Trends in death rates from neoplasms in the US for all ages and detailed analysis for 75-84

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Trends in death rates from neoplasms in the US for all ages and detailed analysis for 75-84

C. Alegria [1,*] **and Y. Nunes** [1,2]

[1] *RiskMath Lda.*[*]*, Portugal*
[2] *LibPhys*[†]*, Department of Physics, FCT-NOVA, Portugal*

Correspondence*:
Corresponding Author
calegria@phinancetech.com

ABSTRACT

We investigate trends in death rates from neoplasms (ICD-10 codes C00-D48) for all age groups in the US using data from the CDC (Centers for Disease Control and Prevention). We also perform a detailed analysis for older individuals aged 75 to 84. We investigate trends in neoplasms where these appear on multiple causes (MC) of death, or as the underlying cause (UC), as well as the trends in the ratio of multiple cause to underlying cause death rates.

For individuals aged 75 to 84 we show a rise in excess mortality from neoplasms reported as the underlying cause of death, which started in 2021 (+4.8%) and increased substantially in 2022 (+11.5%). The increase in excess mortality in both 2021 (Z-Score of 10.5) and 2022 (Z-Score of 25.1) are highly statistically significant (extreme events). When looking at neoplasm deaths reported as multiple cause of death, we observe a similar trend, but starting in 2020, with excess mortality of +3.4% in 2020, +9.2% in 2021, and +16.4% in 2022, which were also highly statistically significant.

The larger rise of excess death rates due to neoplasms in multiple causes compared to underlying cause indicates that some deaths from neoplasms are being brought forward by other causes. However, the rise in cancers as underlying cause indicates that there might also be an unexpected rise in the incidence of fatal cancers, an increase in rapid growth cancers and/or an acceleration of existing cancer cases leading to earlier death.

We also show that excess deaths from cancers occurred for most age groups, with the strongest effect in ages 15-24 and individuals 65 and older. The results indicate that from 2020 a novel phenomenon leading to increased neoplasm deaths appears to be present. An exception was observed for individuals aged 55-64. This cohort did not exhibit excess deaths from neoplasms in 2020, 2021 or 2022.

Keywords: neoplasms, excess mortality, mortality trends

[*] Phinance Technologies - Humanity Projects

[†] LibPhys

1 INTRODUCTION

In the context of ongoing excess all-cause mortality since the outbreak of the SARS-CoV-2 pandemic in 2020[1], we expand on our previous work investigating death rates and morbidity ascribed to malignant neoplasms in the UK (Alegria, et al., 2024)[1] and both malign and benign neoplasms in the US (Alegria, et al., 2024)[2]. The reason for our focus on neoplasms in 15-44 year olds in our previous papers is the emergence of anecdotal reports of unusually aggressive cancers in younger people. As we have previously described, there have been case reports of lymphoma onset after administration of the mRNA COVID-19 vaccinations (Goldman, et al., 2021, (Zamfir, et al., 2022)[3], (Sekizawa, et al., 2022)[4] (Mizutani, et al., 2022)[5], and safety signals for cancers in 11 MedDRA codes in the CDC's Disproportionality Signal Analysis for the COVID-19 vaccinations (Wiseman et al.)[6]

The purpose of our work is not to explain the mechanisms behind the rise in cancer-related deaths. However, we recognize that health professionals working in this field will benefit from further analysis of this phenomenon and the age groups most affected in terms of relative and absolute increased risk. In this paper we therefore expand our analysis to all age groups, and furthermore we focus on older individuals aged 75 to 84, as these correspond to larger absolute numbers of excess deaths from cancer.

As with our previous US study, the data from CDC WONDER enables us to investigate trends in neoplasms where these appear on multiple causes of death (MC), or as the underlying cause of death (UC), as well as the trends in the ratio of multiple cause to underlying cause death rates. This allows us to expand our understanding of the increase in cancer-related deaths and whether the increase is in people dying from cancer, or people with cancer dying from other causes, or both.

2 DATA

2.1 Cause of Death Data

The data utilized in this analysis is comprised of the number of deaths recorded in the USA between 2010 and 2022, categorized by underlying cause code (ICD-10), sex, and 10-year age groups. These data were acquired through the CDC WONDER[2] system, provided by the National Center for Health Statistics of the Centers for Disease Control and Prevention (CDC). The mortality data is considered final up to 2021 but provisional from 2022 onwards. Additionally, to compare trends in multiple cause (MC) of death from neoplasms with those in underlying cause (UC) of death, we retrieved data from both the multiple cause of death databases and underlying cause of death databases.

Query parameters:

For underlying cause of death data, select variable grouped by: *1. Ten-year-age-groups, 2. Gender, 3. Year, 4. UCD – ICD Chapter*

(Link to the underlying cause of death databases).

For multiple cause of death data, select variable grouped by: *1. Ten-year-age-groups, 2. Gender, 3. Year, 4. MCD – ICD Chapter*

(Link to the multiple cause of death databases)

2.2 Underlying Cause (UC) and Multiple Causes (MC) cause of death

The Centers for Disease Control and Prevention (CDC) categorizes the reasons for deaths into two principal classifications: 'Underlying Cause of Death' (UC) and 'Multiple Causes of Death' (MC). These categorizations serve as valuable tools in epidemiological investigations, public health endeavors, and the comprehension of diverse mortality trends. The respective definitions are as follows:

Underlying Cause of Death: The underlying cause of death is defined as "the disease or injury which initiated the train of morbid events leading directly to death, or the circumstances of

[1] Phinance Technologies - Humanity Projects - Excess Mortality Project

[2] CDC Wonder

the accident or violence which produced the fatal injury," according to the World Health Organization (WHO).

Multiple Causes of Death: Multiple causes of death include all causes and conditions reported on the death certificate that contributed to death, not just the underlying cause. This includes the underlying cause, immediate cause, and any other significant conditions contributing to death. Each death certificate contains a single underlying cause of death, and up to twenty additional multiple causes.

2.3 Limitations on CDC Data Utilization

In alignment with the guidelines set forth by the Centers for Disease Control and Prevention (CDC) regarding data utilization, this research paper complies with the following restrictions[3]:

"The Public Health Service Act (42 U.S.C. 242m(d)) provides that the data collected by the National Center for Health Statistics (NCHS) may be used only for the purpose for which they were obtained; any effort to determine the identity of any reported cases, or to use the information for any purpose other than for health statistical reporting and analysis, is against the law. Therefore, users will:

- *Use these data for health statistical reporting and analysis only.*
- *Do not present or publish death counts of 9 or fewer or death rates based on counts of nine or fewer (in figures, graphs, maps, tables, etc.).*
- *Make no attempt to learn the identity of any person or establishment included in these data.*
- *Make no disclosure or other use of the identity of any person or establishment discovered inadvertently and advise the NCHS Confidentiality Officer of any such discovery."*

2.4 Population data

The source for the population data that are used for computing death rates (deaths per 100,000) are the data retrieved from the CDC queries. We opted to utilize CDC population data instead of data from the US Census Bureau to maintain consistency with analyses conducted by other researchers.

2.5 All-cause deaths data

All cause deaths were retrieved from CDC WONDER, by using the following query parameters: *1.Ten-year-age-groups, 2. Gender, 3. Year* The ten-year-age-groups are: 1, 1-4, 5-14, 15-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75-84, 85+.

2.6 Verification and Constraints of Data

The CDC WONDER system offers two distinct databases for accessing underlying cause of death data and multiple cause of death data. Furthermore, each of these databases is segmented into two datasets covering varying time frames. Thus, to compile a time series spanning from 2010 to 2022, several queries were executed.

Moreover, within the multiple cause of death databases, the underlying cause of death data can be retrieved. We obtained all available annual data for both multiple causes of death and underlying causes of death and conducted comparisons across different datasets for consistency whenever there was an overlap in the time periods.

For the years 2010 to 2021, the data on multiple causes and underlying causes of death are finalized, while for 2022, they remain provisional. However, data for 2023 was omitted from analysis due to its provisional nature and incompleteness. Further information on provisional CDC deaths data can be accessed here[4].

3 METHODOLOGY

In this study, we examine the patterns of mortality rates associated with neoplasms, encompassing both malignant and benign cases. Our analysis is conducted using annual data, rendering seasonal adjustments unnecessary.

[3] CDC Wonder - Data Use Restrictions

[4] CDC Wonder Technical Notes for Provisional Mortality

Broadly, our approach to estimating trends in these variables entails computing excess rates, which represent the disparity between observed rates and a predefined baseline (expected rates). Given our objective of elucidating the impact of the COVID-19 pandemic and subsequent periods relative to pre-pandemic conditions, our baselines are established by assessing trends in a period preceding the pandemic.

In this research, we will utilize Method 2C, as outlined in our publication on methodologies for quantifying excess mortality in the population (Alegria, et al., 2024)[7]. Method 2C involves calculating trends in death rates (deaths adjusted by the population) rather than raw death counts, serving as the baseline for estimating excess mortality. This approach substantially diminishes estimation noise by accounting for fluctuations in population size. Additionally, the method incorporates the historical trend in death rates, which typically decrease over time as the population experiences improved health and better management of risk factors.

3.1 Estimating Excess Death Rates - Method 2C

Equation 1 below, represents a general expression for estimating the excess death rates in relation to a specified baseline. The superscript AG is utilized to denote a specific population age range, which is the primary focus of the current analysis. Other groups to which this equation may be applied include distinct geographical regions, genders, or underlying causes of death. The subscript t_i denotes time, indicating the corresponding year for which the additional deaths are computed.

$$\begin{bmatrix} Excess \\ Deaths \end{bmatrix}_{t_i}^{AG} = Deaths_{t_i}^{AG} - Baseline_{t_i}^{AG} \quad (1)$$

For estimating the baseline for "normal or expected" death rates we use a simple linear fit:

$$Baseline(t_i) = \hat{b} + \hat{a}(t_i - t_0) \quad (2)$$

Where $\hat{a}$ and $\hat{b}$ are the estimated coefficients of the death rate trendline from 2010 to 2019. We also compute a Z-score that estimates the normalized deviation from trend:

$$Z = \frac{\Big[Deaths\Big]_{t_i}^{AG} - \Big[Baseline\Big]_{t_i}^{AG}}{\sigma_{2010-2019}} \quad (3)$$

Where σ is the standard deviation of the excess deaths during the pre-pandemic period 2010-2019.

3.2 List of Selected Causes of Death for Neoplasms According to ICD-10 Codes

For this analysis, we included all ICD-10 codes listed within the CDC aggregated chapter lists (Letters C00 to D48). Specifically, codes C00 to C99 denote deaths associated with malignant neoplasms, while codes D00 to D48 correspond to benign neoplasms.

4 YEARLY ANALYSIS OF EXCESS DEATH RATES FOR AGES 75-84

In this section we perform an analysis of the trend in yearly death rates for individuals aged 75 to 84 in the US, using the data from CDC WONDER. In this study, we employ the trend in deaths per 100,000 (death rates) from 2010 to 2019 as the baseline estimate for excess death rates. The excess death rates for the period spanning 2010 to 2019 are considered in-sample, whereas those for 2020, 2021, and 2022 are computed out of sample.

In order to contextualize trends in death rates from neoplasms, we first analyze the trends in all-cause death rates.

4.1 Deaths from All Causes

The analysis of the deaths from all causes allows us to have a context by which we can then compare the death rates from neoplasms. Figure 1-top shows the death rate per 100,000 individuals for all deaths in the US from 2010 to 2022, for the 75 to 84 age

group. Figure 1-bottom shows the actual number of deaths during the period.

We note that the trend in all-cause death rates from 2010 to 2019 for individuals aged 75 to 84 declined over time which is the normal state of affairs in developed countries.

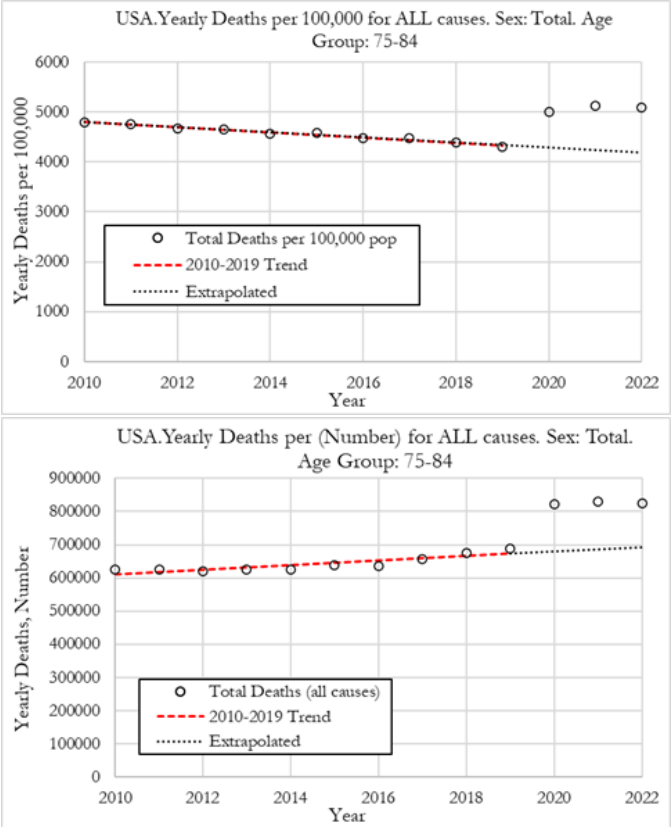

Figure 1. Yearly all-cause deaths for the US for individuals aged 75 to 84. The red dashed line shows the trend from 2010 to 2019. The dotted line shows the extrapolation of the trend from 2020 until 2022. Top: Death rate (per 100,000). Bottom: Deaths (Number).

The all-cause death rate for individuals aged 75 to 84 was 4790 per 100,000 in 2010 declining monotonically to 4308 per 100,000 in 2019, corresponding to a 10% drop over the period. The death rate increased in 2020 to 4997 per 100,000 and then again in 2021 to 5119 per 100,000. In 2022 the death rate dropped slightly to 5089 per 100,000.

4.1.1 Excess all-cause death rates

Figure 2 illustrates the excess death rate for recorded deaths (all-cause) in the US spanning from 2010 to 2022. Figure 2-top, indicates relative deviations from the trend observed during 2010-2019, while Figure 2-bottom displays the Z-Score (signal strength) corresponding to these deviations from the trend.

Figure 2 shows that excess deaths in 2020 were around +16.6%, with a Z-Score of 32.1. These values indicate a very high level of statistical significance, being considered an extreme occurrence. In 2021 excess deaths further increased to around +20.9% with a Z-Score above 40.4, indicating very high statistical significance. Excess deaths in 2022 were +21.7% with a Z-Score of 41.8, again indicating very high statistical significance. Excess death levels increased successively in 2020, 2021 and 2022.

4.2 Trends in Underlying Cause Death Rates for ICD-10 Codes C00 to D48 (Neoplasms)

In this section, we analyze the trends in mortality rates between 2010 and 2022, focusing on cases where neoplasms (ICD-10 codes C00 to D48) were designated as the primary cause of death among individuals aged 75-84.

4.2.1 Underlying Cause Death Rates

Figure 3-top shows the death rate per 100,000 individuals for neoplasm deaths in the US from 2010 to 2022. We can observe that deaths per year from neoplasms in the 75-84 age group have been trending lower from 2010 to 2019, with a significant downward slope. In 2010 the death rate was 1238 per 100,000 and in 2019 it was 1035 per 100,000, a 16.4% drop.

The death rate dropped in 2020 to about 1021 per 100,000 in line with the 2010-2019 trend, and then rose to 1049 per 100,000 in 2021. In 2022 the death rate increased again to 1091 per 100,000, a level that is similar to that observed in 2017.

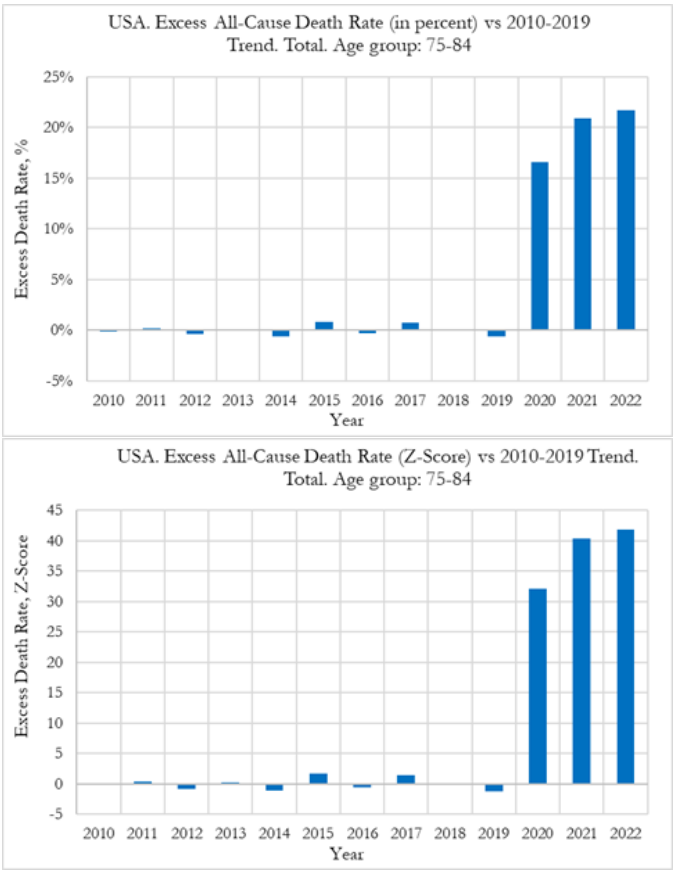

Figure 2. Excess all-cause death rates for both sexes aged 75 to 84 in the US. Top: Relative deviation from trend, percent. Bottom: Deviation from trend Z-Score.

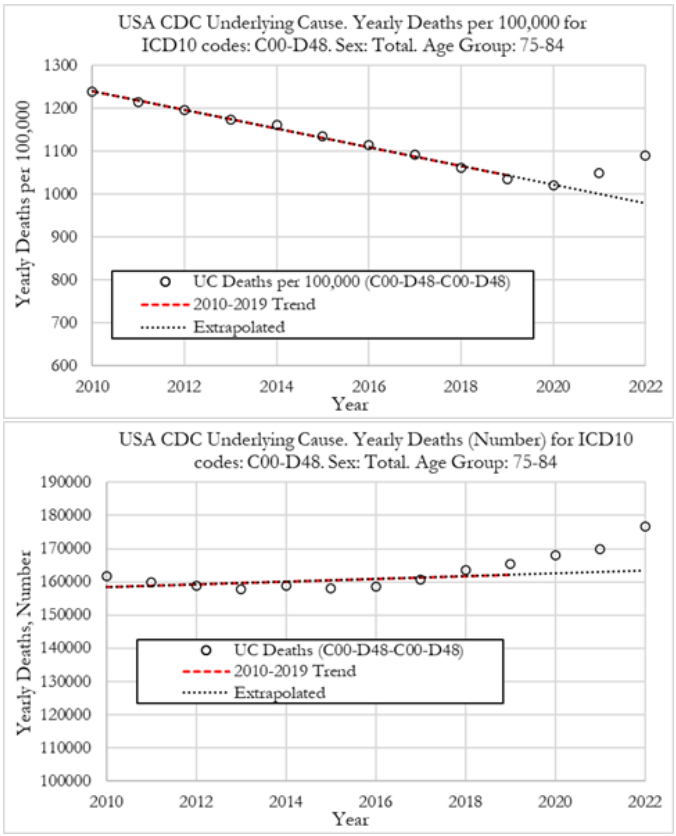

Figure 3. Yearly deaths from neoplasms as underlying cause in the US. The red dashed line shows the trend from 2010 to 2019. The dotted line shows the extrapolation of the trend from 2020 until 2022. Top: Deaths per 100,000. Bottom: Deaths (Number).

When presenting these numbers as the absolute number of deaths for diseases from neoplasms, shown in Figure 3-bottom, we can observe that in 2020 there were 167,957 deaths, while in 2021 there were 169,929 deaths, and 176,784 in 2022.

4.2.2 4.2.2. Excess Underlying Cause Death Rates

Figure 4 presents the excess death rate attributed to neoplasms in the US for the age group of 75 to 84 years from 2010 to 2022. The graphs also display the excess deaths from all causes for the purpose of comparison. Figure 4-top illustrates relative deviations from the trend observed during 2010-2019, while Figure 4-bottom presents the Z-Score (signal strength) corresponding to these deviations from the trend.

In Figure 4-top we can observe that the excess death rates from neoplasms as the underlying cause were slightly negative in 2020 at -0.1%, then rose to +4.8% in 2021, and +11.5% in 2022. By comparison, the excess mortality for all-cause deaths was +16.6% in 2020, +20.9% in 2021, and +21.7% in 2022. Noteworthy is that while excess mortality for all-cause deaths increased only slightly from 2021 to 2022, excess deaths from neoplasms as the underlying cause rose substantially.

When translating the UC excess death rates from neoplasms into absolute number of excess deaths, these values compute to -208 excess deaths in 2020, 7,815 in 2021 and 18,213 in 2022. For comparison, for all-cause death rates, the corresponding number of excess deaths were 117,235 in 2020, 143,592 in 2021 and 147,040 in 2022.

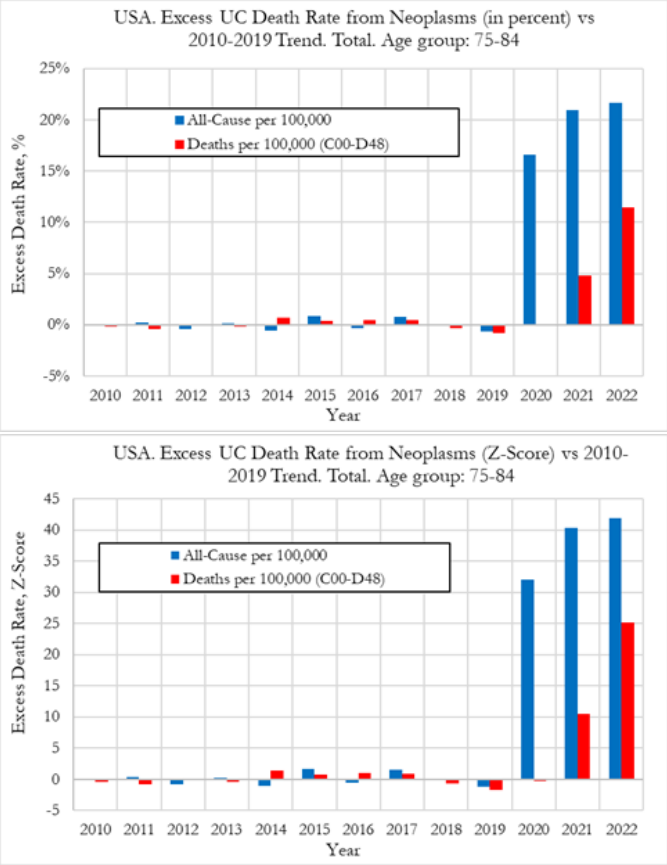

Figure 4. Excess UC death rates from neoplasms from 2010 to 2022 for both sexes of ages 75 to 84 in the US. Top: Relative deviation from trend, percent. Bottom: Deviation from trend Z-Score. Excess deaths from all causes are shown for comparison.

In terms of statistical significance of the excess deaths, we observe from Figure 4-bottom that the Z-Scores for neoplasm death rate deviations from trend were 10.5 in 2021 and 25.1 in 2022. The strength of the excess deaths from neoplasms was of similar magnitude when we analyzed younger individuals aged 15-44 (Alegria, et al., 2024)[2].

4.3 Trends in Multiple Cause Death Rates for ICD-10 Codes C00 to D48 (Neoplasms)

In this section, we explore the trends in mortality rates from 2010 to 2022, focusing on instances where neoplasms (ICD-10 codes C00 to D48) were documented as one of the multiple causes of death (MC), which indicates they were either the underlying cause or a secondary cause of death, among individuals aged 75-84. This investigation offers supplementary insights into comprehending the surge in cancer-related deaths during the pandemic years for individuals within this age group.

4.3.1 Multiple Cause deaths from ICD-10 Codes C00 to D48 (Neoplasms)

Figure 5-top shows the death rate per 100,000 individuals aged 75-84 in the US from 2010 to 2022, where neoplasms appear as one of multiple causes of death (either underlying or contributing). We can observe that MC deaths per year from neoplasms have been trending lower from 2010 to 2019, with a significant downward slope. In 2010 the death rate was 1388 per 100,000 and in 2019 it was around 1168 per 100,000, a 15.8% drop.

The death rate rose slightly in 2020 to about 1188 per 100,000 and then rose to 1228 per 100,000 in 2021 and 1281 per 100,000 in 2022, a level similar to that observed in 2014.

4.3.2 Excess Multiple Cause Deaths Rates

As noted earlier, multiple cause classification of death, encompasses deaths associated with a specific disease, where it either serves as the primary cause or a contributor towards mortality. For instance, respiratory infections are often a contributing factor to death, whereas another condition was the primary cause. Consequently, MC death rates related to respiratory diseases might exceed the underlying cause (UC) respiratory death rate by several folds, and it is important to interpret high MC death rates with caution, as they do not necessarily imply a high rate of deaths from that disease. However, by examining both MC death rates and UC death rates, we can gain deeper insights into the fundamental factors influencing mortality.

When computing excess death rates, whether they relate to multiple cause (MC) death rates or underlying cause (UC) death rates, adjustments are made for preceding trends in mortality rates, and when determining relative deviations from these trends these are also scaled. Moreover, excess death rates are further adjusted for the variability in deviations

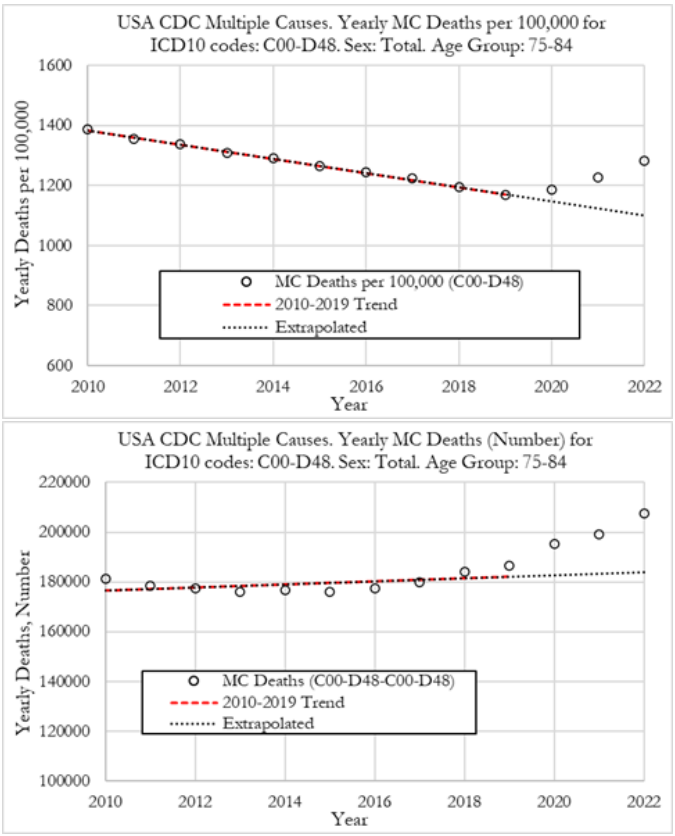

Figure 5. Yearly deaths from neoplasms as one of multiple causes (underlying or contributing factor) in the US. The red dashed line shows the trend from 2010 to 2019. The dotted line shows the extrapolation of the trend from 2020 until 2022. Top: Deaths per 100,000. Bottom: Deaths (Number).

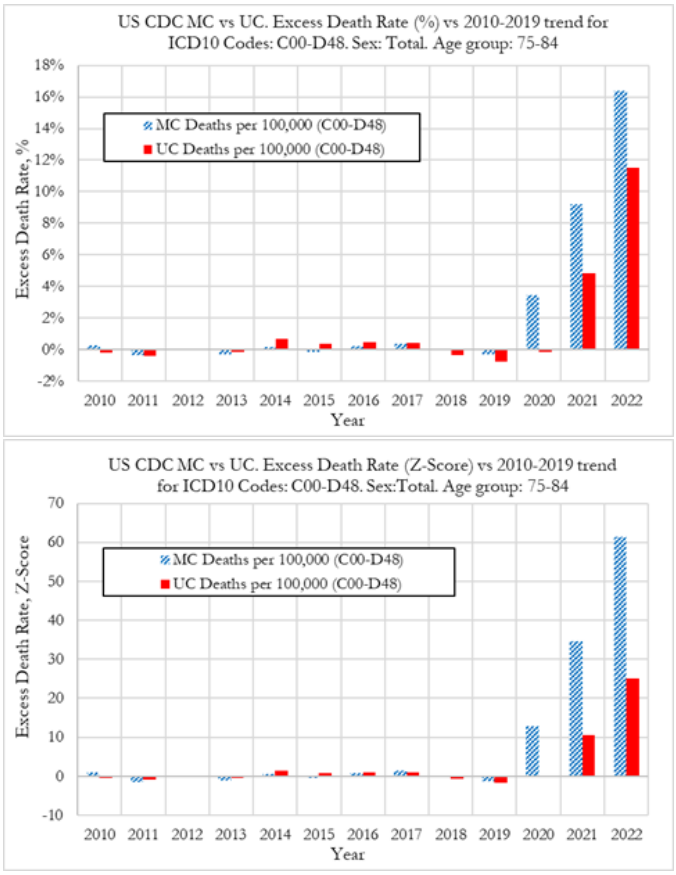

Figure 6. Excess MC death rates from neoplasms from 2010 to 2022 for both sexes of ages 75 to 84 in the USA. Top: Relative deviation from trend, percent. Bottom: Deviation from trend Z-Score. Excess UC death rates are shown for comparison.

from the trend (dispersion around the trend), enabling a direct comparison between excess MC death rates and excess UC death rates.

Figure 6 compares the excess MC death rates from neoplasms from 2010 to 2022, while also showing, for comparison, the excess from UC deaths from neoplasms, in the US. The figure on the top refers to relative deviations from the 2010-2019 trend, while Figure 6-bottom shows the Z-Score (signal strength) for the deviations from trend.

In Figure 6-top we can observe that the excess MC death rates from neoplasms were +3.4% in 2020, then rose to +9.2% in 2021, and +16.4% in 2022. By comparison, the excess UC death rates were -0.1% in 2020, +4.8% in 2021, and +11.5% in 2022. Of note is that the rise in excess mortality for MC deaths from cancer were greater than for UC deaths, particularly in 2020.

In terms of absolute numbers, the MC excess death rates from neoplasms correspond to 6,488 excess deaths in 2020, 16,806 in 2021 and 29,231 in 2022. For UC excess death rates, the corresponding number of deaths were -208 in 2020, 7,815 in 2021 and 18,213 in 2022.

In terms of the statistical significance of the excess deaths, when looking at excess MC deaths from neoplasms, the Z-Score in 2020 was 12.9, indicating that the increase in neoplasm-related deaths is a very strong signal. That trend however accelerated substantially in 2021 and 2022 where we observe Z-Scores of 34.6 and 61.4, respectively. These are extreme events, akin to those observed

for UC cancer deaths. The following section will provide further analysis of the cancer-related deaths where the neoplasm was a contributing factor, attempting to identify whether the increase in neoplasm MC deaths in 2020 represents an increase in cancers per se, or an adverse effect of the pandemic on mortality for people with existing cancers.

4.4 Comparison of MC and UC Death Rates for ICD-10 Codes C00 to D48 (Neoplasms)

In this section we compare the trends in death rates from 2010 to 2022 for the 75-84 age group of both sexes, from MC deaths and UC deaths from neoplasms (ICD-10 codes C00 to D48).

Figure 7-top shows the MC deaths rates and UC death rates from neoplasms in the US, from 2010 to 2022. We can observe that both UC and MC death rates from neoplasms have been trending lower from 2010 to 2019, with a significant downward slope.

Figure 7-bottom shows the ratio of MC/UC death rates and illustrates that the behavior of UC cancer deaths and MC cancer deaths is very similar from 2010 to 2019 where the ratio was relatively stable ranging from 1.11 to 1.12, with a slight increase in the ratio in 2018 and 2019. The fraction of MC deaths to UC deaths then jumped in 2020 to 1.163. Broadly speaking, this indicates a break from the existing trend in which people with cancer were increasingly dying of another condition or reason. In 2020, this could be explained by deaths from COVID-19 or other health effects of the pandemic lockdowns on individuals suffering from cancer. In 2021 the fraction of MC to UC cancer deaths further rose to 1.171, and then to 1.175 in 2022.

4.5 Trends in Underlying Cause Death Rates for Males and Females

In this section, we examine the patterns in underlying cause (UC) death rates attributed to neoplasms among males and females in the 75-84 age group.

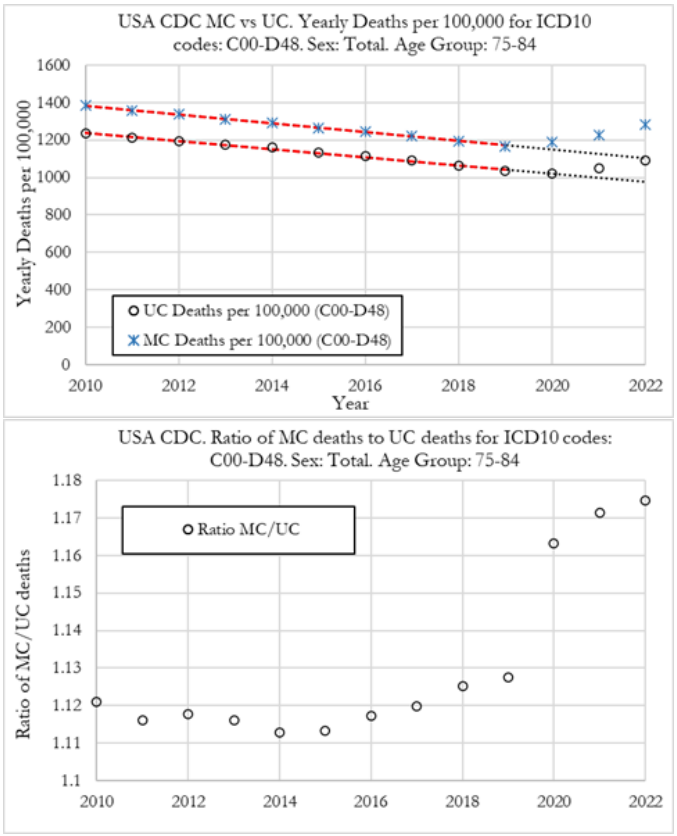

Figure 7. Yearly deaths from neoplasms as multiple cause (underlying or contributing factor) in the US. The red dashed line shows the trend from 2010 to 2019. The dotted line shows the extrapolation of the trend from 2020 until 2022. Top: Deaths per 100,000. Bottom: Deaths (Number).

4.5.1 UC Death Rates from Neoplasms for Males and Females

Figure 8 illustrates the death rates per 100,000 individuals for males and females, specifically when neoplasms were reported as the underlying cause of death. It is evident that underlying cause (UC) death rates have exhibited a downward trend from 2010 to 2019, characterized by a substantial decline, among both males and females in the 75-84 age group.

For females, in 2010 the death rate was 1385 per 100,000 and in 2019 it was 1098 per 100,000, a 20.7% drop. The death rate dropped slightly in 2020 to about 1079 per 100,000 and then rose to 1102 per 100,000 in 2021 and to 1153 per 100,000 in 2022.

For males, in 2010 the death rate was 1561 per 100,000 and in 2019 it was around 1271 per

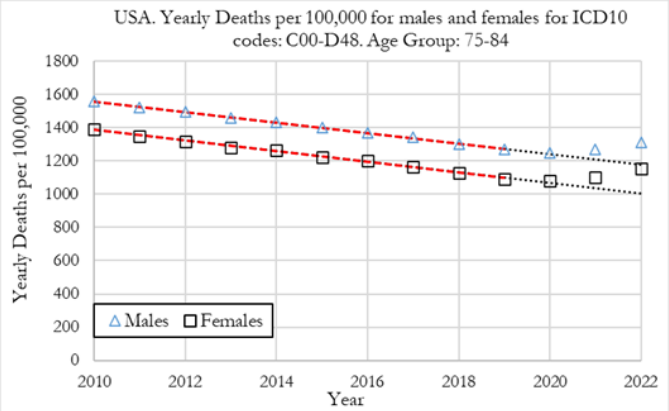

Figure 8. Yearly UC death rates from neoplasms in the US for males and females of ages 75-84. The red dashed line shows the trend from 2010 to 2019. The dotted line shows the extrapolation of the trend from 2020 until 2022.

100,000, an 18.6% drop. The death rate dropped slightly in 2020 to about 1246 per 100,000 and then rose to 1268 per 100,000 in 2021, and 1313 per 100,000 in 2022.

4.5.2 Excess UC Death Rates for Males and Females

When comparing excess UC death rates from neoplasms for males and females, shown in Figure 9, we observe that in 2020, while females had +1.27% excess mortality, males experienced only +0.45% excess mortality, with Z-Scores of 2.8 and 1.8 respectively. The results indicate that the excess neoplasm mortality for females might point to a small signal, with statistical significance, in 2020.

In 2021 excess UC death rates from neoplasms for males was about +5.0% while +6.6% for females, both having Z-Scores above 10, indicating very high statistical significance (as shown in Figure 9-bottom). For individuals aged 75-84 in the US, females experienced higher excess deaths rates from neoplasms compared to males in 2021. This is the opposite of our findings for ages 15 to 44 (Alegria, et al., 2024)[2] where males experienced almost double the excess deaths from neoplasms compared to females in 2021.

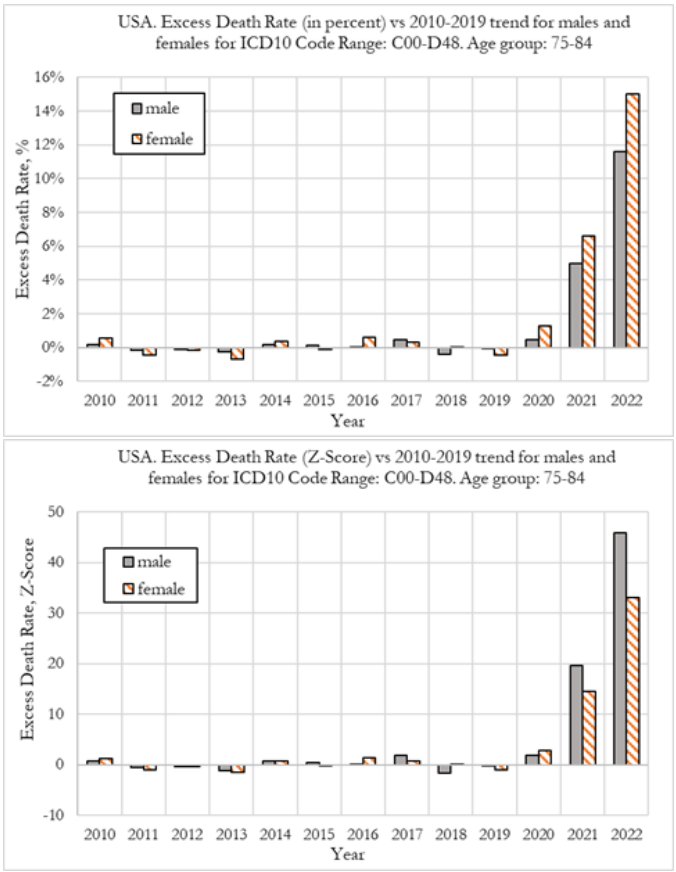

Figure 9. Excess deaths rates from neoplasms for males and females, in the US. Top: Relative deviation from trend, percent. Bottom: Deviation from trend Z-Score.

In 2022 excess UC death rates from neoplasms for males was +11.6% while +15.0% for females, both having Z-Scores above 30, which are extreme occurrences. Females also experienced worse outcomes compared to males in 2022.

5 ANALYSIS OF NEOPLASM EXCESS DEATH TRENDS FOR ALL AGES

In this section we generalize the previous analysis for all age groups. We compute the excess deaths (deviation from trend) from neoplasms, for the different age groups in the US.

5.1 Excess UC Deaths from Neoplasms for Different Age Groups

Here, we compute, for all age groups, the excess UC death rates from neoplasms in 2020, 2021 and

2022, shown in Figure 10. The results are also shown in Table 1, in the appendix, for a more detailed analysis.

In Figure 10-top we plot the excess UC death rate (in percent) while Figure 10-bottom shows the respective Z-Scores. Each datapoint on the graphs is obtained by performing the analysis described in the methodology section where the extrapolated 2010-2019 trendline in death rates is subtracted from the death rates in 2020, 2021 and 2022, for each of the age groups. The highlighted region corresponds to the results for the detailed analysis shown previously for the 75 to 84 age group.

Figure 10 shows that the excess UC death rates from neoplasms seem to have started in 2021 and risen substantially in 2022 for ages 15 and above. One exception however is the 55-64 age group where excess death rates from neoplasms actually decreased over the same period. Individuals aged 5-14 also seem to have experienced excess death rates from neoplasms, but only in 2022, with low signal strength due to the small sample size. For age groups 1 and 1-4, we observe large negative excess deaths due to neoplasms albeit without statistical significance which we attribute to small sample sizes for these age groups.

In 2022, within younger individuals (aged 5-54), excess death rates were highest for age group 15-24. Excess death rates were negative for age group 55-64 which is an exception from the overall pattern of increasing excess deaths from cancers. This observation should be subject for further detailed investigation, to better understand the underlying phenomenon. Older individuals aged 75 and older show the highest rises in UC excess deaths from cancers in 2021 and 2022 with individuals 85 and older being the most affected. Signal strengths for the younger age-groups *vis-à-vis* older age groups is due to larger sample sizes for older individuals.

5.2 Excess MC Deaths from Neoplasms for Different Age Groups

In this section we compute, for all age groups, the excess MC death rates from neoplasms in 2020, 2021 and 2022, shown in Figure 11. For a more detailed analysis the results are also provided in Table 1, in the appendix.

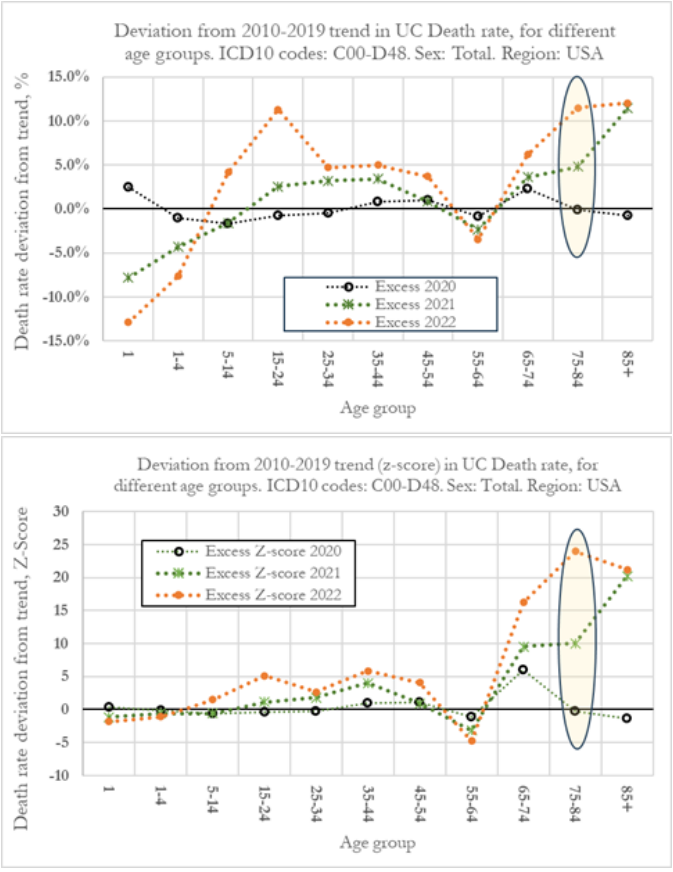

Figure 10. Excess UC death rates from neoplasms for 2020, 2021 and 2022 for different age groups of both sexes in the US. Top: Relative deviation from trend, percent. Bottom: Deviation from trend Z-Score.

In Figure 11-top we plot the excess MC death rate (in percent) while Figure 11-bottom shows the respective Z-Scores. Each datapoint on the graphs is obtained by performing the analysis described in the methodology section where the extrapolated 2010-2019 trendline in death rates is subtracted from the MC death rates in 2020, 2021 and 2022, for each of the age groups. The highlighted region corresponds to the results for the detailed analysis shown previously for the 75 to 84 age group.

When analyzing Figure 11, we can make many different observations, some of which, even though interesting, are not within the scope of this paper.

We will focus on the more general characteristics of the data shown in Figure 11 and how they relate to the equivalent data for excess UC of deaths rates that we discussed previously in Figure 10. We can observe that in general, excess MC death rates from neoplasms are higher than for UC death rates in 2020, 2021 and 2022, for age group 5-14 and older. This is particularly noticeable for 2020 when excess UC death rates from neoplasms were close to zero, while the MC excess death rates were already statistically significantly positive for age group 35-44 and above. This is likely a bring-forward effect of cancer-related deaths occurring during 2020, due to COVID-19 and other pandemic-related causes (Fedeli, et al., 2024)[8].

Secondly, MC and UC excess death rates have very similar age patterns in the sense that for individuals aged 5-14 or older (with the exception of the 55-64 age group), excess cancer death rates were successively higher in 2020, 2021 and 2022, with signals showing very high statistical significance in 2022 (Figure 11-bottom).

In 2022, within younger individuals (aged 5-54), excess death rates were highest for age group 15-24 albeit the signal strengths were not the strongest due to the lower sample sizes compared to for instance the 35-44 age group. Excess death rates were close to zero for age group 55-64 which is an interesting observation, which we also observed previously for UC death rates (in Figure 10). This observation should be subject for further detailed investigation, to understand the underlying phenomenon. Older individuals aged 65 and older show the highest rises in MC excess deaths from cancers in 2020, 2021 and 2022 with individuals 85 and older being the most affected.

6 SUMMARY OF FINDINGS AND COMMENTARY

In this study we investigate trends in death rates from neoplasms (ICD-10 codes C00-D48) for all age groups in the US using data from the CDC. We also perform a detailed analysis for older individuals aged 75 to 84. We investigate trends in

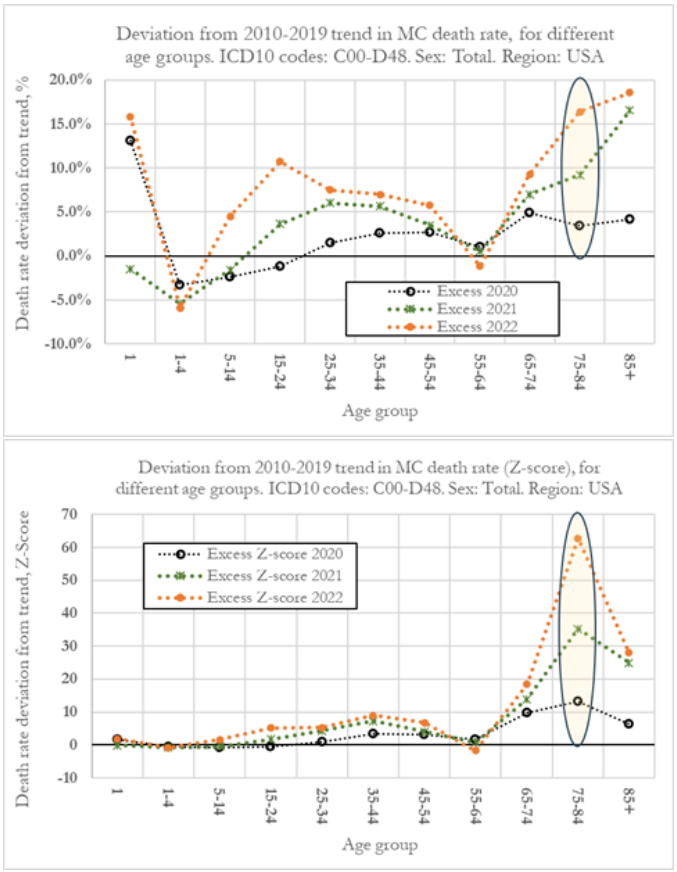

Figure 11. Excess MC death rates from neoplasms for 2020, 2021 and 2022 for different age groups of both sexes in the US. Top: Relative deviation from trend, percent. Bottom: Deviation from trend Z-Score.

neoplasms where these appear on multiple causes (MC) of death, or as the underlying cause (UC), as well as the trends in the ratio of multiple cause to underlying cause death rates.

Excess deaths from neoplasms for age group 75 to 84

Our results show that the excess UC death rates from neoplasms for the 75-84 age group were -0.1% in 2020, +4.8% in 2021, and +11.5% in 2022, with respective Z-Scores of -0.3, 10.1 and 24.0, as shown in Table 1. The excess UC death rates in 2021 and 2022 can be considered extreme occurrences. In 2020 there was no significant deviation from the 2010-2019 trend in UC death rates.

When analyzing MC death rates from neoplasms we show that the excess death rate from neoplasms

was +3.4% in 2020, +9.2% in 2021, and +16.4% in 2022, with Z-Scores of 13.2, 35.3 and 62.7, respectively, as shown in Table 1. The excess death rates were highly statistically significant in 2020, 2021 and 2022.

For comparison, excess mortality for all-cause deaths for individuals aged 75-84 was +16.6% in 2020, +20.9% in 2021, and +21.7% in 2022. Of note is that while excess all-cause mortality more or less stabilized in 2021 and 2022, excess deaths from neoplasms both as UC and MC rose substantially.

When comparing UC death rates for males and females we observe that excess death rates for males were +0.45% in 2020 with low statistical significance (Z-Score of 1.8). In 2020, females experienced +1.27% excess mortality from neoplasms, with a Z-Score of 2.8. In 2021 excess UC death rates from neoplasms for males was +5.0% while +6.6% for females, both having Z-Scores above 10, indicating very high statistical significance (as shown in Figure 9-bottom). In 2022 excess UC death rates from neoplasms for males was 11.6% while 15.0% for females, both having Z-Scores above 30, which are extreme occurrences.

Females experienced higher excess death rates compared to males in 2020, 2021 and 2022, which was in contrast to the results found in our previous paper (Alegria, et al., 2024)[2] on cancer rates in individuals aged 15 to 44, where excess death rates for males much higher than for females in both 2021 and 2022.

Pull-forward effect

In 2020, 2021 and 2022 we observe larger rises in deviations from trend in MC death rates from neoplasms, compared to deviations from trend in UC death rates. The relationship of MC to UC cancer deaths tends to be relatively stable over time as shown in Figure 7-bottom, which shows the ratio of MC/UC death rates from ratio was relatively stable from 2010 to 2019, ranging from 1.11 to 1.13. The ratio of MC deaths to UC deaths then jumped in 2020 to 1.163, increasing again in 2021 to 1.171, and in 2022 to 1.175. This indicates a break from the existing trend in which people with cancer were increasingly dying of another condition or reason, which tracks the rise in all-cause mortality in 2020, 2021 and 2022. In 2020, this could be explained by deaths from COVID-19-related or other health effects related to the pandemic (lockdowns, stress, less exercise, worse food habits, lack of medical care, etc.).

The jump in the ratio of MC to UC deaths in 2020 can be understood as a pull forward of cancer-related deaths which should be followed by a period of negative excess UC neoplasm death rates in subsequent years. We observe that so far the opposite has occurred, with 2021 indicating a larger pull forward effect (due to an even higher MC/UC deaths ratio) and showing even higher excess MC death rates as well as excess UC death rates. This means that in 2022 we should expect an equivalent period of negative excess deaths that compensate the bring-forward effect observed in 2020 and 2021. However, our analysis shows that in 2022 excess UC death rates continued accelerating leading us to conclude that the ongoing rise in neoplasm death rates in 2021 and 2022 is more likely to be caused by a different phenomenon, overlapping in timescale, of increased incidence or severity of cancers.

Given the case studies of neoplasms following COVID-19 vaccination cited in the literature, one possible factor could be adverse effects of the COVID-19 vaccines, which were rolled out from 2021 and prioritized for vulnerable groups such as those with cancer. Additionally, one cannot disregard the possibility of continuous COVID-19 infections or Long COVID (Jangnin, et al., 2024)[9] being contributors towards increased incidence or severity of cancers.

Excess neoplasm deaths for all ages

When investigating different age groups, we observe that excess UC death rates from neoplasms started in 2021 and rose substantially in 2022 for most age cohorts from age 15 and above (Table 1). Older individuals aged 75 and older show the highest rises in UC excess deaths from cancers with individuals 85 and older being the most affected.

For younger cohorts (aged 5-54), excess death rates were highest for age group 15-24. Excess death rates were negative for age group 55-64 which is an exception from the overall pattern of increasing excess deaths from cancers. This observation should be subject for further detailed investigation, to better understand the underlying phenomenon.

Individuals aged 5-14 also experienced excess death rates from neoplasms, but only in 2022 and with low signal strength due to the small sample size. For age groups 1 and 1-4, we observe large negative excess deaths due to neoplasms albeit without statistical significance which we attribute to small sample sizes for these age groups. The lower signal strengths for the younger age-groups relative to older age groups is due to larger sample sizes for older individuals.

Excess MC death rates on the other hand started rising in 2020 for age groups 35-44 and older, which we attribute to the pull-forward effect that tracks the all-cause mortality increase caused by the COVID-19 pandemic in 2020.

Limitations of the study

The primary limitation in our analysis arises from the provisional nature of the 2022 data obtained from the CDC for various causes of death, as of the data retrieval date (December 20th, 2023). This provisional status implies that the data is subject to potential modifications, especially concerning the classification of underlying causes or the inclusion of secondary causes of death. Consequently, discrepancies may arise once the final data is published.

Another confounding variable could be a possible reduction in cancer screening, diagnostics and treatments during the pandemic years leading to higher deaths in subsequent years. This factor, however, might not be very impactful to younger individuals (aged 50 or younger).

Suggestions for future work

Further research is needed to untangle the different contributions towards the rise in cancer-related death rates. Investigation of the underlying causes of increased cancer-related deaths is of the utmost importance, as the observations show an acceleration in deaths both directly due to neoplasms (UC) and with neoplasms as a contributing factor (MC).

Our analysis does not allow us to look in detail at whether cancer incidence has increased since 2020, and when this may have occurred. Given the case studies of neoplasms following COVID-19 vaccination cited above, future studies should focus on COVID-19 vaccinated and unvaccinated individuals and whether the vaccination rollout or COVID-19-related conditions such as Long COVID are contributing factors to the ongoing rise in neoplasm-related deaths.

CONFLICT OF INTEREST STATEMENT

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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APPENDIX

Summary table with MC and UC excess death rates from neoplasms in 2020, 2021 and 2022.

2020	UC Excess Death Rate		MC Excess Death Rate		Ratio MC/UC
Age Group	**Deviation**,%	***Z*-Score**	**Deviation**,%	***Z*-Score**	
1	2.5	0.3	13.1	1.6	1.44
1-4	-1.0	-0.1	-3.3	-0.5	1.05
5-14	-1.6	-0.6	-2.4	-0.8	1.06
15-24	-0.8	-0.4	-1.2	-0.6	1.07
25-34	-0.4	-0.2	1.5	1.0	1.09
35-44	0.8	1.0	2.6	**3.4**	1.08
45-54	1.0	1.2	2.6	**3.1**	1.07
55-64	-0.8	-1.1	1.1	1.6	1.09
65-74	2.3	**6.0**	4.9	**9.7**	1.12
75-84	-0.1	-0.3	3.4	**13.2**	1.16
85+	-0.8	-1.4	4.1	**6.2**	1.26

2021	UC Excess Death Rate		MC Excess Death Rate		Ratio MC/UC
Age Group	**Deviation**,%	***Z*-Score**	**Deviation**,%	***Z*-Score**	
1	-7.8	-1.1	-1.5	-0.2	1.38
1-4	-4.3	-0.6	-5.4	-0.8	1.06
5-14	-1.6	-0.6	-1.5	-0.5	1.07
15-24	2.5	1.2	3.6	1.7	1.09
25-34	3.2	1.8	6.0	**4.3**	1.10
35-44	3.4	**4.0**	5.7	**7.3**	1.08
45-54	0.9	0.9	3.5	**4.1**	1.09
55-64	-2.3	-3.2	0.5	0.8	1.10
65-74	3.6	**9.6**	7.0	**13.9**	1.13
75-84	4.8	**10.1**	9.2	**35.3**	1.17
85+	11.5	**20.3**	16.5	**24.9**	1.25

2022	UC Excess Death Rate		MC Excess Death Rate		Ratio MC/UC
Age Group	**Deviation**,%	***Z*-Score**	**Deviation**,%	***Z*-Score**	
1	-12.9	-1.8	15.8	1.9	1.71
1-4	-7.6	-1.1	-5.9	-0.9	1.10
5-14	4.2	1.5	4.5	1.6	1.07
15-24	11.3	**5.1**	10.7	**5.1**	1.08
25-34	4.7	2.7	7.5	**5.3**	1.10
35-44	5.0	**5.9**	7.0	**8.9**	1.08
45-54	3.7	**4.1**	5.7	**6.7**	1.08
55-64	-3.5	-4.8	-1.2	-1.8	1.10
65-74	6.2	**16.3**	9.3	**18.5**	1.13
75-84	11.5	**24.0**	16.4	**62.7**	1.17
85+	12.0	**21.2**	18.6	**28.0**	1.27

Table 1. UC and MC excess death rates from neoplasms for different age groups in 2020, 2021 and 2022. Excess death rates refer to deviations from 2010-2019 trend. The ratio MC/UC is the ratio of MC deaths to UC deaths from neoplasms.