

Manuscript title: Characterizing all-cause excess mortality patterns during COVID-19 pandemic in Mexico

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## Abstract

**Background:** The low testing rates, compounded by reporting delays, hinders the estimation of the mortality burden associated with the COVID-19 pandemic based on surveillance data alone. A more reliable picture of the effect of COVID-19 pandemic on mortality can be derived by estimating excess deaths above an expected level of death. In this study we aim to estimate the absolute and relative mortality impact of COVID-19 pandemic in Mexico in 2020 by gender and two geographic regions: Mexico City and the rest of the country.

**Methods:** We obtained mortality time series due to all causes for Mexico, and by gender, and geographic region using epidemiological weeks from January to December 2020 and for preceding 5 years. We also compiled data on COVID-19 related morbidity and mortality to assess the timing and intensity of the pandemic in Mexico. We assembled weekly series of the number of tweets about ‘death’ from Mexico to assess the correlation between people’s media interaction about ‘death’ and the rise in pandemic deaths. We estimated all-cause excess mortality rates and mortality rate ratio increase over baseline by fitting Serfling regression models.

**Results:** The COVID-19 pandemic excess mortality rates per 10,000 population in Mexico between March 1, 2020 and January 2, 2021 was estimated at 26.10. The observed total number of deaths due to COVID-19 was 128,886 which is 38.64% of the total estimated excess deaths. Males had about 2-fold higher excess mortality rate (33.99) compared to females (18.53). The excess mortality rate for Mexico City (63.54) was about 2.7-fold higher than the rest of the country (23.25). Similarly, the mortality rate ratio relative to baseline was highest for Mexico City (RR: 2.09). There was no significant correlation between weekly number of tweets on

‘death’ and the weekly all-cause excess mortality rates ( $p=0.309$  (95% CI: 0.010, 0.558,  $p$ -value=0.043).

Conclusion: The excess mortality rate of 26.10 per 10,000 population corresponds to a total of 333,538 excess deaths in Mexico between March 1, 2020 to January 2, 2021. COVID-19 accounted for only 38.21% of the total excess deaths, which reflects either the effect of low testing rates in Mexico, or the surge in number of deaths due to other causes.

Keywords: All-cause mortality, COVID-19, Excess mortality, Mexico, Pandemic, 2020

## Background

SARS-CoV-2 continues to spread unabated in many parts of the world [1]. In particular, Latin American countries are being heavily affected by the COVID-19 pandemic with a total of 15,754,382 cases including 512,233 deaths as of December 27, 2020 [1]. Mexico, one of the highly populated countries in the world with approximately 42% of the people living in poverty [2], documented the first imported COVID-19 case on 27<sup>th</sup> February, 2020 and currently ranks 4<sup>th</sup> in the world in terms of numbers of COVID-19 reported deaths, with a total of 121,837 recorded deaths (6.94% of total deaths globally) as of December 27, 2020 [1]. Factors such as delayed response towards implementing social distancing intervention, mixed reactions towards the stay-at-home order, and phased reopening of country have facilitated a sustained transmission of COVID-19 in Mexico [3].

Mexico has one of the lowest per-capita COVID-19 testing rates in the world with about 17 tests per 1000 people in total [4]. The low testing rates, compounded by reporting delays, hinders the estimation of the mortality burden associated with the COVID-19 pandemic based on surveillance data alone. Instead, a more reliable picture of the effect of COVID-19 pandemic on mortality can be derived by estimating excess deaths above a baseline or expected level of death[5, 6]. These estimates can provide information about the deaths that are directly or indirectly attributed to the pandemic [6]. Indeed, some deaths could be misclassified as COVID-19 deaths, or some could be occurring in the context of overburdened health care systems. Thus, tracking all-cause mortality in near real time can help assess whether excess deaths are occurring during a specific period of time and spatial area [6].

Here we report our estimates of the absolute and relative mortality impact of the COVID-19 pandemic in Mexico using cyclical Serfling regression models together with publicly available weekly all-cause mortality data from 2015 to 2020 by gender and for Mexico City and other areas of Mexico. Further, we collected and analyzed weekly twitter data from Mexico about ‘deaths’ during the COVID-19 pandemic in correlation with the excess all-cause death rate and COVID-19 death rate.

## Methods

*Data:* We obtained all-cause death counts based on epidemiological weeks for Mexico which were also stratified by gender and geographic region from January to December 2020 as well as for the preceding 5 years (2015-2019) in order to establish a baseline mortality level [7]. Based on data availability, we used weekly mortality data available from National Institute of Statistics and Geography (INEGI) for the years from 2015 to 2018, and data available from National Population Registry (RENAPO) for the years 2019 and 2020 [7]. To gauge the timing and relative intensity of the pandemic in Mexico, we examined surveillance data characterizing the weekly number of laboratory-confirmed COVID-19 cases and deaths, which were obtained from the official website of the Mexican Ministry of Health through the Directorate General of Epidemiology [8]. Population size estimates used to calculate mortality rates were obtained from National Population Council (CONAPO) of Mexico [9].

*Statistical analysis:* To investigate and quantify the mortality pattern associated with the COVID-19 pandemic in Mexico, we estimated excess all-cause mortality rates per 10,000 population at the national level and for Mexico City, and other areas of Mexico and by gender. The excess death rate corresponds to the overall mortality rate above a seasonal baseline of the

expected mortality rates in the absence of the COVID-19 pandemic using standard statistical methods [10-12].

*Definition of pandemic periods and excess mortality estimation:* We estimated the baseline mortality level by fitting cyclical Serfling regression models to all-cause deaths in non-COVID-19 period. Once a weekly baseline and 95% CI were established, periods of COVID-19 pandemic were defined as the weeks in 2020 where the observed all-cause mortality rate exceeded the upper 95% confidence limit of the baseline mortality level. The same pandemic period was used for estimating the total excess mortality rate for entire Mexico, Mexico City, Mexico excluding Mexico City, and gender specific excess mortality rates using established methodology [10-12]. Excess all-cause mortality rate was defined as the difference between the observed and model adjusted baseline mortality rates for each week constituting the pandemic period. Negative excess mortality estimates were replaced by zeros in our analyses. Overall pandemic excess mortality attributed to all cause for total population, each gender group, Mexico City, and Mexico excluding Mexico City was calculated by summing the excess death rates across the pandemic weeks in 2020 [10, 12], We also calculated the rate ratio (RR), the ratio of observed all-cause mortality rate during pandemic period to the model predicted baseline mortality level in the absence of COVID-19 for the given group.

*Twitter data analysis:* We used a clean version of the publicly available dataset of tweets version 42 [13], the clean version of this dataset removes all re-tweets, keeping only directly initiated posts by users. We filtered all tweets, by removing all other languages via their ISO 639-1 language code, to only keep the tweets in Spanish (es) and those that originated from Mexico via its country code MX. Additionally, we removed tweets from news agencies and bot accounts.

We used the following terms to subset the tweets per day: "muerto, muerta, fallecio, murio, deceso, fallecimiento, defunción, óbito, expiración, defuncion, obito, expiracion, perdio la vida, sin vida". In English, these terms reflect the meanings “dead, deceased, died, death, expiration, lost life, lifeless”. We collected a total of 1,219,995 unique tweets from March 1 to December 31, 2020. Next, we overlayed the curve of frequency of weekly tweets over the weekly mortality rate curve to inspect the relationship between the mortality rate and the frequency of tweets. We also calculated correlation coefficients between frequency of weekly tweets and the weekly excess death rate and the weekly COVID-19 death rate.

## Results

Between March 1 and December 31, 2020, as of data surveillance data updated on February 26, 2021, a total of 1,348,906 laboratory-confirmed COVID-19 cases, and 127,448 COVID-19-related deaths were captured by the epidemiological surveillance system in Mexico. The national daily series of new cases and deaths due to COVID-19 are shown in Figure 1. The number of cases rapidly rises from April to July followed by a downward trend which again takes off from mid-September. A similar temporal pattern can also be gleaned from the time series of COVID-19 related deaths.

Out of total 44 weeks from March 1, 2020 to January 2, 2021, 38 weeks starting from week 16 (April 12-18, 2020) had the excess death rate greater than 0. The excess death rate peaked on week 29 (July 12-18, 2020) with the excess death rate of 1.01 per 10,000 population, and on week 53 (December 27, 2020-January 2, 2021) with the excess death rate of 1.06 per 10,000 population. The weekly timeseries of all-cause mortality rate per 10,000 population in Mexico is shown in (Figure 2). We found that peaks in all-cause death rates aligned with the peaks in COVID-19 laboratory-confirmed death rates captured by the surveillance system. The curve of weekly number of tweets from Mexico about death is overlaid with the mortality rate curve in Figure 2.

Twitter trends show engagement of people in Mexico with the hashtag terms (Figure 2). This trend has been gradually declining despite the all-cause mortality rate and COVID-19 death rate continued to increase. There was a weak correlation between the weekly frequency of tweets and the weekly excess mortality rate and the weekly COVID-19 mortality rate from March 1 to December 26, 2020, which were estimated at  $\rho=0.309$  (95% CI: 0.010, 0.558,  $p\text{-value}=0.043$ )



and  $\rho=0.177$  (95% CI: -0.130, 0.453, p-value=0.257), respectively. The weekly timeseries of all-cause mortality rate per 10,000 population in the country of Mexico by gender are displayed in Figure 3. Similarly, the weekly timeseries of all-cause mortality rate per 10,000 population for Mexico City and for the rest of Mexico are shown in Figure 4.

In Table 1, we present the estimates of all-cause excess mortality rate per 10,000 population and the rate ratio estimates for each studied group, including the estimates at the national level. We estimated an excess death rate at 26.10 per 10,000 population in Mexico from March 1, 2020 to January 2, 2021. This corresponds to 333,538 excess deaths during the pandemic period. In the same period, a total of 128,886 lab-confirmed COVID-19 deaths corresponds to 38.64% of the total estimated excess deaths.

Table 1. Estimates of all-cause excess mortality rate per 10,000 population and RR during COVID-19 pandemic, Mexico, March 1, 2020- January 2, 2021.

	All-cause excess death rate per 10,000 population	Rate ratio*	Total number of all-cause excess deaths	Deaths due to COVID-19 (% of total number of all-cause excess deaths)
<b>Mexico</b>	<b>26.10</b>	<b>1.67</b>	<b>333,538</b>	128,886 (38.64%)
<b>Mexico City</b>	<b>63.54</b>	<b>2.09</b>	<b>57,304</b>	16,127 (28.14%)
<b>Mexico excluding Mexico City</b>	<b>23.25</b>	<b>1.62</b>	<b>276,148</b>	112,759 (40.83%)
<b>Male, Mexico</b>	<b>33.99</b>	<b>1.76</b>	<b>212,667</b>	81,489 (38.32%)
<b>Female, Mexico</b>	<b>18.53</b>	<b>1.56</b>	<b>120,861</b>	47,397(39.22%)

\* *calculated as the ratio of total observed death rate to total baseline death rate during the pandemic period*

The excess mortality rate in Mexico City (63.54) was about 2.7-fold higher than the rest of the Mexico (23.25). Interestingly, COVID-19 deaths in Mexico City accounted for only 28.14% of

the total estimated excess deaths in Mexico City, compared to 40.83% in the rest of Mexico.

Excess mortality rate among males nearly doubled the rate among females (proportion test, p-value  $<0.0001$ , and the proportion of COVID-19 deaths out of total excess deaths was similar, 38.321% among males and 39.22% among females (proportion test, p-value  $<0.0001$ ).

Our estimates of both the absolute and relative excess mortality rate as measured by the rate ratio of observed vs baseline mortality rate was highest for Mexico City (2.09) compared to other areas of Mexico (1.62) and for males (1.76). The rate ratio (RR) at the national level was estimated at 1.67.

## Discussion

Monitoring the excess mortality rate during the course of a pandemic is one of the key approaches for evaluating pandemic mortality impact [14]. In this study we characterized the excess mortality impact during COVID-19 pandemic in Mexico from March 1, 2020 to January 2, 2021. The pandemic was associated with an excess mortality rate of 26.10 per 10,000 population (a total of 333,538 excess deaths) (Table 1). Further, COVID-19 laboratory-confirmed deaths comprised only 38.64% of total excess deaths during the studied period. Our findings indicate that the COVID-19 pandemic has exerted a particularly devastating mortality burden on the Mexican population (Figure 2, Table 1).

Our estimate of the excess deaths in Mexico is higher compared to other Latin American countries such as Brazil (190,300+ excess deaths from March 2 to Nov 21), Peru (103,600 excess deaths from March to December), and Colombia (46700 excess deaths from March 2 to December 27) [15].

We found that the all-cause excess-death rate among males (33.99 per 10,000) was twice as high as the excess death rate among women (18.53 per 10,000), in Mexico (Table 1). This finding is in line with the previous studies, indicating that more men die from COVID-19 than women [16-18]. Several factors such as differences in the prevalence of comorbidities [19] as well as risk behaviors such as smoking and drinking [20], frequency of hand washing [21-23] and delays in health care seeking [18] could be contributing to a higher risk of COVID-19 death among males.

We found that both the all-cause excess death rate and the rate ratio were highest in Mexico City, compared to rest of the country (Table 1). This implies that, the risk of death has been

significantly higher in Mexico City. Mexico City is one of the most crowded cities in the world [24], and high population density has been shown to be one of the key factors contributing to COVID-19 infection and mortality rate [25, 26]. We also found that COVID-19 deaths directly accounted for only 28.14% of the excess all-cause deaths in Mexico City.

The fraction of COVID-19 attributed excess deaths was lower in Mexico (38.64%) compared to more than 65% in the USA [14, 27], and Germany [28]. From March to May 2020, the number of all cause excess deaths in the US was only 28% higher than the official record of COVID-19 deaths for that period [14]. From March 15, 2020 to January 30, 2021 an estimated 527,500 excess deaths occurred in the USA of which 83.3% were attributed to COVID-19[29] . In developed countries like Germany where the COVID-19 pandemic management has been considered a success story, the estimated excess number of deaths during the first wave of pandemic was lower than the reported number of COVID-19 deaths (+8071 estimated excess deaths vs. 8674 reported COVID-19 deaths) [28].

We observed a gradual decrease in people's Twitter engagement using sentiment hashtag terms indicating death even when the pandemic related mortality is rising. This was surprising, however might be indicative of fatigue. It could also indicate that people are less cautious or less concerned about the risk of death due to COVID-19. The reduced concern of COVID-19 deaths could also be the effect of vaccine availability.

Mortality data during an ongoing pandemic is not complete and in most settings, the differences in the officially reported COVID-19 death counts and the total deaths is due to limited COVID-19 testing rather than undercounting [15]. A review of mortality data of 2020 in 35 countries has

shown that at least 496,000 more people have died during the COVID-19 pandemic than the officially reported COVID-19 deaths [15].

When we compare the shape of weekly death rate in Mexico, and other countries, we see that the all-cause mortality level during the pandemic period always exceeded the upper bound threshold for the expected mortality baseline in Mexico and other countries including the U.S. [15, 27], Brazil, Peru, South Africa, Colombia, and Bolivia [15]. For Europe, the pooled estimate of data from 27 participating countries including heavily affected countries such as Spain and the UK showed that all-cause deaths exceeded the mortality level higher than four z-scores above the baseline (called as substantial excess deaths) in week 11 (March 9-15)/2020, reached the peak on week 14 and then declined below the substantial level on week 20. The curve then started to exceed the substantial excess deaths level from week 41 and gained a second peak in week 53, 2020 [30]. In Mexico, the mortality rate was higher than the upper 95% CI of expected baseline mortality rate from week 16 (April 12-18) of 2020 which peaked in week 29 (July 12-18, 2020), then started to decline gradually until mid-September and then peaked again with the highest excess death rate on week 53 of 2020 (December 27, 2020 to January 2, 2021) with the excess death rate of 1.06 per 10,000 population. The two peaks in excess death rate aligns with the two peaks in COVID-19 mortality rate. Similarly, in the U.S., from January to early October, 2020, deaths exceeded the upper bound threshold of expected deaths starting on week 12 (March 21-27), 2020 and reached their highest points in the weeks ending (April 5-11) and August 1-8, 2020 [27], which then had a third peak last week of 2020.[6].

Several factors could explain the low proportion of laboratory-confirmed deaths (38.64%) out of total estimated excess deaths from all-cause mortality in Mexico. First, Mexico has a high burden

of non-communicable diseases. In 2019, the top 5 leading causes of deaths were ischemic heart disease, diabetes, chronic kidney disease, cirrhosis, and stroke [31]. These comorbidities have been found to be associated with severe outcomes including death due to COVID-19 [32, 33]. Therefore, COVID-19 pandemic in a country like Mexico with high prevalence of chronic diseases, as well as with a health system struggling with absenteeism and health worker infections might have led to this alarming number of excess deaths [34, 35]. It is worth noting that, Mexico has the highest number of health worker deaths due to the COVID-19 pandemic (~1400 deaths) in the world [36, 37]. Another factor contributing to the low proportion of COVID-19 deaths out of total excess deaths could be the low COVID-19 testing rates in the country [4], and delay in reporting the COVID-19 deaths [38].

Our study has several limitations. As excess death rates will be strongly different among subgroups (it is quite high among the elderly, and those with underlying diseases), overall estimate is affected by age structure of the population. A detailed data on death certificate with age and underlying diseases information will provide more accurate estimates. Similarly, the COVID-19 deaths data that we have used might be underestimated because of different factors such as very low testing rates in Mexico, and misclassification of COVID-19 deaths. Further studies are needed to shed light on the extent of deaths directly attributable to COVID-19 and those that are related to other causes.

## Conclusion

Our estimate of all-cause excess mortality rate at 26.10 per 10,000 population during COVID-19 pandemic in Mexico provides a reliable estimate of the mortality impact of COVID-19 in a hard-hit Latin American country with a low testing rate. As the data becomes available on different sub-groups of the population, further studies on excess mortality could elucidate the mortality impact of the COVID-19 pandemic in Mexico.

## Declarations

**Ethics approval and consent to participate:** Not Applicable

**Consent for publication:** Not Applicable

**Availability of data and material:** The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Competing interest:** The authors declare that they have no competing interest.

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**Author Contributions:** Conceptualization, G.C., and S.D.; methodology, G.C., S.D., J.B., K.M.; validation, G.C.; formal analysis, S.D.; investigation, S.D.; resources, G.C., S.D., J.B.; writing—original draft preparation, S.D.; writing, review and editing, S.D., G.C., J.B., A.B., K.M. All authors have read and agreed to the published version of the manuscript.



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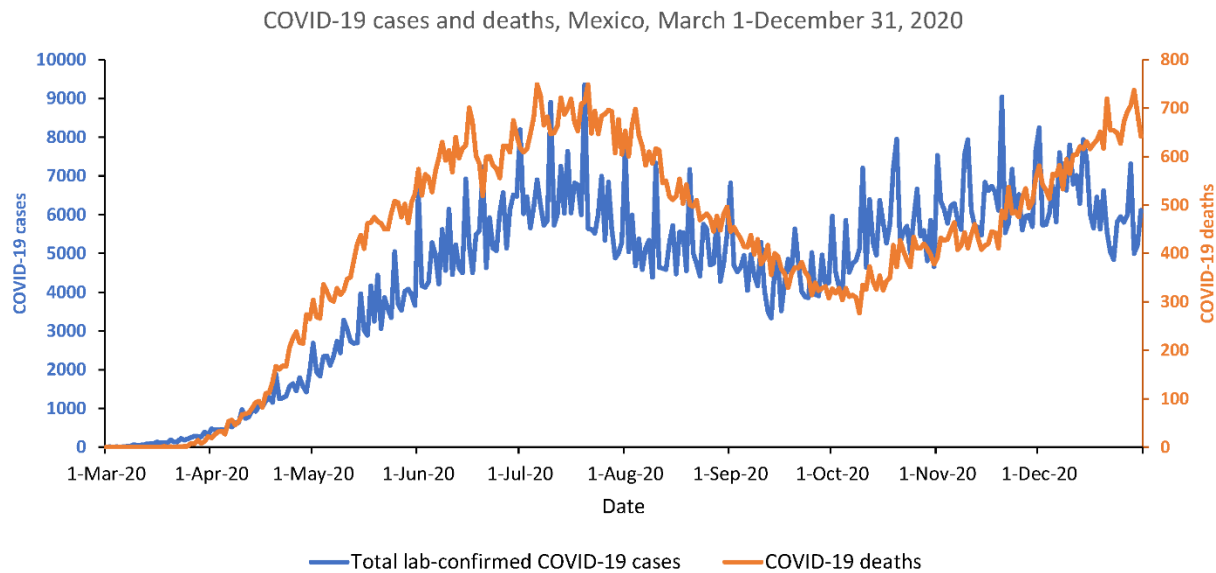


Figure 1. Daily series of new laboratory-confirmed COVID-19 cases and deaths in Mexico, from March 1- December 31, 2020

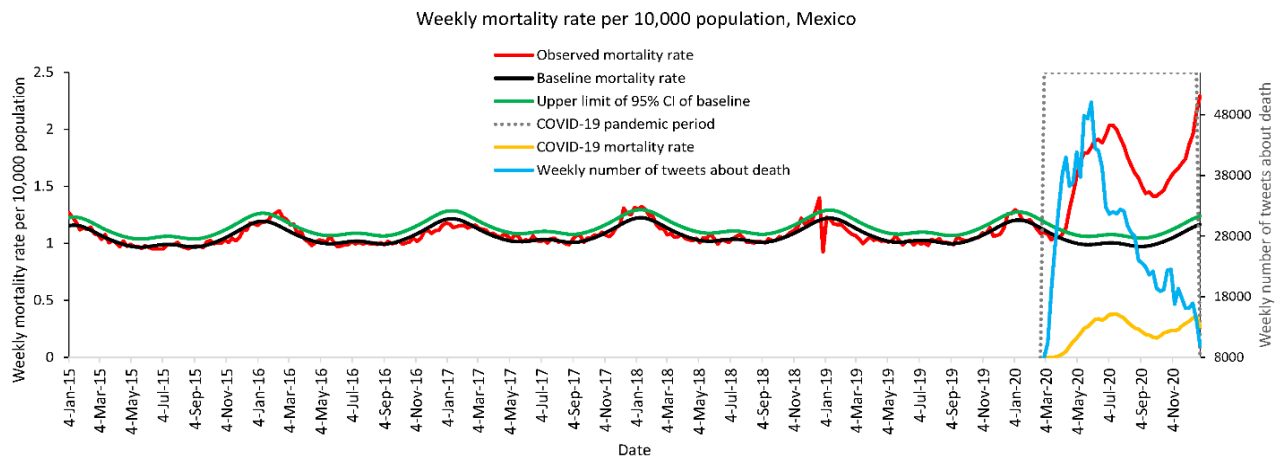


Figure 2. Mortality rate per 10,000 population, Mexico, 2015-2020. The red line is the weekly all-cause death rate. COVID-19 death rate curve is shown in orange color. Dotted lines highlight 2020 COVID-19 pandemic period. The Serfling seasonal regression model baseline (*black*

curve) and corresponding upper limit of the 95% confidence interval of the baseline (green curve) are also shown. The weekly frequency of tweets about death is shown by cyan curve. Excess all-cause mortality rate is the difference between the observed and model adjusted baseline mortality rates for each week where observed total all-cause mortality rate exceeded the upper 95% confidence limit of the baseline.

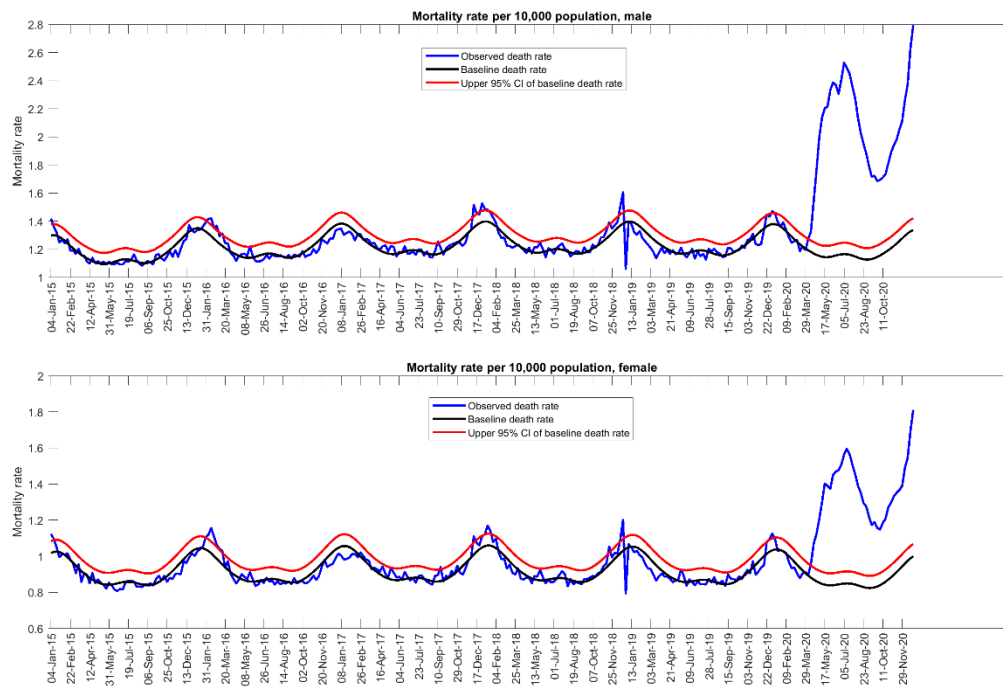


Figure 3. Mortality rate per 10,000 by gender, Mexico. Excess all-cause mortality rate is the difference between the observed and model adjusted baseline mortality rates for each week where observed total all-cause mortality rate exceeded the upper 95% confidence limit of the baseline in the country.

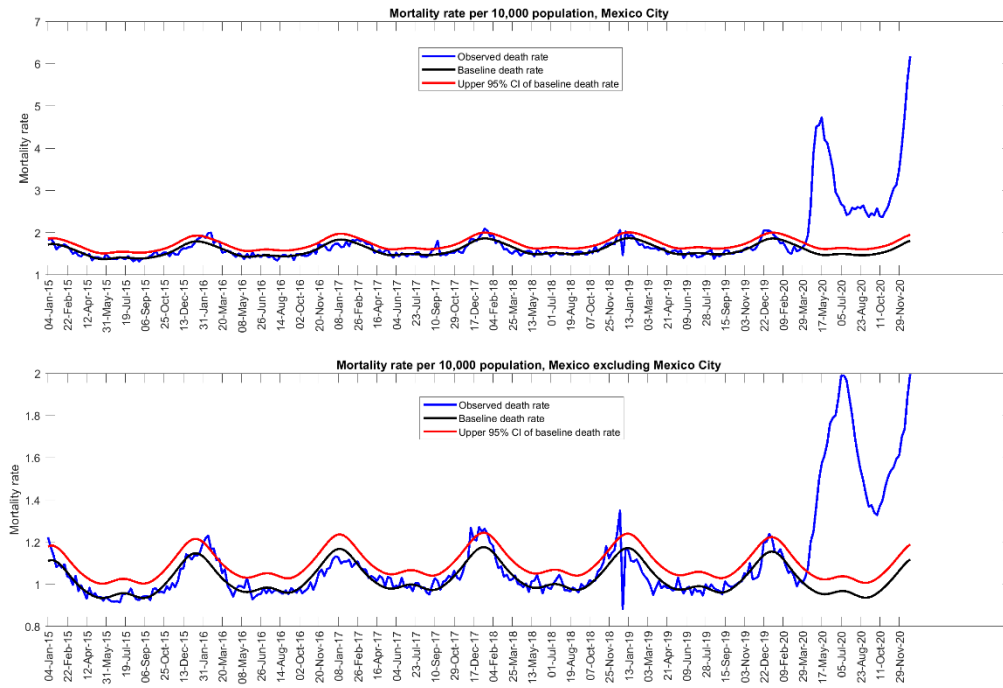


Figure 4. Mortality rate for Mexico City and Mexico excluding Mexico City. Excess all-cause mortality rate is the difference between the observed and model adjusted baseline mortality rates for each week where observed total all-cause mortality rate exceeded the upper 95% confidence limit of the baseline in the country.