Perturbations in Mortality:

How COVID-19 Changed the Face of Death

by

Levi R. Legler

A Capstone Project Submitted to the Faculty of

Utica University

August 2024

in Partial Fulfillment of the Requirements for the Degree of

Master of Science in

Data Science

Abstract

The COVID-19 pandemic, declared a global health emergency by the World Health Organization on March 11, 2020, has had a profound impact on public health and mortality rates. This study presents a comprehensive retrospective analysis of all-cause mortality in the United States from 2014 to 2022. By comparing pre-pandemic years (2014-2019) with the pandemic years (2020-2022), this research quantifies the changes in mortality rates and identifies the most affected causes of death.

Baseline mortality data from 2014-2019 serve as reference points to observe deviations during the pandemic years, revealing significant trends and anomalies. The analysis shows a spike in excess deaths during the pandemic, with the annual mortality rate rising from an average of 2.8 million pre-pandemic to nearly 3.3 million between 2020 and 2022. This study highlights the "crest" phenomenon, characterized by a large deviation from stable mortality rates followed by convergence with expected rates, illustrating the pandemic's extensive, but thankfully temporary impact on most mortality patterns.

The research further explores the exacerbation of health conditions by COVID-19, contributing to excess mortality. Notable increases in deaths related to ischemic heart disease, diabetes mellitus, and other comorbidities were observed, alongside rises in homicide, chronic liver disease, and accidental deaths. The study underscores the critical need for targeted public health interventions and healthcare policy adjustments to address these disruptions.

The findings suggest that the disruptions in healthcare services, particularly during the peak of COVID-19 hospitalizations, were major drivers of excess deaths. As the healthcare system recovers and adapts, mortality rates are expected to normalize, though the long-term impact on life expectancy remains uncertain.

Keywords: COVID-19, mortality rates, public health, healthcare disruptions, excess mortality, comorbidities, retrospective analysis

Acknowledgments

To my son James. I would never have started this journey without you. I hope you seek out and find the things in life that spark your curiosity and that drive you to find the best version of yourself. To Dr. Nathan Tucker for pulling me from perdition and giving me the opportunity to show the world what I can do.

Table of Contents

List of Illustrated Materials……vi
Introduction……1
Data Sources and Methodology……2
Metadata……2
Linear Regression Analysis……3
Deviation Hypothesis Testing……4
Polynomial Regression……5
Literature Review and Findings……5
"The Big Picture"……5
General Mortality Trends……7
Age Related Effects……8
Specific Causes of Death……9
Accidents and Adverse effects……10
Residual Diseases……12
Diabetes mellitus……14
Assault and Homicide……16
Hypertensive Heart Disease……18
Chronic liver disease and Cirrhosis……21
Ischemic Heart Diseases……23
Motor Vehicle Accidents……25
Discussion……27
"The Bad News"……27
Excess Mortality and Healthcare Disruptions……27
Secondary Health Impacts……29
Vaccination and Mortality Trends……29
Baseline Mortality……30
"The Good News"……31
Limitations and Ethical Considerations……32

Future
Directions……...….....33
Conclusion……..…34
References…….…….36

List of Illustrative Materials

Figure 1 – Perturbations in Mortality……...4
Figure 2 – The Covid Crest…….....5
Table 1 – Total Mortality and Excess Death Counts……...6
Figure 3 – Predicted Vs. Observed Mortality……..6
Figure 4 – Mortality Trends by Age (1 -74)……....8
Table 2 – Top 10 Causes of Excess Death 2020…….…9
Table 3 – Top 10 Causes of Excess Death 2021…….…9
Table 4 – Top 10 Causes of Excess Death 2022…….…9
Table 5 –All Other Unspecified Accidents and Adverse Effects Regression Output……....10
Figure 5 – All Other Unspecified Accidents and Adverse Effects Mortality by Year……..…10
Figure 6 – Mortality Trends by Age (25-74)……11
Table 6 – Residual Disease Polynomial Regression Output……..12
Table 7 – Residual Disease Trendline Model Output……12
Figure 7 – Residual Disease Model…….…..13
Table 8 – Diabetes Mellitus Linear Regression Output…….…14
Figure 8 – Diabetes Mellitus Convergence Plot……15
Table 9 – Assault and Homicide Polynomial Regression Output……..16
Figure 9 – Assault and Homicide Related Deaths(2014-2022)…….....16
Table 10 – Hypertensive Heart Diseases Linear Regression Output……18
Figure 10 – Hypertensive Heart Diseases Mortality by Year……18
Figure 11 – Hypertensive Heart Diseases Models……19
Table 11 – Chronic Liver Disease and Cirrhosis Polynomial Regression Output…….21
Figure 12 – Chronic Liver Disease and Cirrhosis Grouped Mortality Models……..22
Table 12 – Ischemic Heart Diseases Linear Regression Output……23
Figure 13 – Ischemic Heart Diseases Mortality Models……24
Table 13 – Motor Vehicle Accidents Polynomial Regression Output……...25
Figure 14 – Motor Vehicle Accidents Mortality Models……...2

Introduction

On January 20, 2020, the Centers for Disease Control (CDC) announced the first confirmed case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (*CDC Museum COVID-19 Timeline*, 2023) in the United States. Within 3 months of this announcement on March 11th, 2020, the World Health Organization (WHO) declared SARS-COV-2 (more commonly known as COVID-19), to be a global pandemic. The pandemic went on to wreak havoc on public health and healthcare systems globally, but the full extent of its long-term impact on mortality rates remains to be thoroughly understood. This project proposes a comprehensive retrospective analysis of all-cause mortality in United States from 2014 to 2022. By comparing pre-pandemic years (2014-2019) with the pandemic years (2020-2022), the study aims to quantify the changes in mortality rates and identify the most affected causes of death. This analysis will provide a deeper understanding of how the pandemic influenced mortality patterns, revealing both direct and indirect effects on various health conditions.

To achieve this, the study uses baseline mortality data calculated from the 2014-2019 multiple-cause mortality files available through the CDC's National Center for Health Statistics. These baselines serve as reference points to observe deviations during the pandemic years. By examining the observed changes from the expected baseline mortality, the study will highlight significant trends and anomalies in mortality rates. This approach will enable a detailed exploration of the pandemic's impact on the landscape of mortality, shedding light on the healthcare system's response and adaptability and demonstrating a powerful diagnostic tool for visualizing major changes in death rates.

Additionally, the study will explore how the COVID-19 virus may have exacerbated certain health conditions, contributing to excess mortality. By identifying these conditions and

their potential relationships, the research can inform future public health strategies and healthcare policies, aiming to mitigate similar impacts in potential future pandemics.

Data Sources and Methodology

Metadata

```
<class 'pandas.core.frame.DataFrame'>
RangeIndex: 26779062 entries, 0 to 26779061
Data columns (total 10 columns):
 #   Column    Dtype
---  ------    -----
 0   educ2003  object
 1   monthdth  object
 2   sex       object
 3   ager52    object
 4   placdth   object
 5   year      int64
 6   mandeath  object
 7   ucod      object
 8   ucr113    object
 9   ucr39     object
dtypes: int64(1), object(9)
memory usage: 2.0+ GB
None
```

The data for this analysis was sourced from the CDC Vital Statistics Repository and the National Bureau of Economic Research. Files were read using Python3 and converted to pandas data frames, obtained from .csv or .DUSMC.PUB files. The master data frame generated included columns such as 'year', 'education level (2003 coding)', 'manner of death', 'place of death', 'sex', 'age (recoded into 52 categories)', 'month of death', ‘underlying cause of death’, 'underlying cause of death recode 39', and 'underlying cause of death recode 113'.

Raw counts were obtained by ICD-10 recode-39, and recode-113, as well as by individual ICD-10 codes from the Vital Statistics Multiple Cause of Mortality files. After filtering for the target columns all rows were complete, with no missing or unknown values. The year-over-year rate of change was calculated using the equation:

$$\text{Rate of Change} = \left(\frac{\text{Number of Deaths in Target Year}}{\text{Number of Deaths in Previous Year}} - 1 \right)$$

Linear Regression Analysis

Predicted values for the years 2020-2022 were calculated via linear regression. The model was built utilizing ICD-10 counts from mortality data spanning the years 2014 to 2019. Excess death counts for each condition were obtained by subtracting observed values from predicted values. The total excess death count was calculated as the sum of these values. Standard deviation values for each condition were calculated using the raw counts for the 39 ICD-10 recode values.

Results were visualized (Figure 1.) to allow for ease of identification. After identifying perturbations visually, the significance level was verified to ensure the change was outside the expected variation, these deviating values were earmarked for further analysis.

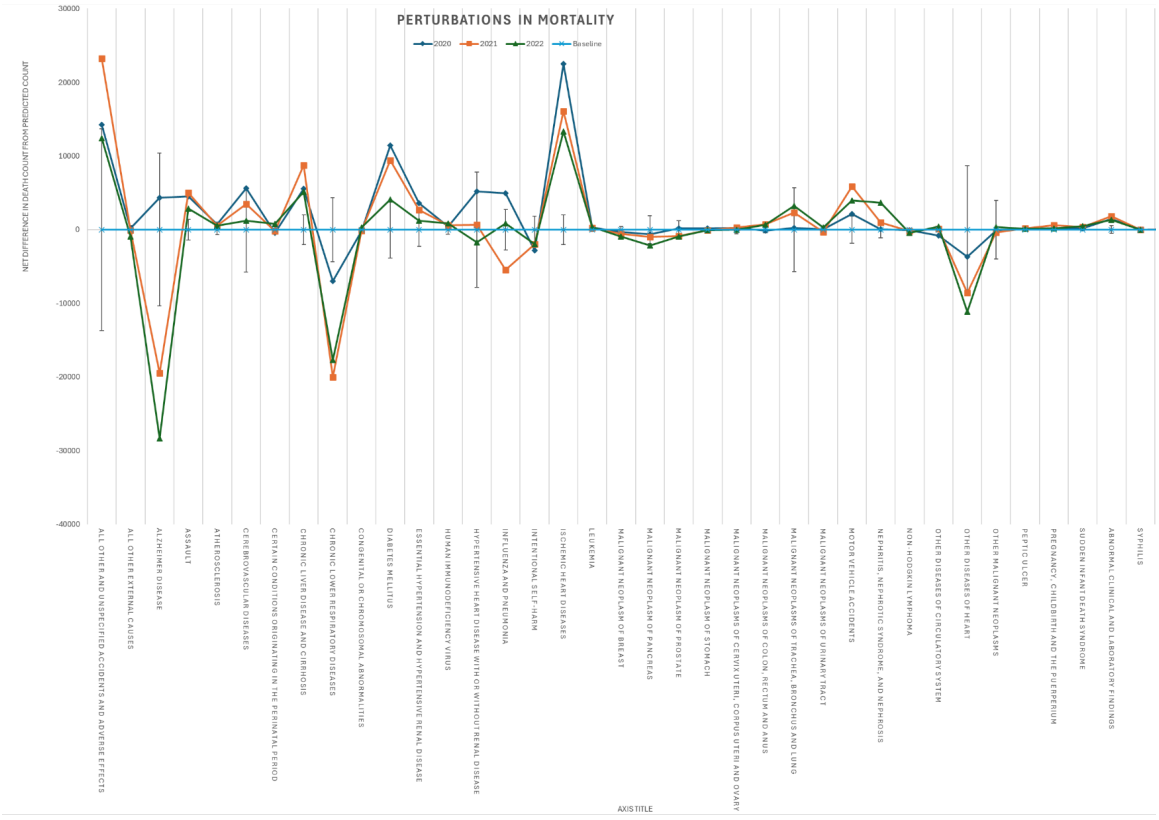

Figure 1. Perturbations in Mortality. Lines represent deviations from the predicted death count for the respective years Dark Blue = 2020, Orange= 2021, Green = 2022, Light Blue = Baseline(0). Standard deviations are represented along the baseline to aid in contextualizing the changes observed.

Deviation Hypothesis Testing

H_0: There is no significant deviation from the expected baseline mortality rate

H_1: There is a significant deviation from the expected baseline mortality rate

Test utilized: 1-Sample Student's T-Test with two tails

Test statistic: T

Degrees of Freedom: 5

Significance Threshold: 0.05

For each ICD-10 code, the null hypothesis was tested with a significance threshold of 5%. The test statistic was calculated based on the magnitude of deviation between the observed

and predicted death counts for each year. Under the null hypothesis, the expected mean difference was assumed to be 0.

Polynomial Regression

Models were generated in Tableau (Version 2024.1). Two types of analysis were performed. First, a polynomial model was generated for the years 2014-2022. Secondly, data were grouped into two categories 2014-2019 and 2020-2022. Individual models were generated for each group to estimate convergence.

Literature Review and Findings

"The Big Picture"

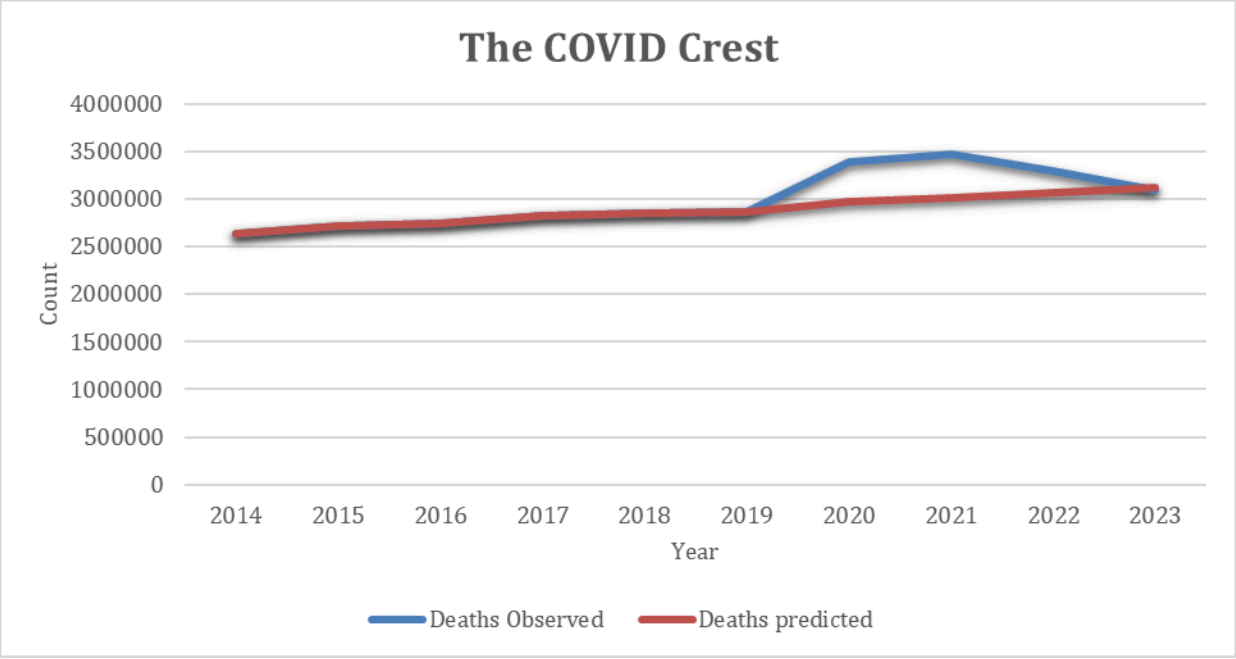

Figure 2. Total annual mortality for the years 2014-2022. All values are shared from 2014-2019. Orange line indicates predicted mortality in the absence of the COVID-19 pandemic. Blue line represents the observed mortality for the years 2020-2022.

Year	Predicted	Observed	Excess Death	p-value
2020	2,965,956	3,390,241	424,285	5.0E-05
2021	3,019,166	3,472,094	452,928	3.7E-05
2022	3,072,377	3,289,557	217,180	1.2E-03
2023	3,125,587	3,090,582*	N/a	N/a
		Total	1,094,393	

Table 1. Total Mortality and Excess Counts 2020-2022. Predicted counts are based on regression analysis of all ICD-10 39 recodes. Excess deaths are the difference between the observed and predicted values for the respective year. *=Due to this value being taken from preliminary data not included in this study, hypothesis testing was omitted for this year.

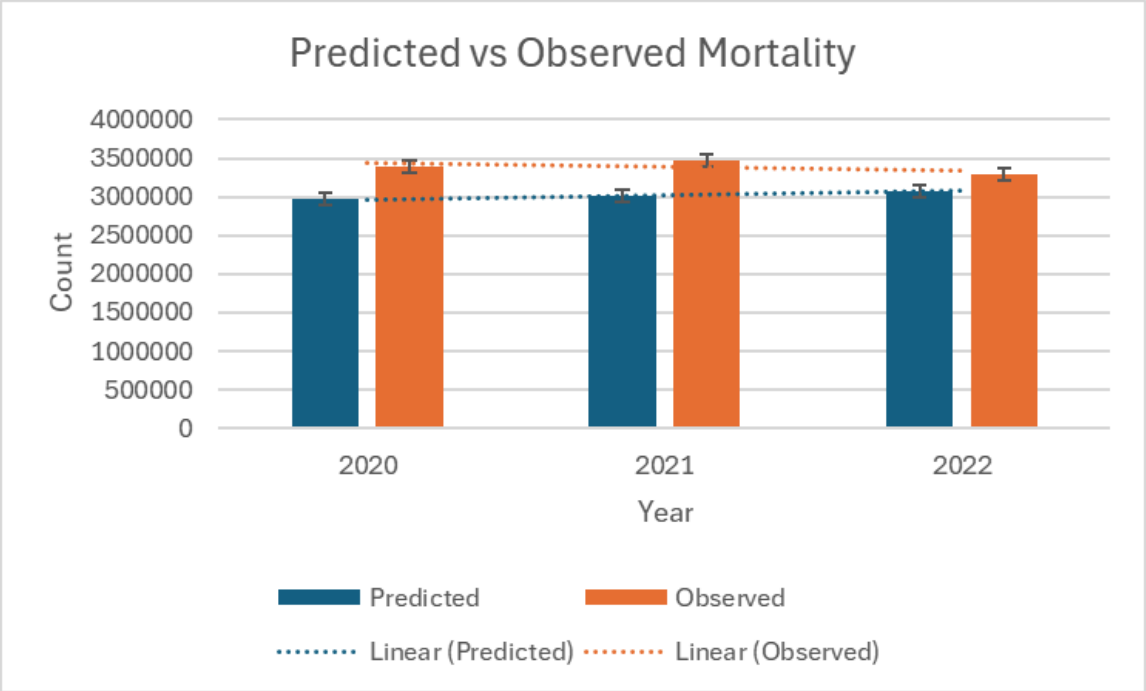

Figure 3. Predicted vs. Observed Mortality. Bar charts of the observed and predicted mortality counts for the years 2020-2022. Error bars represent the standard deviation based on year-over-year changes for the period of 2014-2019.

General Mortality Trends

From 2014 to 2019, there was a downward trend in year-over-year rate changes in mortality, indicating a stabilizing pattern prior to the COVID-19 pandemic. Note that the absolute number of deaths was still increasing despite this stabilizing pattern likely as a natural function of a growing population. The pandemic caused a major spike in excess deaths: 462,770 in 2020, peaking at 715,936 in 2021, and then falling to 474,964 in 2022. The average yearly mortality pre-pandemic was approximately 2.8 million, whereas from 2020 to 2022, the annual mortality count rose to almost 3.3 million. In a world devoid of the emergence of COVID-19, the expected average would be approximately 3.07 million per year in 2022, as we can observe in Table 1.

Provisional data from the National Vital Statistics System reports that the death toll in 2023 dropped to 3,090,582 (Ahmad et al., 2024), which falls just below our predicted value of 3,125,587. This large deviation from the stable mortality rate followed by convergence with the expected mortality rate shall hence be referred to as the “crest” for the remainder of this exploration, in reference to the resemblance of the perturbations to waveforms.

The convergence becomes more apparent when plotting a trendline over representative counts for observed and predicted mortality. An analysis of Figure 2 reveals observed death counts having reached normalized values as of 2023. This full convergence suggests a robust recovery from the effects of the pandemic.

Age-related effects

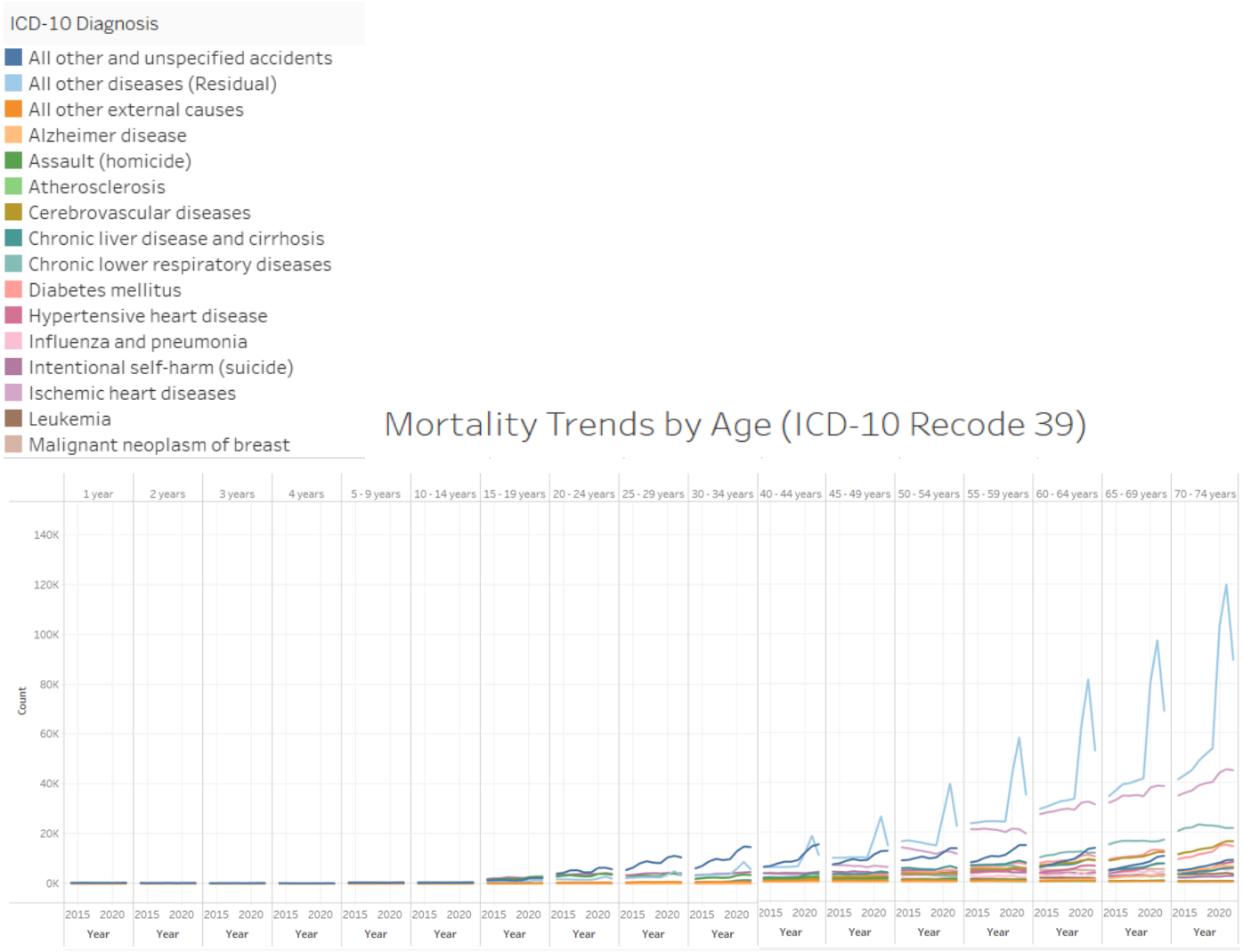

Figure 4. Mortality Trends by Age (1-74) Line plots for the sixteen greatest contributors to mortality from 2014-2022.

Most of the deaths related to Covid-19 were experienced by individuals older than 65. This phenomenon is easily explained by the accumulation of comorbidities and loss of resilience to disease that comes with age. (Mueller et al., 2020) We can confirm from our findings in Figure 2 that from 2020 to 2022, Americans under the age of 20 did not display a significant increase in mortality associated with viral infections. This is consistent with findings previously published regarding the risk of COVID-19 infection in younger populations being less severe (Leidman et

al., 2021). It should be noted that the COVID crest was observed in all age groups above the 15-19 age group, and the magnitude of this deviation was positively associated with age.

Specific Causes of Death

Cause of Death	Year	Predicted Deaths	Observed Deaths	Net	St. Dev.	St. Err.	Test Stat. (T)	p-value
All other diseases	2020	567566	964843	397277	21906.50	8943.29	44.42	1E-07
Ischemic heart diseases	2020	367218	383637	16419	2143.29	874.99	18.77	8E-06
Diabetes mellitus	2020	89489	102297	12808	4109.99	1677.90	7.63	6E-04
Hypertensive heart disease	2020	67882	78289	10407	8525.70	3480.60	2.99	3E-02
Chronic liver disease and cirrhosis	2020	45192	51762	6570	2167.85	885.02	7.42	7E-04
Assault /Homicide	2020	21464	24693	3229	1417.73	578.78	5.58	3E-03
Essential hypertension/Hypertensive renal disease	2020	39181	41961	2780	2439.97	996.11	2.79	4E-02
Abnormal clinical and laboratory findings	2020	32210	32919	709	519.04	211.90	3.35	2E-02
Malignant neoplasm of stomach	2020	11004	11262	258	152.12	62.10	4.15	9E-03
Pregnancy, childbirth and the puerperium	2020	1043	1293	250	92.59	37.80	6.62	1E-03

Table 2. Counts of predicted deaths, standard deviation, and standard error were calculated via linear regression. Net counts were calculated as (Observed Deaths - Predicted Deaths). The test statistic (T) and p-values were obtained via a one-sample student's t-test.

Cause of Death	Year	Predicted Deaths	Observed Deaths	Net	St. Dev.	St. Err.	Test Stat. (T)	p-value
All other diseases	2021	578544	1039854	461310	21906.50	8943.29	51.58	5.2E-08
All other and unspecified accidents/adverse effects	2021	162897	185620	22723	14298.70	5837.42	3.89	1.1E-02
Diabetes mellitus	2021	91602	103424	11822	4109.99	1677.90	7.05	8.9E-04
Chronic liver disease and cirrhosis	2021	46280	56727	10447	2167.85	885.02	11.80	7.7E-05
Hypertensive heart disease	2021	72101	81871	9770	8525.70	3480.60	2.81	3.8E-02
Ischemic heart diseases	2021	367440	376377	8937	2143.29	874.99	10.21	1.5E-04
Assault	2021	22243	26167	3924	1417.73	578.78	6.78	1.1E-03
Motor vehicle accidents	2021	44330	47397	3067	1887.53	770.58	3.98	1.1E-02
Abnormal clinical and laboratory findings	2021	32402	33402	1000	519.04	211.90	4.72	5.3E-03
Pregnancy, childbirth and the puerperium	2021	1018	1691	673	92.59	37.80	17.80	1.0E-05

Table 3. Counts of predicted deaths, standard deviation, and standard error were calculated via linear regression. Net counts were calculated as (Observed Deaths - Predicted Deaths). The test statistic (T) and p-values were obtained via a one-sample student's t-test.

Cause of Death	Year	Predicted Deaths	Observed Deaths	Net	St. Dev.	St. Err.	Test Stat. (T)	p-value
All other diseases	2022	589522	831138	241616	21906.50	8943.29	27.02	1.3E-06
All other and unspecified accidents/adverse effects	2022	171109	187097	15988	14298.70	5837.42	2.74	4.1E-02
Hypertensive heart disease	2022	76321	88444	12123	8525.70	3480.60	3.48	1.8E-02
Diabetes mellitus	2022	93716	101410	7694	4109.99	1677.90	4.59	5.9E-03
Chronic liver disease and cirrhosis	2022	47368	54967	7599	2167.85	885.02	8.59	3.5E-04
Ischemic heart diseases	2022	367662	372794	5132	2143.29	874.99	5.86	2.0E-03
Nephritis, nephrotic syndrome, and nephrosis	2022	54446	58022	3576	1255.75	512.66	6.97	9.3E-04
Assault	2022	23022	25086	2064	1417.73	578.78	3.57	1.6E-02
Human immunodeficiency virus	2022	4120	4981	861	640.85	261.63	3.29	2.2E-02
Sudden infant death syndrome	2022	1087	1533	446	129.30	52.78	8.44	3.8E-04

Table 4. Counts of predicted deaths, standard deviation, and standard error were calculated via linear regression. Net counts were calculated as (Observed Deaths - Predicted Deaths). The test statistic (T) and p-values were obtained via a one-sample student's t-test.

Accidents and Adverse Effects

P-value: < 0.0001

Equation: All other and unspecified accidents and adverse effects (V01,V05-V06,V09.1,V09.3-V09.9,V10-V11,V15-V18,V19.3,V19.8-V19.9,V80.0- = 10659.9*Year + -2.13687e+07

Coefficients

Term	Value	StdErr	t-value	p-value
Year	10659.9	999.108	10.6694	< 0.0001
intercept	-2.13687e+07	2.0162e+06	-10.5985	< 0.0001

Table 5. Describes the linear model used to estimate future mortality rates.

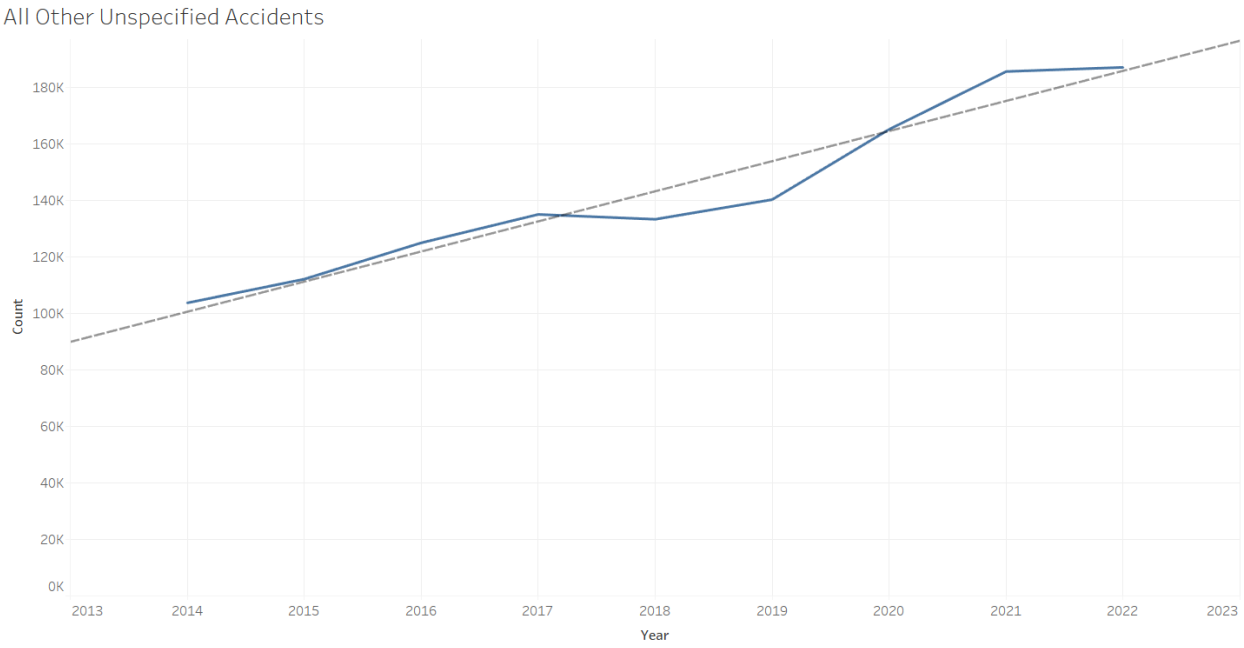

Figure 5. All Other Unspecified Accidents Mortality by Year. This line plot shows the linear nature of mortality growth (R=0.94, p=0.0001).

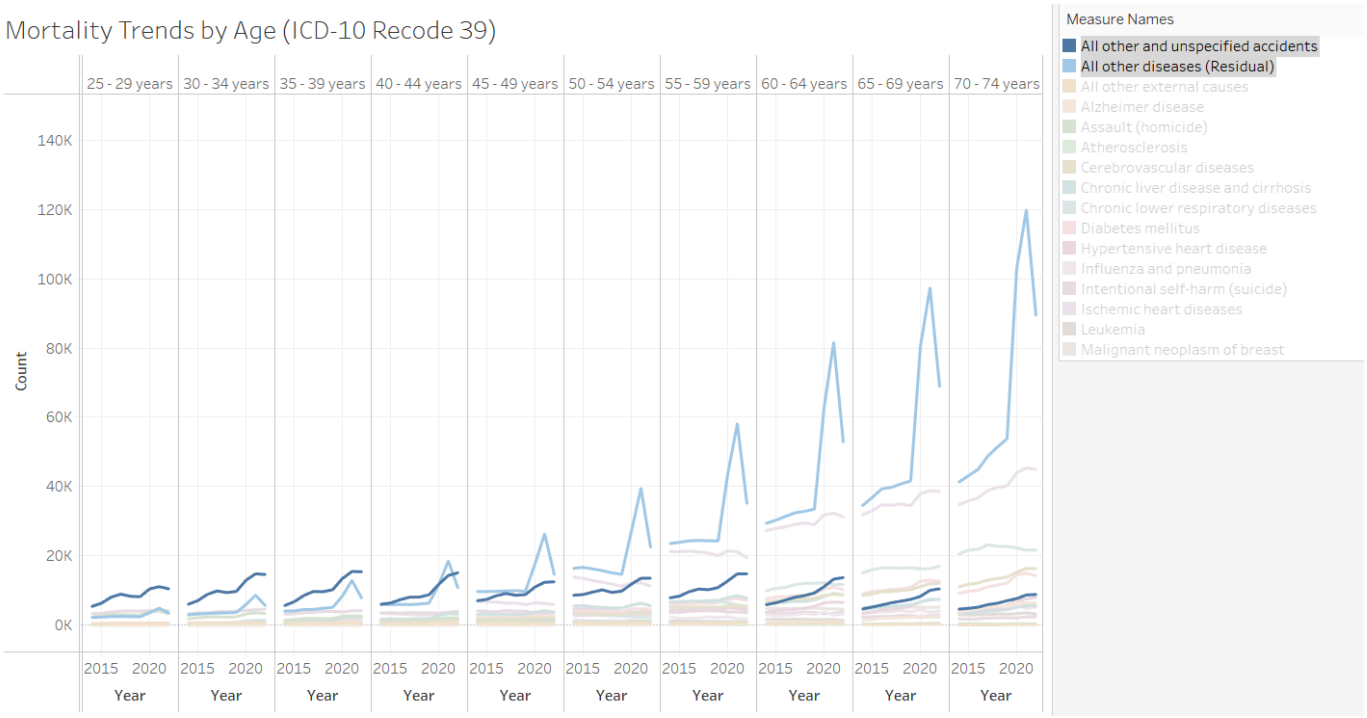

Figure 6. Mortality Trends by Age (25-74) Highlighted line plots of accidental deaths and residual diseases from 2014-2022.

Accidents and adverse effects (ICD codes V01, V05-V06, V09.1, V09.3-V09.9, V10-V11, V15-V18, V19.3, V19.8-V19.9, V80.0-V80.2, V80.6-V80.9, V81.2-V81.9, V82.2-V82.9, V87.9, V88.9, V89.1, V89.3, V89.9, V90-X59, Y40-Y86, Y88) accounted for 3.89% of all deaths, with a rate of change increasing by 11% from 2019 to 2020. These accounted for up to 62,000 excess deaths and were the leading cause of death for individuals under 40. During 2020 and 2021, the crossover event resulting in "all other diseases" becoming the leading cause of death occurred earlier, shifting from the 40-44 age bracket to the 35-39 bracket, indicating an elevated rate across all age groups.

While COVID-19 deaths dropped, accidental deaths remained elevated through 2022. Following the trend that existed prior to the pandemic (Figure 5) So, while it appears that the pandemic exacerbated the rise in accidental deaths, it was almost certainly not the root cause.

Residual Diseases

Trend Lines Model

A polynomial trend model of degree 3 is computed for sum of All other diseases (Residual) (A00-A09,A20-A49,A54-B19,B25-B99,D00-E07,E15-G25,G31-H93,I80-J06,J20-J39,J60-K22,K29-K66,K71-K72, given Year. The model may be significant at p <= 0.05. The factor Year (group) 1 may be significant at p <= 0.05.

Model formula:	Year (group) 1*(Year^3 + Year^2 + Year + intercept)
Number of modeled observations:	9
Number of filtered observations:	0
Model degrees of freedom:	7
Residual degrees of freedom (DF):	2
SSE (sum squared error):	1.51405e+07
MSE (mean squared error):	7.57024e+06
R-Squared:	0.999959
Standard error:	2751.41
p-value (significance):	0.0001227

Table 6. Describes the polynomial model used to estimate future mortality rates.

Analysis of Variance:

Field	DF	SSE	MSE	F	p-value
Year (group) 1	3	8.4328914e+10	2.81096e+10	3713.18	0.0002693

Individual trend lines:

Panes			Color	Line		Coefficients	
Row		Column	Year (group) 1	p-value	DF	Term	Value
All other diseases (Residual) (A00-A09,A20-A49,A54-B19,B25-B99,D00-E07,E15-G25,G31-H93,I80-J06,J20-J39,J60-K22,K29-K66,K71-K72,		Year	2020-2022	N/A	0	Year^3	-46.791
						Year^2	141830
						Year	0
						intercept	-1.93053e+11
All other diseases (Residual) (A00-A09,A20-A49,A54-B19,B25-B99,D00-E07,E15-G25,G31-H93,I80-J06,J20-J39,J60-K22,K29-K66,K71-K72,		Year	2014-2019	0.0094451	2	Year^3	-600.666
						Year^2	3.63483e+06
						Year	-7.33185e+09
						intercept	4.9297e+12

Table 7. Describes the individual models used to generate the trendlines observed in Figure 7.

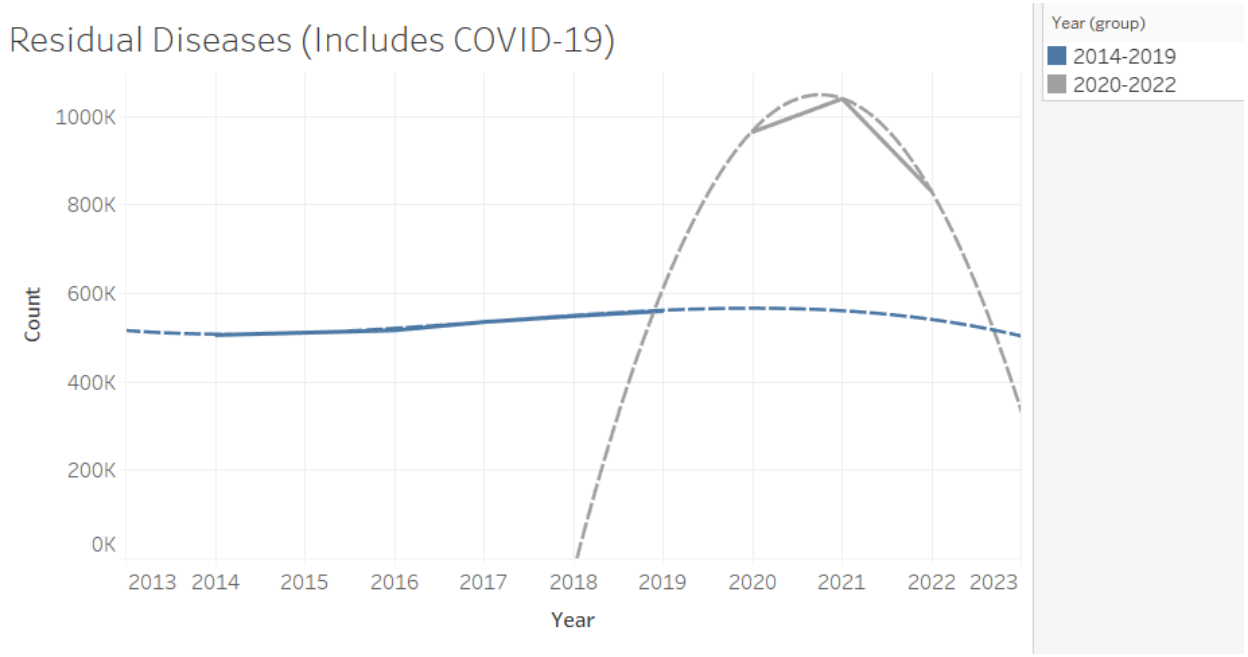

Figure 7. Residual Disease Model. Line graphs of the observed mortality during the period from 2014-2022, with predictive trendlines spanning the period 2014-2023. Trendlines were generated from a polynomial model grouping the years 2014-2019 and 2020-2022.

The category of "all other diseases" (ICD codes A00-A09, A20-A49, A54-B19, B25-B99, D00-E07, E15-G25, G31-H93, I80-J06, J20-J39, J60-K22, K29-K66, K71-K72, K75-M99, N10-N15, N20-N23, N28-N98, U04, U07.0, U07.1) includes COVID-19 (U07.1) and saw upwards of 397,000 excess deaths in 2020 (Table 2.) and more than 450,000 in 2021.

The model plotted in Figure 7 (R=0.99) shows a stable mortality rate from residual disease before the onset of the COVID-19 pandemic. Our model suggests convergence by 2023. Without access to the 2023 data, it is not possible to know for certain if this is the case or if there have been significant improvements in other areas that have driven the convergence observed at the aggregate level. Still, it is promising to note that the model is congruent with these macro trends.

The number of excess deaths decreased in 2022 to ~240,000, with a rate of change from 2021 to 2022 of -20%. The reduction in mortality observed in 2022 corresponds with the increasing population possessing immunity acquired through either vaccination or exposure. While the estimated seroprevalence had reached 96.4%, as many as 244,986 deaths listed COVID-19 as either a primary or secondary condition in 2022 (Ahmad et al., 2023). This discrepancy underlines the complexity of the risks associated with this disease. Despite our best efforts, COVID-19 is here to stay and can be expected to continue to result in thousands of deaths each year.

Diabetes Mellitus

Model formula:	Year (group)*(Year + intercept)
Number of modeled observations:	9
Number of filtered observations:	0
Model degrees of freedom:	4
Residual degrees of freedom (DF):	5
SSE (sum squared error):	3.40105e+06
MSE (mean squared error):	680210
R-Squared:	0.996237
Standard error:	824.748
p-value (significance):	< 0.0001

Analysis of Variance:

Field	DF	SSE	MSE	F	p-value
Year (group)	2	1.003534e+08	5.01767e+07	73.7665	0.0001945

Year (group)	p-value	DF	Term	Value	StdErr	t-value	p-value
2020-2022	0.710397	1	Year	-443.5	906.729	-0.489121	0.710397
			intercept	998690	1.8325e+06	0.544988	0.682335
2014-2019	0.0001634	4	Year	2173.91	158.418	13.7227	0.0001634
			intercept	-4.30153e+06	319450	-13.4654	0.000176

Table 8. Describes the linear model used for estimating mortality and convergence.

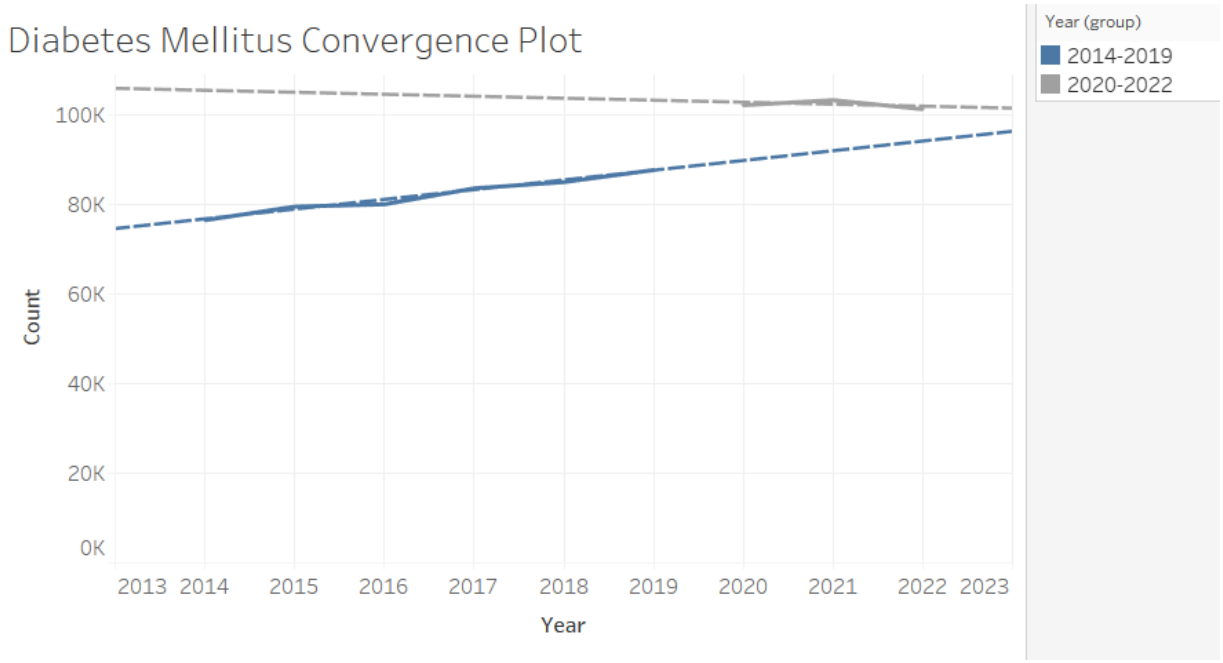

Figure 8. Diabetes Mellitus Convergence Plot. This line plot shows the linear nature of mortality growth (R=0.99) and the trend toward convergence of mortality rates to the expected counts.

In 2020 there was a major spike in mortalities attributed to Diabetes Mellitus leading to an estimated 12808 excess deaths (p=0.00061)(Table 2.). These results are consistent with clinical observations that have strongly linked diabetes as a comorbidity to COVID-19 and implicated a reciprocal relationship where COVID-19 acts as a possible causal contributor to the development or onset of type 1 diabetes (Ssentongo et al., 2022).

Like many other mortality spikes observed during the crest of the COVID-19 pandemic, excess deaths remained high for diabetes in 2021 (11822, p=0.00089) (Table 3.) and fell in 2022 (7694, p=0.0059)(Table 4.). The model shown in Figure 8 suggests that death rates will eventually converge on their expected linear outcomes by 2025. However, we must keep in mind that this 2022 figure is still significantly greater than the predicted number of deaths (Table 4.). Also, the predicted delay in convergence suggests that COVID-19 will still pose a significant

risk to this vulnerable population going forward. Particularly given the implications of the possible role of induction of diabetes by COVID-19 and the nearly doubled COVID-19 mortality risk for patients diagnosed with diabetes (Saha et al., 2021).

Assault and Homicide

A polynomial trend model of degree 3 is computed for sum of Assault (homicide) (*U01-*U02,X85-Y09,Y87.1) given Year. The model may be significant at p <= 0.05.

Model formula:	(Year^3 + Year^2 + Year + intercept)
Number of modeled observations:	9
Number of filtered observations:	0
Model degrees of freedom:	4
Residual degrees of freedom (DF):	5
SSE (sum squared error):	1.68576e+07
MSE (mean squared error):	3.37152e+06
R-Squared:	0.838231
Standard error:	1836.17
p-value (significance):	0.0201614

Table 9. Describes the polynomial model used to estimate future homicide rates.

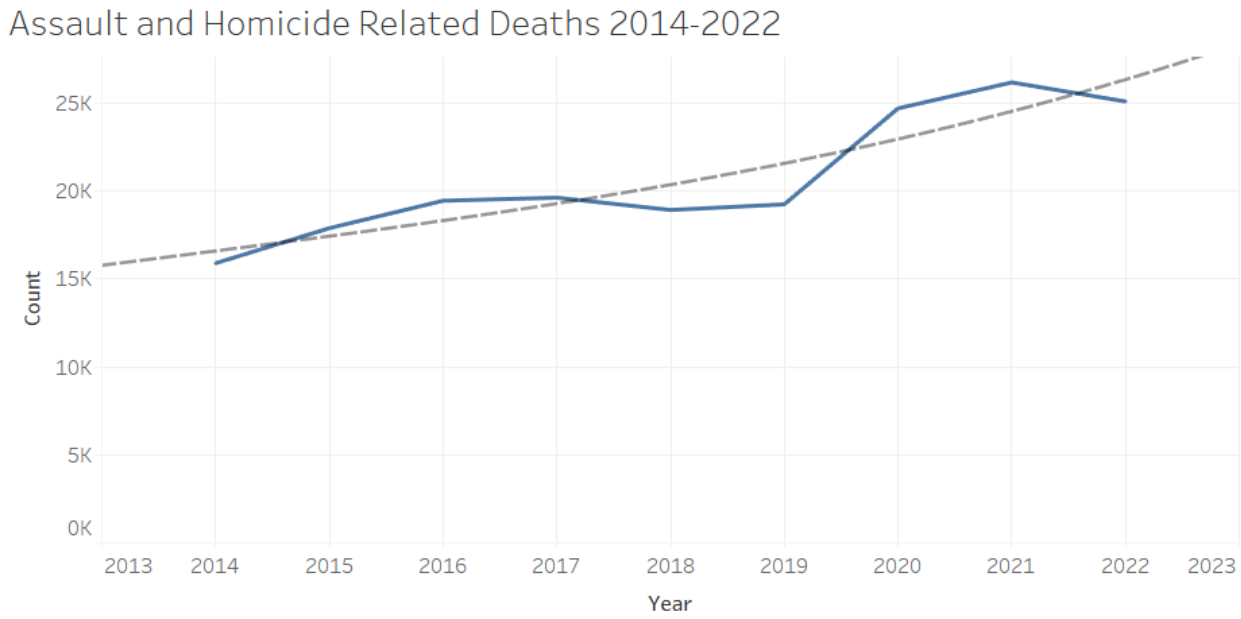

Figure 9. Assault and Homicide Related Deaths 2014-2022. The blue line represents the plotted counts for the period between 2014-2022, the grey trendline was generated from the polynomial model described in Table 8 and estimates the years from 2013 to 2023.

Deaths from assault and homicide jumped by 28.3% to 24,693 in 2020. This jump generated up to 3229 excess deaths. While it is the natural inclination to attribute these deaths to the COVID-19 pandemic, we must also take into consideration the political climate.

The year 2020 was host to a contentious Presidential race. Which saw violent protests become standard operating procedure and culminated with an attack on the capital. Based on this information, we can then make the logical leap to the assumption that this rise in assault and homicide deaths is likely linked to a combination of political tensions and pandemic-related pressures. Many Americans were facing fears of the unknown from multiple fronts. Rising unemployment, shortages in basic necessities, and disruptions to the supply lines, causing food scarcity induced anxiety and depression in huge portions of the population (Guerrini et al., 2021). Stress of this magnitude has been known to induce violent acts and so it is not necessarily unexpected that we would observe an uptick in homicides during this kind of crisis.

This trend continued with a 6.0% rise in 2021 followed by a fall of 4.1% in 2022. The mortalities observed in 2020, 2021, and 2022 exceed the expected count by 3229 ($p=0.003$), 3924 ($p=0.0011$), and 2064 ($p=0.016$) respectively. While the reduction seen in 2022 is a hopeful sign, it is more likely based on our model ($R=0.838$, $p=0.02$) that we will continue to see a rise in assault and homicide-related deaths in the future.

Hypertensive Heart Diseases

Trend Lines Model

A linear trend model is computed for sum of Hypertensive heart disease with or without renal disease (I11,I13) given Year. The model may be significant at p <= 0.05. The factor Year (group) 2 may be significant at p <= 0.05.

Model formula:	Year (group) 2*(Year + intercept)
Number of modeled observations:	9
Number of filtered observations:	0
Model degrees of freedom:	4
Residual degrees of freedom (DF):	5
SSE (sum squared error):	6.69097e+06
MSE (mean squared error):	1.33819e+06
R-Squared:	0.996881
Standard error:	1156.8
p-value (significance):	< 0.0001

Analysis of Variance:

Field	DF	SSE	MSE	F	p-value
Year (group) 2	2	50694780	2.53474e+07	18.9415	0.0046421

Individual trend lines:

Panes		Color	Line	
Row	Column	Year (group) 2	p-value	DF
Hypertensive heart disease with or without renal disease (I11,I13)	Year	2020-2022	0.107231	1
Hypertensive heart disease with or without renal disease (I11,I13)	Year	2014-2019	< 0.0001	4

Table 10. Describes the grouped linear models for the years 2014-2019 and 2020-2022.

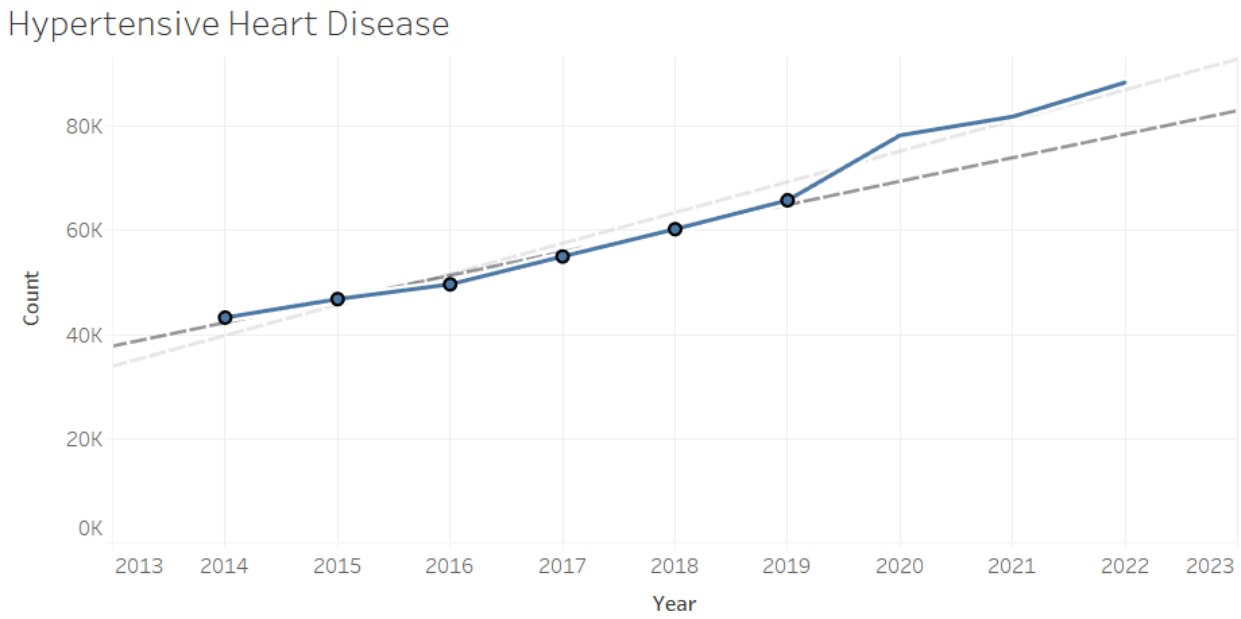

Figure 10. Hypertensive Heart Disease Mortalities by Year. The blue line represents the observed mortality counts for the respective year. The highlighted grey trendline represents the model for the group 2014-2019 described in Table 10. The light grey trendline represents the linear trend for the mortality data from the years 2014-2022.

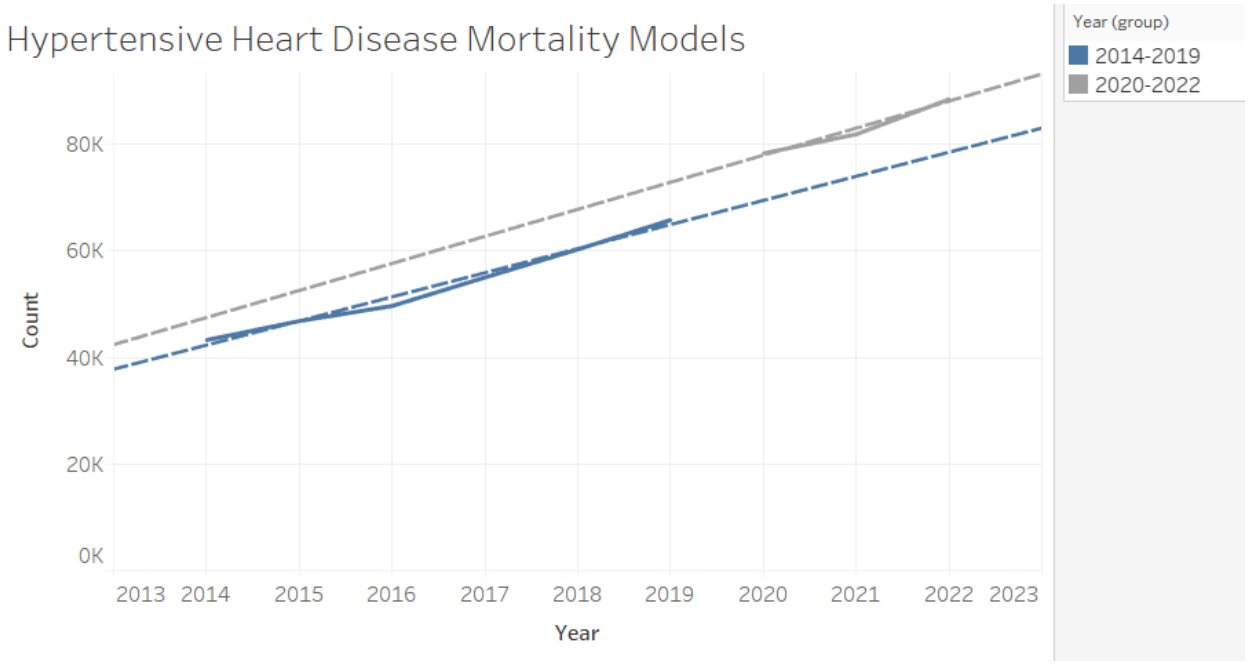

Figure 11. Hypertensive Heart Disease Mortality Models. The blue line represents the observed mortality counts for the years 2014-2019. The grey line represents the observed mortality counts for the years 2020-2022. Dashed lines plot the linear models described in Table 10 of their respective designated colors.

The average year-over-year increase in hypertensive heart disease deaths was 11.1% before the pandemic, rising sharply by 19.0% in 2020, equating to an excess of 10,407 (p=0.03)(Table 2). Rising again at a more stable rate of 4.6% in 2021, unfortunately, this still resulted in an excess death count of 9,770 (p=0.038)(Table 3). The death count for hypertensive diseases rose again by 8.0% in 2022 increasing the excess death count by 12,123 (p=0.018)(Table 4).

Based on the models shown in Figure 10 we are unlikely to observe convergence for hypertensive heart disease mortalities. Figure 11 demonstrates a diverging trend when comparing

the models. This indicates that the changes to the hypertensive heart disease mortality rate are likely to be sustained and will continue to be an increased strain on the healthcare industry.

Observing persistently high rates of hypertensive heart disease deaths following the onset of COVID-19 is not surprising. Hypertension has been consistently found to be a risk factor for COVID-19-associated hospitalization (Ebinger et al., 2022)(Muhamad et al., 2021). While the mechanism is still under investigation, there is some evidence to suggest that the link involves the interplay between the renin-angiotensin system and the ACE-2 receptor (Ebinger et al., 2022), which has been well-established as one of the primary entry mechanisms for the COVID-19 virus and is pivotal to the pathophysiology, disrupting the ACE→Angiotensin II→AT1 receptor axis (Verdecchia et al., 2020).

If these findings are true, then we can expect the levels of hypertensive heart disease deaths to remain elevated as COVID-19 infections continue to exacerbate pre-existing conditions. These clinical findings are consistent with the predictions given by the model shown in Figure 10. This is particularly alarming given the consistency of most other conditions to gravitate toward convergence with the expected values.

Trend Lines Model

A polynomial trend model of degree 2 is computed for sum of Chronic liver disease and cirrhosis (K70,K73-K74) given Year. The model may be significant at p <= 0.05. The factor Year (group) 3 may be significant at p <= 0.05.

Model formula:	Year (group) 3*(Year^2 + Year + intercept)
Number of modeled observations:	9
Number of filtered observations:	0
Model degrees of freedom:	6
Residual degrees of freedom (DF):	3
SSE (sum squared error):	719024
MSE (mean squared error):	239675
R-Squared:	0.998089
Standard error:	489.566
p-value (significance):	0.0002832

Analysis of Variance:

Field	DF	SSE	MSE	F	p-value
Year (group) 3	3	28323736	9.44125e+06	39.3919	0.0065638

Individual trend lines:

Panes		Color	Line		Coefficients	
Row	Column	Year (group) 3	p-value	DF	Term	Value
Chronic liver disease and cirrhosis (K70,K73-K74)	Year	Other	N/A	0	Year^2	-3362.5
					Year	1.35928e+07
					intercept	-1.37371e+10
Chronic liver disease and cirrhosis (K70,K73-K74)	Year	2014, 2015, 2016 and 3 more	0.0053527	3	Year^2	3.28571
					Year	-12110.4
					intercept	1.11015e+07

Table 11. Describes the grouped polynomial models generated for determining convergence.

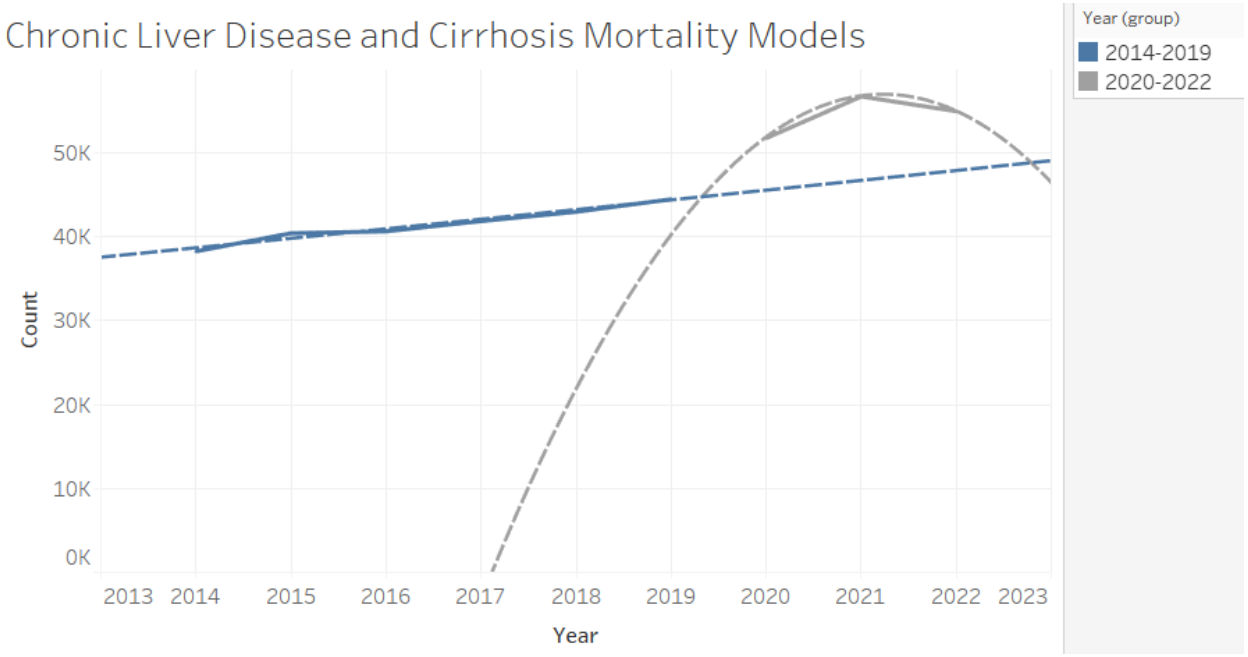

Figure 12. Chronic Liver Disease and Cirrhosis Grouped Mortality Models. The blue line represents the observed mortality data for the years 2014-2019. The grey line represents the observed mortality from 2020-2022. Dashed lines plot the polynomial models described in Table 11 of their respective designated colors.

Mortality associated with chronic liver disease and cirrhosis rose 16% from 2019 to 2020 resulting in an estimated excess death toll of 6530 (p=0.0007) (Table 2). Mortalities rose again in 2021 to 56,727 which is 10,447 over the estimated value of 46,280 (p=0.000077) (Table 3). As observed in many other conditions, there was a reduction in the mortalities observed in 2022 moving toward convergence with estimates based on pre-pandemic mortality data.

It is no secret that the pandemic introduced stressors to the population, which were impossible to prepare for. Often as a source of coping, humans have been known to steer toward alcohol and other intoxicants to "ease the pain" of life's more difficult periods (Sinha, 2022). As such, there were significant increases in alcohol and drug abuse during the pandemic lockdown periods with alcohol sales soaring as much as 477% in the first 4 months (Nielsen, 2020) (Calina

et al., 2021). Alcohol is one of the largest driving factors in liver disease pathophysiology (Roerecke et al., 2019) and so we would expect consequently that we would then see an increase in both diagnosis and mortality associated with chronic liver disease. The reduction in these deaths observed in Figure 12 as the pandemic pressures receded is congruent with these assertions.

Ischemic Heart Diseases

Trend Lines Model

A linear trend model is computed for sum of Ischemic heart diseases (I20-I25) given Year. The model may be significant at p <= 0.05. The factor Year (group) 4 may be significant at p <= 0.05.

Model formula:	Year (group) 4*(Year + intercept)
Number of modeled observations:	9
Number of filtered observations:	0
Model degrees of freedom:	4
Residual degrees of freedom (DF):	5
SSE (sum squared error):	2.10049e+07
MSE (mean squared error):	4.20097e+06
R-Squared:	0.943501
Standard error:	2049.63
p-value (significance):	0.0015142

Analysis of Variance:

Field	DF	SSE	MSE	F	p-value
Year (group) 4	2	2.2016497e+08	1.10082e+08	26.204	0.0022387

Individual trend lines:

Panes		Color	Line	
Row	Column	Year (group) 4	p-value	DF
Ischemic heart diseases (I20-I25)	Year	2020-2022	0.123085	1
Ischemic heart diseases (I20-I25)	Year	2014-2019	0.39661	4

Table 12. Describes the grouped linear models generated for determining convergence.

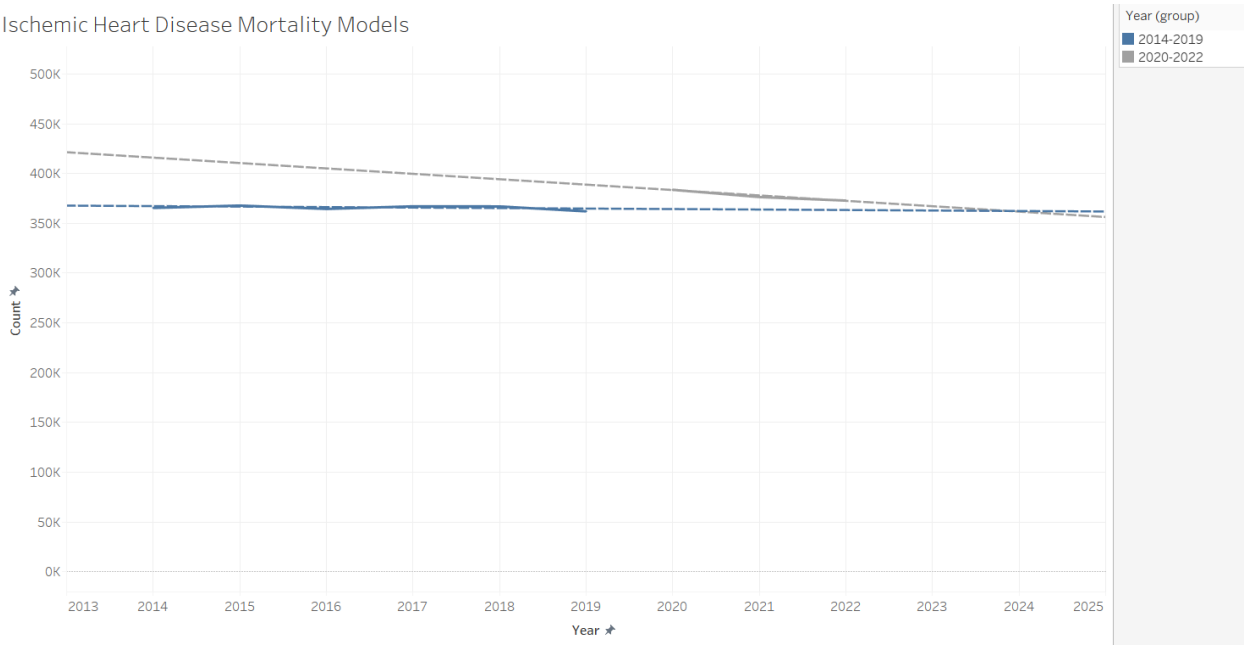

Figure 13. Ischemic Heart Disease Mortality Models. The blue line represents the observed mortality data for the years 2014-2019. The grey line represents the observed mortality from 2020-2022. Dashed lines plot the linear models described in Table 12 of their respective designated colors.

Mortality from ischemic heart diseases exceeded predicted estimates by 16,419 in 2020 (p=0.00000079) (Table 2), 8,937 in 2021 (p=0.00015) (Table 3), and 5,132 (p=0.002) (Table 4). This downward trend is demonstrated in Figure 13 and predicts convergence around 2024. While the trendlines for the respective models did not reach the significance level, this is likely a function of the small sample size rather than a representative statistic for the model's fit. It has been previously described that COVID-19 exacerbates cardiac complications, including viral endocarditis, leading to up to an estimated 7.28 ischemic heart disease diagnoses per 1000 patients presenting with COVID-19 (Abbasi, 2022).

It is too early to tell if the trend toward convergence will materialize or if the ischemic heart disease mortality rate will remain elevated going forward. Published clinical observations

imply this will be an ongoing pressure, but until more data becomes available the jury will remain hung on this matter.

Motor Vehicle Accidents

Trend Lines Model

A polynomial trend model of degree 3 is computed for sum of Motor vehicle accidents (V02-V04,V09.0,V12-V14,V19.0-V19.2,V19.4-V19.6,V20-V79,V80.3-V80.5,V81.0-V81.1,V82.0-V82.1,V83-V86,V87. given Year. The model may be significant at p <= 0.05.

Model formula:	Year (group) 5*(Year^3 + Year^2 + Year + intercept)
Number of modeled observations:	9
Number of filtered observations:	0
Model degrees of freedom:	7
Residual degrees of freedom (DF):	2
SSE (sum squared error):	656080
MSE (mean squared error):	328040
R-Squared:	0.994279
Standard error:	572.748
p-value (significance):	0.0170659

Analysis of Variance:

Field	DF	SSE	MSE	F	p-value
Year (group) 5	3	14760986	4.92033e+06	14.9992	0.0631492

Individual trend lines:

Panes		Color	Line	
Row	Column	Year (group) 5	p-value	DF
Motor vehicle accidents (V02-V04,V09.0,V12-V14,V19.0-V19.2,V19.4-V19.6,V20-V79,V80.3-V80.5,V81.0-V81.1,V82.0-V82.1,V83-V86,V87.	Year	Other	N/A	0
Motor vehicle accidents (V02-V04,V09.0,V12-V14,V19.0-V19.2,V19.4-V19.6,V20-V79,V80.3-V80.5,V81.0-V81.1,V82.0-V82.1,V83-V86,V87.	Year	2014, 2015, 2016 and 3 more	0.0546827	2

Table 13. Describes the grouped polynomial models generated for determining convergence.

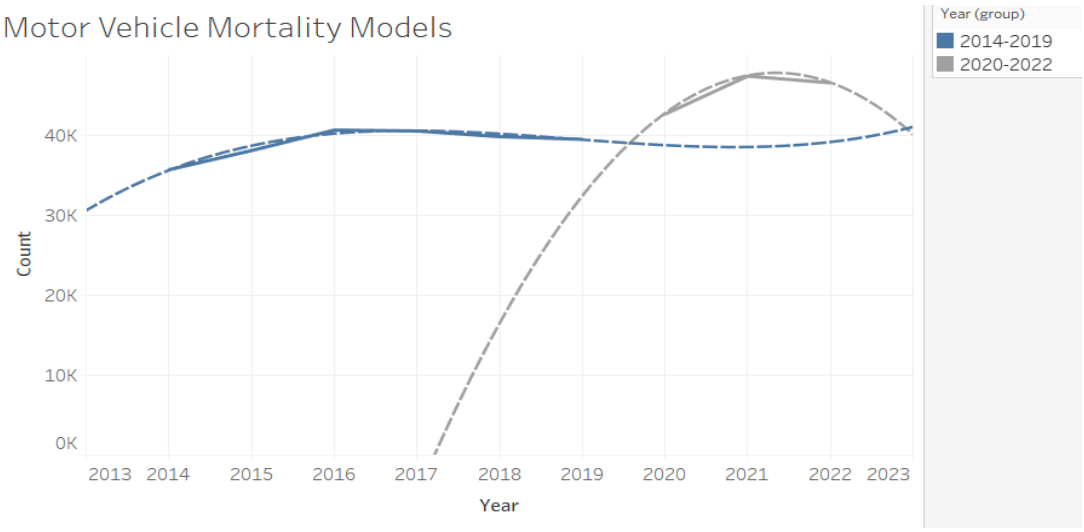

Figure 14. Motor Vehicle Mortality Models. The blue line represents the observed mortality data for the years 2014-2019. The grey line represents the observed mortality rate from 2020-2022. Dashed lines plot the linear models described in Table 13 of their respective designated colors.

Motor vehicle accidents did not deviate from the expected count in 2020 (p=0.34), followed by a steep increase of 7.9% in 2021 resulting in an estimated 3067 excess deaths (p=0.011) (Table 3), and then fell by 1.7% in 2022, still above the pre-pandemic rate, but not a significant deviation (p=0.19). It is unclear what type of relationship exists between the COVID-19 pandemic and the spike in traffic fatalities observed in 2021. However, it is possible that this was a secondary effect stemming from the COVID-19 lockdown policies keeping most drivers off the road for more than a year.

Discussion

"The Bad News"

Excess Mortality and Healthcare Disruptions

Previous publications have established that during the COVID-19 pandemic, significant increases in excess mortality occurred directly due to the COVID-19 virus and indirect effects from healthcare disruptions (Woolf et al., 2022). Excess deaths were observed across various age groups and regions in the U.S., indicating a widespread impact (Weinberger et al., 2020). Individuals with underlying conditions experienced higher mortality risks, emphasizing the vulnerability of certain populations (Banerjee et al., 2020). These types of disruptions and co-morbidity risks are likely candidates to help explain the increase in mortality for conditions like ischemic heart disease and diabetes mellitus observed in this exploration. Nearly all interventions related to ischemic heart diseases are either time-sensitive or require extensive monitoring by a provider. Naturally, any delays in care will dramatically influence the prognosis of individuals requiring care for these types of conditions.

The pandemic disproportionately affected older adults and individuals with comorbidities, leading to higher case-fatality rates in these groups (Onder et al., 2020) (Gold et al., 2021). Other vulnerable populations, such as those with down's syndrome or immunodeficiencies, faced significantly higher mortality risks, these findings strongly imply a necessity for developing targeted healthcare interventions (Clift et al., 2020) (Mishra et al., 2021).

This was likely a two-fold effect. Firstly, these populations are more susceptible to infection as both age and congenital conditions like down syndrome are associated with reduced

efficiency of the immune system (Ram & Chinen, 2011) (Glynn & Moss, 2020). Secondly, there were significant barriers to accessing care during the pandemic. These populations also tend to require a higher level of observation by their healthcare providers in order to maintain equitable outcomes to less vulnerable populations. These factors would exacerbate one another.

As vulnerable populations or those with comorbidities contract COVID-19 they often require hospitalization. These hospitalizations reduce the availability for routine care. Reductions in routine care then led to worsening of the pre-existing conditions or denial of access to preventative care, which then contributes to higher rates of hospitalization for infections and chronic diseases (Cassell et al., 2022). Given the reciprocal nature of this relationship, it is apparent that epidemiologists primary priority in this scenario is to find ways to reduce the strain on hospitals. This contextualizes the controversial push to mandate experimental vaccination techniques as a necessity of preventative intervention. The subsequent recovery of the mortality rate observed in this analysis in the years 2022 and 2023 coincides with the implementation of these preventative interventions and is strong evidence to uphold the argument that while controversial, the decision to mandate prophylactic care may have been the best course of action.

With delays in access to necessary care it was an expected outcome that we would observe increases in mortalities among vulnerable populations. Thankfully, as the healthcare system recovers, and the number of COVID-19 hospitalizations decreases due to a combination of prophylactic care and an improved understanding of the pathophysiology related to COVID-19 severity, we will also see a decline in the number of secondary deaths caused by limited access to care.

Secondary Health Impacts

As early as 2020 COVID-19 was already being associated with an increase in comorbid conditions like cardiovascular diseases, contributing to overall mortality (Reyes-Bueno et al., 2020; Sousa et al., 2020). These reports are consistent with the sudden increase in mortality associated with hypertensive heart disease, Diabetes mellitus, and ischemic heart diseases observed in this study.

It was not only deaths associated with disease or illness that were impacted. We observed an increase of 28.4% in homicide deaths, a 16.4% increase in chronic liver disease, and a 17.7% increase in accidental deaths. These staggering death tolls paint a bleak portrait of violence, substance abuse, and an overworked healthcare sector.

Vaccination and Mortality Trends

Large-scale administration of the first mRNA COVID-19 vaccinations led to a shift in mortality towards younger age groups in countries with effective elderly vaccination strategies, reducing severe outcomes and overall mortality rates (Pastorino et al., 2022). When parsing the data down to individual ICD-10 codes, it was observed that from 2020 to 2021 excess deaths exceeding (20,000) were attributed to “Accidental poisoning by and exposure to other and unspecified drugs, medicaments and biological substances” (X44). This ICD-10 code includes accidental poisonings from drugs that impact the cardiovascular system, anesthetics, systemic antibiotics, and vaccines.

Given that the controversial COVID-19 mRNA vaccinations were implemented in 2021 it is not an unreasonable assumption that this sudden spike in X44-coded mortalities is to some

degree a direct consequence. However, it is important to keep in consideration that this ICD-10 code also encapsulates accidental poisonings from anesthetics and drugs affecting the cardiovascular system. It is well documented that the sheer volume of the number of cases of COVID-19 requiring hospitalization resulted in massive strains on the healthcare infrastructure directly leading to excess deaths. (French et al., 2021) Our finding of a rising rate of X44 coded mortalities in 2020 further supports the notion that this increase was the natural progression of the overloading of the healthcare system as the COVID-19 pandemic wreaked havoc on the global population.

It is important to make these distinctions as a misinterpretation of the vaguely coded ICD-10 classification could lead to problematic consequences for society. For the first time in history, the average person was given a front-row seat to witness the stage upon which the scientific method plays out. The reality of the matter is that uncertainty is the very premise upon which this method is based. This is not a comforting or steadfast platform upon which to build trust in the idea that the response of this community will maintain the safety of the general population. At this juncture, transparency with the public is paramount to reestablishing good faith between the scientific community and the community at large.

Baseline Mortality

Baseline data on U.S. mortality trends before and during the pandemic reveal significant deviations in mortality rates, highlighting the broader impact of the pandemic on public health (Xu et al., 2020; CDC, 2021). The pandemic has also resulted in a notable decline in life expectancy, underscoring its long-term health implications (Arias et al., 2022). This is consistent with the shift in the convergence of accidental deaths and residual disease observed in Figure 7.

While trends indicate that this was a temporary shift, with only three years of data it is not possible to confidently assert that this decline in life expectancy will be a lasting effect. This could also be a function of the disproportionate loss of life in the early years of the pandemic experienced by older Americans. With fewer older Americans in the population as possible mortalities, we would naturally see a downward shift in life expectancy as a nature of the sampling population.

"The Good News"

Out of the 6 highest contributors to excess death that were analyzed in this exploration only 2 ICD-10 recode models did not suggest convergence with expected mortality within the next 5 years. Most of the major perturbations in mortality that were observed followed a wavelike pattern, spiking during the height of the pandemic and falling along with the recession of cases and hospitalizations. This indicates to us that the disruptions in care caused by the high levels of COVID-19 hospitalizations were likely the primary driving factor in excess deaths that were not directly associated with COVID-19 infections.

It is not a matter of contention that limited access to care is an indicator of poor health outcomes. Among Medicare beneficiaries, it has been estimated that limited access to specialists accounts for 40% of the urban-rural difference in preventable mortality (Johnston et al., 2019). Similarly, research suggests a positive correlation between health insurance coverage and patient outcomes (McWilliams, 2009).

At the height of the pandemic, the unemployment rate hit an unprecedented 14.4% (Blazina, 2024). With the majority of Americans relying on their employer for health care, this

led to a massive decline in insurance coverage (Bundorf et al., 2021). Complicating matters further were new barriers to healthcare including limited appointment availability due to government-sanctioned health advisory requirements, reduced resource availability, and fear of infection (Pujolar et al., 2022). This was a perfect storm for producing excess mortality in areas that require specialist care.

The good news is that we can expect normalization of mortality rates as tension eases upon the healthcare system, unemployment rebounds, and the population adapts in response to the extreme wave of mortality that washed over the world during the COVID-19 pandemic.

Limitations and Ethical Considerations

The number of years analyzed for the purposes of this study resulted in underpowered statistical analysis. This was a compromise brought on by a two-fold problem. Firstly, building the master data frame from nearly 28 million entries was highly computationally expensive, requiring both long run times and high memory consumption. Secondly, our test group was taken from only 3 years due to limitations in the availability of data. As a direct consequence, we were able to build well-fit models for the control period from 2014-2019, but the models representing the changes between 2020 and 2022 lacked statistical significance. This does not necessarily mean that conclusions drawn from these models do not hold water, it simply means that we must keep this in mind when making assertions or decisions based on these models.

These analyses are incomplete without greater context. As discussed earlier, there is a problem of vague coding practices, which may lead to problematic or inaccurate interpretations. The mortality counts for each of these ICD-10 coded conditions are only a piece of the story and

do not take into consideration things like misdiagnosis, cultural factors, ethnic factors, or other sociological factors that may play a role in the fluctuation of mortality counts for a given year. What these analyses allow us to do is to identify major fluctuations in mortality, which in turn will then inform future investigation and should not be taken as a final assessment. Instead, we should consider this exploration a dowsing rod, leading us to pools rich with information for downstream analysis.

Future Directions

Several avenues were illuminated, and foundations were established throughout the course of this analysis. Continued monitoring of the mortality rates of conditions known to be comorbid to COVID-19 is essential for re-establishing a stabilized healthcare system and for understanding the overall impact that the pandemic has had on the population at large. It would be beneficial to continue this line of analysis with a larger pool of data. I suggest compiling all mortality data from the National Center for Health Statistics, which reaches back to 1959 and compiling more recent data as it is released. This will help to improve the overall predictive power of the established models

Future experiments should investigate the implementation of several machine learning models to improve excess death calculations. These investigations would also benefit from normalizing the mortality level to account for birth rates and incorporating a greater number of variables including demographic factors into the machine learning models. Combining a more complex data input with effective principal component analysis is likely to yield figures that paint a more complete picture of the changes in mortality caused by the COVID-19 pandemic.

Deeper investigations should be launched into the future of hypertensive heart disease, ischemic heart disease, diabetes mellitus, and chronic liver disease-related mortalities. Each of these conditions has been clinically observed to have a complicated relationship with the pathophysiology of COVID-19 infections. While the analysis conducted here shows promising results, complications related to peripheral effects of COVID-19 infection and reduced vaccination coverage in younger populations (Aldridge et al., 2023) make the future unclear, as the long-term effects of the pandemic unfold.

Conclusion

The major effects on mortality appear to be waning as the population adjusts to this newcomer among the pantheon of pathogens. While mortalities related to some conditions like hypertensive heart disease remain elevated, we can find solace in the knowledge that nearly all other causes of excess death are trending toward predicted levels. The perturbations across mortality that were observed during the pandemic appear to be fluctuations that can be expected to regress toward the norm. Putting on full display the power of the "law of large numbers", bending even population dynamics to its might.

This is not to take lightly the devastation wrought upon society by the juggernaut of virulence that is COVID-19. Based on our analysis we can estimate that from 2020 through 2022 the pandemic caused over 1 million excess deaths. Meanwhile, reports continue to pour in over new variants, contributing to ongoing concerns over the health and safety of global populations (Katella, 2024). This in turn lends itself to driving continued monitoring of mortality trends of conditions associated with COVID-19 comorbidity or which may have complex interplay mechanisms that are still poorly characterized. It is also important to consider that the social,

economic, and psychological effects of the COVID-19 pandemic are more widespread, with greater lasting power than the limited scope of this study allows us to see.

We began this investigation by asking how COVID-19 changed the face of death. It comes to pass that the answer is that generally, it didn't. Some disease states are still experiencing elevated levels of mortality and the future is uncertain regarding the long-term effects of the virus. For this reason, it is imperative that we stay vigilant, investigating all significant perturbations in mortality that arise in the future. With that said, the findings herein suggest that we can expect life to carry on as it did before the onset of this globally traumatic event. Thanks to the power of human ingenuity and the robust nature of our diverse population. There is still a long road to recovery, but this analysis gives us a solid foundation to believe that tomorrow will bring a brighter day.

References

Abbasi, J. (2022). The COVID Heart—One year after SARS-COV-2 infection, patients have an array of increased cardiovascular risks. *JAMA*, *327*(12), 1113. https://doi.org/10.1001/jama.2022.2411

Ahmad, F. B., Cisewski, J. A., Xu, J., & Anderson, R. N. (2023). COVID-19 mortality update — United States, 2022. *MMWR Morbidity and Mortality Weekly Report*, *72*(18), 493–496. https://doi.org/10.15585/mmwr.mm7218a4

Aldridge, R. W., Nellums, L. B., Bartlett, S., Barr, A. L., Patel, P., Burns, R., ... & Abubakar, I. (2023). "Global, regional, and national estimates of the impact of the COVID-19 pandemic on routine childhood vaccination coverage: a modeling study." *Journal of Public Health*, 45(2), e196-e205.

Arias, E., Tejada-Vera, B., & Ahmad, F. (2022). "Provisional Life Expectancy Estimates for 2021." National Center for Health Statistics.

Baker, T. B., Bolt, D. M., Smith, S. S., Piasecki, T. M., Conner, K. L., Bernstein, S. L., Hayes-Birchler, T., Theobald, W. E., & Fiore, M. C. (2023). The Relationship of COVID-19 Vaccination with Mortality Among 86,732 Hospitalized Patients: Subpopulations, Patient Factors, and Changes over Time. *Journal of General Internal Medicine*, *38*(5), 1248–1255. https://doi.org/10.1007/s11606-022-08007-0

Banerjee A, Pasea L, Harris S, Gonzalez-Izquierdo A, Torralbo A, Shallcross L, Noursadeghi M, Pillay D, Sebire N, Holmes C, Pagel C, Wong WK, Langenberg C, Williams B, Denaxas S, Hemingway H. Estimating excess 1-year mortality associated with the COVID-19

pandemic according to underlying conditions and age: a population-based cohort study. Lancet. 2020 May 30;395(10238):1715-1725. doi: 10.1016/S0140-6736(20)30854-0. Epub 2020 May 12. PMID: 32405103; PMCID: PMC7217641.

Blazina, C. (2024, April 14). Unemployment rose higher in three months of COVID-19 than it did in two years of the Great Recession. *Pew Research Center*. https://www.pewresearch.org/short-reads/2020/06/11/unemployment-rose-higher-in-three-months-of-covid-19-than-it-did-in-two-years-of-the-great-recession/

Bundorf, M. K., Gupta, S., & Kim, C. (2021). Trends in US health insurance coverage during the COVID-19 pandemic. *JAMA Health Forum*, *2*(9), e212487. https://doi.org/10.1001/jamahealthforum.2021.2487

Calina, D., Hartung, T., Mardare, I., Mitroi, M., Poulas, K., Tsatsakis, A., Rogoveanu, I., & Docea, A. O. (2021). COVID-19 pandemic and alcohol consumption: Impacts and interconnections. *Toxicology Reports*, *8*, 529–535. https://doi.org/10.1016/j.toxrep.2021.03.005

Cassell, K., Zipfel, C. M., Bansal, S., & Weinberger, D. M. (2022). Trends in non-COVID-19 hospitalizations prior to and during the COVID-19 pandemic period, United States, 2017–2021. *Nature Communications*, *13*(1). https://doi.org/10.1038/s41467-022-33686-y

CDC Museum COVID-19 timeline. (2023, March 15). Centers for Disease Control and Prevention. https://www.cdc.gov/museum/timeline/covid19.html

Centers for Disease Control and Prevention (CDC). (2021). "Provisional Mortality Data — United States, 2020." Morbidity and Mortality Weekly Report (MMWR).

Clarke, K. E. N., Jones, J. M., Deng, Y., Nycz, E., Lee, A., Iachan, R., US Department of Health and Human Services/Centers for Disease Control and Prevention, Gundlapalli, A. V.,

Hall, A. J., & MacNeil, A. (2022). Seroprevalence of Infection-Induced SARS-COV-2 Antibodies — United States, September 2021–February 2022. In *Morbidity and Mortality Weekly Report* (Vol. 71, Issue 17). https://www.cdc.gov/mmwr/volumes/71/wr/pdfs/mm7117e3-H.pdf

Clift, A. K., Coupland, C. A. C., Keogh, R. H., Hemingway, H., & Hippisley-Cox, J. (2020). "COVID-19 mortality risk in Down syndrome: results from a cohort study of 8 million adults." *Annals of Internal Medicine*, 173(6), 442-448.

Ebinger, J. E., Driver, M., Joung, S., Tran, T., Barajas, D., Wu, M., Botting, P. G., Navarrette, J., Sun, N., & Cheng, S. (2022). Hypertension and excess risk for severe COVID-19 illness despite booster vaccination. *Hypertension*, *79*(10). https://doi.org/10.1161/hypertensionaha.122.19694

French, G., Hulse, M., Nguyen, D., Sobotka, K., Webster, K., Corman, J., Aboagye-Nyame, B., Dion, M., Johnson, M., Zalinger, B., & Ewing, M. (2021). Impact of hospital strain on excess deaths during the COVID-19 pandemic — United States, July 2020–July 2021. *MMWR Morbidity and Mortality Weekly Report*, *70*(46), 1613–1616. https://doi.org/10.15585/mmwr.mm7046a5

Guerrini, C. J., Schneider, S. C., Guzick, A. G., Nwankwo, G. N. A., Canfield, I., Fedson, S., Gutierrez, A. M., Sheu, J. C., Song, A. Y., Villagran, A. M., McGuire, A. L., & Storch, E. A. (2021). Psychological distress among the U.S. general population during the COVID-19 pandemic. *Frontiers in Psychiatry*, *12*. https://doi.org/10.3389/fpsyt.2021.642918

Hughes, M. M., Wang, A., Grossman, M. K., Pun, E., Whiteman, A., Deng, L., ... & Kambhampati, A. K. (2021). "County-level COVID-19 vaccination coverage and social

vulnerability—United States, December 14, 2020–March 1, 2021." *BMJ Open*, 11(12), e050525.

Johnston, K. J., Wen, H., & Maddox, K. E. J. (2019). Lack of access to specialists associated with mortality and preventable hospitalizations of rural Medicare beneficiaries. *Health Affairs*, *38*(12), 1993–2002. https://doi.org/10.1377/hlthaff.2019.00838

Katella, K. (2024, July 11). *3 things to know about FLIRT and LB.1, the new coronavirus strains*. Yale Medicine. https://www.yalemedicine.org/news/3-things-to-know-about-flirt-new-coronavirus-strains

Kontis, V., Bennett, J. E., Rashid, T., Parks, R. M., Pearson-Stuttard, J., Guillot, M., Asaria, P., Zhou, B., Battaglini, M., Corsetti, G., McKee, M., Di Cesare, M., Mathers, C. D., & Ezzati, M. (2020). Magnitude, demographics and dynamics of the effect of the first wave of the COVID-19 pandemic on all-cause mortality in 21 industrialized countries. *Nature Medicine*, *26*(12), 1919–1928. https://doi.org/10.1038/s41591-020-1112-0

Leidman, E., Duca, L. M., Omura, J. D., Proia, K., Stephens, J. W., & Sauber-Schatz, E. K. (2021). COVID-19 trends among persons aged 0–24 years — United States, March 1–December 12, 2020. *MMWR Morbidity and Mortality Weekly Report*, *70*(3), 88–94. https://doi.org/10.15585/mmwr.mm7003e1

McWilliams, J. M. (2009). Health Consequences of Uninsurance among Adults in the United States: Recent Evidence and Implications. *Milbank Quarterly*, *87*(2), 443–494. https://doi.org/10.1111/j.1468-0009.2009.00564.x

Mishra, S., Ma, H., Moloney, G., Ibberson, C. B., Allen, D. M., & Fisman, D. N. (2021). "COVID-19 hospitalizations and mortality among children with down syndrome: A nationwide cohort study." *The Lancet Public Health*, 6(9), e640-e647.

Mortality data - Vital Statistics NCHS Multiple cause of death data. (2023, February 1). NBER. https://www.nber.org/research/data/mortality-data-vital-statistics-nchs-multiple-cause-death-data

Mueller AL, McNamara MS, Sinclair DA. Why does COVID-19 disproportionately affect older people? Aging (Albany NY). 2020 May 29;12(10):9959-9981. doi: 10.18632/aging.103344. Epub 2020 May 29. PMID: 32470948; PMCID: PMC7288963.

Muhamad, S., Ugusman, A., Kumar, J., Skiba, D., Hamid, A. A., & Aminuddin, A. (2021). COVID-19 and hypertension: the what, the why, and the how. *Frontiers in Physiology*, *12*. https://doi.org/10.3389/fphys.2021.665064

Nielsen, I. Q. (2020). Rebalancing the COVID-19 effect on alcohol sales. *Nielsen New York (NY)*.

Onder, G., Rezza, G., & Brusaferro, S. (2020). "Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy." *JAMA*, 323(18), 1775-1776.

Pastorino, R., Pezzullo, A. M., Villani, L., Causio, F. A., Axfors, C., Contopoulos-Ioannidis, D. G., Boccia, S., & Ioannidis, J. P. (2022). Change in age distribution of COVID-19 deaths with the introduction of COVID-19 vaccination. *Environmental Research*, *204*, 112342. https://doi.org/10.1016/j.envres.2021.112342

Pujolar, G., Oliver-Anglès, A., Vargas, I., & Vázquez, M. (2022). Changes in Access to Health Services during the COVID-19 Pandemic: A Scoping Review. *International Journal of Environmental Research and Public Health*, *19*(3), 1749. https://doi.org/10.3390/ijerph19031749

Ram, G., & Chinen, J. (2011). Infections and immunodeficiency in Down syndrome. *Clinical & Experimental Immunology*, *164*(1), 9–16. https://doi.org/10.1111/j.1365-2249.2011.04335.x

Reyes-Bueno, J. A., García-Trujillo, L., Urbaneja, P., Luna, C., Alguacil-Guillén, M., & Gómez-Iglesias, P. (2020). "COVID-19 and neurological disorders: A systematic review." *Journal of Neurology*, 267(9), 2809-2821.

Roerecke, M., Vafaei, A., Hasan, O. S., Chrystoja, B. R., Cruz, M., Lee, R., Neuman, M. G., & Rehm, J. (2019). Alcohol Consumption and Risk of Liver Cirrhosis: A Systematic Review and Meta-Analysis. *The American Journal of Gastroenterology*, *114*(10), 1574–1586. https://doi.org/10.14309/ajg.0000000000000340

Rossen, L. M., Branum, A. M., Ahmad, F. B., Sutton, P., & Anderson, R. N. (2021). "Excess Deaths Associated with COVID-19, by Age and Race and Ethnicity — United States, 2020." MMWR.

Saha, S., Al-Rifai, R. H., & Saha, S. (2021). Diabetes prevalence and mortality in COVID-19 patients: a systematic review, meta‐analysis, and meta‐regression. *Journal of Diabetes & Metabolic Disorders*, *20*(1), 939–950. https://doi.org/10.1007/s40200-021-00779-2

Sinha, R. (2022). Alcohol's Negative Emotional Side: The Role of Stress Neurobiology in Alcohol Use Disorder. *Alcohol Research*, *42*(1). https://doi.org/10.35946/arcr.v42.1.12

Sousa, G. J. B., Garces, T. S., Cestari, V. R. F., Florêncio, R. S., Moreira, T. M. M., & Pereira, M. L. D. (2020). Mortality and survival of COVID-19. *Epidemiology and Infection, 148*, e123. https://doi.org/10.1017/S0950268820001405

Ssentongo, P., Zhang, Y., Witmer, L., Chinchilli, V. M., & Ba, D. M. (2022). Association of COVID-19 with diabetes: a systematic review and meta-analysis. *Scientific Reports*, *12*(1). https://doi.org/10.1038/s41598-022-24185-7

Weinberger, D. M., Chen, J., Cohen, T., Crawford, F. W., Mostashari, F., Olson, D., Pitzer, V. E., Reich, N. G., Russi, M., Simonsen, L., Watkins, A., & Viboud, C. (2020). Estimation of excess deaths associated with the COVID-19 pandemic in the United States, March to May 2020. *JAMA Internal Medicine*, *180*(10), 1336. https://doi.org/10.1001/jamainternmed.2020.3391

Woolf, S. H., Chapman, D. A., Sabo, R. T., Weinberger, D. M., Hill, L., & Taylor, D. D. H. (2021). "Excess Deaths From COVID-19 and Other Causes, March-April 2020." JAMA.

Wynants, L., Van Calster, B., Collins, G. S., Riley, R. D., Heinze, G., Schuit, E., ... & Damen, J. A. (2020). "Prediction models for diagnosis and prognosis of COVID-19: systematic review and critical appraisal." *Journal of Clinical Epidemiology*, 126, 84-93.

Xu, J., Murphy, S. L., Kochanek, K. D., & Arias, E. (2020). "Mortality in the United States, 2018." National Center for Health Statistics.

Verdecchia, P., Cavallini, C., Spanevello, A., & Angeli, F. (2020). The pivotal link between ACE2 deficiency and SARS-CoV-2 infection. *European Journal of Internal Medicine*, *76*, 14–20. https://doi.org/10.1016/j.ejim.2020.04.037