Cause-Specific Excess Mortality Patterns in the US During the COVID-19 Pandemic

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Introduction & Background

The COVID-19 pandemic (henceforth: pandemic), caused by the SARS-CoV-2 virus, emerged in late 2019 and quickly became a global health crisis. By early 2020, the United States faced unprecedented challenges in healthcare, public policy, and daily life because of the pandemic's rapid spread (Kaye et al., 2021). The pandemic has resulted in a significant number of direct fatalities, as evidenced by the official COVID-19 death toll of 1,141,782 in the United States as of September 9th, 2023, according to the Centers for Disease Control and Prevention (CDC, 2020). In the US, estimated excess mortality has been higher than official COVID-19 deaths (Faust et al., 2021). This likely reflects both undercounted COVID-19 mortality (Paglino et al., 2023) and increases in other causes of death, reflecting indirect impacts of the pandemic. COVID-19 itself may have longer term impacts on mortality risk after the acute infection period has ended, resulting in more persistent excess mortality (Xie et al., 2022).

Understanding these ripple effects is critical. Historical instances of epidemics have illustrated that although the immediate threat presented by a new infectious disease may decrease, its health ramifications can persist, either through the long-term health impacts of the infection itself or as a result of the indirect consequences of societal response to disease (Eickhoff, 1961; Madhav et al., 2017). In the context of the COVID-19 pandemic, there is evidence of interruptions in healthcare systems (Haldane et al., 2021), social isolation (Brooks et al., 2020), economic difficulties (Nicola et al., 2020), and psychological stress factors (Purtle, 2020).

The United States entered the pandemic with significant population health challenges and elevated mortality compared to peer countries. These challenges included an opioid crises that predated the pandemic (Alexander et al., 2020; Masters et al., 2018) and the rising rates of midlife mortality in the U.S. (Committee on Rising Midlife Mortality Rates and Socioeconomic Disparities et al., 2021). Although some studies have examined the indirect impact of COVID-19 on certain causes and population groups (Chen et al., 2023; Cronin & Evans, 2021; Roberton et al., 2020; Wadhera et al., 2021; Zhu et al., 2021), there is limited work comprehensively evaluating on a full range of causes. This paper will estimate monthly excess deaths in the US by cause of death, age, and sex. We examine five age groups (15-29, 30-44 … 75+), separately by sex, and eight primary causes of death: cardiovascular disease, cancer, influenza and pneumonia, substance use, accidents, suicide, cancer, and a residual category (including deaths due to COVID-19).

Data and Research Methods

Monthly data on deaths in the US from 2015-2022 came from the Multiple Cause of Death Data provided by the Centers for Disease Control and Prevention's (CDC) Wonder system and were stratified by sex and 15-year age groups (15-29, 30-44, 45-59, 60-74, 75+). Eight causes of death were analyzed: cardiovascular diseases, cancer, influenza and pneumonia, substance-

related (drugs and alcohol), accidents, suicide, cancer, and a residual category (including direct deaths from COVID-19).

A stochastic interpretation of the Generalized Additive Model (GAM) was employed. The selection of the GAM was motivated by its versatility as a statistical model class, which expands upon the capabilities of Generalised Linear Models (GLMs) by accommodating non-linear associations between predictor variables and the response variable (Hastie & Tibshirani, 1986).The GAM methodology effectively captures non-linear correlations and fluctuations throughout extensive datasets by employing smooth functions. Due to its ability to detect patterns within time series data, the GAM has shown efficacy in addressing seasonality and producing precise forecasts. This is especially important with monthly death data, as many causes of death vary in their severity across seasons (e.g., influenza and pneumonia is higher in winter months than in summer).

Data from January 2015 to February 2020 were used as the training set, whereby the GAM predicts the number of deaths expected in each month from March 2020 to December 2022 ("expected deaths"). This is then compared with the observed number of deaths in each month ("observed deaths"). The number of excess deaths was then calculated as the difference between expected and observed deaths. The model was simulated 100 times, generating confidence intervals for each cause and age-sex stratum.

Preliminary Findings

Between March 2020 and December 2022, there were an estimated 1,302,846 excess deaths in the United States (95% CI: 1,102,368 to 1,507,630). Excess mortality varied by cause of death and over time, as shown in Figure 1. Cumulatively, cardiovascular diseases accounted for 116,703 excess deaths (95% CI: 67,080 to 168,042), substance use for 87,658 deaths (95% CI: 69,115 to 106,310), and accidents for 25,108 excess deaths (95% CI: 13,229 to 37,189). Figure 1 shows the absolute number of excess deaths by cause in each month. Cardiovascular disease made up the majority of non-Covid excess deaths (reaching a maximum of 11,279 in January 2022). Substance-related deaths remained consistent over time (with a maximum of 3,656 in April 2020), while influenza and pneumonia showed negative excess throughout much of the period. Excess deaths due to residual causes track closely with the deaths directly attributable to COVID-19, though a divergence between the two emerged after May 2022.

Figure 1. **Absolute excess mortality by cause of death, US, Jan 2020 to Dec 2022**

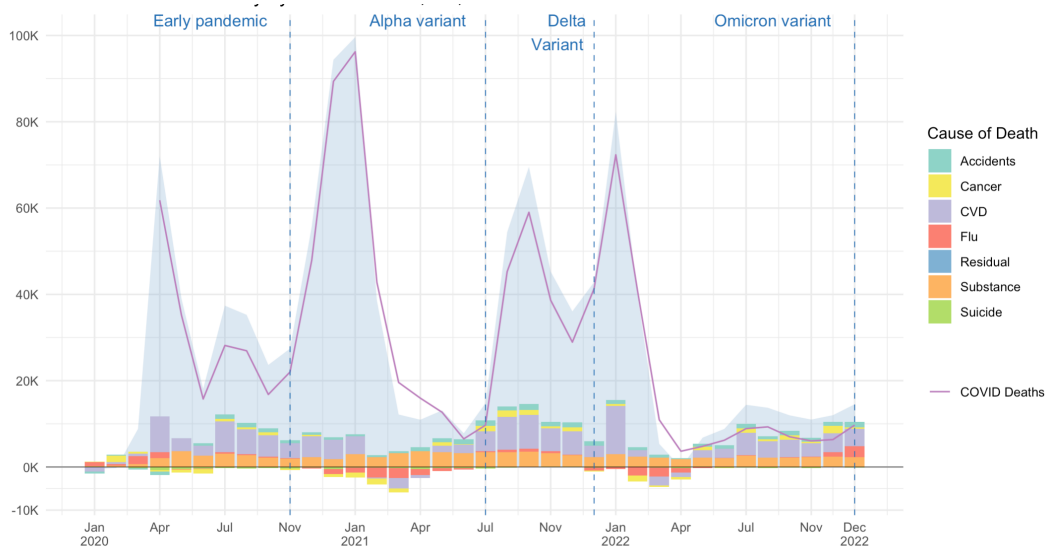
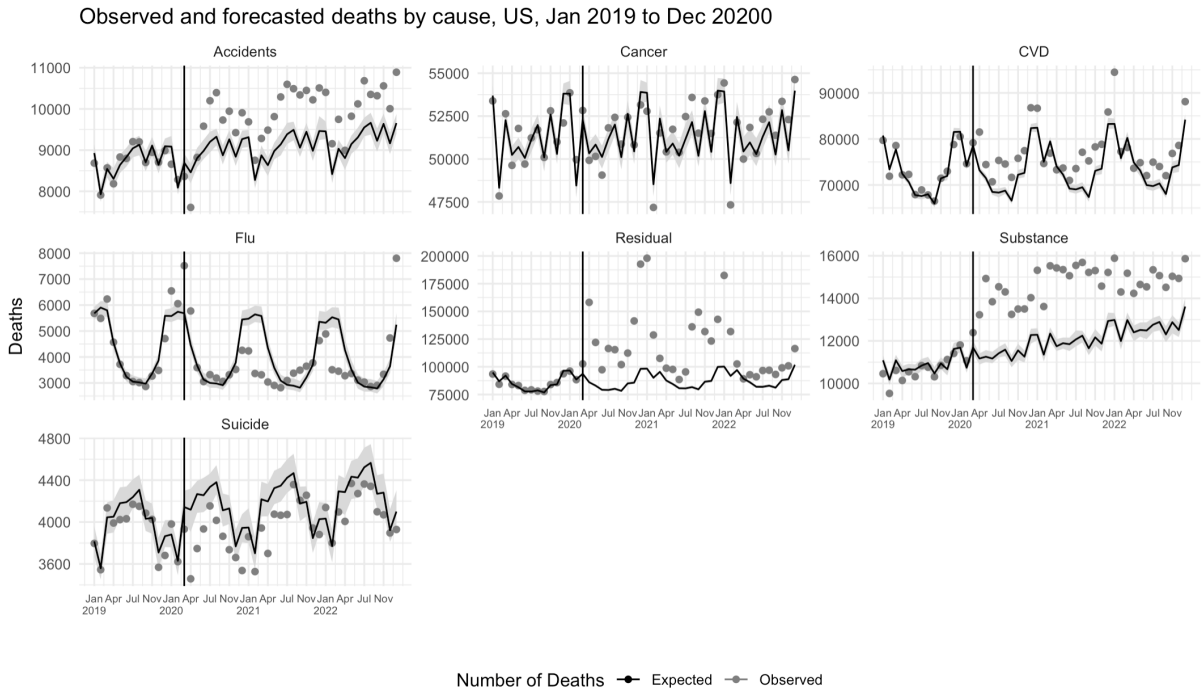


Figure 2 illustrates the difference between expected deaths (line) and observed deaths (dots). This chart illustrates the seasonality of most causes of death, including the lower influenza and flu mortality in summer month, the lower number of suicides in winter months, and the general trends, such as the consistent increase in substance-related deaths. Across the entire study period, deaths from substances (including drug- and alcohol-related) far surpassed the projected upward trend. The presence of seasonality and the magnitude of COVID-19 related excess absorbed by the 'Residual' component are also evident.

Figure 2. **Observed and forecasted deaths by cause, US, January 2018 to December 2020**



Cumulative P-scores by age and sex categories are shown in Table 1, The P-scores represent the standardized increase/decrease in percentage difference and are calculated as follows:

$$P\text{-}score = \frac{Observed\ Deaths - Expected\ Deaths}{Expected\ Deaths} * 100$$

P-scores offer an important and complementary perspective to the absolute excess death values. As an illustration, females aged 75 and above suffered 28,987 cumulative excess cardiovascular deaths (95% CI: 6,361 to 46,219), but P-scores show that this was just 3.36% above expected levels. This table also highlights that the highest relative increase in excess deaths from cardiovascular disease was found at ages 30-44, for both genders. Additionally, deaths due to substances were cumulatively nearly 25% higher than projected for males aged 15-29, 30-44, and 45-59. There was minimal or negative excess mortality attributed to influenza in all groups, consistent with COVID-19 precautions lowering the incidence of other infectious disease. Additionally, there were fewer suicides than expected across nearly all demographic groups, contrary to early concerns about the impact of the pandemic on mental health and isolation.

Table 1. **Cumulative P-scores (%) by cause and age-sex group, US, March 2020 to December 2022**

Sex/Age Group	Cancer	Accidents	CVD	Influenza	Substance	Suicide	Residual (inc. Covid)
Females 15-29	-3.14	16.29	6.42	-22.55	17.90	-1.11	38.24
Males 15-29	2.75	19.26	11.07	-6.08	23.92	-5.88	33.56
Females 30-44	3.49	16.98	18.09	-18.94	27.05	-2.32	55.29
Males 30-44	8.23	21.39	18.06	1.23	25.27	0.42	67.92
Females 45-59	-0.44	8.19	10.11	-14.25	23.32	-10.75	55.52
Males 45-59	1.01	7.38	9.35	-6.64	24.36	-7.83	70.50
Females 60-74	0.20	1.85	7.02	-4.57	16.15	-9.01	41.42
Males 60-74	0.06	5.93	5.40	1.60	15.89	-8.45	49.48
Females 75+	0.54	4.08	3.36	-7.85	12.04	5.54	24.98
Males 75+	-0.29	3.27	3.02	-3.34	5.09	0.57	32.53

Conclusions and Next Steps

The COVID-19 pandemic altered US mortality trends. Deaths due to some causes, such as influenza/pneumonia and suicides decreased, while others, notably cardiovascular diseases, and substance use, were much higher than anticipated. Such patterns reflect both direct and indirect pandemic impacts, underscoring the urgency for public health interventions for the most affected demographic groups and preventable causes. Prior to the European Population Conference in June 2024, we will finalize data visualizations for excess mortality patterns by age, sex and cause and will elaborate in the discussion on the implications of these trends for future mortality and population health in the US.