VIEWPOINT

Challenges Estimating Total Lives Lost in COVID-19 Decisions
Consideration of Mortality Related to Unemployment, Social Isolation, and Depression

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Related article

The coronavirus disease 2019 (COVID-19) pandemic has claimed hundreds of thousands of lives, directly and indirectly, and threatens to claim many more. Nations have made different policy decisions that have affected the rate of infection, mortality, the economy, and the life of the country differently. The choices between various alternative policies have led to different trade-offs between what are arguably incommensurable goods, such as survival, mental health, social connection, and economic growth. It can seem difficult or impossible to weigh these numerous factors, yet policy decisions must be made, with countless implications for society. In the early stages of the pandemic, and when information was limited, a cautious approach was arguably most appropriate. As further information becomes available, it becomes possible to make better-informed decisions. However, the inherent challenges involved in the very real, and very difficult, trade-offs remain.

One approach to weigh these different outcomes, which are difficult to directly compare, is to attempt to use a composite measure such as well-being–adjusted life-years.[1] In such an approach, each year of life saved

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or lost is weighted by a self-assessed overall life-satisfaction score (range, 0-10). This approach, however, has several drawbacks. First, it is difficult to weigh aspects of well-being against survival. Second, many conceptualizations of well-being involve numerous components.[2] While a number of well-being approaches prioritize life satisfaction,[1] it is unclear why this aspect of well-being ought to be prioritized over others, such as having a sense of meaning in life. If different aspects of well-being were assessed (such as meaning and purpose), this would then lead to different assessments of well-being–adjusted life-years. Third, using well-being–adjusted life-years based on life satisfaction is also problematic insofar as it may deprioritize the lives of individuals who are poor, disabled, and vulnerable by giving their lives less weight because their life satisfaction tends to be lower.

An alternative would be to use a "total lives saved" approach that prioritizes life as the highest present good

at stake and requires that decisions be based on lives saved alone. This has been proposed in recent ethical statements concerning clinical care[3] but is arguably applicable more generally in policy decision-making. A total lives saved approach does not mean that economic, social, and well-being outcomes are to be neglected—in fact, these factors also affect mortality rates, sometimes substantially. Meta-analyses of covariate-adjusted longitudinal cohort studies indicate that unemployment, social isolation and lack of community, and late-life depression are all associated with increased all-cause mortality.[2,4-7] The magnitude of associations may, in some cases, be sufficient to considerably shift the evaluations of lives saved or lost when considering different policies.

For example, if everyone younger than 60 years in a particular region who was healthy returned to work but an additional 500 people died of COVID-19 infection, is that a reasonable trade-off, and would it be offset by avoiding the mortality consequences of unemployment and social isolation?[4,5] Another scenario highlights the challenges of trade-offs: In the fall of 2020, decisions will need to be made about children returning to school. Although deaths attributable to COVID-19 among children are exceedingly rare, children who become infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) could infect older individuals. Should millions of children be kept out of school, with substantial and likely lifelong consequences, to "save" 500 or 1000 or 10 000 lives? Do the consequences of keeping children out of school, and potential future adverse effects on health and longevity,[2,4] outweigh the consequences of infection-related deaths, assuming that as much as possible is done to protect older adults, health care workers, and other individuals who ensure a functioning society?

The implementation of such a total lives saved approach faces potential, although not insurmountable, challenges. First, the associations of employment, social isolation, and depression with mortality are likely to vary by context. The association between unemployment and mortality may be more pronounced in midlife than in later life. Conversely, depression may have a stronger association with mortality later in life rather than earlier.

Second, while these meta-analyses were based on prospective cohort data, with multivariate-adjusted covariate control, the data are observational and subject to confounding. It would be important, when using

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meta-analytic estimates to inform policy decisions, to also consider sensitivity analyses that set the values of these relationships to somewhat lower levels than the estimates, to examine whether conclusions change, and to provide estimates that individuals can understand.

Third, and perhaps most challenging, it will be difficult to assess and compare the influence of various alternative self-isolation, social distancing, contact tracing, and other policies on employment, social isolation, and depression. While decades of data are available to inform the association of unemployment, social isolation, and depression with mortality,[4-7] much less data are available regarding the relationships of pandemic policies with these social, psychological, and economic outcomes. Moreover, what is important to assess with regard to decision-making is not so much how the pandemic influences these social, psychological, and economic outcomes but rather how different *policies* for handling the pandemic may influence these outcomes. Even without strict isolation and workplace closure measures, the economy and social relations would still have been adversely affected by the morbidity and mortality related to COVID-19 and the substantial changes in individual behaviors.

These aforementioned challenges, however, are not necessarily an insurmountable barrier to this total lives saved approach. Within the past months, different countries, regions, and cities have made different decisions, essentially resulting in a series of "natural experiments." From these experiences and decisions, it is possible to begin to assess the association between different policies and social, psychological, and unemployment outcomes, as well as SARS-CoV-2 infection rates and COVID-19 fatality rates. However, such data must be used carefully, because different countries, regions, and cities may differ from one another in a host of other ways; some of these factors may not be possible to control for; and societies may prioritize various outcomes in different ways. Nevertheless, a series of analyses, as rigorous as possible, to evaluate various policies, drawing on country-by-country, region-by-region, and city-by-city comparisons, may give considerable insight into the association between implementation of various policies

with social, psychological, and economic outcomes.[8] From estimates of these outcomes, it may be possible to extrapolate to the mortality consequences over time. Simply assessing current total excess mortality rates is insufficient because it will take time for the mortality consequences of unemployment, isolation, and depression to become manifest. More direct mathematical and theoretical modeling of these effects may also give further insight, as has occurred with modeling for infection rates and fatality rates. It will again be important, when using the estimates to inform policy decisions, to also consider how sensitive conclusions are when the strength of the relationships between various policies and outcomes are set to values different from their best estimates.

In the months ahead, while confronting the possibility of a second wave of the pandemic, these calculations of total lives lost, both from SARS-CoV-2 infection and because of social, psychological, and unemployment outcomes, may prove important in policy decisions. Other factors associated with mortality also will require consideration, such as delayed treatments, for example, for heart disease or cancer,[9] and prolonged absence of preventive health care and vaccinations.[10] However, there may come a point at which the number of lives lost from economic, social, and psychological consequences of different policy decisions will outweigh the number of lives lost from infection, and it will be crucial to consider the indirect mortality consequences of these policy decisions. When reasonable and rigorous sensitivity analyses and variations of the parameters indicate that this point has been reached, it would be a mistake to ignore these other considerations. Moreover, this approach of using only total lives saved or lost is effectively conservative in its deference to infection-related fatalities because it does not directly take into account social and other goods but rather places them subordinate to life. With new unemployment claims in the US alone reaching 40 million, and with unemployment associated with all-cause mortality, it may be time to more seriously, and quantitatively, take the social, economic, and psychological consequences of policies into account in decision-making when calculating total lives lost from the COVID-19 pandemic.

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