Trends in Cumulative Incidence and Case Fatality Of COVID-19 In the United States: Extreme Epidemiologic Response

Laurens Holmes, Jr, MD, DrPH*, Glen Philipcien, MD; Keerti Deepika, MD, Chinacherem Chinaka, MPH, Prachi Chavan, MD, PhD, Janille Williams, MPH; Benjamin Ogundele,MPH, Kirk Dabney, MD, MHCDS, Maura Poleon, BSN, RN, DPN (c); Lavisha Pelaez, MPH, Tatiana Picolli, MD,MPH, Valescia John, PhD, MS, Leslie Stalnaker, MPH, Michael Enwere, Ph.D.

***Affiliation**:* Translational Health Disparities Science Research Connectome, Wilmington, DE 19803 (Virtual Collaborative Connectome). *This connectome is directed by Professor Laurens Holmes, Jr., Immunology, Infectious Disease & Epidemiology Translationist, Head & Founding Director, Nemours Healthcare System for Children Translational Health Disparities Science Fellowship Program

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***Correspondence*:** Dr. Michael Enwere. Nemours Children's Healthcare System. email; mikky89@gmail.com. twitter.com/mickky89

ABSTRACT

OBJECTIVES - COVID-19, a respiratory disease caused by SARS-COV2 and transmitted from person-to-person through viral droplets remains a global pandemic. There is a need to understand the transmission modes, populations at risk, and how to mitigate the spread and case fatality in the United States (US) and globally. The current study aimed to assess the global COVID-19 transmission and case fatality, examine similar parameters by countries and determine evidence-based practice in extreme epidemiology response in epidemic curve flattening and case fatality reduction.

METHODS - A cross-sectional ecologic design was used to assess the preexisting data on confirmed COVID-19 cases and mortality in March 2020 from the CDC, WHO, Worldodomter, and STATISTA. A rapid assessment between March 23rd and 31st, 2020, was utilized for the extreme epidemiology response. The case fatality, termed fatality proportion, was examined using mortality in relation to confirmed cases involving the world, United States of America (USA), United Kingdom (UK), Italy, France, Spain, China, Germany, India and South Korea.

RESULTS - The COVID-19 is a global pandemic, with the US as the epicenter for transmission, representing 20.9% of all confirmed cases worldwide, while Italy is the epicenter for case fatality, 30.6% of mortality as at 03/31/ 2020. The fatality proportion (FP) in Italy was 11.4%, Spain (8.8%), France (6.8%) and UK (6.4%). Despite the increased number of confirmed cases, the lowest FP was observed in Germany (0.96%) and South Korea (1.66%). There is increasing linear tends in transmission in the US, R^2=0.97 as well as positive daily percentage change, ranging from 1.27% to 20.5%.

CONCLUSION - The USA remains the epicenter for COVID-19 transmission, while Italy is the epicenter for case fatality. The observed relatively low case fatality in Germany and South Korea

is due to an “extreme epidemiology” response through the application of Wuhan, China’s early data on COVID-19 transmission control measures and optimized patient care. These data are suggestive of relaxing the clinical guidelines in the United States in COVID-19 testing, application of contact tracing and testing, case isolation and most importantly enhancing resources for case management and social and physical distancing globally, hence epidemic curve flattening and case fatality reduction.

KEY WORDS - COVID-19; SARS-CoV2; Extreme Epidemiology Response; Population at Risk, Case Fatality.

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Introduction

"Et causae quoque estimatio saepe morbum solvit", implying that the knowledge of the underlying cause of a disease often leads to the remedy, Celsus, A.D., 25.

The SARS-CoV2, the causative pathogen in COVID-19, remains a global pandemic, suggestive of a reliable scientific control and preventive measures response in flattening the epidemic curve and mitigating case fatality [1]. The utilization of what is scientifically understood about the risk of transmission, incubation period, clinical manifestations, management, and control, is needed now more than ever before in flattening the epidemic curve nationally and globally.

Epidemiologic data reflects a transition from infectious disease as the leading cause of death in the 1900s to chronic disease, namely Cardiovascular diseases (CVDs) in the current era. [2]. This scientific experience provided substantial data to epidemiology on infectious disease modeling in terms of transmission, incubation period, subclinical disease, the period of infectivity, prognosis, and fatality [3]. Additionally, epidemiologic approaches to infectious disease observed in the epidemic curve, which could be due to excess fatality or transmission containment and mitigation through intense screening and pathogen detection.

The coronavirus, also known as COVID-19, a single-stranded RNA enveloped virus that enters the lungs via droplets and binds to Angiotensin-Converting Enzyme-2 (ACE-2) on Type 2 pneumocytes for cell entry is a particular antigenic type of coronavirus-disease causing pathogen, discovered in 2019, which remains pandemic. [4]. This microbe is an intracellular pathogen, meaning that it requires the host cells (humans in this case) in order to replicate and continue to survive.[1] The fatality proportion/prevalence, and not rate in the second week in March was estimated at 1.5%, lower than the estimate of 5.2% in late February and early March, due to the limited capacity in case detection which has moderately improved lately, with

still more to be accomplished in the screening process. The global fatality prevalence was 4.2%, which was due to the experience of 475 mortality in Italy despite the accelerated screening and preventive modalities in lowering the curve [5, 6].

This microbe is transmitted from person-to-person as a community-acquired pathogen. The mode of transmission includes viral droplets from the nose, eyes, and mouth, with the droplet being able to survive on several surfaces over 24 hours. Individuals who are infected with this microbe may transmit the virus to others even though such individuals do not manifest any symptoms. Such carriers are termed asymptomatic [7, 8].

The manifestations of COVID-19 include dry and productive cough, fever, sneezing, shortness of breath, tiredness as decreased vitality, and lower respiratory tract colonization, including pneumonia [9]. Fever is a protective mechanism for the host in order to limit pathogen replication [10]. Early laboratory reports on patients having fever and confusion admitted to intensive care units revealed Hyperferritinemia, lymphopenia, elevated IL-6, C-reactive protein, and soluble CD25. These laboratory data are indicative of Cytokine Storm Syndrome (CSS). CSS often results in acute respiratory distress syndrome (ARDS) and multi-organ failure leading to increased fatality [11]. However, individuals could be infected with this virus without fever manifestation, especially if such individuals are immuno-incompetent, implying a compromised immune system response. The history of infectious disease is indicative of the limited clinically benefits of antipyretic to treat the fever of an infection. However, fever could be regulated in avoiding seizure, especially in children by low/moderate application of antipyretics, such as Paracetamol [12]. Specifically, the role of fever in infection is to protect the host by limiting viral replication via pathogenic transcriptome denaturation. The excessive use of antipyretic, for example in the context of a novel pathogen within the community without antibodies to the

pathogen, is indicative of excessive viral replication and the inability of human interferon-gamma (INF-γ) to protect the non-infected human cells against the virally infected cells, and the subsequent cellular dysfunction and extreme community fatality [13]. This serves in part to explain the fever dysregulation in increased coronavirus fatality observed in Italy. Therefore, when the immune system is compromised, there remains an increased risk of infection and mortality, requiring the immune system potentiation in epidemic curve flattening.

With the current COVID-19 pandemic, there is a need to understand the transmission modes, populations at risk, and how to mitigate the spread and increase of case fatality in the US and globally. The current rapid extreme epidemiology response aimed to : (a) examine the frequency of confirmed COVID-19 cases globally and by countries, (b) assess the frequency of deaths due to COVID-19 , (c) determine the case fatality, (d) provide a possible explanation of the epicenter of spread and case fatality, and (e) to apply extreme epidemiologic scientific data for recommendation in COVID-19 epidemic curve flattening and case fatality reduction, especially in the United States of America.

Material and Methods

Design: Rapid assessment of data from reliable sources on COVID-19 confirmed cases, mortality and recovery using a cross-sectional ecological non-experimental epidemiologic design.

Study population and sample: The study sample comprises world population and selected populations characterized by pandemics in terms of transmission and case fatality. These countries include the UK, USA, France, Italy, Spain, Germany, India, China and South Korea.

Data sources: Online data from Statista, CDC, WHO, and Worldometers were assessed for several cases and deaths. These data sources were examined for accuracy while considering selection bias in their data gathering process.

COVID -19 Clinical features and population risk characterization: The early scientific data on this pathogenic microbe indicates the followings based on the experience in different geographic locale globally:

(a) SARS-CoV2 is a highly contagious single pathogen in COVID-19 and is transmittable without symptoms manifestation from an infected individual, clinically termed carrier or asymptomatic [1, 14].

(b) Genetically, SARS-CoV2 is a single-stranded enveloped RNA virus with a specialized means of gene expression for its genomic stability and proliferation.

   a. Unlike its previous antigenic type or variants, the SARS-CoV2 RNA transcriptome is very pathogenic and highly virulent, meaning an extremely contagious and disease-causing pathogenic microbe.

(c) The incubation period (subclinical stage) ranges between 7 to 14 days and depends on the host immune response.

(d) COVID-19 is transmitted from person-to-person and from animal-to-person and vice versa.

(e) This transmissibility involves eye, nose, and mouth contact with the viral droplets if the suspected or confirmed COVID-19 case coughs or sneezes. Other manifestations include fever, tiredness, difficulty breathing, and pneumonia-like symptoms [15].

(f) ***Risk differentials and populations at higher risk***:

a. Elderly with comorbidities. In the United States, based on the available geriatric data, 76.3 million adults are 60 years of age or older, and are at a higher risk of developing severe illness if infected with COVID-19. Among the 76.3 million adults 60 years of age or older, 41.2 million individuals have an underlying medical condition that has a higher risk of developing a severe illness if infected with COVID-19 and nearly 47.3% adults are 80 years of age or older [16]. An estimated 1.3 to 1.5 million individuals reside in nursing home facilities across the United States, and many residents in nursing homes have chronic medical conditions and will be at risk of serious ill-health if they contract COVID-19. Approximately 16% to 18% of nursing home residents have received respiratory treatment for underlying respiratory illness. Most of the nursing homes have reported a deficiency in Infection control protocol. Resident density will impact on the spread of the Virus in a facility. The Virulence and increased incidence of COVID-19 in elderly individuals can also be at risk of transmitting the infection to vulnerable populations. High incidence of nosocomial transmission of COVID-19 in Long Term Care facilities in geriatric patients as Healthcare-associated amplification of transmission is of concern in emerging infections [17].

b. Males, transmission, and even with similar prevalence of infection, mortality remains higher among males [18].
c. Individuals with chronic diseases such as hypertension, type 2 diabetes, asthma, COPD, cancer patients on chemotherapy [19].
d. Organ transplants patients on immuno-suppressants
    i. Bone marrow transplant patients on immuno-suppressants
e. Individuals with compromised immune systems including autoimmune disorders [1].
f. Children and young adults with chronic diseases such as asthma [19].
g. Pregnancy, especially late maternal age
h. Malnourished children with food insecurity
i. Individuals (young adults and elderly) with psychosocial stress, implying an impaired immune response
j. Socially disadvantaged individuals with low socioeconomic status
k. Alcoholics and substance users/abusers, including smoking and vaping [19].
l. History of recent travel to a location with a high incidence of SARS-CoV-2 can be of high significance and also close contact with persons who have a history of travel or laboratory-confirmed COVID-19 within 14 days of symptom onset.

Statistical Analysis: We estimated the fatality proportion using the number of death/confirmed cases, multiplied by 100 (Fatality Percentage (%) or proportion). Line graphs and bar diagrams were used to illustrate the case fatalities and transmission.

Case Fatality Modeling: To determine the daily percent change (DPC) in case fatality modeling for upward (positive) or downward (negative) trend, we utilized the formula D2-D1/D1*100, implying case fatality in the end result or End Result Case Fatality (ERCF) or (D2) – Baseline Case Fatality (BCF) or D1/BCF * 100.

Results

The reliable sources consulted during the last week in March, (23rd -31st) reflected a global public health emergency and urgent need to flatten the epidemic curve in narrowing the unexpected outcomes of excess universal mortality and decreasing survival with COVID-19. With failure to adhere pandemic epidemic curve flattening evidence-based practice data, as in flu pandemics in 1918, such inadequacies result in the world's population reduction and the long-term effect associated with the economic crisis of COVID-19. The March 28, 2020 fatality prevalence or proportion, not rates were: Global (4.65%), USA (1.72%), UK (5.96%), Italy (10.56%), Spain (7.82%), China (4.03%), India (2.21%), Germany (0.5%), South Korea (1.50%) and France (6.05%) (**Figure I**). An increasing positive trend was observed on 03/31/20) for COVID pandemic , with increasing FP globally and in all the countries, Global (4.81%), USA (2.00%), UK (6.40%), Italy (11.40%), Spain (8.80%), China (4.10%), India (2.80%), Germany (0.96%) and France (6.16%) and South Korea (1.66%). (**Figures II and III**).

The current (March 31st, 2020) lowest fatality rate observed in Germany (0.96%) among the European countries and in South Korea (1.66%) is primarily due to "extreme epidemiology" response through the application of Wuhan, China early data on COVID-19 transmission control measures and the effectiveness of the healthcare system in the application of the resources (ventilators, trained healthcare providers, negative pressure rooms, decontaminants, personal protective equipment (PPE)) and adherence to the infectious disease protocol. [20, 21]. The US fatality proportion (FP) continues to increase due to improvement in screening and case detection, which is indicative of differential application of the strategies in Germany and South Korea, in mitigating COVID-19 pandemic.

The US weekly FP observed this distribution estimates for the 03/23 to 03/31, M (1.10%), T (1.24%), W (1.30%), Th (1.58%), F (1.50%), S(1.63%), SU (1.80%), M2 (1.84%) and T2 (2.0%),(**Figure IV**). The daily percentage change (DPC) is illustrated in **figure V**, and ranges from 1.27% to 21.5%. There is an increasing linear trend, indicative of 97% changes in the daily confirmed cases as a result of COVID-19 spread in the US with time. The observed linear trends and the positive daily percentage change are indicating of the increasing peak in COVID-19 case confirmation. The case fatality modeling in these US confirmed cases and mortality indicated a significant positive linear trend, implying that for every additional 24 hours during the last week of March 2020, there was 0.11 percent increased risk of case fatality. (**Figure V**) As per March 31st, 2020, the US represented 20.9% of all confirmed COVID-19 cases globally (**Figures VI)**, the highest cases and COVID-19 epicenter, but 7.8% of the global fatality, relative to Italy with the highest global fatality proportion, 30.6%.

Discussion

With the restricted guidelines in the US testing strategies, the epidemic curve flattening will be challenging to achieve, requiring the relaxing of the clinical criteria on infectious disease diagnosis, and adopting the testing criteria in pandemic or epidemic to include any suspected cases and individuals concerned with exposure to COVID-19. This study reflects a rapid response to the current COVID global pandemic in addressing the epidemic curve flattening and case fatality reduction. We used data from reliable sources to assess the fatality proportion globally and in selected countries with the United States (US) as the epicenter for transmission. Using the cross-sectional ecologic non-experimental epidemiological design, we observed transmission and case fatality patterns and provided possible explanations of the transmission and case fatality differentials. There are a few relevant findings from this assessment. Firstly, the United States represents a geographic locale with the highest COVID-19 confirmed cases. Secondly, the fatality proportion in terms of case fatality was the highest today in Italy. Thirdly, the lowest fatality rate in Europe was observed in Germany, while South Korea represented the lowest fatality prevalence or proportion in Asia as per today [22]. Fourthly, on average, the transmission is higher among males, while mortality regardless of geographic locale is higher among males.

We have illustrated that COVID-19 transmission is highest in the USA as a global epicenter. The observed excess transmission of COVID-19 in this geographic locale may be due to the inability of the US healthcare system and public health to have initiated appropriate screening for individuals suspected of COVID-19 based on the respiratory symptoms, limited testing kits, and the healthcare system's unpreparedness, as well as limited US public health response to this

pandemic. The contrast in screening and contact tracing was observed in South Korea and Germany, where screening was based on the Chinese model and their healthcare capability with respect to healthcare providers' preparedness, testing kits, Personal Protective Equipment (PPE) appropriate application in donning and doffing, decontaminants, negative pressure rooms, and protected triage and patient area. We project more severe case confirmation, increasing case fatality in the US due to early delays in screening and case detection, as well as the inability to address contact tracing and testing.

This rapid extreme epidemiology response was observed in Italy with the highest case fatality in Europe and globally [23]. The case fatality, which is dependent on COVID-19 survival reflects the healthcare system and public health disaster and emergency preparedness. The possible explanation for the decreased survival from COVID-19 may be due to the aging population with comorbidities and hence impaired immune responsiveness. Secondly, the rapid increase in COVID-19 case confirmation and hospitalization resulted in an extreme lack of resources in terms of ventilators, respirators, and negative pressure rooms as well as PPE. Also, applicable in COVID-19 is a lifestyle in terms of alcohol consumption, smoking, and dietary requirements for healthy living and health maintenance. These lifestyle choices adversely impact natural cell killers (NKC), interferon-gamma (IFN-γ), T-lymphocytes (CD4, CD8), neutrophils, and monocytes' response to pathogenic microbes [24, 25].

We have demonstrated low case fatalities in South Korea and Germany despite increased confirmed cases. The ability to lower mortality in an epidemic or pandemic depends on adherence to the infectious disease control protocol such as hand hygiene, and the donning and

doffing of PPE by those responsible for providing care to patients in a closed environment. The available data observed appropriate COVID-19 disaster and emergency preparedness by the German and South Korean healthcare providers and the healthcare resources. In addressing pandemics adequately, the public health response of any nation must apply scientific data, which is not absolute in terms of accuracy but reliable in flattening the epidemic curve and reducing case fatality. It is also feasible to implicate the role played by the healthcare systems, besides resources in providing preventive health services for an individual's health maintenance and optimal health.

Males relative to females have been observed in this COVID-19 epidemic and pandemic to have a higher incidence of transmission and case fatality. The observed survival disadvantage of males might be due to a healthy lifestyle such as nutrition and routine health checks by females relative to males. Females, compared to males, may also focus on scheduled exercise more than males. These two health attributes tend to enhance the innate and adaptive or specific immune response to inflammation and pathogenic microbes. Relative to individuals with an unbalanced or unhealthy diet, a healthy diet has been illustrated inadequate immunoglobulin (antibodies) response to an antigen, cytokine response, and T-cell activation via IL-1 elaboration from an activated macrophage in the innate immune response [26]. Specifically, moderate and intense exercise had been observed in cytokines elaboration for B-cell growth factors involved in antibodies production. Regular physical activities compared to acute phase response result in the activation of colony-stimulating factors (CSF), leading to neutrophil proliferation and innate and non-adaptive immune response [27]. Also related to physical activities is the influx of natural

killer cells (NKC) and T lymphocytes in the blood, providing an adaptive immune response to a presented antigen, including viral pathogens.

Epidemic Curve Flattening and Case Fatality Mitigation

The extreme epidemiology concept reflects the mobilization of applied epidemiologic principles and concepts in public health disaster and emergency, implying the exploration of rapid/real-time data and evidence-based-practice via quantitative evidence syntheses (QES) and pre-existing data analysis in flattening the epidemic curve of the outbreak, acute and chronic mass conditions, accidents, endemics, and pandemics [28]. This approach allows for empirical strategies in addressing global pandemics, such as COVID-19 in infectivity modeling, epidemic curve flattening, and case fatality mitigation [3]. The history of viral replication in infectious diseases indicates an epidemic curve with or without an intense response. However, flattening the curve in a timely manner reduces the case fatality.

The extreme epidemiologic response today in epidemic curve flattening unequivocally recommends:

- **Testing of all individuals** with clinical manifestations (signs and symptoms) of respiratory infections (cough, sneezing, fever, tiredness, and shortness of breath)
    - Rapid/quick and accurate testing with instant result, resulting in case identification, detection, and isolation (IDI)
- ***SARS-COV2 antibodies test rapid development and utilization for detection and identification of individuals with COVID-19 antibodies, a protective mechanism against re-infection.***
- **Rapid vaccine development**, and time-sensitive clinical trial to phase III

- *Utilization of* ***Investigational Drugs (ID)*** especially in cases with underling conditions (diabetes hypertension, cardiac disorders, etc.)
- *Increased access to ventilators for patients with breathing difficulties for ventilation and ABC achievement, and increased survival.*
- **Contact tracing and testing** of all contacts with or without signs and symptoms of COVID-19.
- ***Social and physical distancing ranging from 6 to 10 feet in reducing the viral spread.***
    - Using modern information technology (iPad, iPhone, e-mails, FaceTime, Zoom, Skype) to interact with family members as a support system and interpersonal relationships to address social distancing adverse psychological effects
- Rigorous ***immune system potentiation*** for all humans globally through planned and scheduled **robust fruit and vegetables consumption** as well as hydration (water and water plus electrolytes)
- ***Microbiome diversity*** through low fat diet, fruits, vegetables and physical activities for inhibition of viral replication, implying the pathogenic microbe's inability the compromise the innate and specific immune system for infectivity.
- Scheduled and planned **daily physical activities** such as walking, jogging, and biking around a safe neighborhood with a distance of 6 to 10 feet during this daily routine.
    - Avoiding public gym until the COVID-19 epidemic curve flattens
- An **adequate amount of sleep** (not less than 7 and half hours) with 5 to 6 hours spent at non-REM sleep (stages 3 and 4) based on the onset of sleep with respect to circadian rhythm

- Utilization of **facemask for infected individuals** (suspected and confirmed cases as well as patients under investigation) to reduce the spread of this novel virus to unexposed community members
- ***Working remotely during this period in enhancing social and physical distancing.***
- *Adherence to healthcare systems and public health departments such as CDC, WHO recommendations in spread mitigation, as well as the Law Enforcement regulations on community physical distancing*
- Adherence to **infectious disease control protocol** by the healthcare system and public health departments
- *Training and education of healthcare providers on **hand hygiene** and **PEE** application inpatient care as well as the availability of resources in providing care to COVID-19 patients with severe respiratory symptoms in red icing case fatality*.

In ensuring a mitigated exposure and infection of healthcare providers in a healthcare system setting, the COVID-19, case detection, control and prevention taskforce guidelines must be utilized and should reflect: (1) facility decontaminants in reducing pathogens within the healthcare facility

(2) rapid isolation of, symptomatic, suspected and confirmed cases, and (3) healthcare professionals protection from COVID-19 transmission. In mitigating the microbe spread in terms of nosocomial viral infection, healthcare facilities should consider limiting the number of elective procedures or surgeries and reducing the number of entrances to the hospital facility as well as ensuring that patients and visitors such as patients care givers or families are screened for respiratory symptoms. The flow of patients to the hospital could be reduced by the hospital

considering the application of telehealth and telemedicine in providing care to patients. Secondly, the healthcare facilities should initiate a properly ventilated triage environment, provide suspected or confirmed cases negative pressure room if feasible or closed private rooms with bath and aerosol-generating procedure (AGP) such as sputum induction, should be performed in Airborne Infection Isolation Room (AIIR). Thirdly, and highly relevant to such guidelines is the healthcare professionals protection involving limited contacts with patient at triage and confirmed COVID-19 patients rooms and areas of care, rigorous hand hygiene, personal protective equipment (PPE) standard implementation as well as limiting the numbers of healthcare professionals delivering care to COVID-19 cases and prioritization of respirators and AIIR for AGP.

This rapid extreme epidemiology response to COVID-19 offers reliable and timely data in transmission and fatality by geographic locale. While the recommendation to epidemic curve flattening and case fatality reduction is adequate and appropriate in this public health emergency, there are some limitations. Firstly, this study is based on aggregate data with a tendency for an ecological fallacy. However, it is highly unlikely that these findings are solely driven by this fallacy, implying individual case level inference, although aggregate data utilization in descriptive epidemiologic generalizability. Secondly, we observed a low fatality proportion in India, which may be due to low case detection, isolation, and hospitalization, but we are unable to provide a reliable explanation. Therefore, given the aggregate nature of these data, caution is required in the interpretation and application of these case fatality estimates, since the exact denominator remains unknown in pandemics as it is challenging to have all data on the confirmed cases at the time of mortality data access and availability.

Conclusion

In summary, COVID-19 remains pandemic, with the United States as the current epicenter in terms of spread, while Italy remains the epicenter for case fatality. The observed transmission and case fatality pandemic require an Extreme Epidemiology Response (EER) to flatten the epidemic curve and case fatality reduction. Relative to emergency department (ED) response to an emergency and the emergence of extreme medicine from ED experience, extreme epidemiology (EE) is indicative of the need for the global initiative, especially the US healthcare system and public health department to apply the available scientific data on COVID-19 transmission and case fatality, as well as adherence to the infectious disease control protocol (hands hygiene, PPE donning and doffing, negative pressure rooms, ventilators, and COVID-19 patient care room and treatment areas requirements), intense case detection and contact tracing and testing as well as social and physical distancing. The inability to do so will not only prolong the epidemic curve flattening but will expand the economic crisis related to COVID-19 spread, and hence population exponential expansion of socially disadvantaged individuals (low SES), increasing health disparities nationally and globally, adversely impacting world health. Specifically, the COVID-19 transmission, if not addressed based on the available scientific data, will increase the US health data pool on health disparities, given the implication of social determinants of health in epidemics and pandemics.

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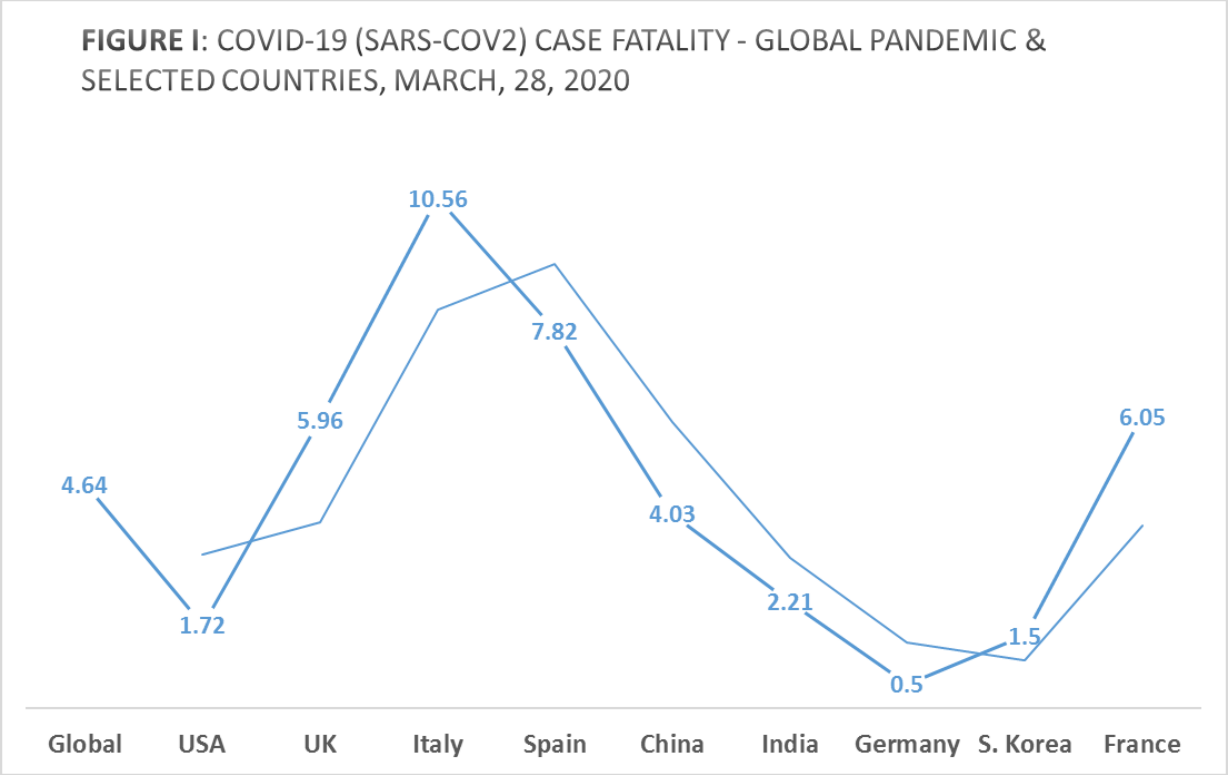
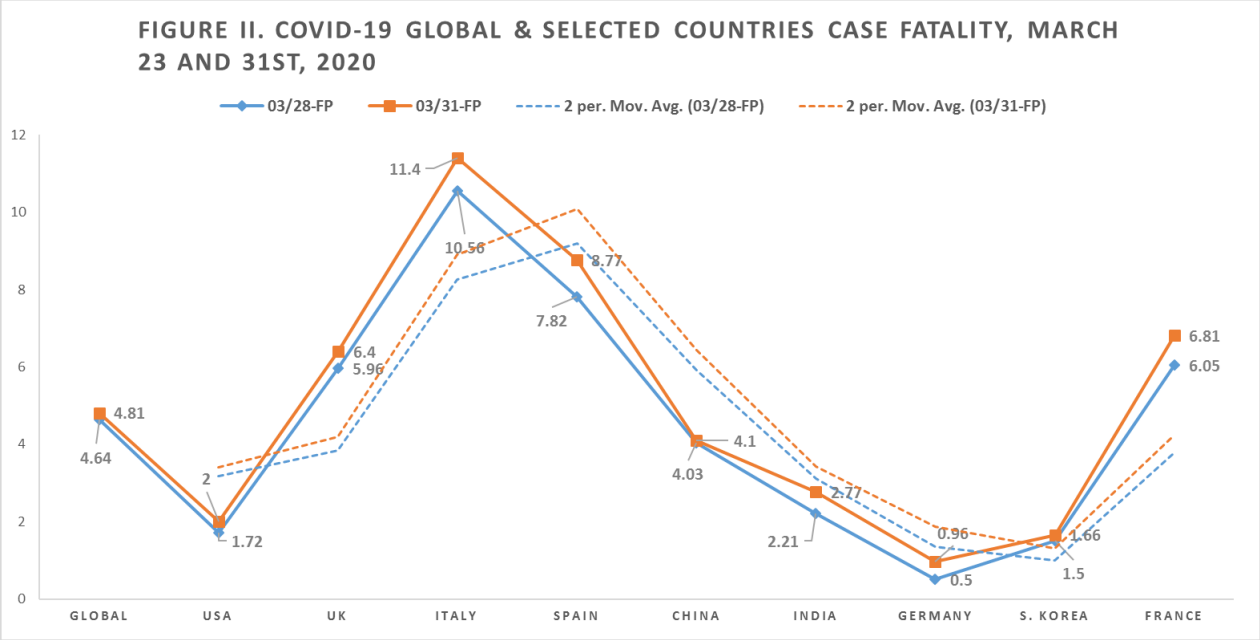
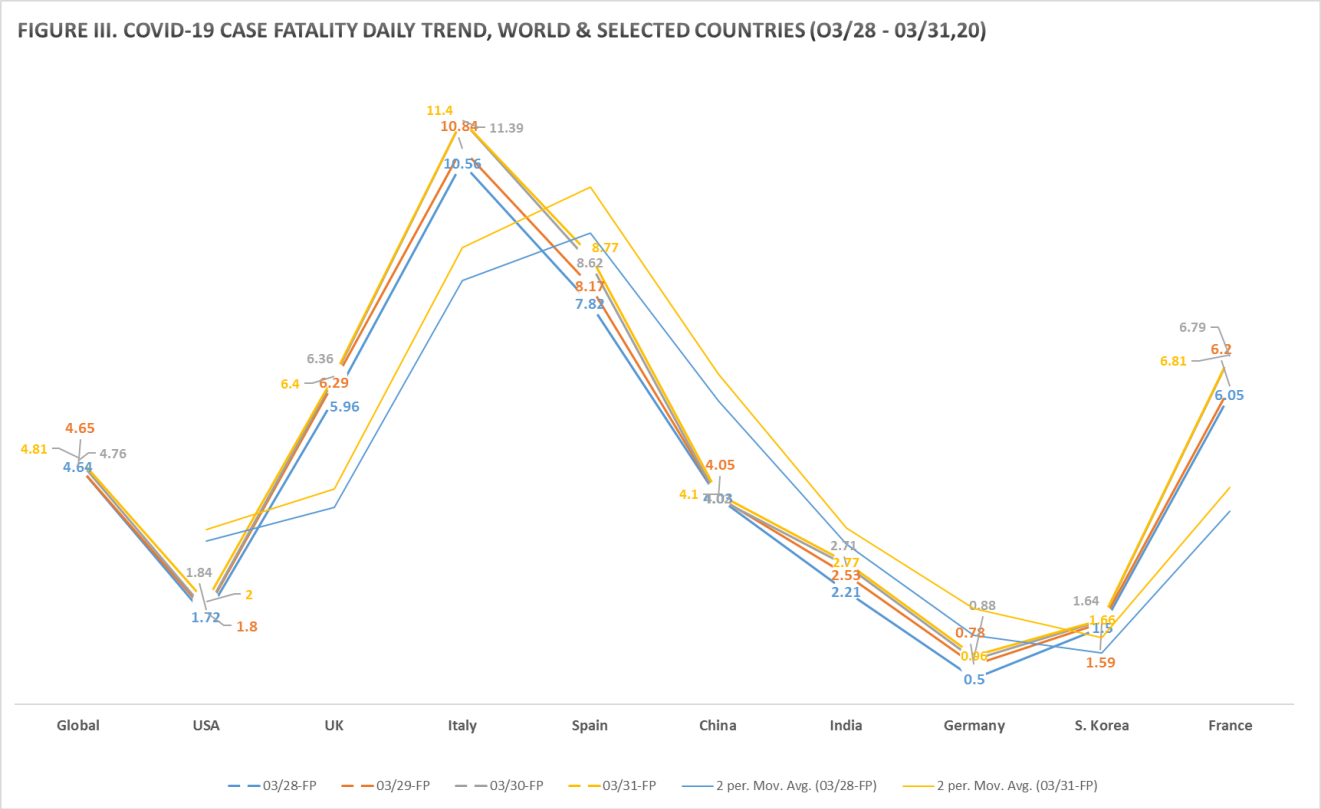


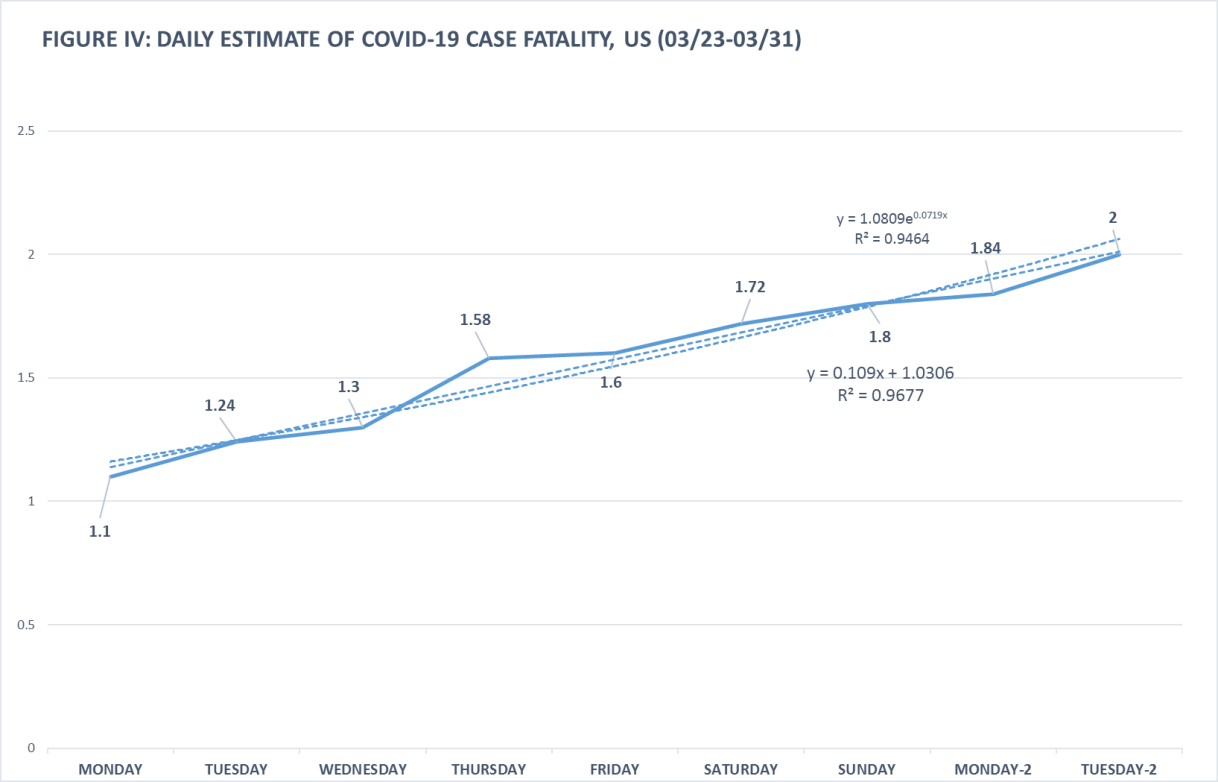
Notes: *COVID-19 illustrates an upward case fatality trends, implying survival disadvantage across the world following this novel viral infection. Italy exhibits the highest case fatality in fatality proportion (FP), implying the nation with the poorest survival, while Germany illustrates survival advantage from COVID-19 on the first day of this investigation, March,23rd, 2020.*



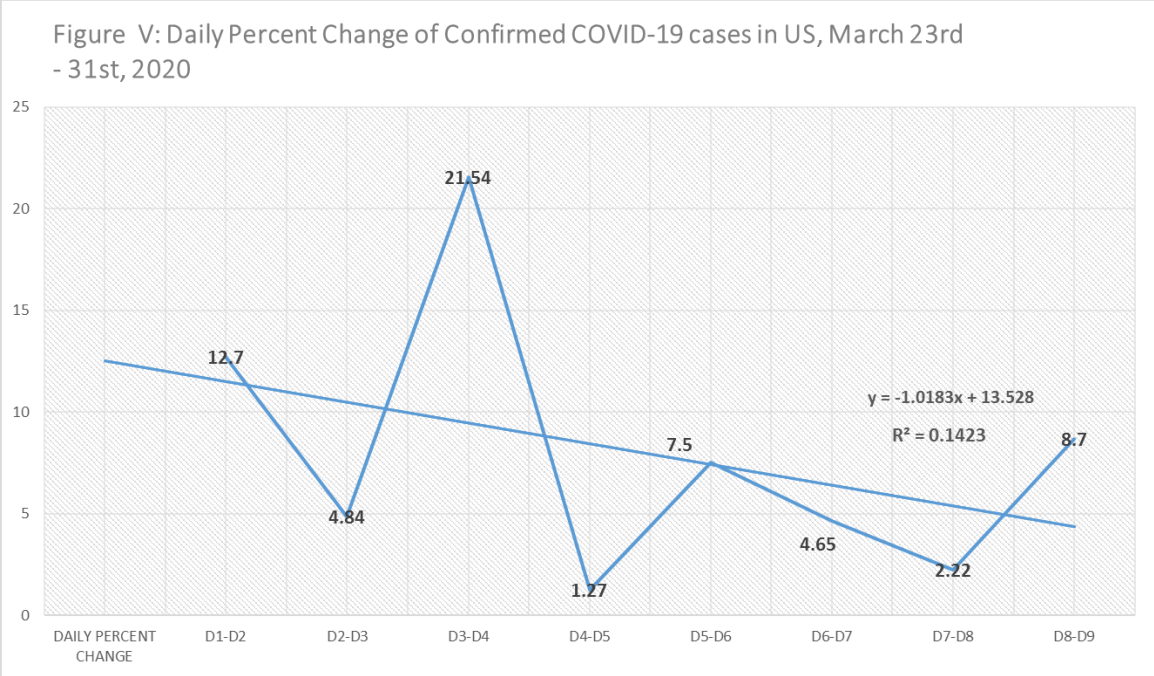
Notes: *This figure illustrates the case fatality for COVID-19 by fatality proportion (FP). The two day FP visualized an upward trend globally and across the world, with the highest case fatality in Italy and the lowest in Germany during 03/28 and 03/31. The graph reflects the FP data for 03/28/20 and 03/31/20, indicative of European COVID-19 case fatality contrast, Italy versus Germany.*



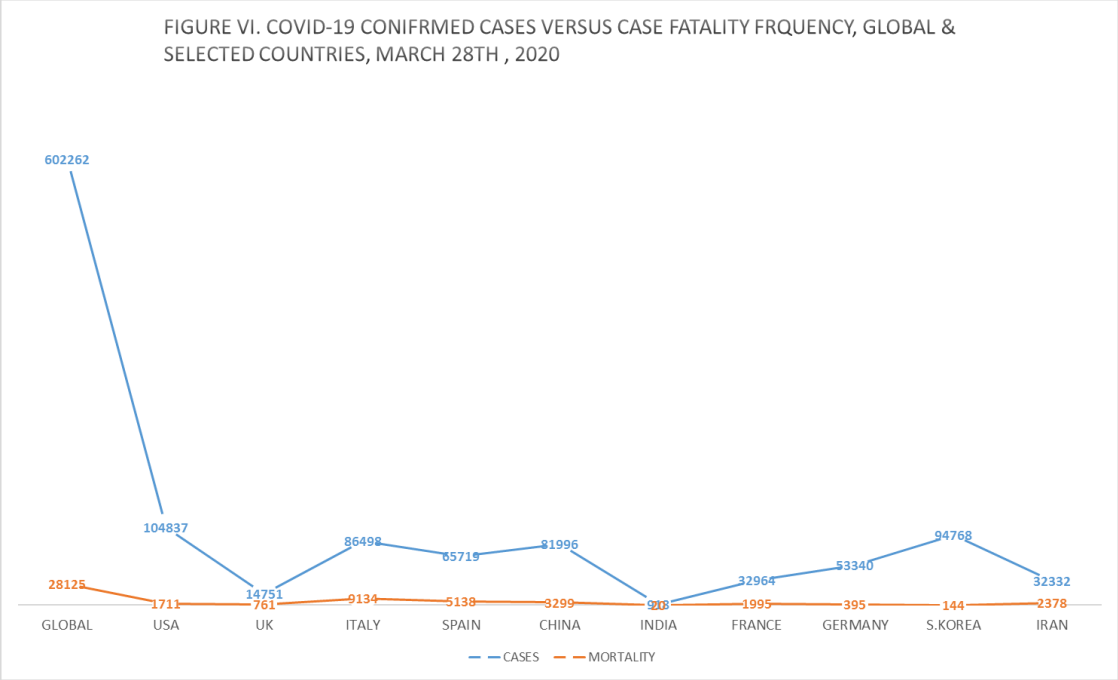
Notes: *This figure illustrates the case fatality for COVID-19 by fatality proportion (FP). The four day FP visualizes an upward trend globally and across the world, with the highest case fatality in Italy and the lowest in Germany during the week, 03/23 – 03/31. The graph reflects the FP data from 03/28/20 to 03/31/20, indicative of European COVID-19 contrast, Italy versus Germany.*



Notes: *A nine day trend in COVID-19 case fatality as fatality proportion (FP) in the USA. This figure illustrates and upward trend, implying the inability of the system to mitigate case fatality and improve survival from COVID-19 infectivity. The nine days range, 1.10-2.0% is indicative of a positive trend (+0.9), requiring care optimization for case fatality reduction and epidemic curve flattening in the USA.*



Notes and abbreviations: *DI=Day 1, Monday, 03/23, and D9= Day 9, Tuesday, 03/31. The figure represents the daily percent change (DPC), implying the fatality proportion (FP) in D2-D1/D1*100.*



Notes: *The graph illustrates confirmed COVID-19 cases and mortality as number of deaths as per 03/28/2020. Of all the countries examined, Italy illustrates worst outcome in Europe and globally, while Germany indicates the contrast, implying the best survival advantage from COVID-19.*