Spring 5-12-2023

Comparing the Mortality Trends of COVID - 19 Comorbidities and Recommendations for the Population at Risk

Ogechukwu Igbokwe

Comparing the Mortality Trends of COVID - 19 Comorbidities and Recommendations for the Population at Risk

by

Ogechukwu D. Igbokwe

Under the Direction of Kevin Maloney, PhD, MPH

A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of

Master of Public Health

in the School of Public Health

Georgia State University

2023

ABSTRACT

AIM: The aim of this research is to assess the impact of COVID-19 on mortality rates among people in the United States with comorbid diabetes or cardiovascular disease (CVD)

METHODS: We utilized mortality data published by the Centers for Disease Control and Prevention for the years 2018–2021. Annual mortality rates were reported, including all-cause mortality, and mortality rates with COVID-19, diabetes and cardiovascular disease listed as a primary or underlying cause of death.

RESULT: Compared to 2018, there was a substantial increase in all-cause mortality across 2019, 2020 and 2021 respectively (0.9%, 18.4% and 20.3%). At the same time, we observed increased rates of CVD mortality (0.9%, 18.4% and 19.8%) and diabetes mortality (2.25% 39.7% and 42.7%).

CONCLUSION: We observed similar increases in the rates of all-cause mortality and CVD mortality in 2020 and 2021, but a more substantial increase in the rate of deaths among people with diabetes.

Comparing the Mortality Trends of COVID - 19 Comorbidities and Recommendations for the Population at Risk

by

OGECHUKWU D. IGBOKWE

Committee Chair: Kevin Maloney

Committee: Ike Okosun

Electronic Version Approved:

Office of Graduate Services

College of Arts and Sciences

Georgia State University

May 2023

AUTHOR STATEMENT

In presenting this thesis as a partial fulfillment of the requirements for an advanced degree from Georgia State University, I agree that the Library of the University shall make it available for inspection and circulation in accordance with its regulations governing materials of this type. I agree that permission to quote from, to copy from, or to publish this thesis may be granted by the author or, in his/her absence, by the professor under whose direction it was written, or in his/her absence, by the Associate Dean, School of Public Health. Quoting, copying, or publishing must be solely for scholarly purposes and will not involve potential financial gain. I understand that any copying from or publication of this dissertation which involves potential financial gain will not be allowed without written permission of the author.

Ogechukwu D. Igbokwe

ACKNOWLEDGEMENTS

I would like to take this opportunity to express my sincere gratitude to God and all those who have contributed to my personal and professional growth. Without their support and encouragement, I would not have achieved the level of success that I have today.

Firstly, I would like to express my heartfelt thanks to my mother and sisters, Mrs. Lovette Igbokwe, Chinelo Igbokwe and Onyee Igbokwe for their unwavering love and support. They have been my pillars of strength, providing me with the motivation and inspiration to pursue my dreams and reach for the stars.

I would also like to extend my gratitude to my thesis chair, Dr. Kevin Maloney who has guided me through this process and imparted invaluable knowledge and skills. I would also like to thank my committee member, Dr. Ike Okosun for his dedication and commitment to this process. Special thanks to Dr. Emily Graybill, and the entire staff of Centers for Leadership in Disability whose guidance and support have been instrumental in shaping me into the person I am today.

To my friends especially Toyosi Ogunmuyiwa, Adetomiwa Adekoya and Fumnanya Abuah, thank you for being there for me through thick and thin. Special thanks to my church community, RCCG – The Rock Center Atlanta for their unwavering support and encouragement. They have been a constant source of strength and motivation for me.

I would also like to thank my colleagues and collaborators for their support and contributions to my work. Their insights and expertise have been invaluable in advancing my research and professional endeavors.

To all those who have contributed to my personal and professional growth, thank you from the bottom of my heart. Your support and encouragement have been invaluable, and I will always be grateful for everything you have done for me.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

Cardiovascular Diseases – CVD

Case Fatality Rate – CFR

Chronic Obstructive Pulmonary Disease – COPD

Human Immunodeficiency Virus – HIV

Coronary Artery Disease – CAD

Centers for Disease Control and Prevention – CDC

Intensive Care Unit – ICU

1 INTRODUCTION

1.1 Background

SARS-CoV-2 is a virus that belongs to the family *Coronaviridae*, which also includes other viruses that can cause respiratory illnesses in humans and animals (WHO, 2021). The name "coronavirus" comes from the crown-like spikes on the surface of the virus particles, which are visible under a microscope. SARS-CoV-2 was first identified in Wuhan, China, in December 2019, and quickly spread around the world, causing a global pandemic (WHO, 2021). The virus causes a respiratory illness known as COVID-19, which can range from mild to severe and can be fatal in some cases, especially among elderly people (65+) and those with underlying health conditions (CDC, 2023).

COVID-19 has had a significant impact on public health, economies, and social systems around the world. As of September 2021, there were over 227 million confirmed cases of COVID-19 worldwide, with more than 4.6 million deaths attributed to the virus (WHO, 2021). The case fatality rate (CFR) is the percentage of confirmed cases that result in death. The CFR for COVID-19 varies by country and region, but it is estimated to be around 2.1% globally. The estimated CFR in the US is 1.1% (Cao et al., 2021). In addition, asymptomatic persons seem to account for approximately 40% to 45% of SARS-CoV-2 infections, and they can transmit the virus to others for an extended period, perhaps longer than 14 days. (Oran & Topol 2020)

1.2 Transmission and Symptoms of the Disease

The virus is primarily spread through respiratory droplets when an infected person coughs, sneezes, talks, or breathes. It can also be spread by touching a surface contaminated with the virus and then touching the mouth, nose, or eyes (Huang et al., 2020). The virus can be transmitted by

people who do not show any symptoms, which makes it difficult to control. The symptoms of COVID-19 vary widely in severity and can range from mild to severe illness. Common symptoms include fever, cough, fatigue, shortness of breath, loss of smell or taste, and body aches. Some people may also experience sore throat, headache, or diarrhea. Severe cases can lead to pneumonia, acute respiratory distress syndrome, and/or death (Zayet et al., 2020)

1.3 Disease Severity and Clinical Manifestation

The severity of the disease can vary depending on various factors, including the presence of comorbidities. Comorbidities are pre-existing medical conditions that make people infected with SARS-CoV-2 more susceptible to developing severe COVID-19 disease (Guan et al., 2020). It is important to note that not everyone with SARS-CoV-2 and these comorbidities will develop severe COVID-19 illness. Similarly, some people without any known comorbidities may still develop severe illness. COVID-19 patients with diabetes, chronic obstructive pulmonary disease (COPD), cardiovascular diseases (CVD), hypertension, malignancies, human immunodeficiency virus (HIV), and other comorbidities could develop a life-threatening situation (Williamson et al., 2020).

SARS-CoV-2 utilizes ACE-2 receptors found at the surface of the host cells to infect the cell. Certain comorbidities are associated with a strong ACE-2 receptor expression and higher release of proprotein convertase that enhances the viral entry into the host cells. These comorbidities along with SARS-CoV-2 infection led to an amplified immune response, more severe disease pathology, and are associated with substantial morbidity and mortality (Hassan et al., 2020). However, having these underlying conditions may increase the risk of severe illness and complications. It is important for people with comorbidities to take extra precautions to protect

themselves from SARS-CoV-2 infection, such as wearing masks, practicing social distancing, and getting vaccinated when possible (Ssentongo et al., 2021).

Preventing the spread of COVID-19 requires individual and collective efforts. Measures such as wearing masks, practicing social distancing, washing hands frequently, and avoiding large gatherings have been recommended by health experts (Chu et al., 2020). Vaccines have also been developed to prevent SARS-CoV-2 infection or reduce symptoms of COVID-19 disease, and vaccine distribution efforts have been ongoing in many countries. Over 5.7 billion doses of COVID-19 vaccines had been administered worldwide, with around 40% of the global population having received at least one dose (Polack et al., 2020). However, there are significant disparities in vaccination rates between different countries and regions. As of May 3rd, 2023, around 66% of the population was fully vaccinated against COVID-19, and 78% had received at least one dose (CDC, 2022). However, vaccination rates varied widely by state and demographic group, with some areas and populations lagging behind in their vaccination rates. COVID-19 has had a significant impact on global health, economies, and societies. The pandemic has caused millions of deaths worldwide and has led to significant economic disruptions, including job losses and business closures. The pandemic has also highlighted existing social and economic inequalities and has led to changes in how people work, learn, and interact with each other (Woolf et al., 2020).

Since the outbreak began, scientists and researchers have been working to understand the virus and develop effective treatments and vaccines. The exact percentage of people in the U.S. who have already contracted and recovered from COVID-19 and have natural immunity is difficult to estimate (Baden et al., 2021). However, as of September 2021, the CDC estimated that about 40% of the U.S. population had been infected with COVID-19 at some point which means there

is a high percentage of herd immunity. Despite the progress made, the pandemic continues to have a significant impact on public health, economies, and daily life around the world.

Research on COVID-19 comorbidity is ongoing, and new information is being discovered regularly. It is essential for individuals with underlying medical conditions to take precautions to reduce their risk of infection and seek medical attention promptly if they develop symptoms of COVID-19 (Zheng et al., 2020).

1.4 Cardiovascular Diseases (CVD) and Diabetes Statistics

According to the American Heart Association's 2021 Heart Disease and Stroke Statistics update, CVD affects approximately 121.5 million adults in the United States, or about 48% of the adult population. About 655,000 Americans die from heart disease each year, which is about 1 in every 4 deaths. Coronary heart disease is the most common type of heart disease and accounts for about 370,000 deaths annually. About 18.2 million adults in the United States have coronary artery disease (CAD). Every 40 seconds, someone in the United States has a heart attack. Every year, about 795,000 Americans have a stroke, with about 610,000 being first-time strokes. About 2 in every 5 adults in the United States have high blood pressure, a major risk factor for CVD. African Americans have a higher risk of death from heart disease compared to non-Hispanic whites (AHA, 2021).

The percentage of adults aged 18 years or older with diagnosed diabetes in the United States was 10.5% in 2018. This represents approximately 34.2 million people. Additionally, an estimated 7.3 million people in the United States have undiagnosed diabetes, which means the actual prevalence of diabetes is likely higher (Zhu et al., 2021).

1.5 Purpose of Study

The purpose of this research is to compare the mortality trends of COVID-19 co-morbidities (diabetes and cardiovascular diseases) from 2018 – 2021, suggest possible recommendations to prevent high mortality rates among those who are at risk for COVID-19 comorbidity, and show the importance for governments and health systems to plan for future pandemics. The role of demographics in this study will also be considered to give a more comprehensive perspective and conclusion on the increased mortality trends for this population at risk. For future planning, the findings of this research will shed light on possible precautions and factors that can impact mortality rates. The study focuses on the pre pandemic phase (2018 – 2019) and the pandemic phase (2020 – 2021).

1.5.1 Research Question #1

Among adults aged 25+ years old in the United States, was there a substantial increase in mortality rates among people with diabetes and/or cardiovascular disease during the COVID-19 pandemic?

1.5.2 Research Question #2

Among the US population during the pre-pandemic phase and the pandemic phase, what is the mortality rate distribution across these six race and ethnicity categories: non-Hispanic blacks, non-Hispanic whites, native Hawaiian or Other Pacific Islander, Asians, American Indian or Alaska Natives, or more than one race?

1.5.3 Research Question #3

Are there reliable recommendations to help reduce mortality and morbidity rates of people who are at risk for COVID-19 comorbidities in the United States?

2 LITERATURE REVIEW

2.1 SARS-COV-2

COVID-19 is a respiratory disease caused by SARS-CoV-2, which was first identified in Wuhan, China in December 2019. Since then, it has rapidly spread across the globe and caused a global pandemic. COVID-19 has affected individuals of all ages, causing mild to severe symptoms, and has led to significant mortality rates (WHO, 2023). The purpose of this literature review is to provide an overview of the current knowledge on COVID-19, including its epidemiology and the several comorbidities associated with it.

2.2 Incidence of COVID-19

COVID-19 has affected people of all ages and has spread rapidly throughout the world. The virus is primarily transmitted through respiratory droplets when an infected person coughs, sneezes, or talks. It can also be transmitted by touching surfaces contaminated with the virus and then touching one's mouth, nose, or eyes (Garg et al., 2020). COVID-19 has affected millions of people worldwide. As of February 2023, there have been over 427 million confirmed cases and over 5.9 million deaths globally (WHO, 2023).

According to data from the Centers for Disease Control and Prevention (CDC), as of September 2021, there were over 40 million confirmed cases of COVID-19 in the United States, with over 650,000 deaths attributed to the disease. The pandemic has affected different regions of the United States in varying degrees, with some areas experiencing higher rates of infection and mortality than others. Factors such as population density, access to healthcare, and adherence to public health guidelines have all played a role in the prevalence of COVID-19 in different regions.

It is important to note that the situation with COVID-19 is constantly evolving, and the prevalence of the disease in the United States has changed significantly (KFF, 2022).

COVID-19 has had a significant impact on elderly adults in the United States, who are at higher risk of severe illness and death from the disease (CDC, 2021). According to data from the CDC, as of September 2021, people aged 65 years and older accounted for over 80% of COVID-19 deaths in the United States. This is due in part to the fact that older adults are more likely to have underlying health conditions that put them at higher risk of severe illness, such as heart disease, diabetes, and chronic lung disease. The pandemic has also had a significant impact on the mental health and well-being of older adults, many of whom have been isolated from friends and family members due to social distancing measures. This isolation can lead to increased feelings of loneliness and depression, which can have long-term health consequences (Krendl & Perry, 2021). To protect older adults from COVID-19, it is important to follow public health guidelines, such as getting vaccinated, wearing masks, practicing social distancing, and washing hands regularly. Additionally, it is important to prioritize the mental health and well-being of older adults by finding safe ways to stay connected with loved ones, such as through video calls or outdoor visits (O'Caoimh et al., 2021).

2.3 Clinical presentation and Diagnosis

COVID-19 can present with a wide range of symptoms, ranging from asymptomatic or mild illness to severe illness requiring hospitalization. Common symptoms include fever, cough, shortness of breath, fatigue, muscle or body aches, headache, loss of taste or smell, sore throat, and congestion or runny nose (Lippi & Plebani, 2021). In severe cases, COVID-19 can lead to respiratory failure, sepsis, and death. The severity of the disease can vary depending on age, underlying health conditions, and other factors. Diagnosis of COVID-19 is typically made through

a laboratory test, such as a PCR test, which detects the virus's genetic material. Antigen tests are also available, which can provide rapid results but are less sensitive than PCR tests. Chest X-rays and CT scans may also be used to evaluate the extent of lung involvement in severe cases. (Kavanagh et al., 2021).

2.3.1 Treatment

Currently, there are several treatment options available for COVID-19, including antiviral medications, corticosteroids, and monoclonal antibodies. The antiviral medication remdesivir has been shown to reduce hospitalization time, and corticosteroids have been shown to reduce mortality in hospitalized patients. Monoclonal antibodies have also been shown to be effective in reducing hospitalization rates and mortality in high-risk individuals (Beigel et al., 2020).

2.4 Comorbidities

Comorbidities refer to the presence of one or more additional health conditions that exist alongside a primary condition or disease. Comorbidities can be either pre-existing or acquired during the course of the primary illness (Salvi et al., 2021). Comorbidities are common in many chronic diseases, such as diabetes, heart disease, and obesity, and can impact the severity of the primary condition, increase the risk of complications and reduce the effectiveness of treatment (de las Heras Gala et al., 2020). For example, a person with diabetes and high blood pressure may be at greater risk for cardiovascular disease. It is important for healthcare providers to identify and manage comorbidities to improve patient outcomes and reduce healthcare costs. Strategies for managing comorbidities may include lifestyle modifications, medication management, and coordinated care among healthcare providers (Wu et al., 2020).

In populations aged 65+, comorbidities are quite common and can have a significant impact on overall health and well-being. Some of the most common comorbidities in elderly people include hypertension which is a condition characterized by high blood pressure and is a major risk factor for heart disease and stroke (Poudel et al., 2021). Arthritis is a condition that causes inflammation in the joints, leading to pain, stiffness, and difficulty moving. Diabetes is a chronic condition that affects the body's ability to regulate blood sugar levels. It can lead to serious health problems such as heart disease, kidney failure, and blindness (Zhu et al., 2021). Osteoporosis is a condition that causes bones to become weak and brittle, increasing the risk of fractures. Chronic obstructive pulmonary disease (COPD) is a group of lung diseases that make it difficult to breathe. It can be caused by long-term exposure to cigarette smoke, air pollution, or other irritants (Williamson et al., 2020). Cardiovascular disease includes a range of conditions that affect the heart and blood vessels, such as coronary artery disease, heart failure, and arrhythmias. These are just a few examples of the comorbidities that are commonly seen in elderly people. Managing these conditions and addressing any potential interactions between them is an important part of providing effective healthcare for this population (Zhou et al., 2020).

2.4.1 COVID-19 and Cardiovascular Diseases (CVD)

Studies have shown that individuals with underlying CVDs are at a higher risk of developing severe complications from COVID-19. The reason for this is because the virus can worsen pre-existing heart conditions, leading to heart attacks, strokes, and other cardiovascular complications (Chow et al., 2020). Additionally, COVID-19 can also cause inflammation in the heart muscles, known as myocarditis, which can further exacerbate CVDs. Furthermore, COVID-19 can also lead to blood clots, which can increase the risk of heart attacks and strokes. This is

because the virus can trigger the body's immune system to produce excess blood clotting proteins, leading to the formation of clots that can block blood vessels and cause damage to the heart (Li et al., 2020). To reduce the risk of COVID-19 and CVDs comorbidity, individuals should adopt healthy lifestyle habits such as eating a balanced diet, engaging in regular physical activity, and managing stress levels. It is also recommended that individuals with pre-existing CVDs should take extra precautions to avoid exposure to COVID-19, such as wearing masks, practicing social distancing, and getting vaccinated.

Bonow et al. (2020), conducted a study that discussed the heightened risk for people with CVD who later contracted COVID-19. The research explained that very little information is known about this but there is an increasing awareness of unique risks of COVID-19 for those with underlying cardiovascular disease. Such information is of paramount importance as we now must begin to consider the potential for direct and indirect adverse effects of COVID-19 on the heart and especially so in those with already established heart disease.

Tadic et al. (2020), conducted a study that investigated the association between hypertension, diabetes, and cardiovascular diseases as prevalent comorbidities among patients with COVID-19. Hypertension has been proven to be more prevalent in patients with an adverse outcome (admission in intensive care unit, use of mechanical ventilation, or death). There are many speculations about this coronavirus and its relationship with different risk factors and underlying diseases. It was also reported that hypertension, cardiovascular disease, and diabetes were more prevalent among COVID-19 patients who died in comparison with survivors. Although one of the limitations of this study is that there was a large difference in age and sex distribution between groups, this means that there is a high probability that age was not adjusted for, and sex might act

as an effect modifier. In conclusion the study indicated that hypertension alongside diabetes and obesity are predictors of mortality in COVID-19 patients.

Another study conducted by Savoia et al. (2021), showed that COVID-19 caused by SARS-CoV-2 associates with a considerably high rate of mortality and represents currently the most important concern in global health. Initial reports from China, Europe, and United States showed that arterial hypertension and cardiovascular diseases (CVDs) were associated with increased COVID-19-related complications.

Pranata et al. (2020) performed a systematic literature review of several databases on studies that assess hypertension and COVID-19 outcomes. The composite of poor outcome, comprising of mortality, severe COVID-19, acute respiratory distress syndrome (ARDS), need for intensive care unit (ICU) care and disease progression were the outcomes of interest. Hypertension was associated with increased composite poor outcomes (risk ratio [RR] = 2.11, 95% confidence interval [CI] = 1.85, 2.40), including mortality (RR = 2.21, 95% CI = 1.74, 2.81). The review concluded that hypertension was associated with increased poor outcomes in patients with COVID-19 and the association was not affected by age, gender, presence of cardiovascular disease, diabetes, or COPD. This designates that hypertension may act as one of the potential prognostic factors for COVID-19 severity. This review provides a strong evidence base that there are higher death outcomes in populations with co-morbidities of COVID-19 and hypertension.

2.4.2 COVID-19 and Diabetes

Diabetes mellitus is a chronic metabolic disorder characterized by high blood sugar levels resulting from defects in insulin secretion, insulin action, or both. It affects millions of people worldwide and is a significant cause of morbidity and mortality (Hussain et al., 2020). In 2019,

diabetes was the 7th leading cause of death in the United States, with a total of 88,776 deaths attributed to the disease. The age-adjusted death rate for diabetes was 20.5 per 100,000 population (CDC 2020).

Diabetes mellitus is a variable of interest in this study due to its impact on various health outcomes. It is a risk factor for several chronic diseases, such as cardiovascular disease, kidney disease, and nerve damage (Guo et al., 2020). However, in this study, it is being considered in relation to the coronavirus. The two primary types of diabetes are type 1 and type 2. Type 1 diabetes is caused by an autoimmune reaction that destroys the insulin-producing cells in the pancreas, while type 2 diabetes results from insulin resistance and impaired insulin secretion (Gupta et al., 2020). Several risk factors increase the likelihood of developing diabetes mellitus, including genetics, obesity, physical inactivity, and poor dietary habits. It is also more prevalent in certain populations, such as African Americans, Hispanic/Latino Americans, and Native Americans (Pal et al., 2020). Diabetes mellitus is commonly diagnosed through blood glucose testing, including fasting glucose and hemoglobin A1c levels. Treatment typically involves lifestyle modifications, such as increased physical activity and dietary changes, as well as medications, such as insulin and oral hypoglycemic agents (Ceriello, 2020).

The study of diabetes mellitus as a variable of interest is critical to understanding its impact on health outcomes, the increase in the mortality trends during the pre-pandemic and the pandemic phase, COVID-19 comorbidities and identifying strategies to prevent and manage the disease. Research has shown that people with diabetes are at increased risk of severe illness and complications from COVID-19. When someone with diabetes contracts COVID-19, they may experience more severe symptoms and have a higher risk of developing complications, such as pneumonia and acute respiratory distress syndrome (ARDS) (Singh et al., 2020). Additionally,

COVID-19 can cause blood glucose levels to fluctuate and become more difficult to manage in people with diabetes.

There are several reasons why people with diabetes may be at increased risk of severe COVID-19. Firstly, diabetes can weaken the immune system, making it harder for the body to fight off infections. Secondly, diabetes can cause damage to the blood vessels and increase the risk of cardiovascular disease, which is also a risk factor for severe COVID-19 (Yang et al., 2020). Finally, people with diabetes are more likely to have other underlying health conditions, such as obesity and high blood pressure, which can also increase the risk of severe COVID-19. A report from China showed that patients with diabetes had a higher prevalence of cardiovascular disease (32.4% vs. 14.6%), and less fever (59.5% vs. 83.2%) compared with patients without diabetes (Guo et al., 2020). The study suggested that it is important for people with diabetes to take extra precautions to protect themselves from COVID-19, washing their hands frequently, and avoiding large gatherings during the pandemic phase. The study also recommended that this population should work closely with their healthcare provider to manage their diabetes and monitor their blood glucose levels closely, especially if they become ill with COVID-19.

3 METHODS

3.1 Source of Data

The data used for this descriptive study is data from the Centers for Disease Control and Prevention (CDC). The National Center for Health Statistics is a part of the CDC and is responsible for producing vital and health statistics for the nation. Mortality information is collected by the States and territories and provided to the National Vital Statistics System. Data are based on death certificates for U.S. residents. Each death certificate contains demographic data and cause of death, including a single underlying cause of death and multiple other causes of death (up to 20). We obtained the total number of deaths and death rates, by place of residence (United States national, State, and county when available), age group, race, Hispanic ethnicity, sex, and cause of death.

3.2 Data Collection and Descriptive Analysis

Tools employed in this study were descriptive graphs and charts. The different mortality rates were calculated using the US census population based on the different years. However, the numerator differed based on the type of mortality rate being determined. The all-cause mortality rate was calculated using the total number of deaths caused by all diseases as the numerator and the US census population as the denominator. The mortality rate for diabetes and CVD were calculated using the US census population as the denominator. The numerator was the total mortality count for diabetes mellitus and the absolute number of deaths for cardiovascular diseases.

The rates for this study are being presented as per 100,000 people. For the comparison, 2018 is the reference group and these mortality rates are being compared and presented as a percentage change across 2019, 2020 and 2021.

3.3 Population of Interest and Study Eligibility Criteria

The population of interest is the entire U.S. population estimated using the US census population. The study considered several mortality types: all-cause mortality, CVD mortality and diabetes mortality. This study will ensure representativeness and generalizability as the data being used is national data that encompasses the total US population.

3.4 Definition of Key Variables

3.4.1 Diabetes

Diabetes as a variable is defined as diabetes mellitus, which covers type 1 and type 2 conditions. Other variables that were considered during data collection were diabetes population across all the fifty-two states in the United States. The age group for the diabetes population was ten-year age groups ranging from 25–34, 35– 44, 45–54, 55–64, 65–74, 75–84 and 85+. Other demographics such as sex and race were also considered.

3.4.2 Cardiovascular Diseases (CVD)

CVD in this study is defined as all major cardiovascular diseases, the variable encompasses a wide range of conditions that include coronary heart disease, heart failure, stroke, hypertension, myocardial infarction, atherosclerotic cardiovascular disease, endocarditis, pericarditis, myocarditis. The CVD variable considered both male and female gender across ages 25–85+, using a ten-year age grouping. It also considered CVD population in these different races; non-Hispanic blacks, non-Hispanic whites, native Hawaiian or Other Pacific Islander, Asians, American Indian or Alaska Natives, and more than one race.

3.4.3 Diabetes – COVID19 Comorbidity

This variable of interest for this study was obtained using COVID-19 as the primary cause of death and diabetes was registered as an underlying condition. The age groups considered were from 25 – 85+ across four consecutive years: 2018, 2019, 2020 and 2021. The comorbid population used had six categories of race and ethnicity; non-Hispanic blacks, non-Hispanic whites, native Hawaiian or Other Pacific Islander, Asians, American Indian or Alaska Natives, and more than one race.

3.4.4 Cardiovascular Diseases – COVID19 Comorbidity

This variable of interest for this study was obtained using COVID-19 as the primary cause of death and CVD was listed as an underlying condition. The CVDs considered were coronary heart disease, heart failure, stroke, hypertension, myocardial infarction, atherosclerotic cardiovascular disease, endocarditis, pericarditis, myocarditis. This variable of interest was considered across 2018 to 2021. The reported places of death used to categorize this variable were medical facilities which included (inpatient, outpatient, dead on arrival, status unknown,), decedent's home, hospice facility and nursing home/long term care. The CVD – COVID 19 comorbid population was also grouped in terms of autopsy, no autopsy and unknown.

4 RESULT

The United States is facing a significant increase in the mortality rate of diabetes and cardiovascular disease, two of the most common chronic diseases affecting the population.

Table 1 shows the mortality rates for all-cause, diabetes and CVD across 2018 – 2021. The reference for this study was 2018 which highlights pre pandemic phase compared with 2019, 2020, and 2021. The percentage increase in all-cause mortality from 2018 to 2019 was approximately 0%. This was because the mortality rates for all-cause in 2018 was 867.8 while 2019 was 869.8. It was a very minimal difference.

The rate of CVD deaths increased 0.9% from 2018 to 2019, which was during the pre-pandemic phase. However, there was an evident increase in these rates in 2020 with an 18.4% increase. The diabetic population recorded a 39.7% increase in the mortality rates in 2020 as compared to 2.25% in 2019.

Table 1: Mortality rates per 100,000 for all-cause, diabetes and CVD across 2018 – 2021 grouped by gender

	All-Cause Mortality		CVD		Diabetes	
	Rate	% Change	Rate	% Change	Rate	% Change
Total						
2018	867.8	Reference	471.3	Reference	84.3	Reference
2019	869.8	0.0	475.4	0.87	86.2	2.25
2020	1027.0	18.35	558.0	18.4	117.8	39.74
2021	1043.8	20.28	564.5	19.78	120.3	42.7
Men						
2018	905.2	Reference	490.9	Reference	95.0	Reference
2019	911.7	5.06	498.2	1.49	97.6	2.74
2020	1090.8	25.7	592.1	20.62	134.4	41.47
2021	1118.2	28.85	602.4	22.71	137.1	44.32
Women						
2018	831.6	Reference	452.2	Reference	73.9	Reference
2019	829.0	-0.31	453.3	0.24	75.0	1,49
2020	965.1	16.04	524.8	16.05	101.7	37.62
2021	970.8	16.74	527.4	16.63	103.9	40.6

+

From Table 2, comparing the reference 2018 to 2019, a lower mortality rate increase of 0.9% and 2.25% in CVD and diabetes mortality rates respectively was observed. There was also a 39.7% increase in the diabetes mortality rate from 2018 to 2020 and an 18.4% increase in 2020 CVD mortality rate compared to 2018.

Table 2: Percentage increase in mortality rates per 100,000 for all-cause, diabetes and CVD across 2018 – 2021 stratified by gender.

	All-Cause Mortality			CVD			Diabetes		
% Change	2019	2020	2021	2019	2020	2021	2019	2020	2021
Total	0.9	18.35	20.28	0.87	18.4	19.78	2.25	39.74	42.7
Sex									
Male	5.06	25.7	28.85	1.49	20.62	22.71	2.74	41.47	44.32
Female	0	16.04	16.74	0.24	16.05	16.63	1.49	37.62	40.6

Table 3: Mortality rates per 100,000 for all-cause, diabetes and CVD across 2018 – 2021 stratified by gender and race/ethnicity.

	CVD COVID Comorbidity Mortality Rates		Diabetes COVID Comorbidity Mortality Rates	
	2020	2021	2020	2021
Total	47.5	52.2	17.2	17.8
Sex				
Male	54.0	60.8	20.3	20.9
Female	41.2	43.6	14.1	14.7
Race				
American Indian or Alaska native	41.3	43.6	24.9	30.5
Asian	30.9	30.1	12.1	11.5
Black/ African American	61.2	55.3	26.0	20.6
Native Hawaiian/Pacific Islander	39.1	59.7	26.15	25.75
White	48.1	55.2	16.4	18.1
More than one race	6.5	9.7	2.7	4.3

Table 3 shows the racial disparities across these six racial groups. In 2020, Asians recorded the lowest mortality rates for both diabetes and CVD COVID-19 comorbidities. Non-Hispanic black Americans had the highest CVD comorbidity mortality rate as compared to the other races. Native Hawaiian had the highest diabetes comorbidity mortality rate. Comparing 2020 to 2021 in the six races, most of the mortality rates slightly increased. Although there are no statistics yet

for the post pandemic phase (2023), vaccination introduction may have likely impacted the mortality rates for 2023.

In Figures 1 and 2, we observed a substantial increase in all-cause mortality in 2020. There was also a 39.7% increase in the diabetes mortality rate between these dates and an 18.4% increase in CVD mortality rate compared to 2019 where we observed a lower mortality rate increase of 0.9% and 2.25% in CVD and diabetes mortality rates respectively.

Figure 1: Column graph showing the mortality rate per 100,000 for all-causes, diabetes and cardiovascular diseases from 2018-2021

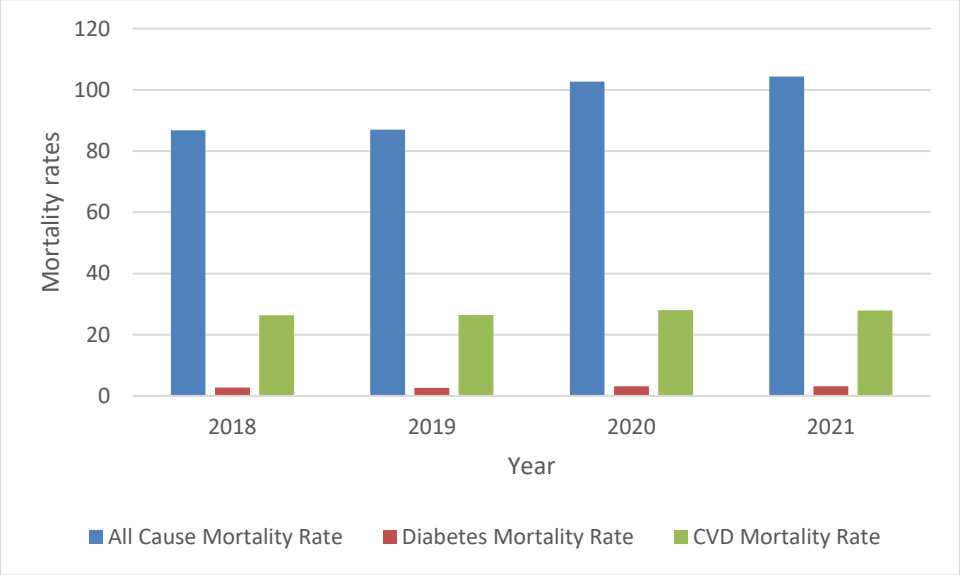
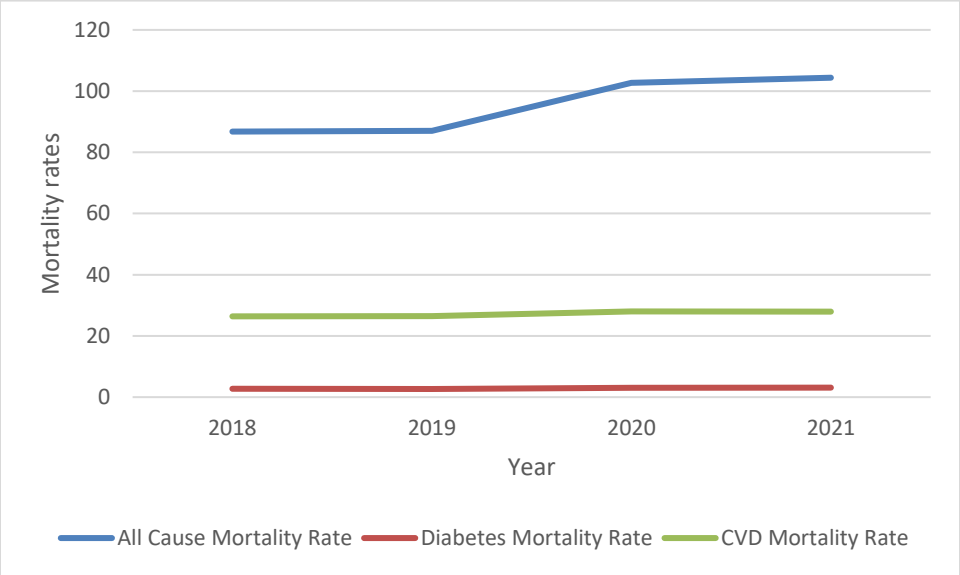


Figure 2: Line graph showing the mortality rate per 100,000 for all-causes, diabetes and cardiovascular diseases from 2018-2021



Figures 3 and 4 show a meaningful increase in the diabetes mortality rate and the comorbidity mortality rate. In comparison to the reference population, the mortality count had a steady decline until after the beginning of 2020 where a meaningful increase was observed. The numbers increased rapidly until 2021 where the increase in diabetes mortality count began to decline. The diabetes COVID-19 comorbidity count has a similar pattern with the total diabetes mortality count from 2019 – 2021.

Figure 3: Graph showing the total diabetes mortality count in the United States from 2018 -2021

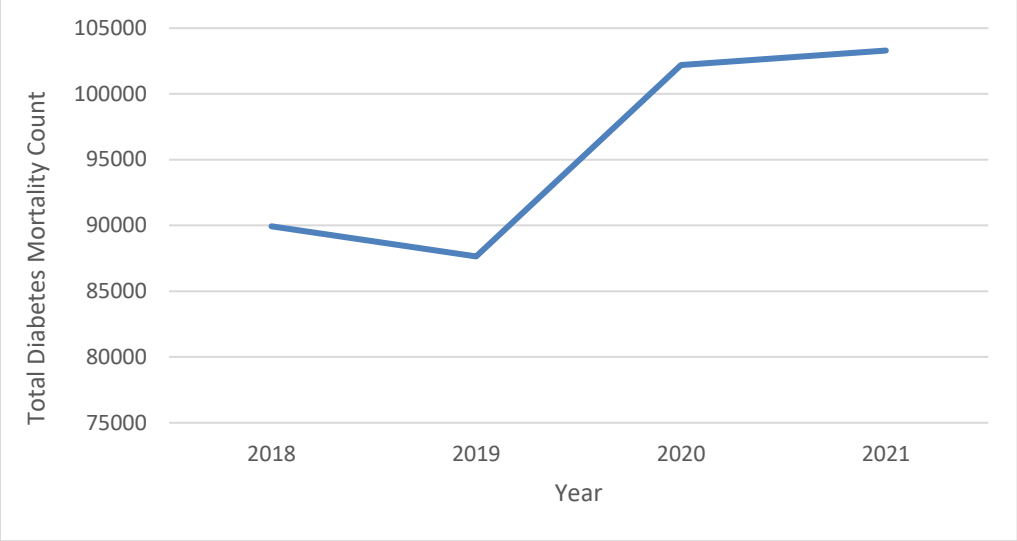
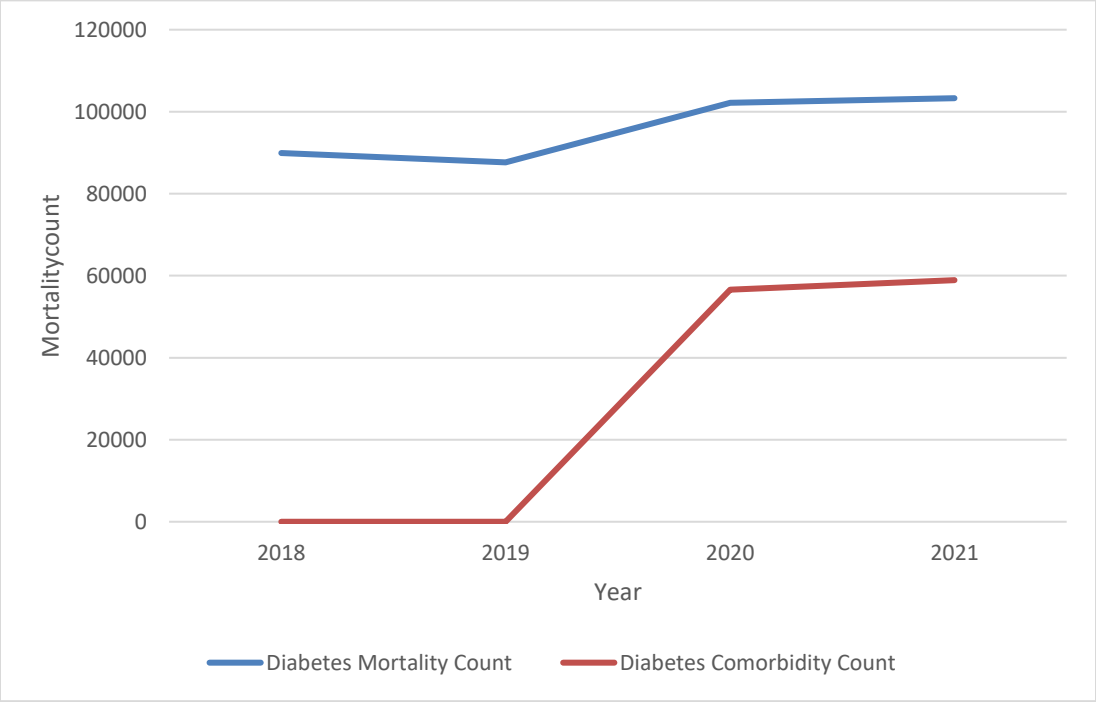


Figure 4: Graph comparing the total diabetes count with the diabetes comorbidity count from 2018 – 2021



Figures 5 and 6 suggest a slow increase in CVD mortality count between 2018 and 2019. However, the CVD mortality count increased rapidly during the pandemic phase from 870,000 persons to about 925,000 persons. From both figures, we observed a similar trend in the mortality count increase from 2019 to 2021.

Figure 5: Graph showing the total mortality count for cardiovascular diseases in the US from 2018 -2021

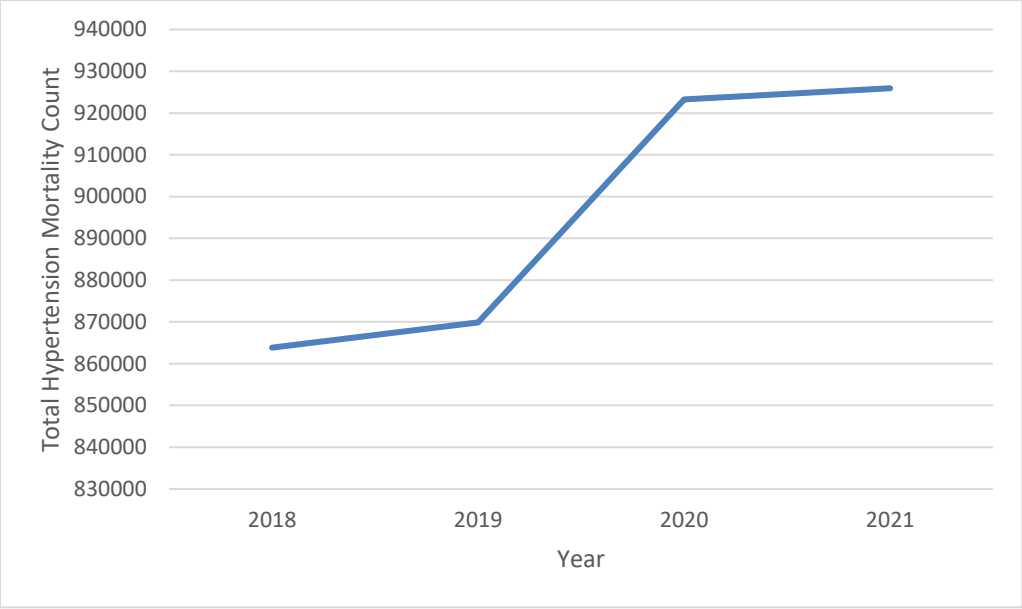
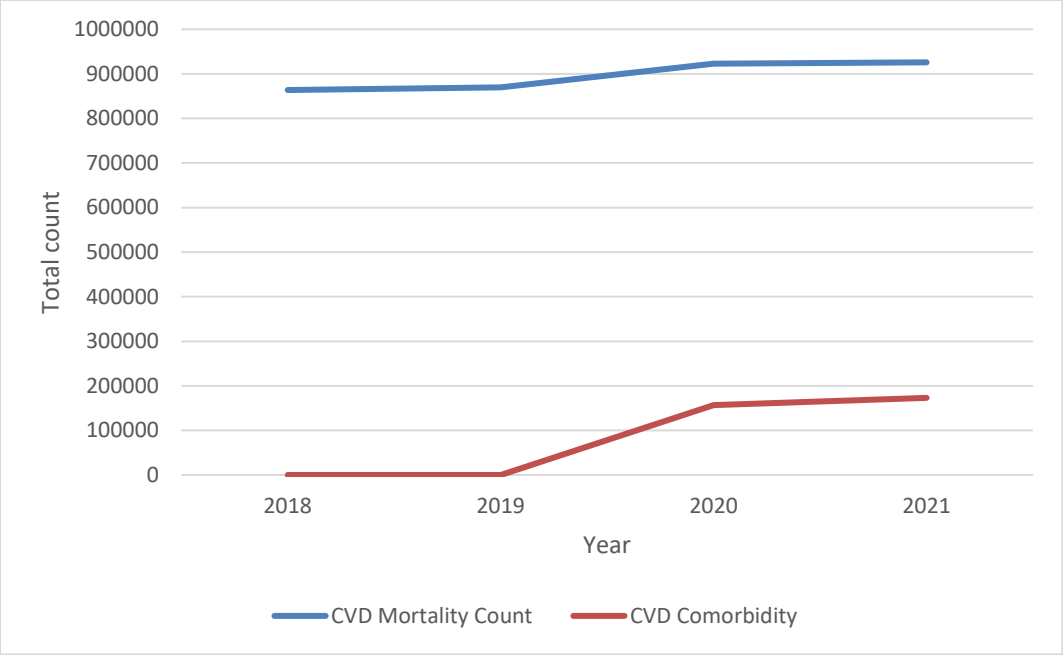


Figure 6: Graph comparing the total CVD count with the CVD comorbidity count from 2018 – 2021.



Figures 7 and 8 show that the mortality rates of both comorbidities were higher in males than females. We also compared all-cause mortality, CVD mortality and diabetes mortality, the rates for males were higher compared to females. The reasons for this gender difference may be attributed to several factors. Hormonal differences between males and females may also play a role in the disparity of COVID-19 comorbidities.

Figure 7: Graph showing the diabetes COVID-19 comorbidity mortality count stratified by gender from 2018 – 2021.

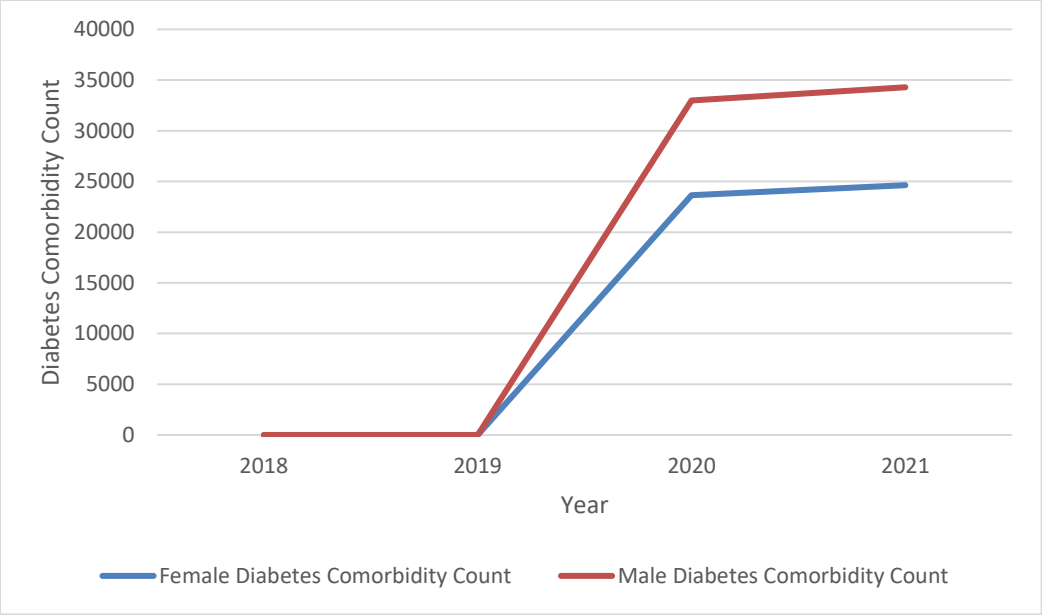
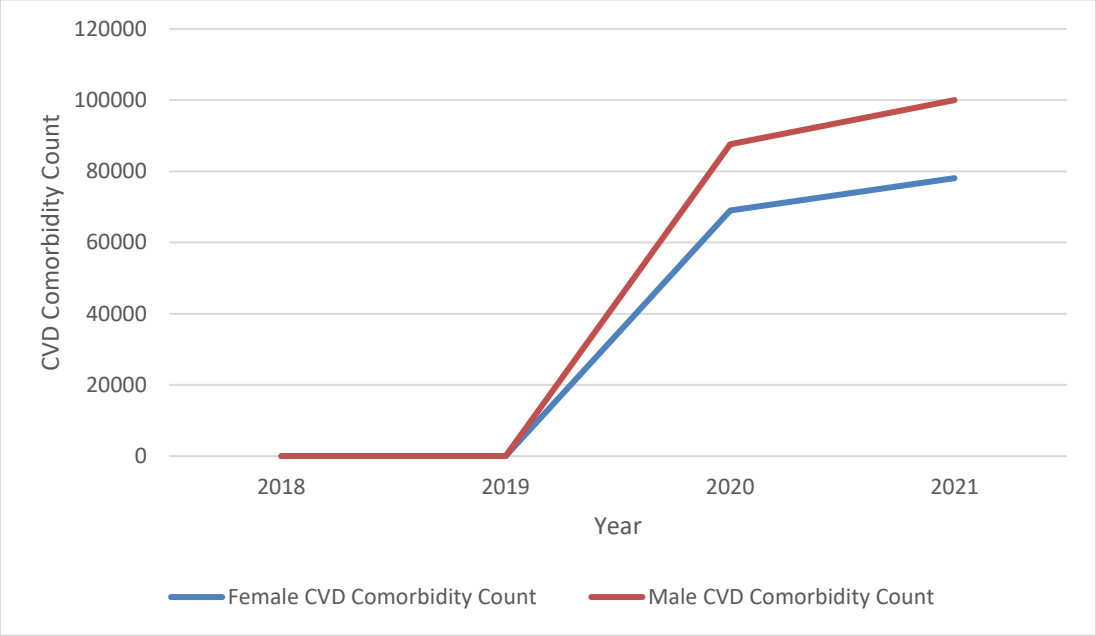


Figure 8: Graph showing the CVD COVID-19 comorbidity mortality count stratified by gender from 2018 – 2021.



Figures 9 and 10 show a comparison in the different mortalities and the overall mortality trends for the comorbidities and the single mortalities. The CVD and the diabetes mortality count increased, however the conclusion observed from the figures suggest that the COVID-19 comorbidities may have made a meaningful impact in causing an increase in the mortality rates in these populations. Overall, the mortality trends show that CVD mortality rates were rising steadily compared to diabetes mortality rates which declined from 2018 – 2019. The figures suggest that diabetes mortality rates started increasing from the inception of the pandemic (2020).

Figure 9: Column graph showing the overall mortality trends for diabetes and CVD across 2018 – 2021.

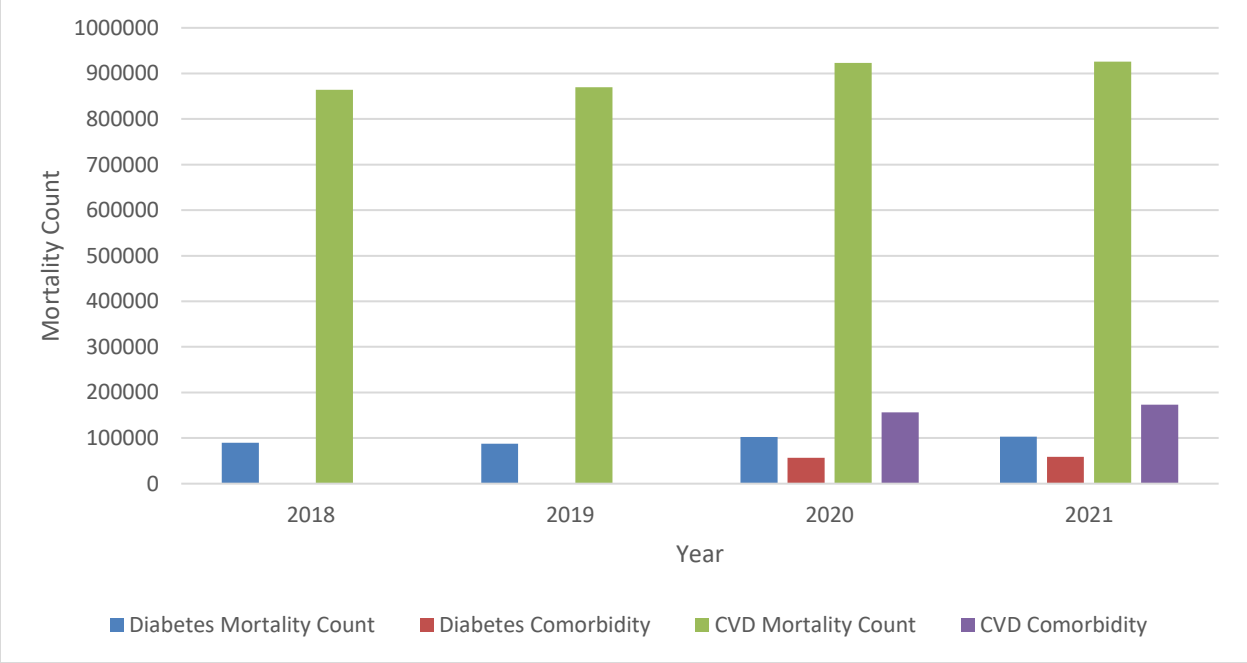
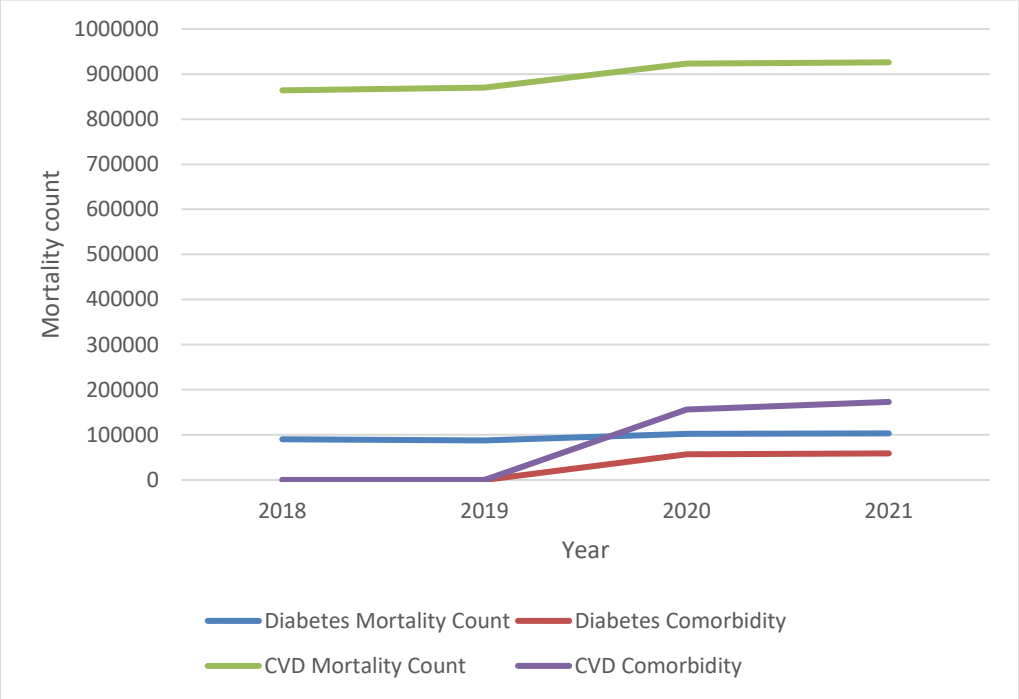


Figure 10: Line graph showing the overall mortality trends for diabetes and CVD across 2018 – 2021.



Figures 11 and 12 show a comparison of the CVD comorbidities and diabetes comorbidities across all six races/ethnicity.

In 2020 (Pandemic Phase), non-Hispanic blacks recorded the highest CVD/COVID-19 comorbidity mortality rate, which was 61.2 per 100,000, the non-Hispanic whites were second with a rate of 48.1 per 100,000. The race with the lowest mortality rate recorded were Asians with a rate of 30.9 and 30.1 respectively for 2020 and 2021. Native Hawaiian or Other Pacific Islander recorded the highest diabetes COVID-19 comorbidity mortality rate, which was 26.15 per 100,000, the American Indian or Alaska Natives were second with a rate of 24.9 per 100,000. The race with the lowest mortality rate recorded were Asians with a rate of 12.1.

Figure 11: Graph showing the mortality rates for CVD comorbidity across all races from 2018 - 2021.

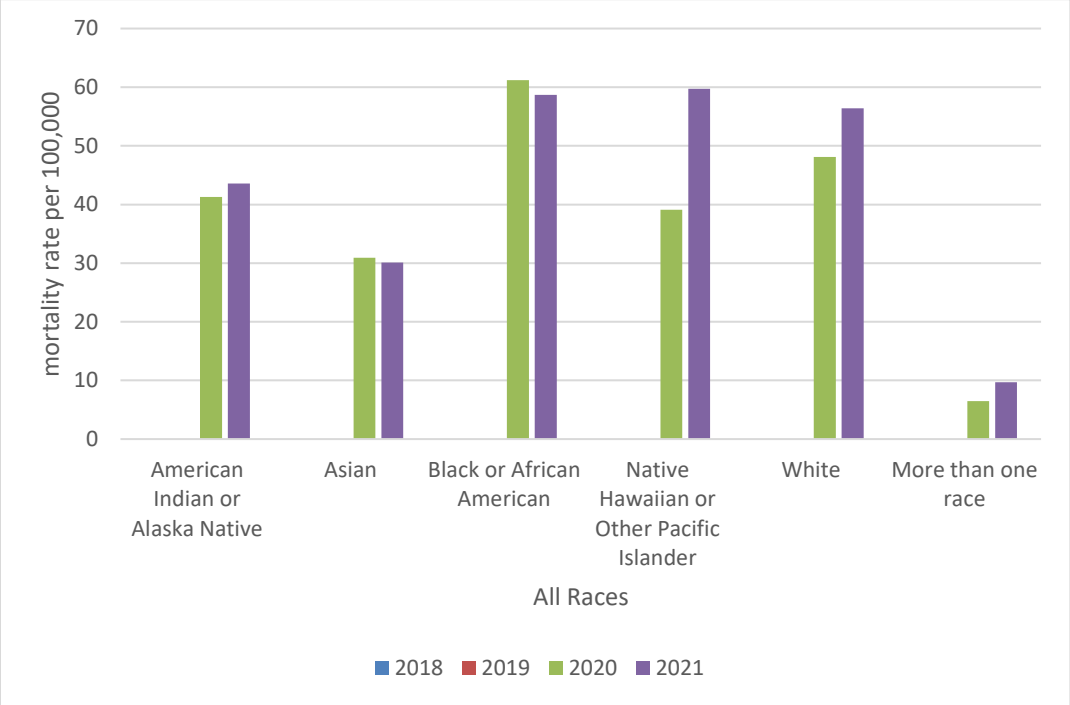
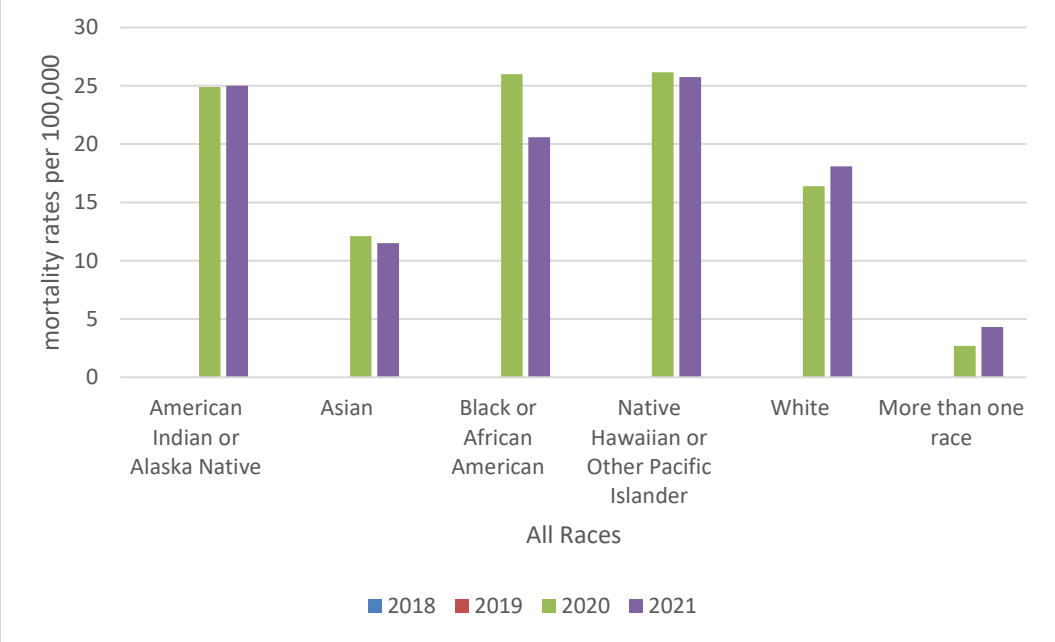


Figure 12: Graph showing the mortality rates for diabetes comorbidity across all races from 2018 - 2021.



5 DISCUSSION

5.1 Discussion

The main findings suggest that CVD mortality rates were higher than diabetes mortality rates. Although the rates were higher, there was a higher percentage increase in the diabetes mortality rate compared to the CVD mortality rate. The denominator was the whole US population for the different years (2018, 2019, 2020 and 2021) and the numerator differed depending on the type of mortality rate being used. There was also a substantial increase in all-cause mortality in 2020. The study suggests that an increase in the mortality rates of diabetes and CVD may have impacted the all-cause mortality rate in 2020.

Comparing the reference 2018 to 2019, a lower mortality rate increase of 0.9% and 2.25% in CVD and diabetes mortality rates respectively was observed. There was also a 39.7% increase in the diabetes mortality rate from 2018 to 2020 and an 18.4% increase in 2020 CVD mortality rate compared to 2018. This study suggests that the diabetes COVID-19 comorbidity may have impacted the diabetes mortality rate during the pandemic phase. Fedeli et al (2022) had a similar conclusion, the author discussed that during the COVID-19 pandemic an increase in mortality from diabetes has been reported in the US and in a number of European countries. In March-April 2020 in Italy, diabetes mortality showed a large excess; an increase, although more limited, was observed also in Spain and England. It must be remarked that in England most excess deaths due to diabetes/cardiovascular diseases occurred during the first half of the first wave of the pandemic (April to mid-May), with a second, smaller increase from mid-July to August. In Norway, the most striking finding of mortality analyses was the large and significant growth in deaths from diabetes. The findings from this descriptive study suggest that there has been a slow increase in the overall mortality rates for both diabetes and CVD. From 2018 to 2019, the mortality rate for diabetes

increased from 84.3 to 86.2 per 100,000 population, while the crude rate for CVD increased from 471.3 to 473.4 per 100,000 population. It can be concluded that in 2020, the COVID-19 pandemic may have led to a more meaningful increase in mortality rates for both diabetes and CVD. The major findings were assessed based on race and gender.

5.2 Findings Stratified by Gender

There was a stratification of this descriptive study based on gender. The risk of more severe COVID-19 deaths was higher in males but may have also increased due to the presence of these chronic comorbidities. Ortolan et al., 2020 also had a similar conclusion, the study concluded that the men's mortality rate was higher compared to women (66.67% vs. 33.33%). There was a systematic literature review and meta-analysis done by data pooling which resulted in a significant association between male sex and mortality (OR = 1.81; 95% CI 1.25–2.62). We also compared all-cause mortality, CVD mortality and diabetes mortality, the rates for males were higher compared to females. The reasons for this gender difference may be attributed to several factors. Hormonal differences between males and females may also play a role in the disparity of COVID-19 comorbidities. Studies have shown that estrogen has a protective effect against viral infections and inflammation. In contrast, testosterone can suppress the immune system, leading to an increased risk of developing chronic diseases such as hypertension, other cardiovascular diseases, and type 2 diabetes. Males are also more likely to be deficient in Vitamin D, which has been shown to reduce the severity of COVID-19 symptoms (Al-Lami et al., 2018).

5.3 Findings Based on Race

From the result, Asians recorded the lowest mortality for both comorbidities. There is significant variation in life expectancy among different Asian populations and among different racial groups in general (Park et al., 2022). However, on average, Asians tend to have a higher life

expectancy than some other racial groups in the United States, such as Black and Hispanic populations. It may be as a result of their traditional Asian diets (Ooraikul et al., 2008). It has been linked to lower rates of heart disease and other chronic illnesses. Another reason could be that many Asian cultures have lower rates of smoking and alcohol consumption than Western cultures (Acciai et al., 2015). This reduces the risk of many health problems and lastly certain genetic factors may contribute to longer life spans among Asians.

5.4 Strengths and Limitations of the Study

This study was useful for providing a broad overview of diabetes comorbidity and CVD comorbidity with COVID-19. Through this study patterns were identified, trends, and relationships among CVD COVID-19 comorbidity variable and diabetes COVID-19 comorbidity variable were seen clearly.

A knowledge gap still remains yet to be filled with regards to the relationship between CVD and its relation to COVID-19. The study was a descriptive study, so our findings only describe ecological associations between variables and we could not determine causal mechanisms.

5.5 Interventions and Recommendations for the Population at Risk

Non-Hispanic Blacks recorded the highest CVD COVID-19 Comorbidity rates. Improving social determinants of health (SDOH) can have a significant impact on reducing mortality rates particularly in black communities. SDOH refers to the conditions in which people are born, grow, live, work, and age that can affect their health outcomes. These factors include access to quality healthcare, safe and affordable housing, nutritious food, education, employment, and social support networks.

Improving SDOH factors such as access to healthcare can help detect and treat diseases earlier, leading to better health outcomes and reduced mortality rates. This can be achieved through initiatives such as increasing healthcare coverage, improving healthcare quality, and addressing healthcare disparities.

Improving access to safe and affordable housing can also have a significant impact on health outcomes. Studies have shown that poor housing conditions, such as overcrowding, are one of the easiest ways to contract respiratory infectious diseases. By improving access to safe and affordable housing, individuals can avoid these health risks, leading to improved health outcomes and reduced mortality rates. Access to nutritious food can also play a significant role in reducing mortality rates. It can help prevent chronic diseases such as obesity, diabetes, and heart disease. The COVID-19 virus attaches itself to the ACE-2 receptors which is found on the surface of many different types of cells in the body. The problem is that people with pre-existing conditions such as diabetes and hypertension have higher levels of ACE-2 receptors in their lung cells. By blocking ACE-2, the virus would not be able to enter the cells and cause infection. Further research should be conducted to get more understanding on how ACE-2 receptors can help reduce the COVID-19 comorbidity mortality rates.

The COVID-19 vaccines and the booster doses have been shown to be safe and effective in reducing the risk of severe illness, hospitalization, and death from COVID-19. Health promotion centered around getting the booster doses should be done in clinics where the prevalent diabetes and CVD populations see their primary care physicians. It could also be done in wellness centers, fitness centers and pharmacies. The COVID-19 pandemic has taken a toll on mental health, and individuals with diabetes or CVD may experience additional stress and anxiety. Providing access

to mental health services and support can help individuals manage their mental health and improve overall health outcomes.

5.6 Conclusion

Similar increases in the rates of all-cause mortality and CVD mortality in 2020 and 2021 were observed, but there was a more substantial relative increase in the rate of deaths among people with diabetes. Interventions are needed to decrease the burden of COVID-19 among people with comorbid CVD and/or diabetes. Other studies suggest that public health measures such as vaccination and receiving booster doses are vital to protect vulnerable individuals with comorbidities.

It is important to note that disparities in mortality rates across racial groups are also attributed to social determinants of health, including access to healthcare, poverty, and discrimination. Efforts to address these disparities through public health policies and interventions are crucial to reducing mortality rates for comorbidities like diabetes and CVD as well as COVID-19.

REFERENCES

CDC. (2021). Comorbidities and COVID-19. Centers for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/evidence-table.html

Wang T, Du Z, Zhu F, Cao Z, An Y, Gao Y, et al. Comorbidities and multi-organinjuries in the treatment of COVID-19. Lancet 2020;395(10228):e52, http://dx.doi.org/10.1016/s0140-6736(20)30558-4.

Patel A, Jernigan DB. Initial public health response and interim clinical guidance for the 2019 novel coronavirus outbreak-United States, December 31,2019–February 4, 2020. MMWR Morb Mortal Wkly Rep 2020;69(5):140, http://dx.doi.org/10.15585/mmwr.mm6905e1

Simonnet A, Chetboun M, Poissy J, Raverdy V, Noulette J, Duhamel A,et al. High prevalence of obesity in severe acute respiratory syndromecoronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. Obesity2020;2020:22831, http://dx.doi.org/10.1002/oby.22831.

CDC. (2021). Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19: Information for Healthcare Providers. Centers for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html

Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382(18):1708–20, http://dx.doi.org/10.1056/NEJMoa2002032.

Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patientsdying in relation to COVID-19 in Italy. JAMA 2020;323(18):1775–6, http://dx.doi.org/10.1001/jama.2020.4683.

Chow N, Fleming DK, Gierke R, Hall A, Hughes M, Pilishvili T, et al. Preliminaryestimates of the prevalence of selected underlying health conditions amongpatients with coronavirus disease

2019–United States, February 12–March 28,2020. MMWR Morb Mortal Wkly Rep 2020;69(13):382–6, http://dx.doi.org/10.15585/mmwr.mm6913e2.

Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features ofpatients infected with 2019 novel coronavirus in Wuhan, China. Lancet2020;395(10223):497–506, http://dx.doi.org/10.1016/S0140-6736(20)30183-5.

Dong X, Cao YY, Lu XX, Zhang JJ, Du H, Yan YQ, et al. Eleven faces of coronavirusdisease 2019. Allergy 2020;14289:1–11, http://dx.doi.org/10.1111/all.14289.

Maddaloni E, Buzzetti R. Covid-19 and diabetes mellitus: unveiling the inter-action of two pandemics. Diabetes Metab Res Rev 2020;31:e33213321, http://dx.doi.org/10.1002/dmrr.3321.

Coronavirus disease (COVID-19) Weekly Epidemiological Update. Available from: https: //www.who.int/docs/default-source/coronaviruse/situation-reports/20200928-weekly-epi update.pdf?sfvrsn=9e354665_6.

Cao Y, Hiyoshi A, Montgomery S. COVID-19 case-fatality rate and demographic and socioeconomic influencers: worldwide spatial regression analysis based on country-level data. *BMJ Open* 2020;**10:**e043560. doi: 10.1136/bmjopen-2020-043560

Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020;395(10223):497-506. doi: 10.1016/S0140-6736(20)30183-5

World Health Organization. Clinical management of COVID-19: interim guidance. 27 May 2020. https://www.who.int/publications-detail/clinical-management-of-covid-19

Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet. 2020;395(10223):507-513. doi: 10.1016/S0140-6736(20)30211-7

Lippi G, Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. Clin Chem Lab Med. 2020;58(7):1131-1134. doi: 10.1515/cclm-2020-0198

Zayet S, Kadiane-Oussou NJ, Lepiller Q, Zahra H, Royer PY, Toko L, et al. Clinical features of COVID-19 and influenza: a comparative study on Nord Franche-Comte cluster. Microbes Infect. 2020;22(9):481-488. doi: 10.1016/j.micinf.2020.06.001

Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708-1720. doi: 10.1056/NEJMoa2002032

Pan F, Ye T, Sun P, Gui S, Liang B, Li L, et al. Time course of lung changes at chest CT during recovery from coronavirus disease 2019 (COVID-19). Radiology. 2020;295(3):715-721. doi: 10.1148/radiol.2020200370

Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ. 2020;368:m1091. doi: 10.1136/bmj.m1091

Garg S, Kim L, Whitaker M, O'Halloran A, Cummings C, Holstein R, et al. Hospitalization rates and characteristics of patients hospitalized with laboratory-confirmed coronavirus disease 2019 - COVID-NET, 14 States, March 1-30, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(15):458-464. doi: 10.15585/mmwr.mm6915e3

Guan WJ, Liang WH, Zhao Y, et al. Comorbidity and its impact on 1,590 patients with COVID-19 in China: A Nationwide Analysis. Eur Respir J. 2020;55(5):2000547. doi:10.1183/13993003.00547-2020

Williamson E, Walker AJ, Bhaskaran KJ, et al. OpenSAFELY: factors associated with COVID-19 death in 17 million patients. Nature. 2020;584(7821):430-436. doi:10.1038/s41586-020-2521-4

Ssentongo P, Ssentongo AE, Heilbrunn ES, Ba DM, Chinchilli VM. Association of cardiovascular disease and 10 other pre-existing comorbidities with COVID-19 mortality: A systematic review and meta-analysis. PLoS One. 2021;16(1):e0247461. doi:10.1371/journal.pone.0247461

Polack FP, Thomas SJ, Kitchin N, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med. 2020;383(27):2603-2615. doi:10.1056/NEJMoa2034577

Baden LR, El Sahly HM, Essink B, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-Vaccine. N Engl J Med. 2021;384(5):403-416. doi:10.1056/NEJMoa2035389

Centers for Disease Control and Prevention. COVID-19 Vaccinations in the United States. 2023. https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-total-admin-rate-total

Our World in Data. Coronavirus (COVID-19) Vaccinations. 2023. https://ourworldindata.org/covid-vaccinations

Zheng Z, Peng F, Xu B, et al. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. J Infect. 2020;81(2):e16-e25. doi:10.1016/j.jinf.2020.04.021

Gupta S, Hayek SS, Wang W, et al. Factors Associated With Death in Critically Ill Patients With Coronavirus Disease 2019 in the US. JAMA Intern Med. 2020;180(11):1436-1446. doi:10.1001/jamainternmed.2020.3596

American Heart Association. COVID-19 and Cardiovascular Disease: What We Know in 2021. March 2021. https://www.heart.org/en/coronavirus/coronavirus-covid-19-resources/covid-19-and-cardiovascular-disease

Centers for Disease Control and Prevention. People with Certain Medical Conditions. December 10, 2021.. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

Woolf SH, Chapman DA, Sabo RT, Weinberger DM, Hill L. Excess Deaths From COVID-19 and Other Causes, March-April 2020. JAMA. 2020;324(5):510-513. doi:10.1001/jama.2020.11787

McKibbin WJ, Fernando R. The Global Macroeconomic Impacts of COVID-19: Seven Scenarios. Asian Econ Pap. 2020;20(1):1-30. doi:10.1162/asep_a_00769

Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2020. https://www.cdc.gov/diabetes/library/features/diabetes-stat-report.html

Menke A, Casagrande S, Geiss L, Cowie CC. Prevalence of and Trends in Diabetes Among Adults in the United States, 1988-2012. JAMA. 2015;314(10):1021-1029. doi:10.1001/jama.2015.10029

Zhu Y, Sidell MA, Arterburn D, et al. Racial/Ethnic Disparities in the Prevalence of Diabetes and Prediabetes by BMI: Patient Outcomes Research to Advance Learning (PORTAL) Multisite Cohort of Adults in the U.S. Diabetes Care. 2021;44(4):910-918. doi:10.2337/dc20-1812

Kaiser Family Foundation. State COVID-19 data and policy actions. https://www.kff.org/coronavirus-covid-19/dashboard/state-vaccine-dashboard/

Krendl AC, Perry BL. The impact of sheltering in place during the COVID-19 pandemic on older adults' social and mental well-being. J Gerontol B Psychol Sci Soc Sci. 2021;76(2):e53-e58. doi:10.1093/geronb/gbaa129

O'Caoimh R, O'Donovan MR, Monahan MP, et al. COVID-19: protecting the older population. Int Psychogeriatr. 2020;32(10):1189-1194. doi:10.1017/S1041610220000984

Kavanagh O, Zeng T, O'Connell NH, et al. Diagnostic accuracy of antigen tests for the detection of SARS-CoV-2: systematic review and meta-analysis. BMJ. 2021;374:n1676. doi:10.1136/bmj.n1676

Beigel, J. H., Tomashek, K. M., Dodd, L. E., Mehta, A. K., Zingman, B. S., Kalil, A. C., ... & López de Castilla, D. (2020). Remdesivir for the treatment of Covid-19—final report. New England Journal of Medicine, 383(19), 1813-1826.

de las Heras Gala, T., Sánchez Mora, C., & García-Agua Soler, N. (2021). Impact of comorbidity on COVID-19: A review. Revista Clínica Española, 221(6), 346-353. https://doi.org/10.1016/j.rce.2021.02.005

Poudel, A., Peel, N. M., Nissen, L. M., Mitchell, C. A., & Gray, L. C. (2020). Comorbidities of older adults with COVID-19: a rapid review. The Australian Journal of Ageing, 39(3), 184-186.

Wu, Z., & McGoogan, J. M. (2020). Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. Jama, 323(13), 1239-1242.

Bonow, R. O., Fonarow, G. C., O'Gara, P. T., & Yancy, C. W. (2020). Association of coronavirus disease 2019 (COVID-19) with myocardial injury and mortality. *JAMA cardiology*, *5*(7), 751-753.

Tadic, M., Cuspidi, C., Mancia, G., Dell'Oro, R., & Grassi, G. (2020). COVID-19, hypertension and cardiovascular diseases: Should we change the therapy?. *Pharmacological research*, *158*, 104906.

Pranata, R., Huang, I., Lim, M. A., Wahjoepramono, E. J., & July, J. (2020). Impact of cerebrovascular and cardiovascular diseases on mortality and severity of COVID-19–systematic review, meta-analysis, and meta-regression. *Journal of stroke and cerebrovascular diseases*, *29*(8), 104949.

Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., ... & Guan, L. (2020). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet, 395(10229), 1054-1062.

Guan, W. J., Ni, Z. Y., Hu, Y., Liang, W. H., Ou, C. Q., He, J. X., ... & Zhong, N. S. (2020). Clinical characteristics of coronavirus disease 2019 in China. New England Journal of Medicine, 382(18), 1708-1720.

Li, B., Yang, J., Zhao, F., Zhi, L., Wang, X., Liu, L., ... & Liu, Y. (2020). Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clinical Research in Cardiology, 109(5), 531-538.

Chow, N., Fleming-Dutra, K., Gierke, R., Hall, A., Hughes, M., Pilishvili, T., ... & Roguski, K. (2020). Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019—United States, February 12–March 28, 2020. Morbidity and Mortality Weekly Report, 69(13),

Hussain, A., Bhowmik, B., & do Vale Moreira, N. C. (2020). COVID-19 and diabetes: Knowledge in progress. Diabetes Research and Clinical Practice, 162, 108142.

Singh, A. K., Gupta, R., & Misra, A. (2020). Comorbidities in COVID-19: Outcomes in hypertensive cohort and controversies with renin angiotensin system blockers. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 14(4), 283-287.

Pal, R., & Bhadada, S. K. (2020). COVID-19 and diabetes mellitus: An unholy interaction of two pandemics. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 14(4), 513-517.

Gupta, R., Ghosh, A., Singh, A. K., & Misra, A. (2020). Clinical considerations for patients with diabetes in times of COVID-19 epidemic. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 14(3), 211-212.

Guo, W., Li, M., Dong, Y., Zhou, H., Zhang, Z., Tian, C., ... & Liu, S. (2020). Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes/Metabolism Research and Reviews, 36(7), e3319.

Zhu, L., She, Z. G., Cheng, X., Qin, J. J., Zhang, X. J., Cai, J., ... & Li, H. (2020). Association of blood glucose control and outcomes in patients with COVID-19 and pre-existing Type 2 diabetes. Cell Metabolism, 31(6), 1068-1077.

Ceriello, A. (2020). Hyperglycemia and COVID-19: What was known and what is really new? Diabetes Research and Clinical Practice, 167, 108383.

Chen, Y., Yang, D., Cheng, B., Chen, J., Peng, A., Yang, C., ... & Cheng, Z. (2020). Clinical characteristics and outcomes of patients with diabetes and COVID-19 in association with glucose-lowering medication. Diabetes Care, 43(7), 1399-1407.

Yang, J. K., Feng, Y., Yuan, M. Y., Yuan, S. Y., Fu, H. J., Wu, B. Y., ... & Wang, L. (2020). Plasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. Diabetic Medicine, 23(6), 623-628.

Park, S. S., Goldman, N., & Andrasfay, T. (2022). The Impact of COVID-19 on Life Expectancy among Asian American Subgroups. medRxiv, 2022-10.

Baluran, D. A., & Patterson, E. J. (2021). Examining ethnic variation in life expectancy among Asians in the United States, 2012–2016. Demography, 58(5), 1631-1654.

Acciai, F., Noah, A. J., & Firebaugh, G. (2015). Pinpointing the sources of the Asian mortality advantage in the USA. J Epidemiol Community Health, 69(10), 1006-1011.

Ooraikul, B., Sirichote, A., & Siripongvutikorn, S. (2008). Southeast Asian diets and health promotion. Wild-Type Food in Health Promotion and Disease Prevention: The Columbus Concept, 515-533.

Danaei, G., Rimm, E. B., Oza, S., Kulkarni, S. C., Murray, C. J., & Ezzati, M. (2010). The promise of prevention: the effects of four preventable risk factors on national life expectancy and life expectancy disparities by race and county in the United States. PLoS medicine, 7(3), e1000248.

Fedeli, U., Casotto, V., Schievano, E., Bonora, E., & Zoppini, G. (2022). Diabetes as a cause of death across different COVID-19 epidemic waves. Diabetes Research and Clinical Practice, 190, 109984.

Ortolan, A., Lorenzin, M., Felicetti, M., Doria, A., & Ramonda, R. (2020). Does gender influence clinical expression and disease outcomes in COVID-19? A systematic review and meta-analysis. International Journal of Infectious Diseases, 99, 496-504.