COVID-19 Mortality Rates by Age and Gender:

Why Is the Disease Killing More Men than Women?

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Abstract

According to <u>New York State Department of Health</u>, around 60% of those in New York who died from COVID-19 were male. The <u>European Centre for Disease Prevention and Control</u> (ECDC) reported that the male-to-female ratio for COVID-19 deaths across the EU was 2.1. The U.K.'s <u>Office for National Statistics</u> (ONS) reported that rate of death due to COVID-19 for males was double that of the rate for females. For reasons that remain unclear, the novel coronavirus appears to present a significantly higher mortality risk to men than women.

In this paper we investigate how COVID-19 mortality risk differs between men and women across different age groups and different countries. A better understanding of the relationship between age, sex, and COVID-19 mortality, and how this differs by country, will help us to:

- Stratify COVID-19 mortality risk within a population
- Understand why there are differences in COVID-19 mortality rates among countries
- Understand how COVID-19 mortality risk for insured populations may differ from general population risk, due to differences in age and sex profiles

We extract publicly available age- and gender-stratified COVID-19 death data for Australia, Belgium, Germany, Italy, the Netherlands, South Korea, Spain, the U.K., and the U.S. Using these data, we explore COVID-19 mortality rates for males and females across different age segments and compare them with all-cause mortality rates taken from the Human Mortality Database.

We show that COVID-19 mortality rates differ by age and sex in the nine countries studied. The male-to-female differences in COVID-19 mortality rates were observed to be greater and have a bigger variation than the differences in all-cause mortality rates, although part of this may be due to low data volumes at some ages in some countries. COVID-19 mortality rates exponentially increase by age for both males and females. The male COVID-19 mortality rate is generally higher than the COVID-19 female mortality rate across all ages in the countries investigated. The age shape is broadly similar by sex within a country, although there were some notable differences between countries.

Finding, extracting, and analyzing COVID-19 deaths data

Publicly available data sources

The totals for COVID-19 reported deaths by sex and age were extracted from the following sources:

Country	Source	Date
Australia	Department of Health	29 Jun 2020
Belgium	Belgian Health Institute, Sciensano	27 Jun 2020
Germany	Robert Koch Institute	29 Jun 2020
Italy	EpiCentro, Italian National Institute of Health	23 Jun 2020
Netherlands	National Institute for Public Health and the Environment	29 Jun 2020
South Korea	Korea Centers for Disease Control and Prevention	28 Jun 2020
Spain	Ministry of Health, Consumer Affairs and Social Welfare	29 May 2020
U.K.	Office for National Statistics	19 Jun 2020
U.S.	Centers for Disease Control and Prevention	20 Jun 2020

It is important to note that what counts as a COVID-19 death differs by country. Most countries currently include only deaths in hospitals, although some countries may include deaths outside of the hospital setting and the definition may change over time. See the <u>Appendix</u> for a fuller discussion on the data limitations.





The date shown in the table is the date of the source report used for each country. Data were compiled on July 3, 2020. Age segments younger than 40 years were excluded due to lack of COVID-19 death data. Death data for Germany, the U.K., and the U.S. were smoothed into age segments of 10 years (assuming the counts followed a Weibull distribution by age).

The age- and sex-stratified population data for year 2020 were extracted from the <u>Department of Economic and</u> <u>Social Affairs, United Nations</u>. This was used to calculate the mortality rate of COVID-19 for each segment.

The male-to-female ratio of the COVID-19 mortality rate was compared to the corresponding male-to-female ratio of the population all-cause mortality rate. The age- and sex-stratified all-cause death and population data were extracted from the Human Mortality Database. This was used to calculate the all-cause mortality rate at the population level for each segment. The confidence interval was calculated using the delta method.

Calculating the mortality rate

The mortality rate (per 1,000 population) for each age segment, X, was calculated separately for males and females as follows:

Mortality rate (per 1,000 population) for X =

Total number of deaths in X Total population (in thousands) of X

Calculating the gender mortality ratio

The gender mortality ratio (GMR) for each age segment, X, was calculated as follows:

Gender mortality ratio for X = -

Male mortality rate for X Female mortality rate for X



COVID-19 mortality rates by age and gender from around the world

COVID-19 mortality rates

Figure 1 shows COVID-19 mortality rates per 1,000 population by age and sex in adults aged 40 years and older for the U.K., Belgium, Spain, the Netherlands, Italy, the U.S., Germany, South Korea, and Australia.

Figure 1: COVID-19 mortality rates per 1,000 population by age and gender in adults aged 40 years and older



Figure 2 presents the data in Figure 1 on the \log_{10} scale. Note the broadly similar shape of the lines representing the mortality rates for males and females within each country, demonstrating that mortality risk exponentially increases by age similarly for both men and women. However, there are differences between countries – for example, the difference in slope between males (solid lines) in Italy and the Netherlands indicates a variation in the mortality rates for those countries.







Figure 2: COVID-19 mortality rate per 1,000 population on the log scale by age and gender in adults aged 40 years and older

There are two observably distinct groupings: South Korea and Australia comprise a subgroup that exhibits lower overall mortality rate, while the U.K., Belgium, Spain, the Netherlands, Italy, the U.S., and Germany exhibit higher overall mortality rates.

Male mortality rates are consistently higher than female mortality rates across all age groups aged 50 and older, regardless of the overall level of mortality. The same holds true for ages 40 to 49 with the exception of the Netherlands, which may be due to low levels of data.

COVID-19 gender mortality ratios

The left side of Figure 3 shows the age-stratified gender mortality ratio (GMR) of COVID-19 mortality rates (solid lines), while the right side shows the all-cause mortality GMR (dashed lines). To better view and compare data from specific countries, we have split the data into three country groupings in Figures 4, 5, and 6. Four interesting features can be seen in Figure 3:

- The COVID-19 GMR is generally higher than the all-cause GMR, suggesting that there is a bigger sex differential in COVID-19 than in all-cause mortality.
- This sex differential differs by country see how the magnitude of COVID-19 GMR compared to all-cause GMR varies significantly by country.
- The all-cause GMR converges at ages 80+ to a ratio between 1.1 and 1.3, demonstrating a diminishing difference between male and female mortality rates at old ages. While the COVID-19 GMR exhibits convergence at ages 80+, the ratio is higher at between 1.2 and 1.9.
- South Korea and Spain have notably higher all-cause GMRs than the other countries.





Figure 3: COVID-19 (solid lines) and all-cause (dashed lines) GMRs by age in adults aged 40 years and older for nine countries







Figure 4 shows the COVID-19 and all-cause GMRs by age for Italy and Germany. The dashed lines and shaded regions represent 95% confidence intervals for each GMR. Italy and Germany have broadly similar all-cause GMRs. These two countries have the highest COVID-19 GMRs among the countries investigated, with male COVID-19 mortality 2.5 to 3.5 times that of females for all but the oldest age groups. Consequently, they also exhibit the largest gap between the COVID-19 GMR and the all-cause GMR – indeed, the sex difference for COVID-19 mortality is generally more than 2.0 times the sex difference seen in all-cause mortality.

Note the contrast in how Italy and Germany have experienced the pandemic so far. Some hospitals in Italy have been overwhelmed, with a high number of COVID-19 deaths, whereas COVID-19 mortality in Germany has been lower.

Figure 4: COVID-19 and all-cause GMRs by age in adults aged 40 years and older for Italy and Germany





Age Segment (Years)

Figure 5 shows the COVID-19 and all-cause GMRs by age for the U.K., the U.S., Spain, and the Netherlands. The U.K., the U.S., and the Netherlands have relatively flat all-cause GMRs around 1.5, and COVID 19 GMRs generally between 1.5 and 2.5. The difference compared to all-cause GMRs is broadly similar and relatively constant across ages and countries. The exception is the Netherlands at ages 40 to 49, for which there is less data. Spain is broadly similar but with some potentially important differences: Spain has higher all-cause and COVID-19 GMRs with more of an inverted U-shape by age.

Figure 5: COVID-19 and all-cause GMRs by age in adults aged 40 years and older for the U.K., the U.S., Spain, and the Netherlands



U.K. Gender Mortality Ratio





Netherlands Gender Mortality Ratio





Figure 6 shows the COVID-19 and all-cause GMRs by age for South Korea, Australia, and Belgium. South Korea shows the highest all-cause GMR out of all nine countries, meaning that it already has a bigger difference in male and female all-cause mortality compared to the other countries. In addition, unlike the countries discussed previously, the COVID-19 GMRs for South Korea, Australia, and Belgium are broadly similar in terms of both level and shape to the all-cause GMRs. However, South Korea and Australia have experienced relatively low levels of COVID-19 mortality throughout the pandemic so far, which is reflected in the wide confidence intervals, so the results should be treated with caution.

Figure 6: COVID-19 and all-cause GMRs by age in adults aged 40 years and older for South Korea, Australia, and Belgium





Belgium Gender Mortality Ratio



Discussion

This research report demonstrates how COVID-19 mortality rates differ by age and sex in nine countries. COVID-19 mortality exponentially increases by age for both males and females. The male COVID-19 mortality rate is generally higher than the female COVID-19 mortality rate across age segments in all countries. The age shape is broadly similar by sex within a country, although there are some differences between countries – for example, compare the mortality rates for males in Italy and the Netherlands.

Initially, smoking was thought to be one of the primary drivers of the sex difference in COVID-19 mortality risk. An elevated COVID-19 male death rate was first observed in data from China in February; a study of <u>44,672 confirmed</u> <u>cases</u> in Wuhan calculated the case fatality rate as 2.8% and 1.7% in men and women, respectively. Smoking prevalence in China is <u>52.1% among men and just 2.7% among women</u>. In Italy, however, smoking rates are much closer between men and women – 28% of men are smokers, while 19% of women are smokers. This suggests that while the difference in smoking rates by sex is expected to be a contributory factor, it is not the critical factor explaining an elevated male death rate.

The variation in COVID-19 mortality is likely to reflect both sex differences (understood to mean the biological factors we associate with a person's sex assigned at birth) and gender differences (taken to mean the combined effect of differences in social, political, legal, cultural, and economic norms). In terms of biological characteristics, it is well known that women produce stronger immune responses than men and are better at fighting off infection, including viral infection. The weaker male immune system leaves men more susceptible to a range of infectious diseases. One potential explanation is that sex hormones are involved in the way the immune system triggers an inflammatory response to pathogens. Some researchers think these differences may also explain why men have been hit harder by COVID-19.

The SARS-CoV-2 coronavirus is closely related to the virus that caused the 2003 SARS outbreak. In SARS, more women than men suffered from the disease, but an <u>analysis of all 1,755 cases in Hong Kong</u> showed that the case fatality rate was significantly higher for men – 22.3% of males with the disease died compared with 13.2% of females. It is possible that differences in smoking prevalence may have contributed to this. However, <u>research in mice infected</u> with the SARS virus concluded that male mice suffered higher mortality, suggesting sex differences in the immune response were in some way accountable.

Angiotensin-converting enzyme 2 (ACE2), the host cell receptor that the SARS-CoV-2 coronavirus uses to invade human cells, might play an important role in in COVID-19 survival. <u>Some researchers</u> suggest gender differences in ACE2 expression levels may explain why more men are dying of the disease. <u>Other researchers</u> have suggested that the occurrence of ACE2 on the X chromosome could also drive worse survival in men – having only a single copy of the gene can enhance the harmful effects of X-chromosome-linked diseases.

In the current pandemic, we also see a higher number of confirmed cases in females compared to males in many countries. The table on the following page is taken from <u>globalhealth5050.org</u>. In Canada and many European countries, around 40-50% of confirmed cases are male (which means more female cases than male, similar to the 2003 SARS outbreak), while 50-60% of deaths are male (implying a higher case fatality rate for males).

In contrast, countries such as Peru, China, Pakistan, and Indonesia have more male cases than female, suggesting the possibility of testing bias or social and cultural gender differences in infection rates by country that are compounding the mortality difference by sex.

Country	Total Number of Confirmed Cases	Confirmed Cases (% male)	Total Number of Deaths	Deaths (% male)	Date Reported
U.S.	2,239,121	NA	103,337	54%	17 Jun 2020
Peru	257,447	58%	8,223	71%	22 Jun 2020
Spain	248,335	43%	20,527	57%	21 May 2020
Italy	238,050	46%	33,209	58%	16 Jun 2020
England	228,742	43%	37,664	57%	17 Jun 2020
Germany	190,431	48%	8,880	55%	22 Jun 2020
Mexico	185,122	55%	22,584	66%	22 Jun 2020
Pakistan	185,034	74%	3,695	71%	22 Jun 2020
Bangladesh	115,786	71%	1,502	77%	23 Jun 2020
South Africa	105,308	43%	2,100	52%	23 Jun 2020
Canada	101,276	44%	8,412	46%	23 Jun 2020
Sweden	60,837	41%	5,161	55%	23 Jun 2020
Belgium	60,567	37%	7,016	51%	19 Jun 2020
China	55,924	51%	2,114	64%	28 Feb 2020
Netherlands	49,631	38%	6,095	55%	23 Jun 2020
Indonesia	47,896	53%	2,535	61%	23 Jun 2020
Argentina	42,785	51%	1,016	57%	22 Jun 2020
Columbia	40,719	55%	1,308	61%	08 Jun 2020

Table 1: Data on total confirmed cases, deaths, and percentage of totals that are male, by country

It is possible that behavioral differences as simple as compliance with handwashing advice could also play a part in infection rates.



In this report, we compared COVID-19 GMRs against all-cause GMRs to determine if the sex difference in COVID-19 mortality is greater than in all-cause mortality. The sex difference in COVID-19 mortality was observed to be greater and to have a bigger variation than the sex difference in all-cause mortality, although part of this may be due to low data volumes at some ages in some countries.

At ages 80 and older, where COVID-19 death data is relatively more abundant and hence more credible, we saw some level of convergence in COVID-19 GMRs across countries, at around 1.2 to 1.9. This is slightly higher than the level at which the all-cause GMRs converge (1.1 to 1.3).

We split results into country groupings; the GMR results are summarized below. South Korea and Australia have low data volumes, so their results should be treated with caution.

Countries	Ratio of male to female COVID-19 mortality	Comparing COVID-19 GMRs to all-cause GMRs	
Italy, Germany	2.5-3.5x	2.0x	
U.K., U.S., Spain, Netherlands	Around 2.0x	1.3x	
South Korea, Australia, Belgium	1.5-3.0x	Similar	

Trends in COVID-19 mortality rates will change as the pandemic progresses, due to such factors as relaxation of mitigation measures and other government strategies. RGA continues to monitor the emerging data. The varying COVID-19 mortality rates by age, gender, and country illustrated in this paper also reflect differences in population health, lifestyle behaviors, and sociodemographic factors, as well as government policies. We hope to include other stratifiers of risk in future reports if the data are available.

A number of research studies have started to explore multivariable associations with COVID-19 mortality. For example, in a U.K. study, male sex remained a significant predictor for risk of dying from COVID-19 (hazard ratio equal to 1.99, which is remarkably similar to what we observe) after controlling for age, BMI, smoking, ethnicity, socioeconomic status, and underlying health conditions. Other research, also based on multivariable models of risk, has demonstrated higher mortality risk for males in U.K. hospitals. In addition, recent research suggests that susceptibility to SARS-CoV-2 infection is also dependent on sex, with men having an odds ratio of approximately 1.55 compared to women.

RGA's Global Data and Analytics associates are continually investigating COVID-19's infection rate, case fatality rate, and mortality rate, as well as other COVID-19 research questions. Please <u>contact us</u> for more information.



Appendix

Limitations

There are a number of limitations associated with our analysis.

1. Limitations of death reporting data

Countries report COVID-19 deaths differently, and the definitions used may also change over time. In Italy, for example, a COVID-19 death is defined as the hospitalized death of someone who tested positive for SARS-CoV-2, regardless of whether they had underlying illnesses that could have independently led to death.

In contrast, in the U.K., the ONS-reported deaths are based on mentions of COVID-19 on death certificates, whether it was the main cause or an underlying factor. ONS figures include nursing homes, at-home deaths, and any other place of death, and the deceased does not have to have tested positive for coronavirus for inclusion.

Death reporting is also affected by the following considerations:

- Any COVID-19-related deaths that occur outside of a hospital setting may not be included in official statistics (i.e., an under-reporting of COVID-19 deaths).
- Patients dying with COVID-19 are deemed to be dying from the disease (i.e., an over-reporting of COVID-19 deaths).
- Asymptomatic people with mild clinical symptoms may not be tested for the coronavirus (i.e., an underreporting of COVID-19 deaths).
- There can be delays in death reporting.
- 2. Uncertainty where data volume is low

Some countries have low death counts (for example, Germany and South Korea) at the time of data collection, particularly at younger age segments. Hence, the best estimates produced from the data are of high uncertainty, which could be compounded when taking a ratio (the GMR) of the two proportions. This will occur where death counts are low in both sexes. We attempted to illustrate these uncertainties using confidence intervals.

3. Aggregated data

Different countries report their data in different age groups, and some are more granular than others. Larger groupings may introduce more uncertainty and make comparisons challenging. For example, the underlying distribution of ages in each 10-year age group may not be consistent across countries between COVID-19 and all-cause mortality and between males and females, and this could explain some of the variations in the GMRs.

4. Care homes

Deaths due to COVID-19 in care homes are typically not included in reported COVID-19 death data, although they may be for some countries. The very old and frail could be dying in care homes soon after infection before being admitted to a hospital. As a result, the all-cause mortality data and the COVID-19 death data will have different age profiles. Moreover, care homes could have a different male and female pattern. If that is the case, it could lead to gender bias in reporting of deaths and could affect the gender ratio of mortality.

5. Development with time

COVID-19 reported data captures a specific point in time and covers only a short period. COVID-19 deaths will continue to increase; therefore, the age and gender pattern will continue to develop. In contrast, the all-cause GMRs that we are comparing against are for a full calendar year.

6. Heterogeneity among countries

Gender differences in mortality rates among the countries studied for this report could be confounded by differences in social, economic, legal, cultural, and political factors.

