

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/382947553>

Trends in death rates from musculoskeletal diseases in the US for all ages and detailed analysis for 75–84

Preprint · August 2024

CITATIONS

0

READS

87

2 authors:



Carlos Alegria
Riskmath Ida

53 PUBLICATIONS 784 CITATIONS

SEE PROFILE



Yuri Nunes
Universidade NOVA de Lisboa

47 PUBLICATIONS 538 CITATIONS

SEE PROFILE

Trends in death rates from musculoskeletal diseases 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 musculoskeletal diseases (ICD-10 codes M00-M99) 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 analyze trends in musculoskeletal diseases where these appear on the death certificate under 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 our results show that the excess UC death rates from musculoskeletal diseases (M00-M99) diseases for individuals aged 75 to 84 were 4.7% (*Z*-Score of 1.7) in 2020, 15.2% (*Z*-Score of 5.6) in 2021, 16.6% (*Z*-Score of 6.1) in 2022 and 26.6% (*Z*-Score of 9.8) in 2023. Excess death rates rose in each consecutive year from 2020 to 2023, and from 2021 onwards, statistical significance of excess deaths can be considered extreme occurrences. We also observe that the rises of musculoskeletal MC* musculoskeletal excess death rates (deaths involving musculoskeletal diseases as either an underlying or contributory cause but where COVID-19-related deaths are excluded) in 2020, 2021, 2022 and 2023 mirror the excess UC death rates, suggests that an underlying factor is at play.

When analyzing the most common causes of death for older individuals aged 75-84, within the musculoskeletal system, namely arthropathies (M00-M25) and osteopathies and chondropathies (M80-M94) we find similar patterns of behavior.

When investigating musculoskeletal diseases as underlying cause for all age groups we observe that the rise in excess deaths occurred for all age groups, however there are different patterns for younger and older individuals. For younger individuals, excess death rates from musculoskeletal diseases appear to be related to rises in all-cause mortality in 2020, peaking in 2021 and with subsequent normalization in 2022 and 2023. For older individuals, excess death rates rose consecutively from 2020 to 2023. The results indicate that from 2020 a novel phenomenon leading to increased musculoskeletal death rates appears to be present particularly in older individuals. From 2021 onwards, excess death rates for older individuals could be explained by adverse effects from COVID-19 vaccinations or lingering effects of multiple SARS-CoV-2 exposures, which requires further research.

*Phinance Technologies - Humanity Projects

†LibPhys

Keywords: neoplasms, excess mortality, mortality trends

1 INTRODUCTION

A number of unanswered questions remain regarding the impact of the COVID-19 pandemic, ranging from the effects of the SARS-CoV-2 virus itself, to the impacts of the pandemic measures (lockdowns, masking, social distancing), COVID-19 treatment protocols, and the introduction of COVID-19 vaccines based upon novel mRNA technology.

We have previously shown excess mortality in the United States from a range of underlying causes, including neurological diseases (Alegria, et al., 2024)[1] and neoplasms (Alegria, et al., 2024)[2] and (Alegria, et al., 2024)[3], beginning in 2020. Despite our efforts to eliminate the direct impact of COVID-19, in terms of ‘pulling forward’ the deaths of individuals made vulnerable to the infection by other underlying causes, our analyses so far suggest that excess mortality has persisted or even increased for some diseases and age groups, through 2021-2023 when vaccines were readily available and COVID-19 variants were generally becoming milder (Mostert, et al., 2024)[4].

One of the aspects that is still not well researched is the impact of the pandemic on musculoskeletal diseases. (Park, et al., 2023)[5] found that non-fatal inflammatory musculoskeletal conditions such as plantar fasciitis, rotator cuff syndrome, and bursitis, were more common in individuals who had received any COVID-19 vaccine than those who had not been inoculated.

Musculoskeletal diseases are most often considered to be contributing factors when mentioned on death certificates and are less frequently given as the underlying cause. Nevertheless, as inflammatory reactions can be triggered by both infectious diseases such as COVID-19, and by vaccination, we consider it credible that the pandemic could have resulted in increased musculoskeletal pathologies that could be contributing to the overall excess mortality that we are observing in the US. In this paper, we therefore investigate trends in musculoskeletal diseases (ICD-10 codes M00 to M99) where these appear on death certificates as

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. Additionally, we also analyze trends in MC death rates where COVID-19-related deaths are excluded.

We first provide a detailed analysis of the older 75-84 age group. These individuals were found to be the most affected by musculoskeletal disease excess deaths, with statistically significant excess deaths starting in 2020 and then increasing substantially in 2021, 2022 and 2023. We also investigate different sub-categories within the musculoskeletal system so that we can have an idea of the relative contribution of the different types of categories of musculoskeletal diseases. We compare trends in death rates for arthropathies (M00-M25), systemic connective tissue disorders (M30-M35), dorsopathies (M40-M54) and osteopathies and chondropathies (M80-M94).

After the detailed analysis of individuals aged 75-84, we analyze excess death trends for the whole musculoskeletal system (M00-M99) for all ages, in ten-year age groups, as provided by the CDC (US Centers for Diseases Control and Prevention) WONDER system.

2 DATA

2.1 Cause of Death Data

The data used in this analysis are the number of deaths that occurred in the USA between 2000 and 2023, by underlying cause code (ICD-10), sex, and 10-year age groups, obtained using the CDC WONDER¹ system provided by the National Center for Health Statistics of the Centers for Disease Control and Prevention (CDC). The mortality data is final up to 2021 but provisional from 2022 onwards. Additionally, for comparing multiple cause (MC)² of death trends from musculoskeletal diseases with underlying cause (UC)³ of death trends, we download data from both the multiple

¹ CDC Wonder

² CDC Wonder Multiple Cause of Death

³ CDC Wonder Underlying Cause of Death

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 Definition of MC of Death and UC of Death

The Centers for Disease Control and Prevention (CDC) classifies deaths based on cause into two primary categories: "Underlying Cause of Death" and "Multiple Causes of Death." These classifications are useful for epidemiological studies, public health, and understanding different mortality patterns. The definitions are:

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

Multiple Causes (MC) 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 Data Use Restrictions

In this research paper we abide by the CDC's restrictions on data use which are⁴:

"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 chose to use the CDC population data instead of data from the US Census Bureau for consistency with other researchers' analyses.

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 Data verification and limitations

The CDC WONDER system provides two separate databases from which to query underlying cause of death data and multiple cause of death data. Additionally, each is separated into two datasets comprising different time periods, so that in order to obtain time series from 2000 to 2023, multiple queries were performed.

⁴ CDC Wonder - Data Use Restrictions

Within the multiple cause of death databases, it is also possible to obtain the underlying cause of death data. We downloaded all the available yearly data (for MC of death and UC of death) and compared the different datasets for consistency, whenever the time periods overlapped.

From 2010 to 2021 the MC and UC of death data is final, while for 2022 and 2023 it is provisional. Details on provisional CDC deaths data can be found here ⁵

3 METHODOLOGY

In this study, we analyze the trends in death rates for musculoskeletal diseases. We investigate these trends using yearly data and therefore a seasonal adjustment to the data is unnecessary.

In general terms, to estimate trends in these variables we use a methodology of computing excess death rates, which is the difference between the actual observed rates and a given baseline (expected rates). Because we want to describe the impact of the COVID-19 pandemic and post-pandemic periods relative to the prior state of the world, our baselines are based upon the estimation of the trend for a period prior to the pandemic.

In this study we will use method 2C, as described in our report on methodologies for measuring excess deaths in the population (Alegria, et al., 2024)[6]. Method 2C is based on computing the trends in death rates (deaths adjusted by the population) instead of deaths, as the baseline for estimating excess mortality. This method significantly reduces the noise of the estimation as it adjusts for population growth or decline, and by also providing different rates for each age category, we adjust for changes in population age distribution. The method also considers the prior trend in death rates, which tend to decline over time as the population grows healthier and risk factors are better managed.

3.1 Method 2C for Estimating Excess Death Rates

$$\left[\begin{array}{c} Excess \\ Deaths \end{array} \right]_{t_i}^{AG} = Deaths_{t_i}^{AG} - Baseline_{t_i}^{AG} \quad (1)$$

Equation 1 is a general expression for estimating the excess absence rates relative to a given baseline. We use the superscript AG to indicate a given population age range, as this is the primary focus of the current analysis. Other cohorts which this equation could apply to include a specific region, sex, or underlying cause of death. The subscript t_i refers to time, that is, the corresponding year for which the excess deaths are computed.

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 2013 to 2019. We also compute a Z -score that estimates the normalized deviation from trend:

$$Z = \frac{\left[Deaths \right]_{t_i}^{AG} - \left[Baseline \right]_{t_i}^{AG}}{\sigma_{2013-2019}} \quad (3)$$

Where σ is the standard deviation of the excess deaths during the pre-pandemic period 2013-2019.

3.2 ICD-10 Code List of Selected Causes of Death for: Diseases of the musculoskeletal system and connective tissue

For this analysis we selected all the ICD-10 codes from the CDC aggregated chapter lists (Letters M00 to M99), which refer to deaths attributed to diseases of the musculoskeletal system and connective tissue (Musculoskeletal Diseases). We also compare death rates from the major sub-categories within the M00-M99 codes, in order to investigate the most common

⁵ CDC Wonder Technical Notes for Provisional Mortality

musculoskeletal diseases that lead to or contribute towards death.

Additionally, as death rates from musculoskeletal diseases tend to affect mostly older individuals, we also perform an in-depth analysis of arthropathies (ICD-10 codes M00-M25) and osteopathies and Chondropathies (ICD-10 codes M80-M94), as these are shown to be responsible for most of the deaths in older individuals.

4 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 analysis we use the 2013-2019 trend in deaths per 100,000 (death rates) as the baseline estimate for excess death rates. Excess death rates for the 2013-2019 period are in-sample while the rates for 2020, 2021, 2022 and 2023 are out of sample computations.

In our study we investigate trends in MC (multiple-cause) and UC (underlying cause) deaths rates from musculoskeletal diseases, and also, trends in MC* death rates (MC deaths where COVID-19-related death are removed).

To contextualize trends in death rates from musculoskeletal diseases, we first analyze the trends in all-cause death rates. We then investigate trends in death rates for the musculoskeletal system (M00-M99) and the main sub-categories within, namely, arthropathies (M00-M25), systemic connective tissue disorders (M30-M35), dorsopathies (M40-M54) and osteopathies and chondropathies (M80-M94) in order to understand the relative contribution of each category of musculoskeletal disease towards mortality in the 75-84 age group.

We then investigate in detail the major categories that contribute to deaths which for the 75-84 age group, which are: arthropathies (M00-M25), and osteopathies and chondropathies (M80-M94).

4.1 Deaths from All Causes

The analysis of the all-causes deaths rates allows us to have a context by which we can then compare the death rates from musculoskeletal diseases. Figure 1 shows the death rate (per 100,000 individuals) for all deaths in the US from 2000 to 2023, for the 75 to 84 age group.

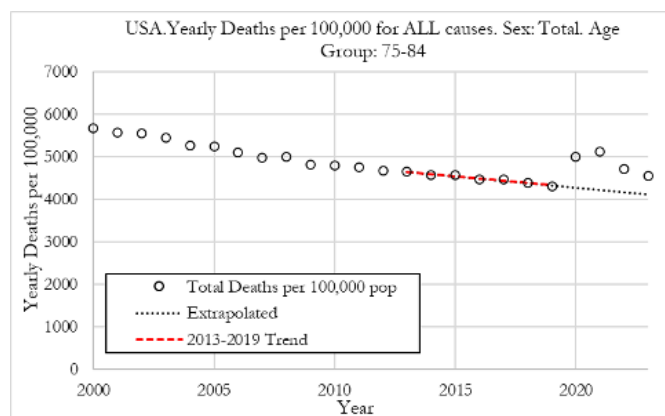


Figure 1. All-cause death rate (per 100,000) for the US for individuals aged 75 to 84, from 2000 to 2023. The red dashed line shows the trend from 2013 to 2019. The dotted line shows the extrapolation of the trend from 2020 until 2023.

The all-cause death rate for individuals aged 75 to 84 was 5667 per 100,000 in 2000, decreasing steadily to 4308 per 100,000 in 2019, corresponding to a 24.0% decline over the period (which equates to a 1.2% drop per annum during 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 4708 per 100,000 and in 2023 the death rate dropped further to 4555 per 100,000 (still above the 2013-2019 extrapolated trend).

4.1.1 Excess All-Cause Death Rates

Figure 2 shows the excess death rate for registered deaths (all-cause) in the US from 2010 to 2023 for the 75-84 age group. The columns in Figure 2 refer to relative deviations from the 2013-2019 trend while the dashed line refers to the respective Z-Scores.

Figure 2 shows that excess deaths in 2020 were 16.8%, with a Z -Score of 28.1, indicating a very high level of statistical significance, being considered an extreme occurrence. In 2021 excess deaths further increased to around 21.1% with a Z -Score above 35.4. Excess deaths in 2022 were 12.8% with a Z -Score of 21.4, again indicating an extreme occurrence. In 2023 excess deaths were 10.5%, with a Z -Score of 17.6. Although excess death levels have reduced from their peak in 2021, they have remained persistently high in the 75-84 age group following the pandemic.

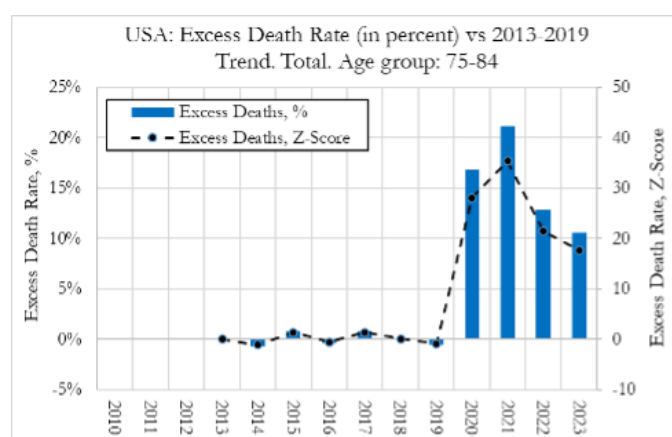


Figure 2. Excess all-cause death rates for both sexes aged 75 to 84 in the US. The columns refer to percent deviations from 2013-2019 trend while the dashed line refers to the respective Z -Scores.

4.2 Trends in UC and MC Death Rates for different categories within the Musculoskeletal system

In this section we investigate the trends in MC and UC death rates from 2000 to 2023 for musculoskeletal diseases (ICD-10 codes M00 to M99), for the 75-84 age group of both sexes. We also investigate different sub-categories within the musculoskeletal system so that we can have an idea of the relative contribution of the different types of musculoskeletal diseases. We compare trends in death rates for arthropathies (M00-M25), systemic connective tissue disorders (M30-M35), dorsopathies (M40-M54) and osteopathies and chondropathies (M80-M94)

It should be noted that we also investigated soft tissue disorders (M60-M79) which are not shown in the charts below as these are rarer as causes of death in older individuals and consequently of negligible impact for death rates within the musculoskeletal system.

4.2.1 UC and MC Death Rates (M00-M99)

Figure 3 shows the death rate per 100,000 individuals from musculoskeletal diseases in the US, for individuals aged 75-84, from 2000 to 2023. The top figure shows UC (underlying cause) death rates while the figure on the bottom refers to MC (multiple cause) death rates. Note that the top figure is shown in log scale in order to have a better idea of the behaviors of the less prevalent sub-categories.

We can observe that both UC and MC death rates from musculoskeletal diseases (M00-M99) have been trending lower from 2000 to 2019. We also note that the two most important sub-categories within the musculoskeletal system-related deaths are arthropathies (M00-M25) and osteopathies and chondropathies (M80-M94). These account for more than half of musculoskeletal deaths for older individuals aged 75-84 and will be investigated in further detail in the following sections.

Figure 3 also illustrates that from 2020 (for MC death rates) there was a clear break from the prior trend in death rates, while for UC death rates the break in trend appears to have occurred from 2021 onwards. These aspects will be also investigated in detail in the following sections.

4.3 M00-M99 - Diseases of the musculoskeletal system and connective tissue

We now investigate in detail the trends in MC, and UC death rates from 2000 to 2023 for musculoskeletal diseases (ICD-10 codes M00 to M99), for the 75-84 age group of both sexes. MC death rates need to be analyzed with a degree of caution as they refer to death rates for a given disease where it is either the underlying cause or a contributing factor towards death. Musculoskeletal

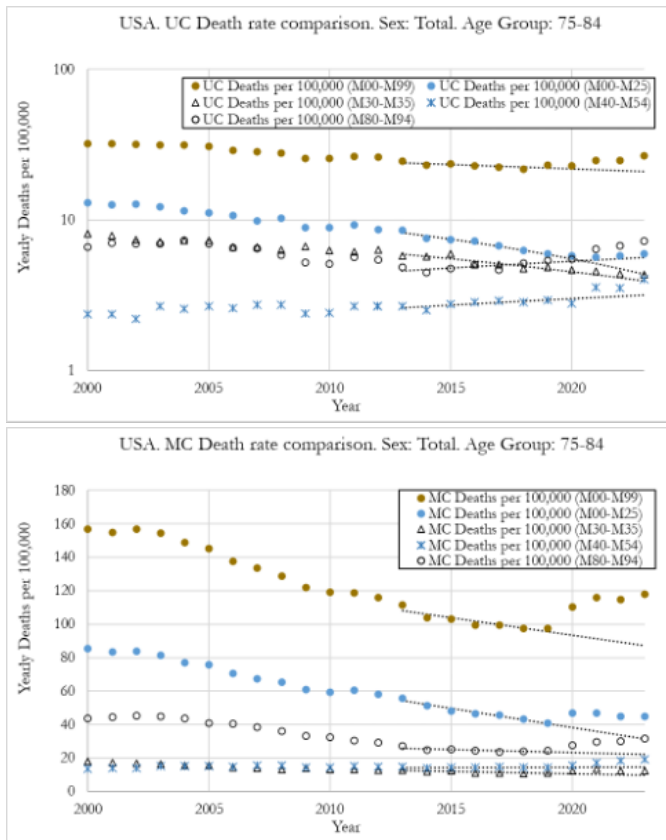


Figure 3. UC and MC death rates (per 100,000) from musculoskeletal diseases and relevant sub-categories in the US for ages 75 to 84. The dotted line shows the trend from 2013 to 2019 and its extrapolation from 2020 until 2023. Top: UC death rates. Bottom: MC death rates.

diseases tend to be contributing causes of death rather than the underlying cause which means that MC death rates from musculoskeletal diseases could amount to several times the UC death rate (as illustrated in Figure 4-bottom). By analyzing both MC death rates and UC death rates, we can have a better understanding of the underlying phenomena that lead to musculoskeletal-related deaths.

Figure 4-top shows the death rate per 100,000 individuals for deaths from musculoskeletal diseases in the US from 2000 to 2023. We can observe that both UC and MC death rates with musculoskeletal diseases in the 75-84 age group have been trending lower from 2000 to 2019. For MC death rates, in 2000 the death rate was 156.8 per 100,000 and in 2019 it was 97.4 per 100,000, a 37.9% decline (which corresponds to a 1.89% drop

per annum). For UC death rates, in 2000 the death rate was 32.2 per 100,000 and in 2019 it was 23.1 per 100,000, a 28.3% decline (which corresponds to a 1.41% drop per annum).

We also observe in Figure 4-bottom that the ratio of MC to UC deaths also declined steadily from 2000 to 2019, from a value of about 4.9 in 2000 to about 4.1 in 2019. It should be noted that MC and MC* (except COVID-19) death rates were the same from 2000 to 2019 as COVID-19 deaths only started in 2020.

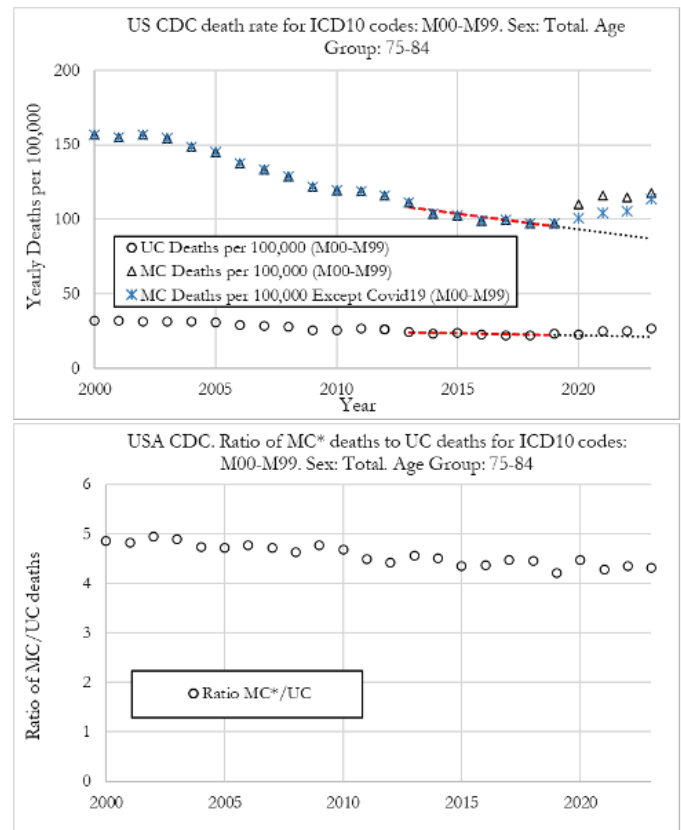


Figure 4. Yearly death rates from musculoskeletal diseases in the US for ages 75 to 84. The red dashed line shows the trend from 2013 to 2019. The dotted line shows the extrapolation of the trend from 2020 until 2023. Top: Death Rates per 100,000. Bottom: Ratio of MC* to UC deaths.

The MC death rate rose in 2020 to 110.4 per 100,000, and then rose again to 116.0 per 100,000 in 2021. In 2022 the MC death rate dropped slightly to 114.8 per 100,000 and in 2023 it rose again to 117.8 per 100,000.

After removing COVID-19-related deaths, we see that the MC* death rate rose in 2020 to 101.4 per 100,000, and then rose again to 104.4 per 100,000 in 2021, to 105.4 per 100,000 in 2022 and in 2023 it rose again to 113.4 per 100,000. Even after removing COVID-19 related deaths, we observe an increase in MC* musculoskeletal deaths in 2020, 2021, 2022, and 2023.

The UC death rate dropped in 2020 to 22.9 per 100,000, and then rose to 24.9 per 100,000 in 2021. In 2022 the UC death rate was again 24.9 per 100,000 and in 2023 it rose further to 26.7 per 100,000.

The ratio of MC* to UC deaths remained stable in 2021, 2022 and 2023, after a slight rise in 2020.

4.3.1 Excess UC Death Rates (M00-M99)

Figure 5 shows the excess death rate from musculoskeletal diseases in the US (M00-M99), for the 75 to 84 age group from 2010 to 2023. The plots also show the excess all-cause deaths for comparison. The figure on the top refers to relative deviations from the 2013-2019 trend, while Figure 5-bottom shows the *Z*-Score (signal strength) for the deviations from trend.

In Figure 5-top we can observe that the excess death rates from musculoskeletal diseases as the underlying cause (UC) were 4.7% (*Z*-Score of 1.7) in 2020, then rose to 15.2% (*Z*-Score of 5.6) in 2021, 16.6% (*Z*-Score of 6.1) in 2022 and 26.6% (*Z*-Score of 9.8) in 2023. By comparison, the excess mortality for all-cause deaths was 16.8% in 2020, 21.1% in 2021, 12.8% in 2022, and 10.5% in 2023.

It is noteworthy that while excess all-cause mortality peaked in 2021 and then dropped in 2022 and 2023, excess deaths from musculoskeletal diseases as the underlying cause rose consecutively in 2021, 2022 and 2023. Additionally, while excess all-cause deaths suffered an extreme rise of 16.8% (28 standard deviation rise) in 2020, excess musculoskeletal death rates were subdued at about 4.7% (*Z*-Score of 1.7), showing low statistical significance.

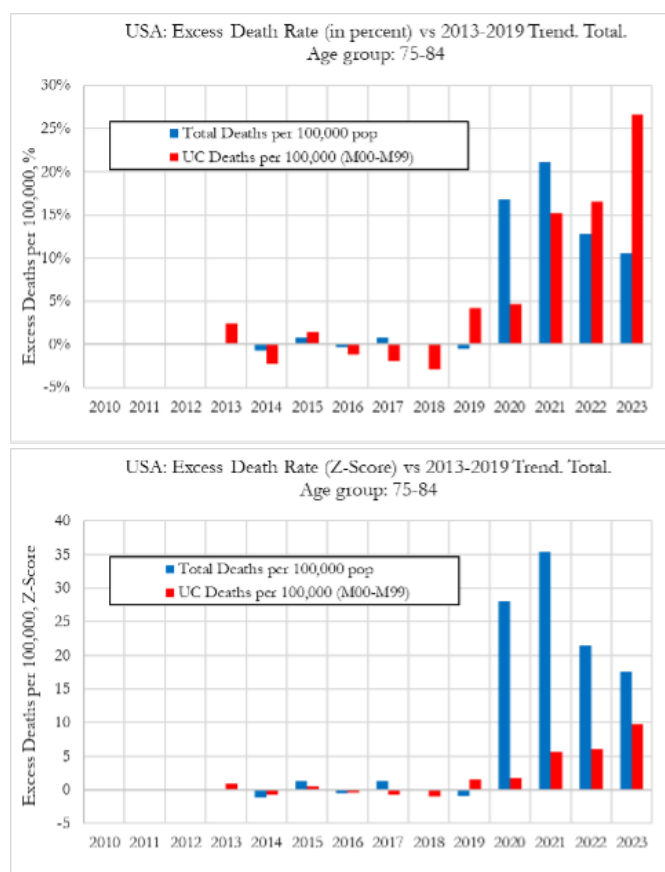


Figure 5. Excess UC death rates from musculoskeletal diseases (M00-M99) from 2010 to 2023 for both sexes of ages 75 to 84 in the US. Top: Relative deviation from trend, percent. Bottom: Deviation from trend *Z*-Score. Excess deaths from all causes are shown for comparison.

4.3.2 Excess MC Death Rates (M00-M99)

We now analyze excess MC deaths rates and excess MC* death rates (by excluding COVID-19 related deaths) from musculoskeletal diseases (M00-M99), for ages 75 to 84 in the US, as shown in Figure 6. The figure on the top refers to relative deviations from the 2013-2019 trend, while figure on the 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 musculoskeletal diseases were 18.3% (*Z*-Score of 9.0) in 2020, then rose to 27.2% (*Z*-Score of 13.4) in 2021, and to 28.8% (*Z*-Score of 14.2) in 2022, and 35.3% (*Z*-Score of 17.4) in 2023. In terms of the statistical significance of the

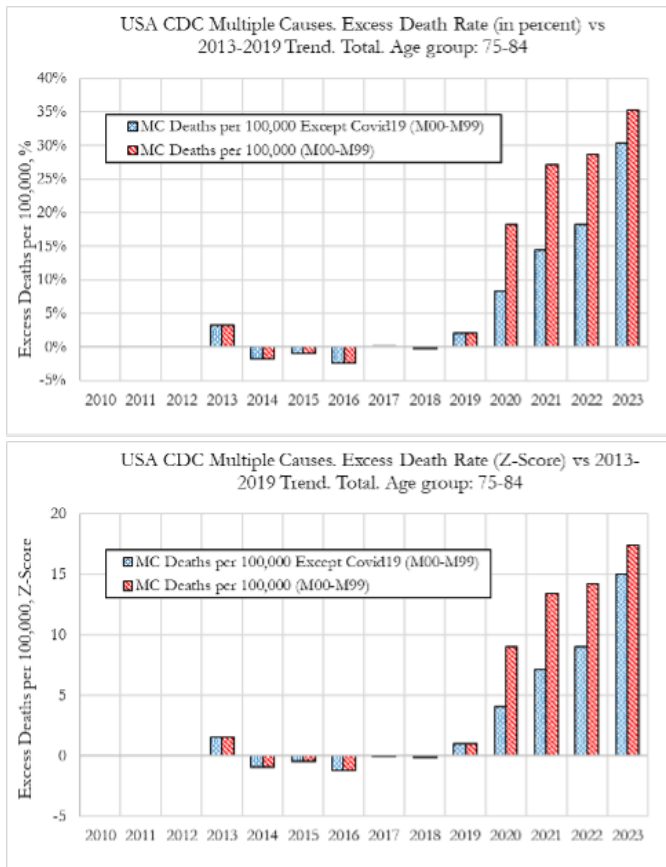


Figure 6. Excess MC death rates from musculoskeletal diseases (M00-M99) from 2010 to 2023 for both sexes of ages 75 to 84 in the USA. Top: Relative deviation from trend, percent. Bottom: Deviation from trend Z -Score. Excess MC* death rates (where COVID-19-related deaths are removed) are shown for comparison.

excess deaths, these can be considered extreme events.

By comparison, the excess MC* death rates from musculoskeletal diseases where COVID-19-related deaths were removed, were 8.3% (Z -Score of 4.1) in 2020, 14.5% (Z -Score of 7.1) in 2021, 18.2% (Z -Score of 9.0) in 2022 and 30.3% (Z -Score of 15.0) in 2023. Of note is that the rise in excess mortality for MC deaths from musculoskeletal diseases where COVID-19-related deaths were removed, exhibited a similar pattern to UC excess death rates from musculoskeletal diseases (shown in Figure 5).

We also observe that MC* death rates are substantially higher than UC death rates from musculoskeletal diseases, as illustrated by the ratio

of MC*/UC death rates (Figure 4-bottom) which is ranges between 4 to 5 across the 2010-2023 period. The ratio did not vary significantly during the pandemic years, 2020, 2021, 2022 and 2023, indicating that both MC* and UC death rates from musculoskeletal diseases had similar behaviors during those years.

4.3.3 Observations on M00-M99

The excess death rates from UC musculoskeletal deaths are in alignment with a previous analysis for neoplasm deaths (Alegria, et al., 2024)[3]. The paper showed that excess UC death rates from neoplasms for individuals aged 75 to 85 in the US were -0.3% in 2020, 4.8% in 2021, and 11.5% in 2022, with Z -Scores of -0.3, 10.1 and 24.0, respectively. The paper did not present results for 2023. The main difference being that for musculoskeletal deaths, the percent deviations from prior trends were of larger magnitude, and that in 2020, excess UC death rates were 7.4% albeit with a relatively low statistical significance (Z -Score of 2.1). The subsequent increase in death rates from musculoskeletal diseases in 2021 and 2022, in similarity to what was observed in neoplasm deaths, suggests that there perhaps a common underlying factor at play. While a new factor was introduced in the form of the novel COVID-19 vaccinations which could have played a significant role (Park, et al., 2023)[5], in parallel with persisting effects from multiple SARS-CoV-2 exposures.

We also observe that the rises of excess both MC* and UC death rates from musculoskeletal diseases in 2020, 2021, 2022 and 2023 suggests that an underlying factor is at play. The rise in excess UC death rates alone cannot explain the rises in MC* death rates as MC death rates are about 5 times larger than UC death rates. This suggests that a common factor is leading to persistent rises in excess mortality related to musculoskeletal diseases.

Next, we'll analyze in detail the two major sub-categories for deaths from musculoskeletal diseases, namely arthropathies (M00-M25) and osteopathies

and chondropathies (M80-M94), which are diseases that typically impact older individuals.

4.4 M00-M25 - Arthropathies

We now investigate in detail the trends in MC, MC* (except COVID-19-related deaths) and UC death rates from 2000 to 2023 for arthropathies (ICD-10 codes M00 to M25), for the 75-84 age group of both sexes. Arthropathies tend to be contributing causes of death instead of underlying cause which means that MC death rates from arthropathies could amount to several times the UC death rate (as illustrated in Figure 7-bottom).

Figure 7-top shows the death rate per 100,000 individuals for deaths from arthropathies from 2000 to 2023. We can observe that both UC and MC death rates with arthropathies in the 75-84 age group have been trending lower from 2000 to 2019.

MC death rates, in 2000 were 85.6 per 100,000 and in 2019 it was 40.8 per 100,000, a 52.3% decline (which corresponds to a 2.62% drop per annum). As for UC deaths, in 2000 the death rate was 13.0 per 100,000 and in 2019 it was 5.9 per 100,000, a 54.6% decline (which corresponds to a 2.73% drop per annum).

We also observe in Figure 7-bottom that the ratio of MC to UC deaths were stable from 2000 to 2019, with a value of about 6.5, which is slightly higher than for the overall musculoskeletal system meaning that arthropathies tend to be classified as a mostly as a contributing caused instead of the underlying cause of death.

MC death rates rose in 2020 to 46.9 per 100,000, and then to 47.0 per 100,000 in 2021. In 2022 the MC death rate dropped slightly to 44.9 per 100,000 and in 2023 it remained at 44.9 per 100,000. MC* death rates (after removing COVID-19-related deaths) rose in 2020 to 41.8 per 100,000, and then dropped to 41.0 per 100,000 in 2021, to 40.4 per 100,000 in 2022 and in 2023 it rose to 43.1 per 100,000.

The UC death rate dropped in 2020 to 5.8 per 100,000, and then to 5.7 per 100,000 in 2021. In

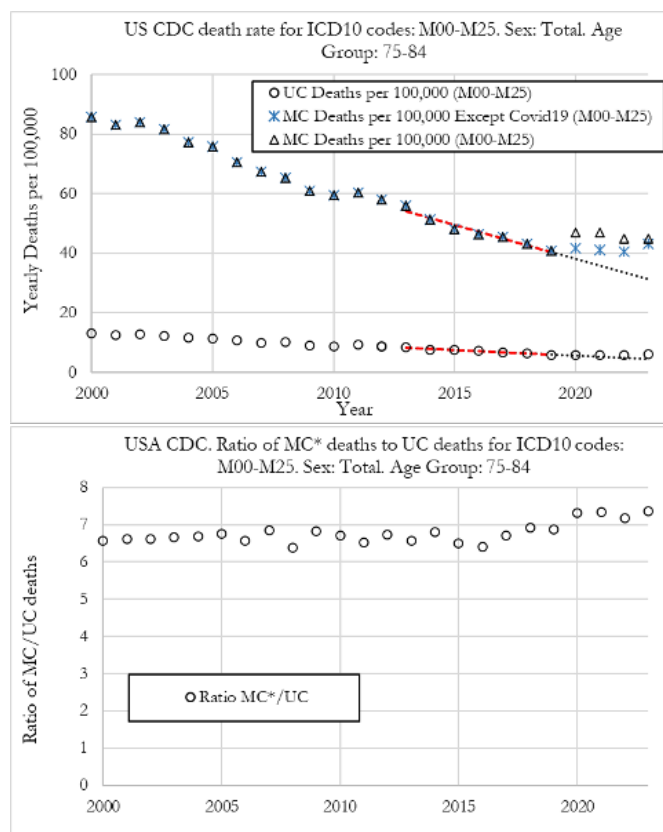


Figure 7. Yearly death rates from arthropathies (M00-M25) in the US for ages 75 to 84. The red dashed line shows the trend from 2013 to 2019. The dotted line shows the extrapolation of the trend from 2020 until 2023. Top: Death Rates per 100,000. Bottom: Ratio of MC* to UC deaths.

2022 the UC death rate was 5.8 per 100,000 and in 2023 it rose further to 6.0 per 100,000.

The ratio of MC* to UC deaths remained stable in 2020, 2021, 2022 and 2023, after a slight rise in 2020.

Even after removing COVID-19 related deaths, we observe a break in MC* arthropathies death rates from the prior 2013-2019 trend.

4.4.1 Excess UC Death Rates (M00-M25)

Figure 8 shows the excess death rate from arthropathies in the US (ICD10 codes: M00-M25), for the 75 to 84 age group from 2010 to 2023. The plots also show the excess all-cause deaths for comparison. The figure on the top refers to relative deviations from the 2013-2019 trend, while Figure

8-bottom shows the Z -Score (signal strength) for the deviations from trend.

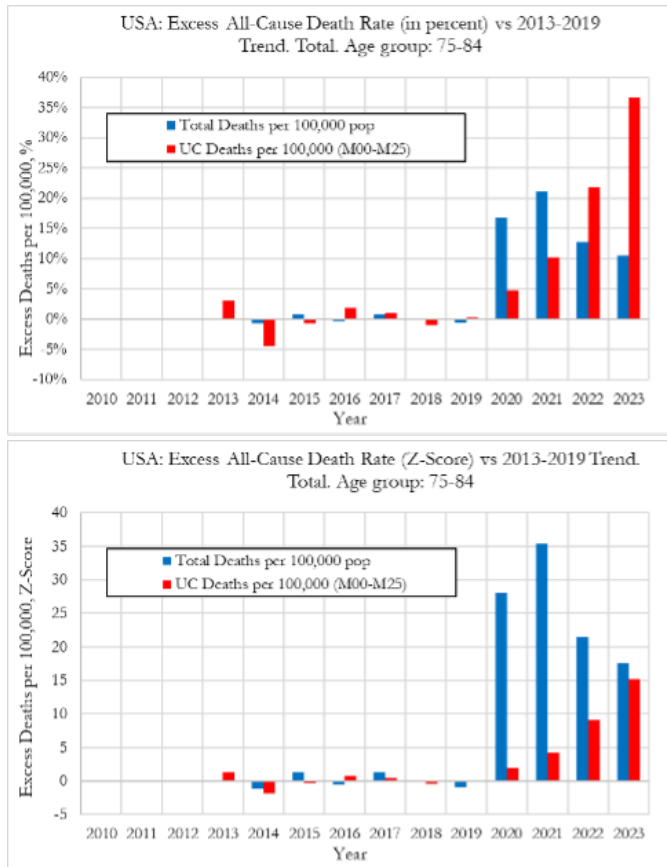


Figure 8. Excess UC death rates from arthropathies (M00-M25) from 2010 to 2023 for both sexes of ages 75 to 84 in the US. Top: Relative deviation from trend, percent. Bottom: Deviation from trend Z -Score. Excess deaths from all causes are shown for comparison.

In Figure 8-top we can observe that the excess death rates from arthropathies as the underlying cause (UC) were 4.8% (Z -Score of 2.0) in 2020, then rose to 10.3% (Z -Score of 4.3) in 2021, 21.9% (Z -Score of 9.1) in 2022 and 36.7% (Z -Score of 15.2) in 2023. By comparison, the excess mortality for all-cause deaths was 16.8% (Z -Score of 28.1) in 2020, 21.1% (Z -Score of 35.4) in 2021, 12.8% (Z -Score of 21.4) in 2022, and 10.5% (Z -Score of 17.6) in 2023.

Noteworthy is that while excess mortality for all-cause deaths dropped substantially from 2021 to 2022 and 2023, excess deaths from arthropathies

as the underlying cause increased substantially. Furthermore, while excess all-cause deaths rose 16.8% (with a Z -Score of 28.1) in 2020, excess death rates from arthropathies were subdued at about 4.8% (Z -Score of 2.0).

4.4.2 Excess MC Deaths Rates (M00-M25)

We now analyze excess MC death rates and excess MC* death rates (by excluding COVID-19 related deaths) from arthropathies (M00-M25), for ages 75 to 84 in the US, as shown in Figure 99. The figure on the top refers to relative deviations from the 2013-2019 trend, while figure on the bottom shows the Z -Score (signal strength) for the deviations from trend.

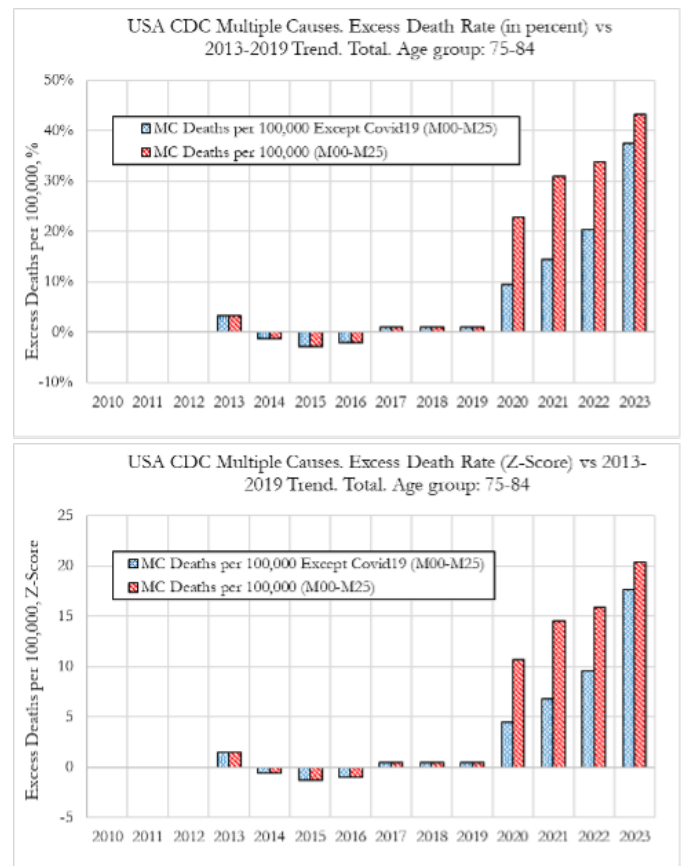


Figure 9. Excess MC death rates from arthropathies (M00-M25) from 2010 to 2023 for both sexes of ages 75 to 84 in the USA. Top: Relative deviation from trend, percent. Bottom: Deviation from trend Z -Score. Excess MC* death rates (where COVID-19-related deaths are removed) are shown for comparison.

In Figure 9-top we can observe that the excess MC death rates from arthropathies were 22.8% (Z -Score of 10.7) in 2020, then rose to 30.9% (Z -Score of 14.6) in 2021, and to 33.7% (Z -Score of 15.9) in 2022, and 43.3% (Z -Score of 20.4) in 2023. In terms of the statistical significance of the excess deaths, these can be considered extreme events.

Excess MC* death rates from arthropathies (where COVID-19-related deaths were removed), were 9.4% (Z -Score of 4.4) in 2020, 14.4% (Z -Score of 6.8) in 2021, 20.3% (Z -Score of 9.6) in 2022 and 37.6% (Z -Score of 17.7) in 2023.

The rise in excess mortality for MC* deaths from arthropathies (where COVID-19-related deaths were excluded), exhibited a similar pattern to UC excess death rates from arthropathies (shown in Figure 8).

We also observe that MC* death rates are substantially higher than UC death rates from arthropathies diseases, as illustrated by the ratio of MC*/UC death rates (Figure 7-bottom) which was stable close to 7.0 across the 2000-2019 period. The ratio rose slightly in 2020 and then remained stable through 2021, 2022 and 2023, indicating that both MC* and UC death rates from these diseases had similar behaviors during those years, after the rise in MC deaths in 2020. Next, we'll analyze in detail osteopathies and chondropathies (M80-M94), which are the other class of musculoskeletal diseases that typically impact older individuals.

4.5 M80-M94 - Osteopathies and chondropathies

In this section we investigate in detail the trends in MC, MC* (except COVID-19-related deaths) and UC death rates from 2000 to 2023 for osteopathies and chondropathies (ICD-10 codes: M80 to M94), for the 75-84 age group of both sexes. As with other musculoskeletal diseases, osteopathies and chondropathies tend to be contributing causes of death instead of underlying cause which means that MC death rates from these diseases could amount to several times the UC death rate (as illustrated in Figure 10-bottom).

Figure 10-top shows the death rate per 100,000 individuals for deaths from osteopathies and chondropathies from 2000 to 2023. We can observe that both UC and MC death rates with these conditions in the 75-84 age group have been trending lower from 2000 to 2019. MC death rates, in 2000 were 43.8 per 100,000 and in 2019 it was 24.5 per 100,000, a 44.1% decline (which corresponds to a 2.20% drop per annum). As for UC deaths, in 2000 the death rate was 6.6 per 100,000 and in 2019 it was 5.4 per 100,000, a 18.2% decline (which corresponds to a 0.90% drop per annum).

We also observe in Figure 10-bottom that the ratio of MC to UC deaths also declined steadily from 2000 to 2019, from a value of about 6.7 in 2000 to about 4.3 in 2019.

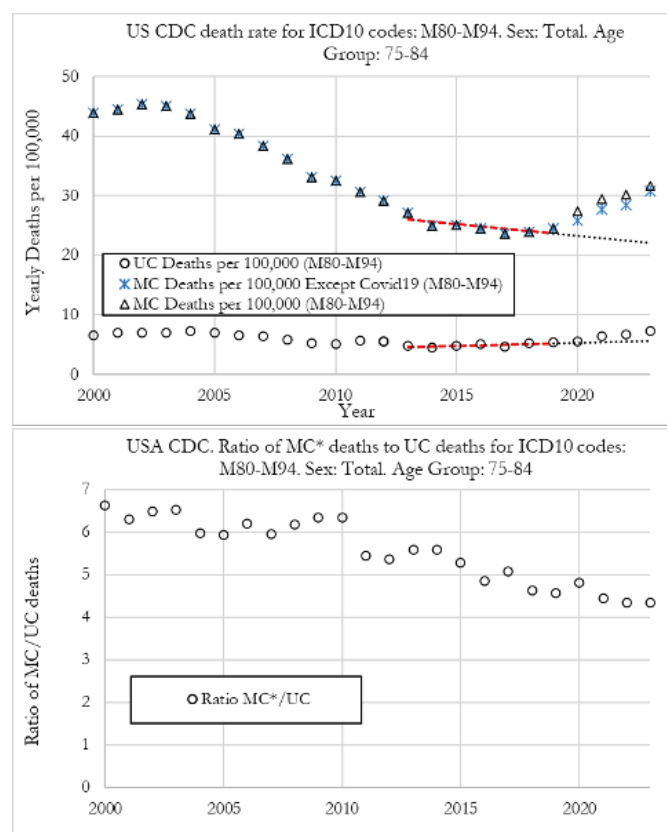


Figure 10. Yearly death rates from osteopathies and chondropathies (M80-M94) in the US for ages 75 to 84. The red dashed line shows the trend from 2013 to 2019. The dotted line shows the extrapolation of the trend from 2020 until 2023. Top: Death Rates per 100,000. Bottom: Ratio of MC* to UC deaths

MC death rates rose in 2020 to 27.4 per 100,000, and then to 29.5 per 100,000 in 2021, to 30.2 per 100,000 in 2022 and to 31.7 per 100,000 in 2023.

MC* death rates (after removing COVID-19-related deaths) rose in 2020 to 25.9 per 100,000, and then to 27.7 per 100,000 in 2021, to 28.5 per 100,000 in 2022 and to 30.8 per 100,000 in 2023. Even after removing COVID-19 related deaths, we observe an increase in MC* death rates from osteopathies and chondropathies in 2020, 2021, 2022 and 2023.

The UC death rate rose slightly in 2020 to 5.5 per 100,000, and then jumped to 6.4 per 100,000 in 2021. In 2022 the UC death rate rose further to 6.8 per 100,000 and to 7.2 per 100,000 in 2023. Figure 10-bottom shows that the ratio of MC* to UC deaths has been on a downward trend from 2000 to 2019 which continued in 2020, 2021, 2022 and 2023, after a slight rise in 2020. The decline seems to be driven mainly by the declining trends in MC death rates.

4.5.1 Excess UC Death Rates (M80-M94)

Figure 11 shows the excess death rate from osteopathies and chondropathies in the US (ICD10 codes: M80-M94), for the 75 to 84 age group from 2010 to 2023. The plots also show the excess all-cause deaths for comparison. The figure on the top refers to relative deviations from the 2013-2019 trend, while Figure 11-bottom shows the Z -Score (signal strength) for the deviations from trend.

From Figure 11-top we observe that the excess death rates from osteopathies and chondropathies as the underlying cause (UC) were 3.3% (Z -Score of 0.7) in 2020, then rose to 17.5% (Z -Score of 3.8) in 2021, 22.1% (Z -Score of 4.8) in 2022 and 28.1% (Z -Score of 6.1) in 2023. By comparison, the excess mortality for all-cause deaths was 16.8% (Z -Score of 28.1) in 2020, 21.1% (Z -Score of 35.4) in 2021, 12.8% (Z -Score of 21.4) in 2022, and 10.5% (Z -Score of 17.6) in 2023.

Of note was that while excess mortality for all-cause deaths dropped substantially from 2021 to 2022 and 2023, excess deaths from osteopathies and

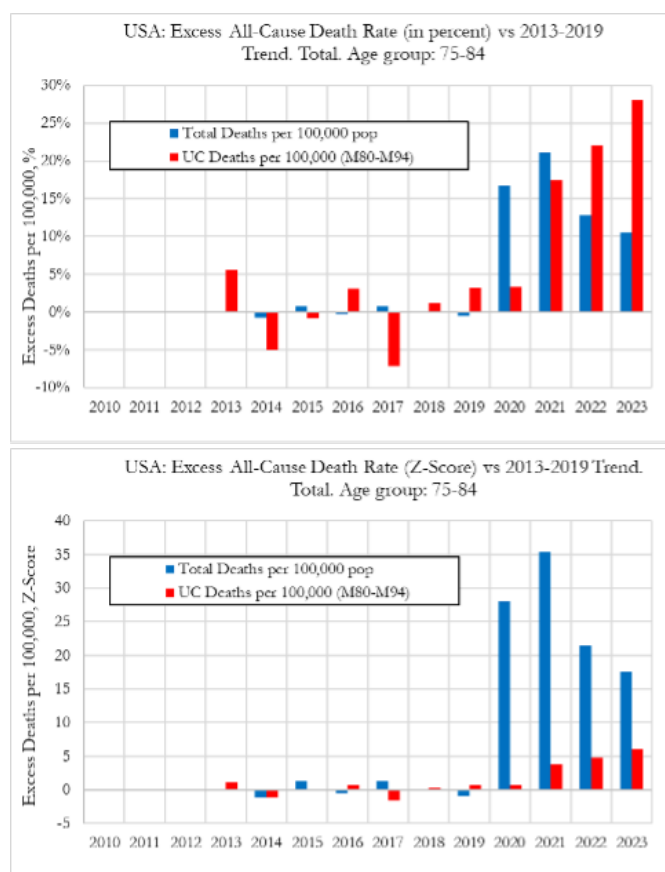


Figure 11. Excess UC death rates from osteopathies and chondropathies (M80-M94) from 2010 to 2023 for both sexes of ages 75 to 84 in the US. Top: Relative deviation from trend, percent. Bottom: Deviation from trend Z -Score. Excess deaths from all causes are shown for comparison.

chondropathies as the underlying cause increased substantially. Furthermore, while excess all-cause deaths rose 16.8% (with a Z -Score of 28.1) in 2020, excess death rates from osteopathies and chondropathies were subdued at about 3.3% (Z -Score of 0.7) showing no statistical significance.

4.5.2 Excess MC Deaths Rates (M80-M94)

We now analyze excess MC death rates and excess MC* death rates (by excluding COVID-19 related deaths) from osteopathies and chondropathies (M80-M94), for ages 75 to 84 in the US, as shown in Figure 12. The figure on the top refers to relative deviations from the 2013-2019 trend, while figure on the bottom shows the Z -Score (signal strength) for the deviations from trend.

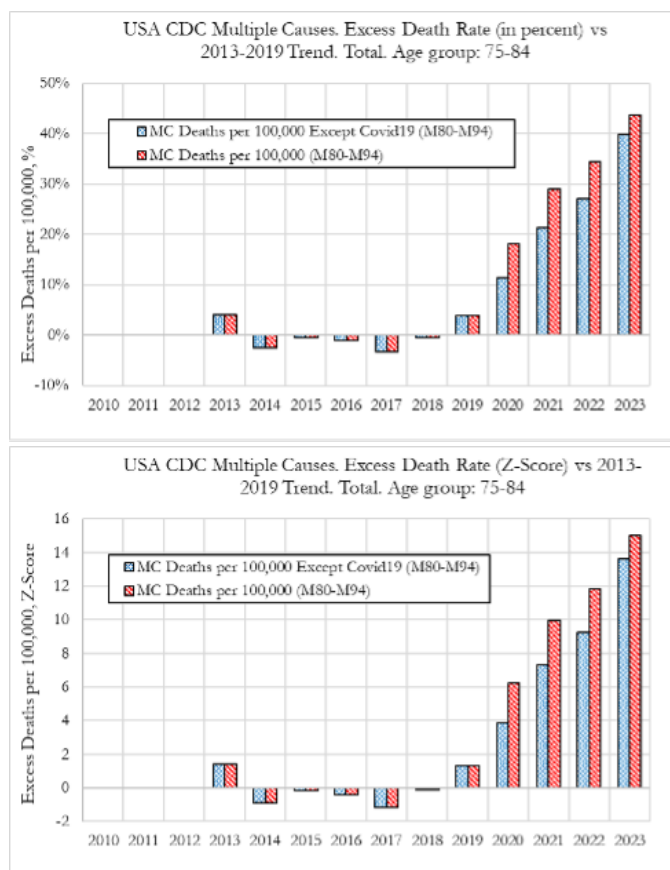


Figure 12. Excess MC death rates from osteopathies and chondropathies (M80-M94) from 2010 to 2023 for both sexes of ages 75 to 84 in the USA. Top: Relative deviation from trend, percent. Bottom: Deviation from trend Z -Score. Excess MC* death rates (where COVID-19-related deaths are removed) are shown for comparison.

In Figure 12-top we can observe that the excess MC death rates from osteopathies and chondropathies were 18.1% (Z -Score of 6.2) in 2020, then rose to 29.1% (Z -Score of 9.9) in 2021, and to 34.5% (Z -Score of 11.8) in 2022, and to 43.8% (Z -Score of 15.0) in 2023. In terms of the statistical significance of the excess deaths, these can be considered extreme events.

Excess MC* death rates from osteopathies and chondropathies (where COVID-19-related deaths were removed), were 11.3% (Z -Score of 3.9) in 2020, 21.4% (Z -Score of 7.3) in 2021, 27.0% (Z -Score of 9.3) in 2022 and 39.8% (Z -Score of 13.6) in 2023.

The rise in excess mortality for MC* deaths from osteopathies and chondropathies (where COVID-19-related deaths were excluded), exhibited a similar pattern to MC excess death rates, and was already noticeable in 2020. As for UC excess death rates previously reported, these only rose significantly from 2021 onwards, which implies that severe cases of osteopathies and chondropathies are possibly associated with either the COVID-19 vaccines or cumulative inflammatory effects of multiple SARS-CoV-2 exposures. The rise in excess MC or MC* death rates from these conditions tracked the rise in all-cause mortality in 2020 and 2021, but the continued rise in excess death rates in 2022 and 2023 did not follow the drop in all-cause mortality, which suggests again that a new persistent phenomenon is at play

5 ANALYSIS OF EXCESS DEATH TRENDS FROM MUSCULOSKELETAL DISEASES FOR ALL AGES

In this chapter we generalize the previous analysis of trends in death rates from musculoskeletal diseases for all age groups. We compute the excess deaths (deviation from trend) from musculoskeletal diseases (ICD10 codes: M00-M99), for the different age groups in the US.

The data for age groups 1, 1-4 and 5-14 cannot be computed as the number of deaths in these age groups are very low, falling below CDC suppression limitations that do not allow for publication.

5.1 Excess UC Death Rates from Musculoskeletal Diseases for Different Age Groups

Here we compute, for all age groups, the excess UC death rates from musculoskeletal diseases in 2020, 2021, 2022 and 2023, shown in Figure 13. The detailed results are also shown in the tables in the appendix.

In Figure 13-top we plot the excess UC death rate (in percent) while Figure 13-bottom the respective

Z-Scores are shown. Each datapoint on the graphs is obtained by performing the analysis described in the methodology section where the extrapolated 2013-2019 trendline in death rates is subtracted from the death rates in 2020, 2021, 2022 and 2023, for each of the age groups.

The results from Figure 13 show that the excess UC death rates from musculoskeletal diseases seem to have impacted mostly older individuals aged 65 and above. For individuals below the age of 35 there is no sign of abnormal excess death rates.

Figure 13 shows that for age groups 35-44, 45-54 and 55-64 we observe statistically significant excess death rates, particularly in 2020 and 2021. For the younger age group 35-44 excess death rates dropped substantially to “normal” values in 2022 and 2023, while for age groups 45-54 and 55-64 the excess death rates were high in 2022 and only dropped in 2023. For these individuals excess UC death rates appear to track all-cause mortality during the 2020-2023 period.

As example, within these age groups, as shown in Figure 13, the largest percentage of excess deaths were observed in the 45-54 age group, where excess death rates were 18.4% (Z-Score: 5.7) in 2020, 14.6% (Z-Score: 3.3) in 2021, 18.9% (Z-Score: 5.8) in 2022 and 9.9% (Z-Score: 3.0) in 2023.

For older age groups 65-74, 75-84 and 85+ we observe statistically significant excess death rates, that increased consecutively from 2020 to 2023. The signal strengths in 2020 were weaker than for younger individuals as illustrated by the 4.7% excess death rate for individuals aged 75 to 84 with a 1.7 Z-Score.

For the older age groups, excess deaths increased substantially in 2021, 2022 and 2023, showing extreme deviations from the prior 2013-2019 trend. Additionally, as illustrated by the detailed analysis of the 75-84 age group, in section 4.2, even as excess all-cause deaths declined in 2022 and 2023, excess death rates from musculoskeletal diseases continued to rise. The results for older individuals

suggest that COVID-19 or even pandemic lockdowns are unlikely explanations for the rise in excess musculoskeletal death rates.

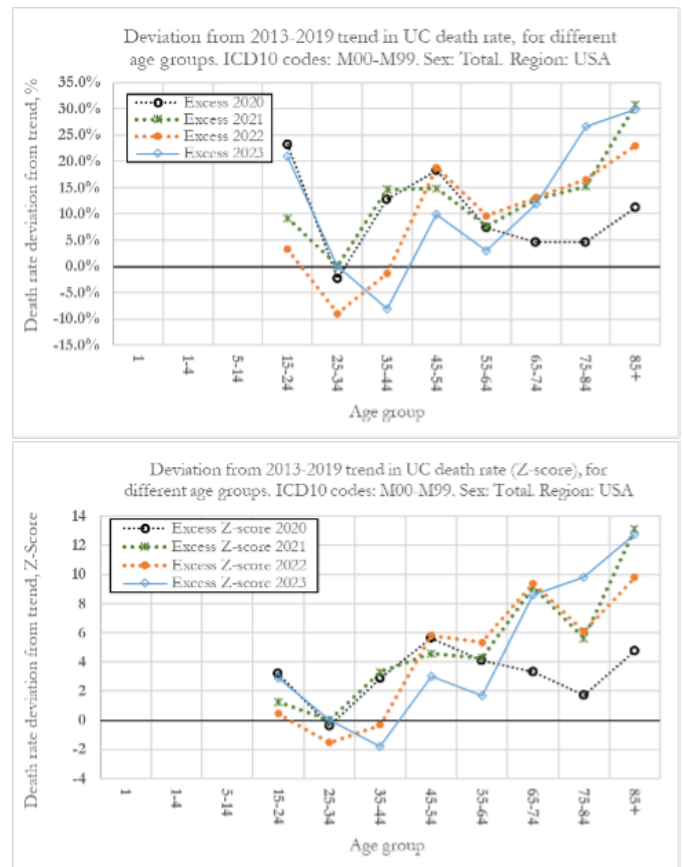


Figure 13. Excess UC death rates from musculoskeletal diseases (M00-M99) for 2020, 2021, 2022 and 2023 for different age groups of both sexes in the US. Top: Relative deviation from trend, percent. Bottom: Deviation from trend Z-Score.

5.2 Excess MC Death Rates with Musculoskeletal Diseases for Different Age Groups

In this section we compute, for all 10-year age groups, the excess MC death rates from musculoskeletal diseases (ICD10 codes: M00-M99) in 2020, 2021, 2022 and 2023, shown in Figure 14. For a detailed view of the results refer to section 8.1, in the appendix. In Figure 14-top we plot the excess MC death rate (in percent) while Figure 14-bottom shows the respective Z-Scores.

In Figure 14 we can observe that in general, excess MC death rates from musculoskeletal diseases were higher than for excess UC death rates in 2020, 2021, 2022 and 2023, for all age groups, despite the fact that multiple-cause musculoskeletal deaths are multiple times underlying-cause deaths (as shown in the MC/UC ratios in the tables in section 8.1 in the appendix). This and can be explained by MC musculoskeletal death rates increasing with all-cause mortality increases, due to the impact of COVID-19 during the pandemic years. To adjust for COVID-19-related deaths, in the next section we analyze excess MC musculoskeletal deaths where COVID-19-related deaths are excluded.

For the younger age groups, we notice from Figure 14 that MC excess death rates from musculoskeletal diseases were already very high in 2020, around 25% for the 35-44 and 45-54 age groups and 15% for individuals aged 55-64. Excess deaths increased in 2021 and remained high in 2022 for these age groups. In 2023 excess deaths dropped but still remained at abnormally high levels when compared to prior trends. These values had a very high statistical significance being considered extreme occurrences, even in 2023.

For older individuals (age groups 65-74, 75-84 and 85+) we observe from Figure 14 that MC excess death rates from musculoskeletal diseases were also very high in 2020, around 20% with very high statistical significance. Excess deaths increased further in 2021, 2022 and 2023 for these age groups, while peaking above 35% for the 75-84 age group in 2023. Contrary from what occurred with younger individuals, excess deaths rates for older individuals kept rising in 2022 and 2023, indicating a worsening of the phenomenon.

5.3 Excess MC* Death Rates with Musculoskeletal Diseases for Different Age Groups

We now calculate, for all age groups, the excess MC* death rates from musculoskeletal diseases in 2020, 2021, 2022 and 2023. As a reminder, MC* death rates refer to MC deaths from musculoskeletal

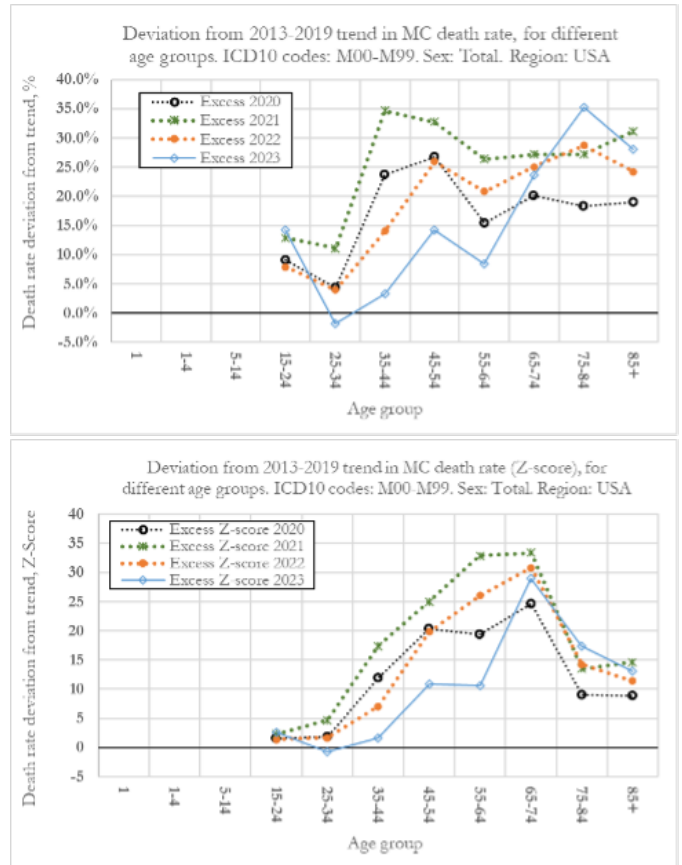


Figure 14. Excess MC death rates from musculoskeletal diseases (M00-M99) for 2020, 2021, 2022 and 2023 for different age groups of both sexes in the US. Top: Relative deviation from trend, percent. Bottom: Deviation from trend Z-Score.

diseases except for those where COVID-19 is also reported (either as underlying cause or a contributing cause).

In Figure 15-top we plot the excess MC* death rates while Figure 15-bottom shows the respective Z-Scores. The results show that the excess MC* death rates exhibit a similar pattern to UC excess death rates for the different age groups. After removing deaths related from COVID-19, we can still observe excess MC death rates in 2020, 2021, 2022 and 2023 ages 35 and above. This is likely due to the rise in MC* death rates being driven by the rises in UC death rates.

For older individuals, aged 65-74, 75-84 and 85+ we observe statistically significant excess death

rates, that increased consecutively from 2020 to 2023. For Younger individuals aged 35-44 and 45-54, excess death rates peaked in 2020 and 2021 and then declined in 2022 and 2023. While for younger individuals, the brunt of the effect was felt in 2020 and 2021, for older individuals, the excess death rates continued rising in 2022 and 2023. The excess death rates in general show very high levels of statistical significance with Z -Scores of 4 and above.

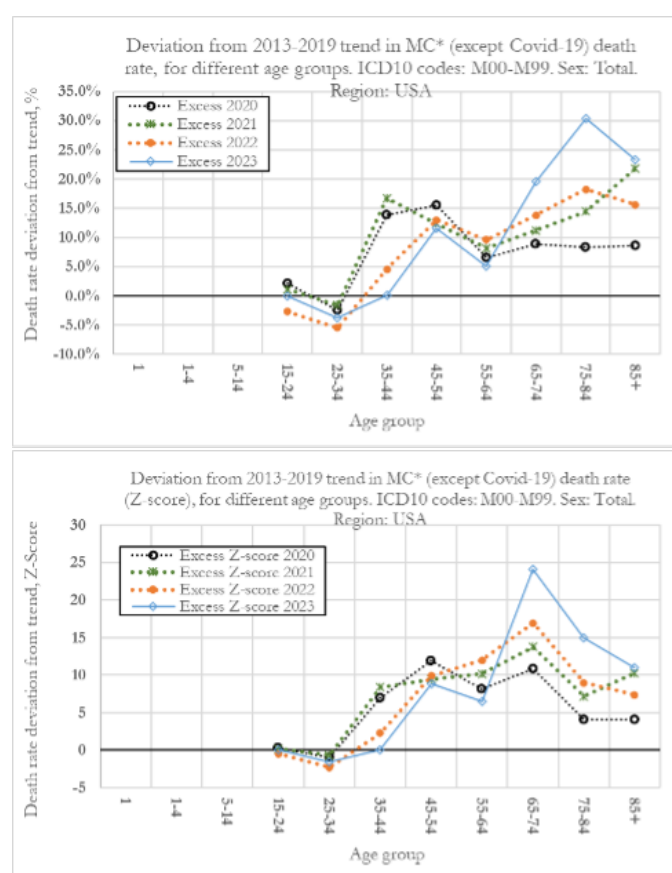


Figure 15. Excess MC* death rates (except COVID-19-related deaths) from musculoskeletal diseases (M00-M99) for 2020, 2021, 2022 and 2023 for different age groups of both sexes in the US. Top: Relative deviation from trend, percent. Bottom: Deviation from trend Z -Score.

6 SUMMARY OF FINDINGS AND COMMENTARY

6.1 Excess Deaths Rates from Musculoskeletal Diseases for Age Group 75 to 84

Our results show that the excess UC death rate from musculoskeletal diseases (ICD10 codes: M00-M99) diseases for individuals aged 75 to 84 was 4.7% (Z -Score of 1.7) in 2020, 15.2% (Z -Score of 5.6) in 2021, 16.6% (Z -Score of 6.1) in 2022 and 26.6% (Z -Score of 9.8) in 2023. Excess death rates rose in each consecutive year from 2020 to 2023. The excess death rate in 2020 was not statistically significant, while from 2021 onwards, the statistical significance of the excess death rates can be considered extreme occurrences. By comparison, the excess mortality for all-cause deaths was 16.8% (Z -Score of 28.1) in 2020, 21.1% (Z -Score of 35.4) in 2021, 12.8% (Z -Score of 21.4) in 2022, and 10.5% (Z -Score of 17.6) in 2023, which shows that while all-cause deaths peaked in 2021 and then dropped in 2022 and 2023, excess deaths from musculoskeletal deaths continued rising in 2022 and 2023.

We also observe that the rises of excess MC* death rates (where COVID-19-related deaths are excluded) from musculoskeletal diseases in 2020, 2021, 2022 and 2023 mirror the excess UC death rates, suggests that an underlying factor is at play.

When analyzing the most common causes of death for older individuals aged 75-84, within the musculoskeletal system, namely arthropathies (ICD10 codes: M00-M25) and osteopathies and chondropathies (ICD10 codes: M80-M94) we find similar patterns of behavior.

Excess death rates from osteopathies and chondropathies as the underlying cause (UC) were 3.3% (Z -Score of 0.7) in 2020, then rose to 17.5% (Z -Score of 3.8) in 2021, 22.1% (Z -Score of 4.8) in 2022 and 28.1% (Z -Score of 6.1) in 2023.

Excess MC death rates were already present in 2020, which could be explained by deaths from

health effects related to the pandemic management measures such lock-downs and lack of medical care, or other related factors such as stress, less exercise, worse food habits, or from under-diagnosed COVID-19 itself, or related side effects. MC deaths signify that the musculoskeletal disease was not severe enough to be the underlying cause of death and consequently the rise in MC deaths can be explained by the overall rise in all-cause mortality in 2020. However, from 2021 onwards acute COVID-19-associated deaths are an unlikely explanation to the observed excess mortality, as observed by the MC* analysis and more likely explanations are likely to be the COVID-19 vaccines (Park, et al., 2023)[5], long COVID, or cumulative inflammatory effect of multiple SARS-CoV-2 exposures.

Excess death rates from musculoskeletal diseases from 2020 to 2023 for older individuals, for which the 75-84 age group is a typical case, have a different pattern of behavior when compared to excess deaths rates from musculoskeletal diseases for younger individuals. We discuss these differences on the discussion of excess death rates for all age groups.

6.2 Excess Musculoskeletal Disease Deaths Rates for all ages

We observe statistically significant excess UC death rates from musculoskeletal diseases for age groups 35-44, 45-54 and 55-64, particularly in 2020 and 2021. For the younger age group 35-44 excess death rates dropped substantially to “normal” values in 2022 and 2023, while for age groups 45-54 and 55-64 the excess death rates were high in 2022 and only dropped in 2023. Our results are corroborated by the analysis of MC* death rates (where COVID-19-related deaths are excluded) from musculoskeletal diseases, which shows a similar pattern of to UC excess mortality.

As example, within these age groups, as shown in Figure 13, the largest percentage of excess UC deaths were observed in the 45-54 age group, where excess UC death rates were 18.4% (Z -Score: 5.7)

in 2020, 14.9% (Z -Score: 4.6) in 2021, 18.9% (Z -Score: 5.8) in 2022 and 9.9% (Z -Score: 3.0) in 2023. By comparison, excess MC* deaths rates were 15.6% (Z -score: 11.9) in 2020, 12.4% (Z -Score: 9.5) in 2021, 13.0% (Z -Score: 9.9) in 2022 and 11.6% (Z -Score: 8.9) in 2023.

Our results indicate that for younger individuals, excess death rates from musculoskeletal diseases appear to be closely related with all-cause mortality during the COVID-19 pandemic. The factors that are driving the excess death rates could be either the societal lock-downs (in 2020), sequelae from the COVID-19 disease (in 2020 through 2023), or COVID-19 vaccinations from 2021 onwards (Alessandria, et al, 2024)[7]. We cannot exclude other possible contributing factors such as pandemic-related changes in lifestyles or other factors. It should be mentioned that as musculoskeletal deaths tend to be classified as a contributing cause instead of underlying cause of death, acute COVID-19-associated deaths are an unlikely explanation to the observed excess mortality. Furthermore, the relatively low excess deaths from UC for younger individuals might be a consequence of a pull forward effect resulting from excess mortality in these age groups (which is evidenced by a rise in MC excess death rate, shown in Figure 14).

For older age groups 65-74, 75-84 and 85+ our results show statistically significant excess UC death rates, that increased from 2020 to 2023. The signal strengths in 2020 were weaker than for younger individuals, as illustrated by the 4.7% excess death rate for individuals aged 75 to 84 with a 1.7 Z -Score. For the same age group, UC excess death rates increased to 15.2% (Z -Score of 5.6) in 2021, 16.6% (Z -Score of 6.1) in 2022 and 26.6% (Z -Score of 9.8) in 2023, as shown in the tables in appendix.

The results suggest that there are different patterns for older individuals when compared to younger individuals. For older individuals the pattern of excess mortality from musculoskeletal diseases is different, as for these individuals,

excess deaths continued to rise in 2022 and 2023, indicating a worsening of the underlying phenomenon. Additionally, one must also consider the “dry tinder” effect where fragile individuals who suffer from chronic conditions were deceased earlier than expected. If this was the case, one would expect to observe low or negative excess death rates in 2022 and 2023, which is not the case.

As for possible causes for this phenomenon, a larger body of evidence is pointing towards the continuous uptake of COVID-19 inoculations within the older age groups being a factor that is driving the phenomenon, as for example, the from evidence of side effects from the vaccines is shown by Fraiman et al. (Fraiman, et al., 2022)[8], and in particular for inflammatory musculoskeletal diseases in shown in Park et al. (Park, et al, 2023)[5]. Furthermore, the recent paper by Alessandria et al. points to higher all-cause mortality COVID-19 vaccinated individuals when compared to unvaccinated ones (Alessandria, et al., 2024)[7].

One cannot exclude other possible contributing factors such as pandemic-related changes in lifestyles, inflammatory processes due to cumulative exposures to SARS-CoV-2, “Long COVID” (Jangnin, et al., 2024)[9] or other factors. It should be mentioned that as musculoskeletal deaths tend to be classified as a contributing cause instead of underlying cause of death, acute COVID-19-associated deaths are an unlikely explanation to the observed excess mortality.

Limitations of the study

The main limitations of this study are data-related:

One of the limitations of our analysis is that the 2022 and 2023 data from the CDC for the different causes of death is provisional, at the date of the data download (5th April 2024), which signifies that it might be subject to change, particularly in the classification of underlying cause or when adding secondary causes of disease. This might lead to some discrepancies once the final data is released. Furthermore, the CDC population denominator, used to compute the death rates, is also provisional

in 2023, as the population values for 2023 are the same as 2022, for each of the age groups. This might lead to changes in the death rate calculations once final values for both MC death classification and the population denominator are released.

The second limitation is the data suppression that the CDC WONDER system imposes on deaths with fewer than 10 individuals. This suppression means that it is not possible to perform a more granular analysis, such as analyzing deaths that are conditional on several distinct causes (disaggregating MC deaths), and in particular for younger age groups.

Future work

Given the literature showing adverse effects following COVID-19 vaccination cited above, which include musculoskeletal diseases, future studies should focus on COVID-19 vaccinated and unvaccinated individuals and whether the vaccination roll out or COVID-19-related conditions such as Long COVID are contributing factors to the ongoing rise in musculoskeletal-related deaths shown in this paper.

ACKNOWLEDGMENTS

The authors would like to acknowledge Elizabeth Walsh for valuable comments and suggestions towards the writing of the paper.

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.

FUNDING SOURCES

There was no funding source associated with this research. The research was a product of independent work by the authors.

REFERENCES

- [1] Alegria C, Nunes Y. Trends in death rates from Neurological diseases in the US for all ages and detailed analysis for 15-44. *Research Gate* (2024). doi:10.13140/RG.2.2.30832.67845. ([link](#)).
- [2] Alegria C, Wiseman D, Nunes Y. US - Death Trends for Neoplasms ICD codes: C00-D48, Ages 15-44. *Research Gate* (2024). doi:10.13140/RG.2.2.16068.64645. ([link](#)).
- [3] Alegria C, Nunes Y. Trends in death rates from neoplasms in the US for all ages and detailed analysis for 75-84. *Research Gate* (2024). doi:10.13140/RG.2.2.16221.01760. ([link](#)).
- [4] Mostert S, Hoogland M, Huibers M, Kaspers G. Excess mortality across countries in the Western World since the COVID-19 pandemic: ‘Our World in Data’ estimates of January 2020 to December 2022. *BMJ Public Health* 2 (2024) e000282. doi:10.1136/bmjph-2023-000282. ([link](#)).
- [5] Park YH, Kim MH, Choi MG, Chun EM. Correlation between COVID-19 vaccination and inflammatory musculoskeletal disorders. *MedRxiv* (2023). doi:10.1101/2023.11.14.23298544. ([link](#)).
- [6] Alegria C, Nunes Y. On measuring excess mortality. *ResearchGate* (2024). doi:10.13140/RG.2.2.16889.44646. ([link](#)).
- [7] Alessandria M, Malatesta GM, Berrino F, Donzelli A. A Critical Analysis of All-Cause Deaths during COVID-19 Vaccination in an Italian Province. *Microorganisms* 12 (2024) 1343. doi:10.3390/microorganisms12071343. ([link](#)).
- [8] Fraiman J, Erviti J, Jones M, Greenland S, Whelan P, Kaplan RM, et al. Serious adverse events of special interest following mRNA COVID-19 vaccination in randomized trials in adults. *Vaccine* 40 (2022) 5798–5805. doi:10.1016/j.vaccine.2022.08.036. ([link](#)).
- [9] Jangnin R, Ritruangroj W, Kittisupkajorn S, Sukeiam P, Inchai J, Maneeton B, et al. Long-COVID Prevalence and Its Association With Health Outcomes in the Post-Vaccine and Antiviral-Availability Era. *Journal of Clinical Medicine* 13 (2024). doi:10.3390/jcm13051208. ([link](#)).

APPENDIX

Summary tables with MC, MC* and UC excess death rates from neurological diseases in 2020, 2021, 2022 and 2023, for all age groups.

MC* - Refers to Multiple Cause Deaths with the exception of those with COVID-19 ICD-10 code U07.1

n.a. - Data not possible to calculate due to data suppression rules for CDC WONDER

2020 Age Group	MC Excess Death Rate		MC* Excess Death Rate		UC Excess Death Rate		Ratio MC/UC
	Deviation,%	Z-Score	Deviation,%	Z-Score	Deviation,%	Z-Score	
1	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
1-4	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
5-14	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
15-24	9.1	1.6	2.1	0.4	23.2	3.2	2.25
25-34	4.4	1.9	-2.4	-1.0	-2.3	-0.4	2.40
35-44	23.7	11.9	13.9	7.0	12.8	2.9	2.60
45-54	26.7	20.4	15.6	11.9	18.4	5.7	3.11
55-64	15.5	19.3	6.5	8.1	7.4	4.1	3.61
65-74	20.1	24.7	8.8	10.8	4.6	3.3	4.15
75-84	18.3	9.0	8.3	4.1	4.7	1.7	4.81
85+	19.0	8.9	8.7	4.1	11.2	4.8	6.10

Table 1. UC, MC and MC* excess death rates from musculoskeletal diseases (M00-M99) for different age groups in 2020. Excess death rates refer to deviations from 2013-2019 trend. The ratio MC/UC is the ratio of MC deaths to UC deaths from musculoskeletal diseases.

2021 Age Group	MC Excess Death Rate		MC* Excess Death Rate		UC Excess Death Rate		Ratio MC/UC
	Deviation,%	Z-Score	Deviation,%	Z-Score	Deviation,%	Z-Score	
1	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
1-4	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
5-14	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
15-24	12.9	2.3	1.1	0.2	9.2	1.3	2.78
25-34	11.1	4.7	-1.6	-0.7	0.1	0.0	2.55
35-44	34.7	17.4	16.7	8.4	14.6	3.3	2.79
45-54	32.8	25.0	12.4	9.5	14.9	4.6	3.39
55-64	26.3	32.9	8.2	10.2	7.7	4.3	3.97
65-74	27.2	33.4	11.2	13.8	12.7	9.1	4.09
75-84	27.2	13.4	14.5	7.1	15.2	5.6	4.66
85+	31.1	14.6	21.9	10.3	30.8	13.1	5.65

Table 2. UC, MC and MC* excess death rates from musculoskeletal diseases (M00-M99) for different age groups in 2021. Excess death rates refer to deviations from 2013-2019 trend. The ratio MC/UC is the ratio of MC deaths to UC deaths from musculoskeletal diseases.

Trends in death rates from musculoskeletal diseases in the US

2022 Age Group	MC Excess Death Rate		MC* Excess Death Rate		UC Excess Death Rate		Ratio MC/UC
	Deviation,%	Z-Score	Deviation,%	Z-Score	Deviation,%	Z-Score	
1	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
1-4	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
5-14	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
15-24	7.9	1.4	-2.7	-0.5	3.3	0.5	2.99
25-34	4.0	1.7	-5.4	-2.3	-8.9	-1.5	2.70
35-44	14.1	7.1	4.6	2.3	-1.3	-0.3	2.76
45-54	26.0	19.9	13.0	9.9	18.9	5.8	3.14
55-64	20.8	26.0	9.6	12.0	9.6	5.4	3.76
65-74	25.1	30.8	13.8	17.0	13.1	9.4	4.02
75-84	28.8	14.2	18.2	9.0	16.6	6.1	4.61
85+	24.2	11.4	15.7	7.4	23.0	9.8	5.62

Table 3. UC, MC and MC* excess death rates from musculoskeletal diseases (M00-M99) for different age groups in 2022. Excess death rates refer to deviations from 2013-2019 trend. The ratio MC/UC is the ratio of MC deaths to UC deaths from musculoskeletal diseases.

2023 Age Group	MC Excess Death Rate		MC* Excess Death Rate		UC Excess Death Rate		Ratio MC/UC
	Deviation,%	Z-Score	Deviation,%	Z-Score	Deviation,%	Z-Score	
1	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
1-4	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
5-14	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
15-24	14.3	2.5	n.a.	n.a.	20.9	2.9	2.88
25-34	-1.8	-0.8	-3.7	-1.6	0.1	0.0	2.38
35-44	3.3	1.6	0.1	0.1	-8.0	-1.8	2.69
45-54	14.3	10.9	11.6	8.9	9.9	3.0	3.11
55-64	8.5	10.6	5.2	6.4	3.0	1.7	3.62
65-74	23.6	29.0	19.7	24.1	12.0	8.6	4.03
75-84	35.3	17.4	30.3	15.0	26.6	9.8	4.41
85+	28.0	13.2	23.4	11.0	29.8	12.7	5.41

Table 4. UC, MC and MC* excess death rates from musculoskeletal diseases (M00-M99) for different age groups in 2023. Excess death rates refer to deviations from 2013-2019 trend. The ratio MC/UC is the ratio of MC deaths to UC deaths from musculoskeletal diseases.