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Spotlight Article

# Age-Related Vulnerability to Coronavirus Disease 2019 (COVID-19): Biological, Contextual, and Policy-Related Factors

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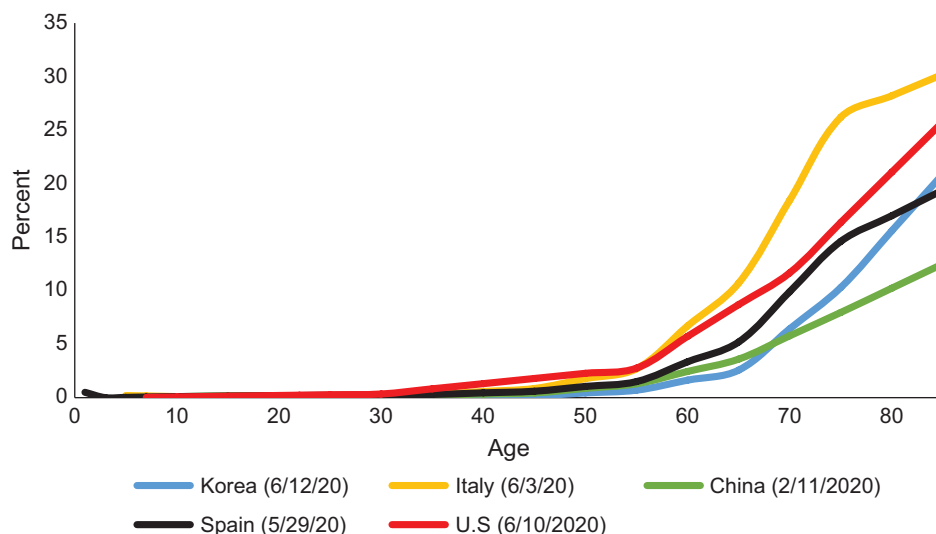
The detailed facts surrounding the coronavirus disease 2019 (COVID-19) pandemic are still evolving; however, one of the most shocking aspects of the COVID-19 pandemic is how lethal this condition is for the older population (Dowd et al., 2020). The risk for death and severe illness with COVID-19 is best predicted by age. The likelihood of death increases exponentially with age among those who contract the virus in all countries where this has been examined (Figure 1). Figure 1 shows the percent of confirmed cases ending in mortality, by age, for five countries near the beginning of June. In every country, the percent dying increases sharply after age 50, and the highest rates occur among the oldest persons. The age pattern is clear across the countries even though the mortality levels are quite different; the United States has had a much greater number of cases and deaths than the other countries in this figure, but the mortality level was higher in Italy. This difference in levels could be influenced by the proportion of diagnosed cases, which depends on testing, treatment of cases, and whether COVID-19 deaths include only those confirmed with a diagnostic test or include both confirmed and probable deaths (Sung & Kaplan, 2020). Even with these differences, the pattern of an exponential increase in death with age is clear.

## Age, Morbidity, and Biology

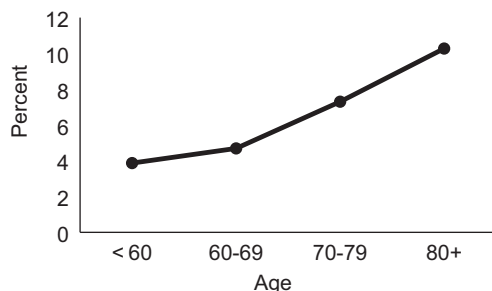There are several likely biological explanations for why COVID-19 is more deadly for older persons, and why older people have much higher death rates no matter what the level of overall infection is. The first is that older persons may be more vulnerable to getting the disease when exposed to the virus because of changes in the immune system with age. Immunosenescence increases markedly with age; as COVID-19 is a novel virus, not before encountered, having more available immune cells to fight it is important (Nikolich-Žugich, 2018). As age increases, the availability of naive T cells and the ratio of CD4/CD8 T cells to address any new pathogen become depleted, and this depletion has been linked to poor responses to COVID-19 (Aviv, 2020). The prevalence of low CD4/CD8, often used as an indicator of immunosenescence, increases markedly with age in a large, representative sample of the American population; it is 3 times higher among those older than 80 than it is for those in their 50s and 60s (Figure 2A).

In addition to having less ability to fight off a novel virus, other aspects of immune functioning also may be worse for older people. Hyperinflammation has been linked to poor outcomes with COVID-19 due to "cytokine storms," or an out-of-control immune reaction that can overwhelm systems and lead to death (D'Elia et al., 2013; Liu et al., 2016; Wang et al., 2020). Hyperinflammation has been characterized by increases in levels of specific cytokines (Blanco-Melo et al., 2020; Vabret et al., 2020; Zhang et al., 2020). Levels of dysregulation in five cytokines by age among Americans over 50 are shown in Figure 2B. The average number of dysregulated cytokines doubles from ages in the 50s to the 80s.

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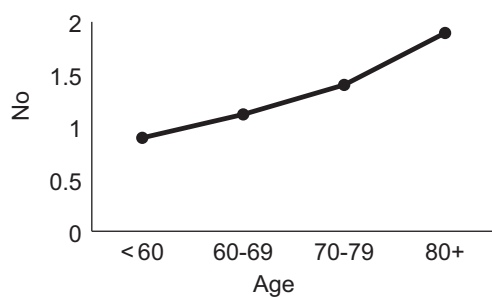
**Figure 1.** Deaths (% dying) among confirmed COVID-19 cases by age. Data sources by country: United States (as of June 10, 2020), Centers for Disease Control and Prevention (https://data.cdc.gov/NCHS/Provisional-COVID-19-Death-Counts-by-Sex-Age-and-W/vsak-wrfu); Spain (as of May 29, 2020), Ministry of Health, Consumption and Social Welfare (https://www.isciii.es/QueHacemos/Servicios/VigilanciaSaludPublicaRENAVE/EnfermedadesTransmisibles/Paginas/InformesCOVID-19.aspx); Korea (as of June 12, 2020), Korea Center for Disease Control and Prevention (http://ncov.mohw.go.kr/bdBoardList_Real.do?brdId=1&brdGubun=11&ncvContSeq=&contSeq=&board_id=&gubun=); Italy (as of June 3, 2020), Laboratory of Epidemiology and Biostatistics of the Istituto Superiore di Sanita (the National Institute of Health of Italy; https://www.epicentro.iss.it/coronavirus/bollettino/Bollettino-sorveglianza-integrata-COVID-19_3-giugno-2020.pdf); and China (as of February 11, 2020), Chinese Center for Disease Control and Prevention (http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51, https://doi.org/10.46234/ccdcw2020.032). Abbreviations: COVID-19, coronavirus disease 2019.
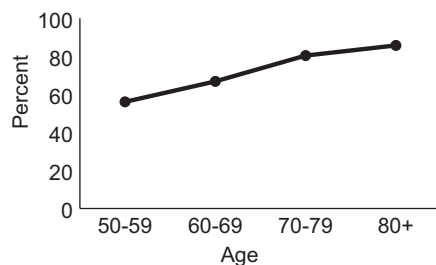


**Figure 2.** Immunosenescence, dysregulated cytokines: United States population, 50+. Cytokines include interleukin 6, interleukin 10, interleukin-1 receptor antagonist, tumor necrosis factor receptor-1, and transforming growth factor beta 1. Source: Health and Retirement Study, 2016 (https://hrs.isr.umich.edu/).

A third factor making COVID-19 more serious for older persons is that they are more likely to have underlying conditions, such as heart disease, hypertension, diabetes, and lung disease, and COVID-19 mortality is higher for those with underlying conditions (Centers for Disease Control and Prevention Conronavirus Disease 2019 Response Team, 2020). These conditions may be linked to COVID-19 because they are associated with greater expression of angiotensin-converting enzyme 2, which is a protein by which COVID-19 viruses bind to cells. In addition, these conditions are linked to higher levels of inflammation. In New York City, 88% of deaths among confirmed COVID-19 cases occurred among people who had an underlying condition; this percentage did not vary much by age, as it was 82% even for those under 17 years of age (New York City Department of Health, 2020). Underlying conditions increase with age to become more common in the older population. Figure 3 shows that at every age group over 50, more than half of Americans have either heart disease, lung disease, diabetes, stroke, or hypertension; by age 70, four out of five people have at least one of these five conditions. These biological changes linked to aging and morbidity are one of the reasons deaths have been concentrated among older persons around the world.
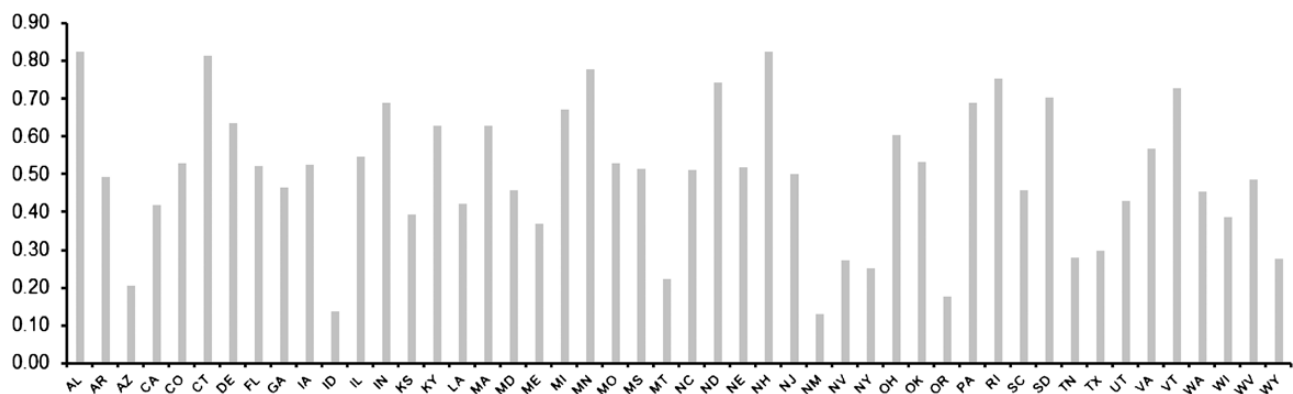
**Older persons have borne the brunt of the worst outcomes of COVID-19.**

## Social Contact, Living Arrangements, Socioeconomic Status, and Age

Biological factors may strongly affect how people respond to infection with COVID-19, but social rather than biological factors primarily determine the likelihood that people of different ages get infected with COVID-19, get diagnosed with the disease, and get treated in a timely fashion. In addition, the level of infection in a country or geographic area appears to be highly related to policies and behavioral responses in the population, as well as macro social and economic circumstances. The age structure of who gets infected also depends on differences in social contact and living arrangements by age. Within the United States, one of the most affected groups by COVID-19 has been members of the Navajo Nation (Navajo Nation Department of Health, 2020). Cases and case fatality rates are especially high among older Navajos, who tend to live with many members of their extended families, many of whom may be regularly exposed to people outside the home because they need to work, but live in dwellings with small numbers of rooms. In Italy, the fact that older persons were well integrated into families both socially and

residentially was thought to expose them to more disease and even higher death rates than in other countries (Dowd et al., 2020). The amount of contact with infected persons is a factor promoting infection, so the less the contact, the less likely an infection will result.

Older members of the Navajo Nation also are much more likely than people in the rest of the country to be of low economic status and to live in dwellings without running water, which makes it difficult to wash hands frequently, one of the most important anticontagion activities. Low socioeconomic status can also be attached to having more difficulty social distancing, because of living arrangements and being in contact with more people due to household members having an essential job.

The most egregious example of the selective impact on older adults has occurred within nursing and other residential care facilities. Residents of these settings are most at risk of getting COVID-19 and dying from COVID-19 in the United States and in a number of other countries (Fallon et al., 2020). A relatively reliable estimate in early June was that 42% of all COVID-19 deaths in the United States had occurred in nursing facilities and other long-term care residences (Girvan & Roy, 2020). These homes have the deadly combination of older residents who are in poor health, are in close contact with both staff and other residents, and live in confined spaces. This, coupled with inadequate testing for COVID-19 among residents and staff and inadequate infection control, has caused this disaster. The proportion of all COVID-19 deaths in each state occurring among those in nursing facilities and other long-term care facilities is shown in Figure 4. The estimates are probably low, as some states do not report deaths for those whose deaths were not diagnosed with testing; some states have not fully disclosed facility deaths; and some states are not even included, as they do not report deaths by residence (Paulin, 2020). For 26 of the states shown in

**Figure 3.** Percent of U.S. population with at least one chronic disease by age. Chronic diseases include heart disease, lung disease, diabetes, stroke, and hypertension. Source: Health and Retirement Study, 2016.

**Figure 4.** Percent of state COVID-19 deaths occurring to nursing home/long-term care residents. Sources: The data represent the percentage of nursing home and long-term care resident deaths divided by the statewide total number of COVID-19 deaths as of June 12, 2020. Most data came from the Nursing Home COVID-19 Public File Data from the Centers for Medicare & Medicaid Services (https://data.cms.gov/stories/s/bkwz-xpvg), except for states where state nursing home data were also available from the state website. The reporting dates for the nursing home death data ranged from May 31, 2020, to June 12, 2020. Data shown for 48 contiguous states and District of Columbia. Abbreviations: COVID-19, coronavirus disease 2019.

the figure, the proportion of all deaths from COVID-19 in the state that occurred among residents of long-term care facilities is at least 50%. In addition, it is suspected that untested formal caregivers and other relatively young asymptomatic workers moved from one facility to another, spreading disease (Furuse et al., 2020). The overall lack of testing, infection control, and the high levels of viral exposure from extremely close contact among staff and residents over extended periods of time contributed to such a rapid spread of cases.

> **The most egregious lack of response in the U.S. was what has happened in nursing and residential care homes.**

## Directions for a Post–COVID-19 Presidency

At the time this was written, the United States was undergoing a renewed surge in COVID-19 cases in the South and the West, while control of the pandemic was being gained in the Eastern states with initially high levels of cases (e.g., New York, New Jersey, Massachusetts). It remains unclear how long this initial wave of the pandemic will last, when a second wave will come again, or whether a vaccine will be available in the coming year. Meanwhile, research to better understand why the United States has become a world leader in the number of COVID-19 cases and mortality has only just begun (U.S. Government Accountability Office, 2020).

The delayed ability to test for COVID-19 at the beginning is widely accepted as an initial challenge that got the United States on the wrong path. The Centers for Disease Control and Prevention was not ready with an accurate and available test, resulting in very few people being tested in the initial months; this contributed to cases spreading rapidly across the country. In comparison, countries with a greater capacity to test in the early phases of the pandemic were able to contact trace and contain the spread of the disease more effectively (e.g., Singapore, Japan, Taiwan, Hong Kong, and Canada). Other countries also used fairly severe "lock downs" and issued quarantines to effectively limit the spread (e.g., China, New Zealand; Wilasang et al., 2020).

Another early problem in the United States was the lack of personal protective equipment (PPE) for medical workers (U.S. Government Accountability Office, 2020). The United States did not identify sources of supplies early, nor did the federal government oversee the acquisition and distribution of supplies across the country so as to target distribution to those states and localities in greatest need. PPE remains in short supply in many parts of the United States even now, and this has been especially problematic for nursing facilities.

In conducting an initial assessment of what went wrong in U.S. nursing facilities, Senators Casey, Peters, and Wyden (2020) reported that it took nearly four months after the first outbreak in a Washington state nursing facility before data collection on facility-specific deaths was federally mandated. While initial efforts involved "locking down" nursing facilities, the lack of resident and staff testing and quarantines did little to ameliorate the situation. These homes still remain short of testing capability and PPE, and what has occurred in other long-term care settings (e.g., assisted living) still remains unclear. Without accurate and timely data, a targeted and effective public response will continue to lag, and efforts to mitigate COVID-19 outbreaks may continue to be unnecessarily inconsistent from one facility to the next.

Perhaps most notable was how, in contrast to other countries, the current administration decided to substantially reduce federal support for the administration and financing of the nation's public health infrastructure and withdraw from international partnerships designed to identify and coordinate responses to such worldwide public health emergencies. Had the current administration maintained (or even expanded and improved) the nation's public health infrastructure and international partnerships, the development of international supply chains and the efficient distribution of tests and PPE arguably would have been improved.

Interestingly, several of the other "more successful" countries that experienced the severe acute respiratory syndrome epidemic in 2003 responded by increasing national investments in public health infrastructure, and were better prepared for COVID-19, as coordinated plans and response approaches to this infectious pandemic were already in place (Sung & Kaplan, 2020). Whether federal and state policy-makers learn from this current experience and begin planning and acquiring resources to prepare for the next pandemic or other public health emergency remains to be seen.

The U.S. Government Accountability Office (2020) indicated that one of the lessons for our government to learn concerns the benefit of "establishing clear goals and roles and responsibilities for the wide range of federal agencies and other key players," as any pandemic, by definition, is a national emergency. The Government Accountability Office also emphasized the need for public officials to follow scientifically based approaches to alleviating the disease, and "provide clear, consistent communication among all levels of government, with health care providers, and the public" so that recommended public heath practices are less likely to be subject to varied interpretation of rules, regulations, and recommended practices across states and localities, and to mitigate the politicization and corresponding dissemination of misinformation across news and social media (U.S. Government Accountability Office, 2020, "Providing" page 3, para.19).

Finally, when considering older Americans in particular, a post–COVID-19 presidency should embrace how changes linked to biological aging and the social lives of

older Americans placed them at higher risk for morbidity. This understanding then may lead to assigning a greater value to investing in basic scientific studies. On one hand, there is a need to better understand the long-term effects of having COVID-19 on the health trajectory of those individuals who were infected: do older persons with COVID-19 experience organ damage from the infection or have their immune systems become compromised and place them at even greater risk when the next viral outbreak occurs? On the other hand, the federal government should invest in basic and applied research to better identify, protect, and treat those older Americans most at risk from future infectious outbreaks and other public health emergencies.

## Funding

## Conflict of interest

None declared.

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