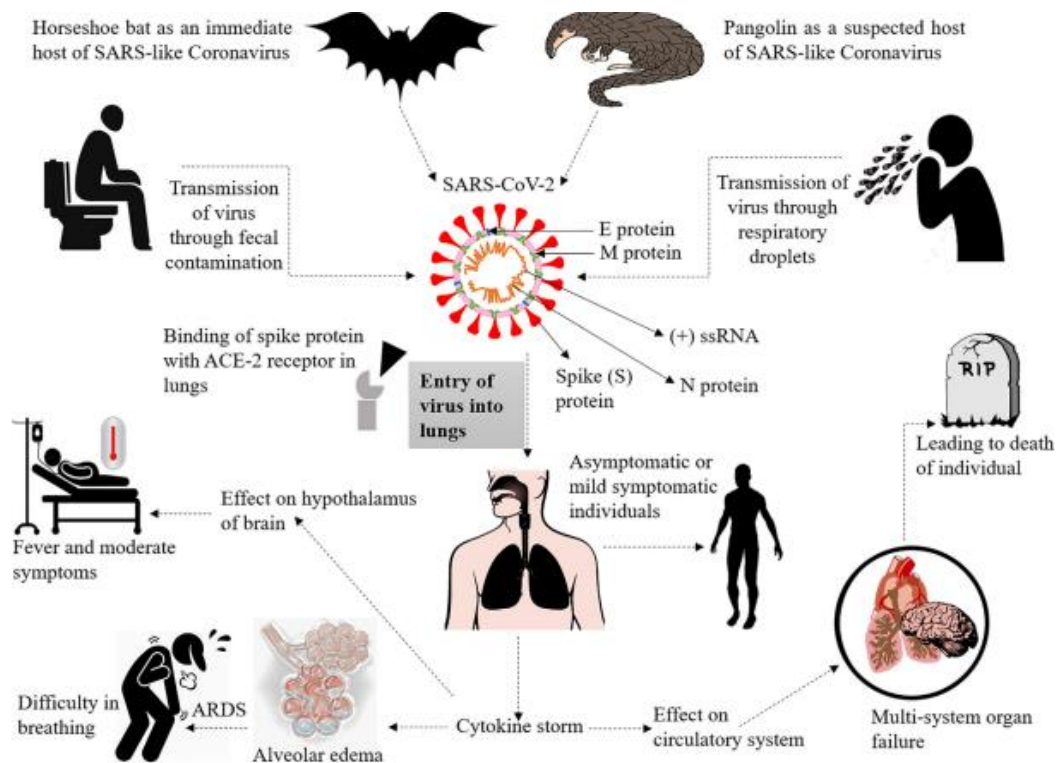


Figure 4: This shows how the SARS-CoV-2 virus utilizes the ACE-2 receptor present in alveolar cells in the lungs, hepatocytes, and kidneys, and affects the host’s biochemistry by

entering cells. SARS-CoV-2 causes acute respiratory distress syndrome (ARDS) by entering into the lungs and generating cytokine storms, which can affect the circulatory system that leads to morbidity and mortality (Ejaz et al. 2020, pg. 1835).

Hypertension and COVID-19:

Hypertension is a common risk factor for COVID-19 as well as a high case of fatality rate (Ejaz et al. 2020). Patients suffering from hypertension experience uncontrolled levels of blood pressure (Ejaz et al. 2020). However, the entry of COVID-19 in patients with hypertension is influenced by a high amount of inhibitors that upregulate the expression of ACE-2 receptors (Ejaz et al. 2020). Thus, the greater the expression of these receptors, the more vulnerable a patient is to COVID-19 and other cardiovascular infections (Ejaz et al. 2020). This ACE-2 receptors are often present in the alveolar cells of the lungs, liver, kidney, and hepatocytes; thus, affecting the circulatory, respiratory and other vital systems which could lead to morbidity and mortality (See figure 4; Ejaz et al. 2020).

Asthma and COVID-19:

Asthma is regarded as a potent risk factor which is associated with late and slow immune response as well as the secretion of interferons (IFN) (Ejaz et al. 2020). This secretion is responsible for the susceptibility to severe cardiac complications (Ejaz et al. 2020). Although asthma is assumed to be a major risk factor, no studies have provided specific evidence on SARS-CoV-2 in asthmatic patients (Ejaz et al. 2020). In addition, studies by researchers in Wuhan reported that there is no risk factor associated with SARS-CoV-2 in asthmatic patients (Ejaz et al. 2020). However, COVID-19 patients with asthma

are likely to be susceptible to other respiratory diseases along with pneumonia-like-symptoms (Ejaz et al. 2020).

Sickle cell and COVID-19:

Previous studies have shown that patients with sickle cell diseases become susceptible to comorbidities such as pulmonary hypertension, renal insufficiency, and hypertension (Menapace and Thein 2020). In addition, Sickle cell diseases lead to acute coronary syndrome which is associated with high death rates (Menapace and Thein 2020). Patients with sickle cell diseases are reported to be susceptible to thrombo inflammatory and thrombotic events due to endothelial dysfunction and abnormal expression of procoagulants (Menapace and Thein 2020).

Diabetes mellitus and COVID-19:

Diabetes was reported as a major risk factor for mortality in patients during the major pandemic that occurred in 2009 as a result of Influenza (H1N1) (de Lucena et al 2020). Previous studies have shown a strong correlation between diabetes and increased lung inflammation with macrophage infiltrates (de Lucena et al 2020). In the immune system, specific immune responses are induced via the recognition and binding of oligosaccharide to C-type lectin receptors (de Lucena et al. 2020). Thus, a major connection between SARS-CoV-2 and uncontrolled hyperglycemia (de Lucena et al. 2020). Uncontrolled hyperglycemia induces alterations of both ACE2 and protein glycosylation which results in SARS-COV2 binding with ACE2 as well as reducing the response of the immune system (de Lucena et al 2020). Reports suggest that comorbidities increase susceptibility to COVID-19 by generating

immune response dysregulation (Thakur et al. 2021).

COVID 19 Vaccine:

To develop effective vaccines with the purpose of long-term immunity, it is important to understand the genome and functionalities of SARS-CoV-2 (Thakur et al. 2021). To develop a vaccine, the identification and quantification of theoretical safety risks against potential benefits is considered (Vasireddy et al. 2021). The development of a vaccine includes the following steps, 1) research and discovery stage 2) preclinical stage 3) clinical stage (Vasireddy et al. 2021). After these stages, the vaccine undergoes Food and drug administration (FDA) assessment and approval before clinical trials can be conducted (Vasireddy et al. 2021). The main objective of the clinical trials is to enhance the safety, efficacy and tolerability of these vaccines in healthy adults after one or two doses (Vasireddy et al. 2021). Reports suggest that these trials are randomized, observer-blinded and placebo controlled (Vasireddy et al. 2021). The United States FDA has approved three (3) COVID-19 vaccines for emergency use namely, Moderna, Pfizer and Janssen (Vasireddy et al. 2021). However, there are other vaccines approved in other parts of the world (See table 2; Vasireddy et al. 2021).

Table 2:

Vaccines Approved in USA and Other Countries for Emergency Use (Vasireddy et al. 2021, pg. 207).

Country of development	Developer	Type of vaccine	Usage
USA/Germany	Pfizer-BioNTech	mRNA	Approved in several countries. Emergency use in USA, EU, UK, Bahrain, Canada, Saudi Arabia, Mexico, etc.
USA	Moderna	mRNA	Approved in Switzerland. Emergency use in USA, UK and EU
Russia	Gamaleya	Viral vector	Early use in Russia
UK/Sweden	Oxford-AstraZeneca	Viral vector	Emergency use in UK and EU
China	CanSino	Viral vector	Approved in China
USA/Belgium	Johnson and Johnson	Viral vector	Emergency use in USA and Bahrain
Russia	Vector Institute	Protein subunit	Early use in Russia
China	Sinopharm	Inactivated virus	Approved in China, UAE and Bahrain. Emergency use in Egypt
China	Sinovac	Inactivated	Approved in China. Emergency use in Brazil

Moderna COVID-19 Vaccine:

The Moderna vaccine is an mRNA vaccine with a high level of efficacy rates (Uddin et al. 2021). Reports have shown that mRNA vaccines have the ability to encode for SARS-CoV-2 antigen (spike protein) using the host ribosome (Uddin et al. 2021). This is very important because the spike protein plays a major role in the attachment of ACE2 receptors in the human body as well as inducing T-cell response (Uddin et al. 2020). The production of these spike proteins by the immune cells causes the body to create antibodies that can help fight the COVID-19 virus (See figure 5; Mayo clinic, 2022). An advantage Moderna and other mRNA vaccines have over other vaccines is the delivery of viral nucleic acid to the

host nuclei, thus avoiding integration in the host DNA (Uddin et al. 2021). The Moderna vaccine contains small amounts of ingredients which serve specific purposes in immune response (See table 3; Information about the Moderna COVID-19 Vaccine, 2022)

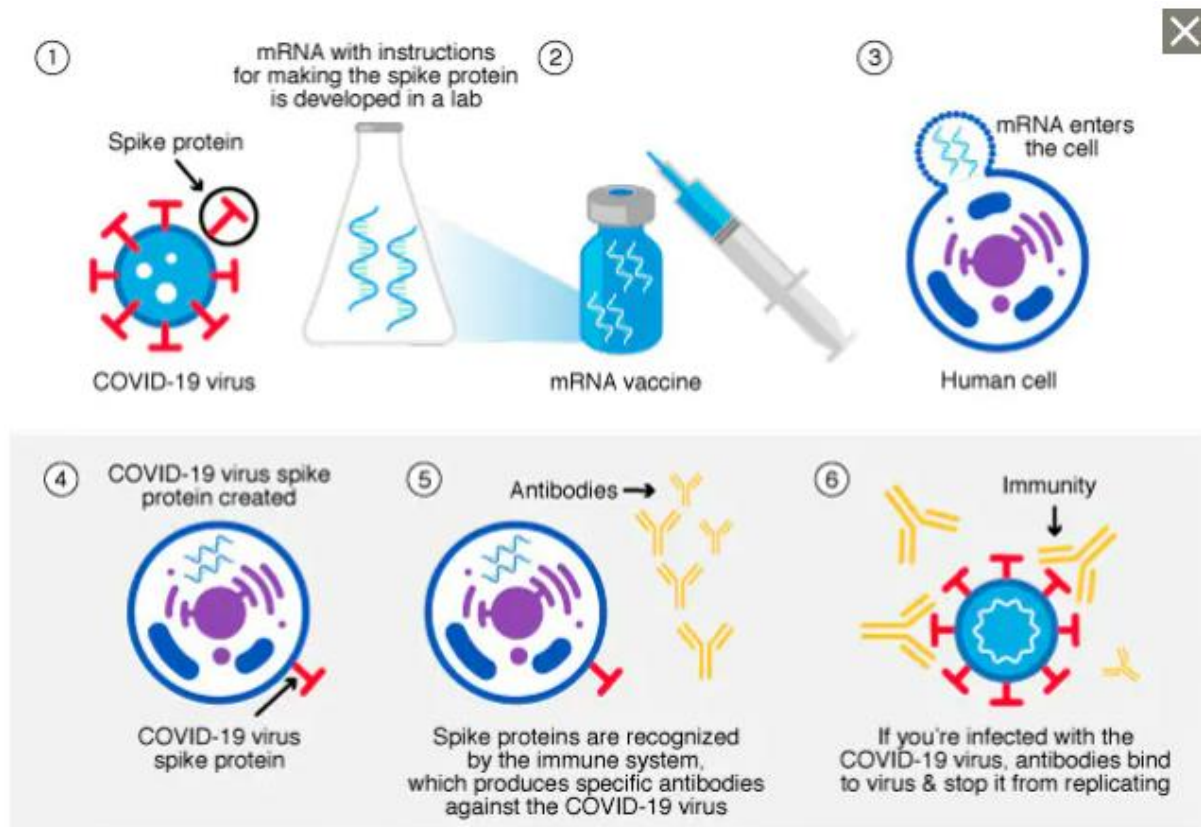


Figure 5: This shows how the mRNA Moderna vaccine helps fight against COVID-19 virus (Mayo clinic 2022, pg. 2)

Table 3: Major ingredients contained in the Moderna Vaccine (Information about the Moderna COVID-19 Vaccine, 2022, pg. 5).

Type of Ingredient	Ingredient	Purpose
Messenger ribonucleic acid (mRNA)	<ul style="list-style-type: none"> Nucleoside-modified mRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2 	<ul style="list-style-type: none"> Provides instructions the body uses to build a harmless piece of a protein from the virus that causes COVID-19. This protein causes an immune response that helps protect the body from getting sick with COVID-19 in the future.
Lipids (fats)	<ul style="list-style-type: none"> PEG2000-DMG: 1,2-dimyristoyl-rac-glycerol, methoxypolyethylene glycol 1,2-distearoyl-sn-glycero-3-phosphocholine BotaniChol[®] (non-animal origin cholesterol) SM-102: heptadecane-9-yl 8-((2-hydroxyethyl) (6-oxo-6-(undecyloxy) hexyl) amino) 	<ul style="list-style-type: none"> Work together to help the mRNA enter cells.

Pfizer-BioNTech:

Pfizer is a lipid non-particle formulated RNA vaccine that targets the S protein of SARS-CoV-2 virus (Francis et al. 2021). The neutralization of the S protein is important because SARS-CoV-2 virus is dependent on S protein for the entry into the human body via

ACE2 receptors (Francis et al. 2021). This neutralization induces an expansion of spike protein-specific T cells (CD4+ and CD8+) (See figure 6; Lamb, 2021). The surface spike protein also plays a major role in the binding and attachment of the virus to host cells (Lamb, 2021). The mechanism of Pfizer involves the translation of mRNA into SARS-CoV-2 protein which is expressed on the surface of the host (Lamb, 2021). This mechanism induces antibodies and quick cellular immune responses which helps in protection against COVID-19 virus. Studies show that Pfizer was 95% effective against COVID-19 during clinical trials in participants (Lamb 2021). Based on FDA approval, Pfizer is authorized for individuals 12 years and older. Similar to other mRNA vaccines, Pfizer contains exactly the same ingredients in small amounts (See table 3; Information about the Moderna COVID-19 Vaccine, 2022).

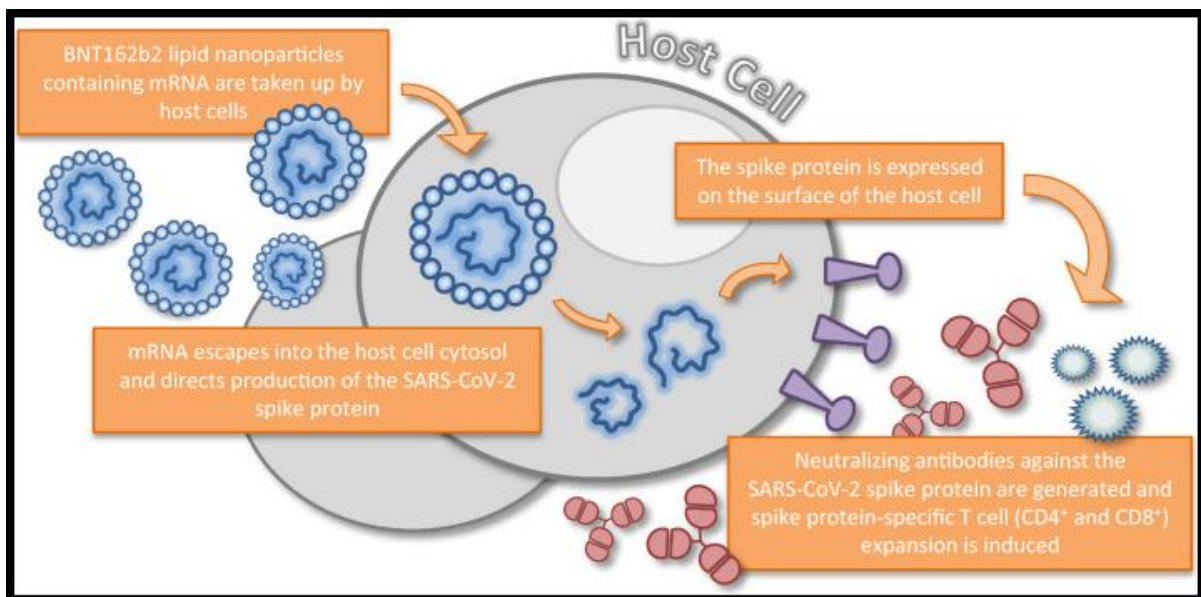


Figure 6: Mechanism of action of BNT162b2 Pfizer following intramuscular administration

(Lamb 2021, pg. 497).

Johnson & Johnson's Janssen:

The Janssen vaccine is known as a viral vector vaccine that contains a modified virus called vector virus which is not a virus that causes COVID-19 (See figure 7; Understanding Viral Vector COVID-19 Vaccines, 2022). It is important to note that this vector virus cannot undergo reproduction, thus unable to cause COVID-19 (Understanding Viral Vector COVID-19 Vaccines, 2022). This vector virus plays an important role in the creation of immune responses in the body (See figure 7; Understanding Viral Vector COVID-19 Vaccines, 2022).

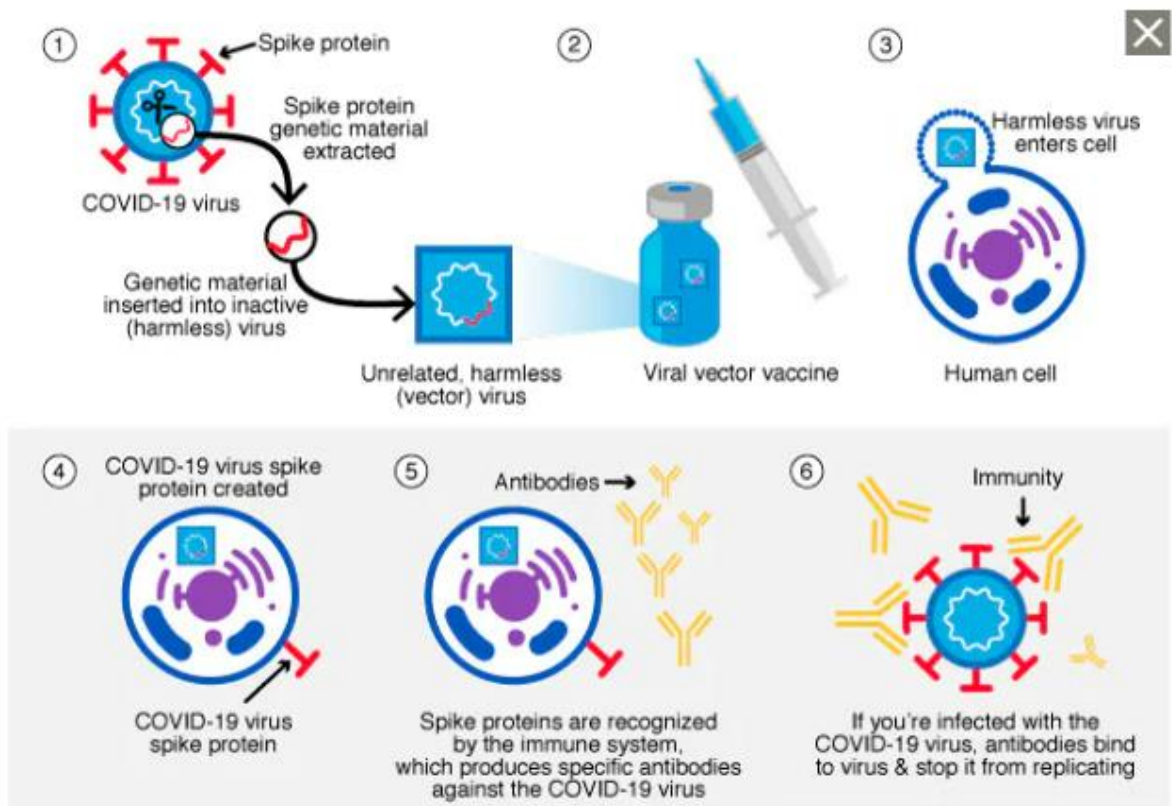


Figure 7: Mechanism of action of a vector viral vaccine in the human body (Mayo clinic

2022, pg. 2).

Once immune response has been induced, the body gets rid of all vaccine ingredients (Understanding Viral Vector COVID-19 Vaccines, 2022). Unlike mRNA vaccines, viral vector vaccines do not interact or integrate with DNA (Understanding Viral Vector COVID-19 Vaccines, 2022). Reports have shown that Janssen vaccine was 66.3% effective during clinical trials at preventing laboratory confirmed COVID-19 infection in people who received the vaccine and had no evidence of being previously infected (Understanding Viral Vector COVID-19 Vaccines, 2022). The Janssen vaccine contains a small amount of ingredients which is generated from food- fats, sugar, salts (See table 4; Understanding Viral Vector COVID-19 Vaccines, 2022).

Table 4: Major Ingredients contained in the Janssen Vaccine (Understanding Viral Vector COVID-19 Vaccines, 2022, pg.5)

Type of Ingredient	Ingredient	Purpose
A harmless version of a virus unrelated to the COVID-19 virus	<ul style="list-style-type: none"> Recombinant, replication-incompetent Ad26 vector, encoding a stabilized variant of the SARS-CoV-2 Spike (S) protein 	Provides instructions the body uses to build a harmless piece of a protein from the virus that causes COVID-19. This protein causes an immune response that helps protect the body from getting sick with COVID-19 in the future.
Sugars, salts, acid, and acid stabilizer	<ul style="list-style-type: none"> Polysorbate-80 2-hydroxypropyl-β-cyclodextrin Trisodium citrate dihydrate Sodium chloride (basic table salt) Citric acid monohydrate (closely related to lemon juice) Ethanol (a type of alcohol) 	Work together to help keep the vaccine molecules stable while the vaccine is manufactured, shipped, and stored until it is ready to be given to a vaccine recipient.

Sides Effects of Moderna, Pfizer and Janssen Vaccine:

Side effects after COVID-19 vaccination tend to be mild, temporary and in some rare cases include adverse events such as allergic reactions (What to Expect after Getting a COVID-19 Vaccine, 2022). Studies have shown that side effects after vaccination include cough, fever, fatigue, headache, shortness of breath, chills, muscle pain, sore throat, diarrhea, or vomiting (See table 5; Vasireddy et al. 2021). However, adverse effects which are noticeably rare include paroxysmal ventricular arrhythmia, right leg paresthesia and shoulder injury (Vasireddy et al. 2021).

Table 5: Side Effects From Pfizer-BioNTech, Moderna and Janssen COVID-19 Vaccines

(Vasireddy et al. 2021, pg. 207).

COVID-19 vaccine	Common side effects	Other adverse effects
Pfizer-BioNTech	Fever, cough, fatigue, headache, shortness of breath, chills, muscle pain, sore throat, diarrhea, or vomiting, local injection site redness or swelling.	Lymphadenopathy, Bell's palsy, paroxysmal ventricular arrhythmia, right leg paresthesia and shoulder injury.
Moderna	Fever, local pain, swelling, tenderness and erythema at the injection site. Axillary lymphadenopathy, fatigue, headache, myalgia, arthralgia, chills and nausea/vomiting.	Hypersensitivity reactions, Bell's palsy and some other lymphadenopathy.
Janssen	Mild to moderate febrile episode, injection site pain, fatigue, headache and myalgia.	

As part of a larger study on comorbidities associated with responses to COVID-19 vaccine, this research sought to analyze if comorbidities influence the human body after COVID-19 vaccinations. We collected medical data with a high level of anonymity for individuals within our study area. Therefore, our objectives were to: 1) determine the influence of comorbidities on responses to the COVID-19 vaccinations and 2) determine if there is a correlation between comorbidities and the type of vaccine received.

CHAPTER II

MATERIALS AND METHOD

Study Area and Data Collection:

A voluntary survey with guaranteed anonymity for participants was emailed to the Maryville College Campus to students, staff, and faculty on 31st of August-2nd September (See appendix 1). In addition, individuals were solicited to fill out the survey in the Maryville College library. Data for this study was collected using a blank quiz survey (See appendix 2). This research project was approved by the IRB of Maryville College (See appendix 3).

Data Analysis

After data were collected, participants' responses were collected and data was input into an Excel worksheet for results collection. Data were organized to compare (1) the influence of vaccine type on symptoms after the first and second dose, (2) percent of younger (<35) and older (>35) individuals experiencing sore arms (the most common symptom, and (3) the impact of BMI on symptoms. Statistical analyses were not conducted due to the fact that the survey respondents were not a representative population (as they were all Maryville College individuals and mostly younger).

CHAPTER III

RESULTS

Overall, this study included 68 participants of which 57 (83%) were younger adults (age 18-35) and 11 (17%) were older adults (age 35-61). From the data, 52.9% were females and 47.1% were males. Data from the survey showed that 41 (60.3%) received the Pfizer vaccine whereas 20 (29.4%) and 7 (10.3%) received Moderna and J&J respectively. The total percent of symptoms in participants were compared in all 3 vaccines (see figure 8), with sore-arm being the most common symptom in participants (over 40% for all vaccines). Tiredness was the second most common symptom among all participants (See figure 8) with over 20% for all vaccines. The remaining symptoms included chills, joint pain, difficulty in breathing, swollen lymph nodes, nausea, and vomiting.

The severity of sore arms amongst young and old participants after 1st and 2nd dose of vaccination was calculated and is shown in Figures 9 and 10. The age bracket for young age was between 18-35, whereas old age was 35-above. Analysis was carried out on the correlation between BMI and total number of symptoms amongst participants after 1st and 2nd dose (Figures 11 and 12). BMI was grouped into 3 categories: Underweight (<18.5), Healthy (18.5-24.9) and Overweight (>24.9). Due to the small sample size, overweight and obese were grouped as one category. Figure 13a and b analyzes the impact of comorbidities

on the total number of symptoms experienced by participants after 1st and 2nd dose respectively.

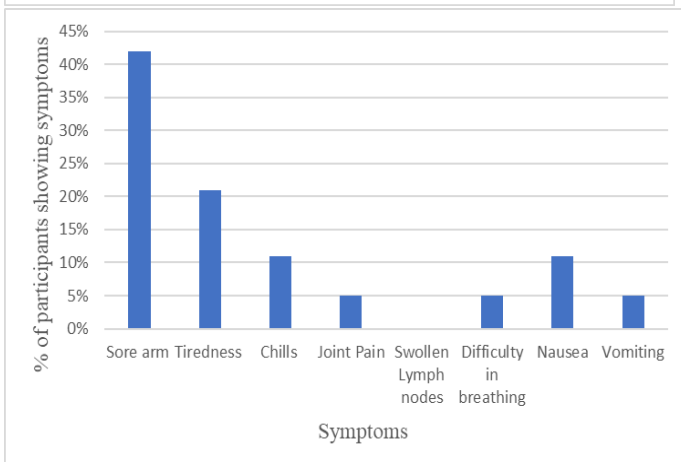
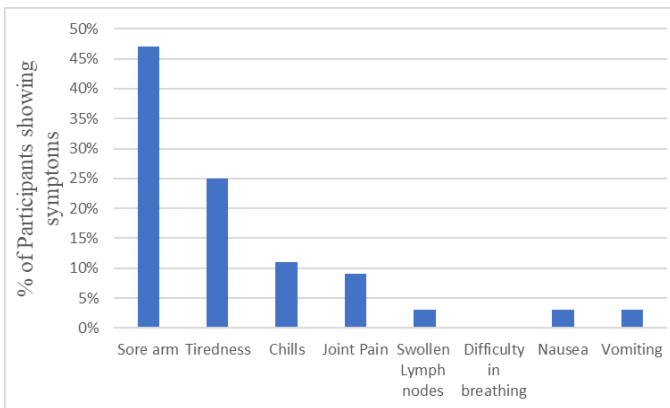
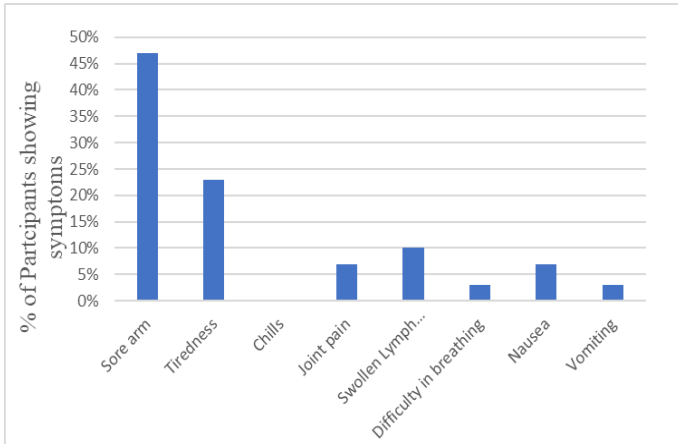


Figure 8. Percent of respondents showing any severity of symptoms to (A) Moderna, (B) Pfizer, and (C) Johnson and Johnson vaccinations.

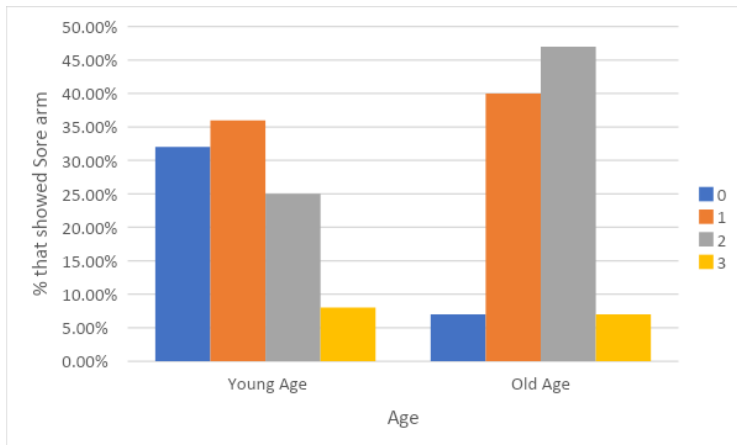


Figure 9. Percent of young and old individuals exhibiting no soreness, mild soreness, moderate soreness, or severe soreness in the arm after the 1st Dose (0=none, 1= Mild, 2= Moderate, 3= Severe).

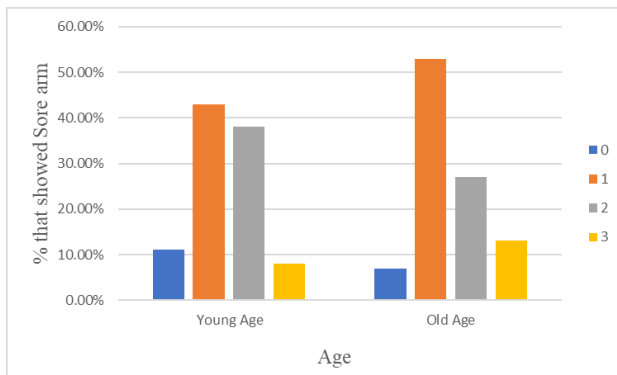


Figure 10. Percent of young and old individuals exhibiting no soreness, mild soreness, moderate soreness, or severe soreness in the arm after the 2nd Dose (0=none, 1= Mild, 2= Moderate, 3= Severe).

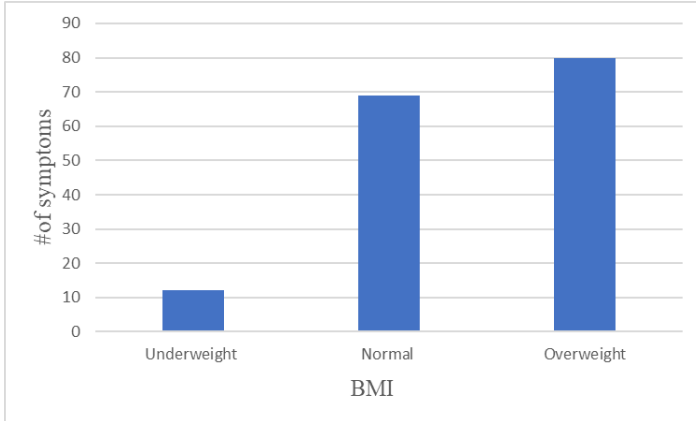


Figure 11: This shows a comparison between BMI and total number of symptoms amongst participants after 1st dose of vaccination. (Underweight = below 18.5 BMI, Normal weight= 18.5-24.9 BMI, Obesity= 25.0-above).

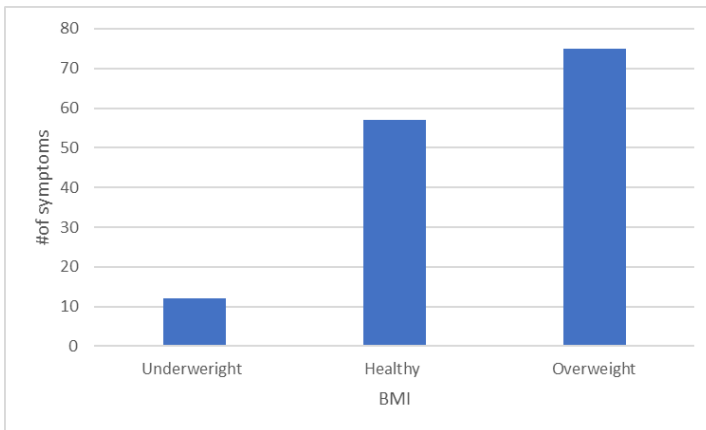


Figure 12: This shows a comparison between BMI and total number of symptoms amongst participants after 2nd dose of vaccination. (Underweight = below 18.5 BMI, Normal weight= 18.5-24.9 BMI, Obesity= 25.0-above).

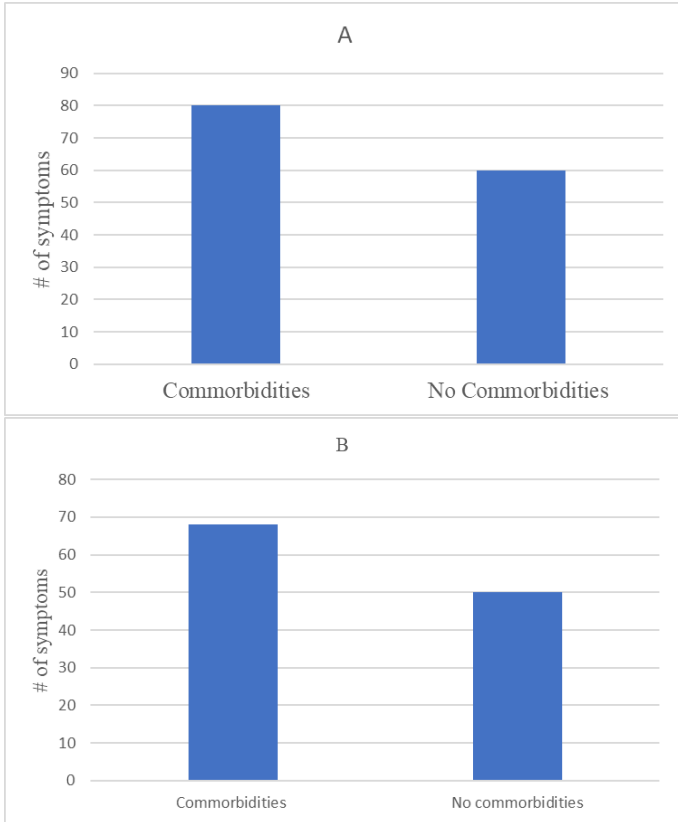


Figure 13: Figure shows the impact of comorbidities on the total number of symptoms experienced by participants (A= after 1st dose, B= after 2nd dose).

CHAPTER IV

DISCUSSION

COVID 19 Vaccines and Severity of Symptoms in Participants:

Reports from CDC have shown that there is great variation in people's confidence on Covid-19 vaccines. This is due to varied awareness about vaccines, possible associated-risk, and religious and political aspects (Vasireddy et al. 2021). Delivering a conformationally accurate protein is crucial for any vaccine that aims to induce antibody mediated immunity (Al Khames et al 2021). The safety of vaccines to the human body is the first priority in production of any vaccine (Al khames et al. 2021). Thus, identifying, quantifying and examining possible risk factors against potential advantages are potential aspects of designing any vaccine (Al khames et al. 2021).

Studies have shown that side effects and symptoms are natural reactions provided by the body due to foreign drug injections (Vasireddy et al. 2021). When the body's neutrophils detect antigens vaccine protein molecules, a release of cytokines occurs (Vasireddy et al. 2021). These cytokines are chemical signals that trigger immune responses such as fever, sore arm, nausea, chills (Al khames et al. 2021). However, there is no scientific data showing correlation between adverse vaccine side effects and adaptive responses by the body (Al khames et al 2021).

This study was not designed to determine the efficacy of the three vaccines but rather to primarily analyze the possible side effects and symptoms expressed by participants as well as comparing them between all three vaccines. Our best-supported model for severity of symptoms to the type of vaccine received (See figure 8) included sore arms as the most common symptom experienced by participants (over 45%) for all vaccines. This result is in agreement with studies conducted by the CDC which shows sore arms as the most common side effect experienced by participants (CDC, 2020). The COVID-19 vaccine is an intramuscular injection which is injected into the deltoid muscle (CDC, 2020). The deltoid muscle is the large muscle that gives the shoulder its range of motion. Studies have shown that the sore arm is as a result of inflammation at the injection site which is triggered by the vaccine (CDC, 2020). These results are also in agreement with results recorded by El-shitany et al. 2021, who reported sore arms being the most common side effect experienced by COVID vaccine recipients. Studies conducted by CDC have shown that 45% of participants experienced soreness after receiving flu shots compared to 90% of participants who received Moderna (CDC, 2020). This is in agreement with our results showing that participants who received Moderna experienced more soreness of arm than those who received Pfizer and J&J. However it is important to note that both flu and Covid-19 vaccines are received via intramuscular injection and the most common side effects experienced by participants is soreness of the arm (CDC, 2020).

Results from data shows that participants who received Moderna reported more sore arms (48%) than those who received Pfizer (46%) and Johnson and Johnson (42%) vaccines.

However, only participants who received Moderna and J&J reported difficulty in breathing. In addition, chills were common only in participants who received Moderna and J&J. Results conducted by Salah & Mehta show that myocarditis (Difficulty in breathing) was associated in 60% of participants who received Pfizer, 33% in Moderna and 7% in J&J participants. It was important to note that 6 out of 9 participants experienced difficulty breathing after receiving the 2nd dose of Moderna (Salah & Mehta, 2021). However, our data analyzed via excel shows that 7 participants experienced difficulty in breathing with 3 occurring after 1st dose and 4 occurring after 2nd dose. Differences in results could be a result of the small sample size for participants who received Pfizer compared to Moderna.

Other notable symptoms included tiredness, chills, joint pain, swollen lymph nodes, nausea, difficulty in breathing, vomiting. However, only participants who received Pfizer (3%) and J&J (5%) reported difficulty in breathing. In addition, chills were common only in participants who received Moderna (12%) and J&J (11%). Analysis conducted by Salah and Mehta showed that associated effects (difficulty in breathing) of myocarditis related to COVID vaccines has an overall fast recovery with no short-term complications.

Figure 11 and 12 shows a clear comparison between COVID-19 vaccine side effects and Body Mass Index amongst participants. Results from figure 11 and 12 shows that participants who were overweight experienced more total side effects (70) than the normal and underweight participants after 1st and 2nd dose. Little to no studies have assessed the impact of weight status on possible adverse reactions (Iguacel et al., 2021). Due to low sample size, overweight and obese participants were categorized as one group (overweight).

Obesity is a major risk factor of COVID-19, but does that conclude that an obese patient is likely to experience more side effects than a normal patient? Our results were not in agreement with results conducted by Iguacel et al. (2021) who reported more side effects experienced in those who were non-overweight compared to overweight. A major factor in the difference in results was the inclusion of age in the Iguacel study when calculating the total BMI of a person, which was not considered in this study. Most studies have shown that obesity reduces the effectiveness of a vaccine (CDC, 2020). However, it is important to note that there is no correlation between vaccine side effects and strength of immunity provided by the vaccine. However, studies conducted by Piernas et al. 2022, showed adverse effects in underweight and obese patients than in healthy patients even after 2nd dose of vaccinations. It is important to note that the sample size for underweight participants was low in the present study and, thus, might have played a major role in the difference in results.

Conclusion:

Individuals with severe comorbidity are more susceptible to SARS-COV-2 infection due to immune response dysregulation (de Lucena et al. 2020). To date, the current vaccines against COVID-19 have shown a high level of efficacy. However, the scarcity of studies on comorbidities in relation to COVID-19 vaccines makes it advisable to promote research that contributes to a deeper understanding of these vaccines. The most common side effect reported by participants was sore arm (>40%). Other common side effects included tiredness, nausea, chills, difficulty in breathing, joint pain and swollen lymph nodes. We found a high

risk of presenting some side effects against COVID-19 vaccine in those with higher BMI (obesity and overweight) compared to those with lower BMI (normal and underweight). In addition, our data shows that people with comorbidities experienced more side effects than those with no comorbidities.

One of the major limitations in this study was the sample size being small (n=68). Because of this, it is difficult to get a clear depiction of the data as well as make definitive conclusions on the results such as comparing BMI to COVID-19 side effects. Additionally, responses for this study were restricted to only the Maryville college community. Thus, it is difficult to make definitive conclusions concerning the vaccines based on the results obtained from this study.

APPENDICES

APPENDIX 1: Brief summary of survey and guarantee of anonymity

Comorbidities associated with responses to COVID-19 vaccine.

The purpose of this survey is to investigate comorbidities associated with responses to the COVID-19 vaccinations. The type of questions involved in this survey include age, height, weight, previously diagnosed medical conditions, type of vaccine received as well as responses to the vaccination.


This survey will take no more than 10 minutes to complete and will help us understand why people respond differently to the vaccine. The benefit of participating in this survey is that participants would be able to understand how comorbidities influence individual's responses to COVID-19 vaccination.

This survey is fully voluntary, and participants are free to discontinue at any point. To assure a high level of anonymity for individuals, personal data such as your name are not components of the survey data. Therefore, all responses from participants are anonymous and are stored on the researchers secured Google cloud account and computer.



For questions about the research, please feel free to contact me via email at nzube.ndubueze@my.maryvillecollege.edu or my advisor (drew.crain@maryvillecollege.edu). You have full rights as a research volunteer to stop participating before submitting the survey at any time without any penalty. If you do not take part in this survey, you will receive no penalty. Once your survey is submitted, your responses are fully anonymous with a high level of confidentiality. If you have questions about your right as a research volunteer that I may not have addressed, you may write the Chair of the Maryville College IRB.
Institutional Review Board
Maryville College

APPENDIX 2: Blank Quiz survey

⋮

Height (Inches)  Short answer ▾

Short answer text

Answer key (0 points)   Required ⋮

Age *

Short answer text

Weight (pounds) *

Gender *

Male

Female

non-binary

Medical health issues? "Has been previously diagnosed with" (Please select all that apply) *

Cancer

Cardiovascular diseases

Neurological conditions

Diabetes

Immunocompromised state

Overweight/Obesity

Stroke

Asthma

Sickle cell disease

Tuberculosis

Other

If you chose other, please specify medical health issue.

Short answer text

Name of vaccine *

Pfizer

Moderna

Johnson & Johnson

Date of 1st dose *

Month, day, year



Did you experience any symptoms after receiving 1st dose? *

	none	Mild	Moderate	Severe
Chills	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Tiredness	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Sore arm	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Joint Pain	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Vomiting	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Nausea	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Diarrhea	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Swelling of the face	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
-	-	-	-	-
Swollen lymph nod...	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Difficulty in breathi...	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Myocarditis	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Date of 2nd dose *

Month, day, year



Did you experience any symptoms after receiving 2nd dose? *

	none	Mild	Moderate	Severe
Chills	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Tiredness	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Sore arm	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Joint Pain	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Vomiting	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Nausea	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Diarrhea	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Swelling of the face	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Swollen lymph nod...	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Difficulty in breathi...	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Myocarditis	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Have you received the Covid-19 booster?

- Yes
- No

Type of Covid-19 booster

- Pfizer
- Moderna
- Johnson & Johnson

Did you experience any symptoms after receiving the booster?

	none	Mild	Moderate	Severe
Chills	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Tiredness	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Sore arm	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Joint Pain	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Vomiting	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Nausea	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Diarrhea	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Swelling of the face	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Swollen lymph nod...	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Difficulty in breathi...	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Myocarditis	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

APPENDIX 3: IRB approval document



Maryville College Institutional Review Board
OHRP IRB#: IRB00007383
FWA Assurance #: FWA00015150

Principal Researcher: Nzube Henry Ndubueze

Faculty Supervisor: Dr. Drew Crain

Division: National Sciences

Title: Comorbidities associated with Responses to Covid-19 Vaccinations

Protocol#: 130422.01

Approval Status: Approved

April 22, 2022

Dear **Nzube**:

The Maryville College Institutional Review Board (IRB) has carefully considered your proposal referenced above. The proposed procedures afford reasonable protection to the human participants involved and therefore you are granted approval for the study.

Your approval is effective April 22, 2022 and will expire one year from this date. Thereafter, continued approval is contingent upon submission of a progress report that must be reviewed and approved prior to the expiration date.

Approval is contingent upon your agreement to obtain informed consent from your participants, to abide by the protocol summarized in the approved IRB application, and to keep appropriate records concerning your participants.

You are required to submit to the Maryville College IRB for review any changes in procedures involving human participants prior to the implementation of such changes.

If you have any questions concerning this approval or regulations governing human participant activities, please contact Ryan Mickey, Chair of the Maryville College IRB, by e-mail at IRB.Review@maryvillecollege.edu or by phone (865) 981-8262.

Sincerely,

A handwritten signature in black ink that reads "Ryan Mickey". The signature is written in a cursive, flowing style.

Ryan Mickey, Ph.D.
Institutional Review Board, Chair

502 E. Lamar Alexander Parkway, Maryville, Tennessee 37804-5907
Voice 865.981.8000 | Fax 865.981.8010 | maryvillecollege.edu

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