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COVID-19 represents a major crisis with major loss of life. We should use the best science, in a data-driven, evidence-based approach to minimize human loss from this pandemic. We need to consider both the benefits and harms of each of our policy interventions and to adjust our interventions according to continuous feedback with reliable data.

Shelter-in-place and lockdown orders were justified initially, when announcements declared a new, contagious virus with 3.4% fatality rate and no asymptomatic infections. Prospects of 60 million deaths worldwide led to comparisons against 1918 influenza. However, currently we know that asymptomatic or mildly symptomatic infections are very common. The numbers of people infected are far more than those documented to-date with PCR testing. Infection fatality rate is accordingly much lower than the crude fatality rates derived from dividing the number of deaths by the number of documented cases. While this is a contagious virus and many people can be infected, to-date person-years of life lost from COVID-19 worldwide is probably in the range of 100- to 1000-fold less than the person-years of life lost from influenza in 1918. Of course, a second wave cannot yet be excluded. Its occurrence and potential magnitude can only be speculated with mathematical models, but models have not been very successful so far in COVID-19 predictions. Therefore, we need to proceed with caution in lifting lockdown and monitor the impact of any changes in policy measures with real data, as opposed to just using models.

The fatality rate from COVID-19 is highly dependent on age and modulated by the presence of comorbidities. For children and young adults, it appears that infection fatality rate is

lower than seasonal influenza, and for middle age adults it is about the same. Infection fatality rate can increase sharply, however, when nursing homes are massively infected and when unprepared hospitals are overwhelmed and the infection spreads to hospitalized patients (nosocomial infection). This explains the paradox why COVID-19 is typically a very mild, benign infection, but it also has the potential to become devastating in specific settings.

While lockdowns were justified initially, their perpetuation may risk many lives. Unemployment may create more marginalized citizens without health insurance. Mental health can be affected with increases in depression, suicides, domestic violence and child abuse. Gun sales have increased. Famine is becoming a global threat. Moreover, deaths from common chronic diseases and treatable conditions such as heart attacks may increase, as patients avoid hospitals, interaction with their care-givers is disrupted, and hospitals become financially devastated. Excess deaths accruing during COVID-19 weeks may reflect both COVID-19 itself but also deaths from health care disruption. COVID-19 overwhelmed a few dozen hospitals, while COVID-19 measures may jeopardize services and multiple health outcomes in thousands of hospitals.

Moving forward, we need to defend hospitals and nursing homes with strict infection control and hygienic measures; universal and periodic testing of all personnel; and quarantine for infected and exposed personnel. Conversely, we should reassure most citizens – those of younger ages without serious preexisting conditions - that they are at very low risk.

Re-opening efforts require great caution, with continuous feedback to identify and limit any potential surge of hospitalizations and deaths upon re-opening. Re-opening should be gradual, with continuous feedback on epidemic activity. This includes data on seroprevalence (proportion of people already infected) and incidence of new infections. These data should be balanced against bed capacity reserves. It is unrealistic to expect new PCR-detected cases to disappear before re-opening. PCR remains positive for a while in many patients who are no longer infectious.

Moreover, with increased testing and with a large pool of previously undetected infections, numbers of PCR-positive samples may seem to remain quite high, even though the epidemic wave has largely passed. It is also unrealistic to expect COVID-19 deaths to stop accruing before re-opening. Deaths may happen 3 weeks after infection, and modern medical technology can maintain some people on mechanical support even for months. Finally, it is unrealistic to expect that complete contact tracing will need to be feasible before re-opening. In most locations, the number of people infected is already too large and their casual contacts may include a large portion, if not the large majority of the entire population, thus making complete contact tracing infeasible. Complete contact tracing can be more feasible when the epidemic activity has ceased, e.g. in the future when trying to catch early and extinguish potentially new waves.

The pace of re-opening may differ across locations, depending on their evolving levels of infection, hospital capacity, and population vulnerability structure. While treatment advances and vaccine efforts may be successful eventually, lockdown measures cannot be prolonged until we find treatments and vaccines that save many lives, since such breakthroughs may take a long time (or may even never happen). For example, remdesivir has shown promising results in shortening duration of disease, but no conclusive evidence yet for saving lives.