

event in a pandemic—by the prompt availability of vaccines that are not only safe but also extremely effective in eliciting a ‘superhuman’ protective immunity: on the one hand, vaccine-induced immunity is more potent than that elicited by the infection⁵. On the other hand, the most-potent vaccines seem to dramatically hinder viral replication and thus transmission⁶. Because of this, a considerable advantage for the virus could therefore be provided by mutations that cause the emergence of variants that evade vaccine-induced immunity. These would still replicate in the vaccinated host in communities in which the proportion of vaccinated people is very high (e.g., Israel and the United States). However, despite vigorous replication of the virus in these highly vaccinated communities, the world is yet to witness the emergence of variants able to ‘break through’ the vaccine-induced immunity⁷. We cannot, of course, exclude the possibility of their emergence even in the near future, but molecular data gathered thus far have made it clear that the ‘evolutionary space’ that SARS-CoV-2 has for evading

vaccine-induced immunity is remarkably narrow relative to that available for increases in transmission rates. Some evolutionary virologists believe complete or nearly complete resistance to the current vaccines is an inevitability⁸, which is a prediction that cannot be discounted or ignored.

Therefore, while the world needs to remain on full alert in order to promptly detect the emergence of ‘vaccine-piercing’ variants and, in that case, rapidly update the available vaccines, there is reason for very cautious optimism. In any case, what is certain is that the emergence of such vaccine-evading variants, if at all possible, will be made more likely by viral spread and replication. May this serve as a reminder that, once infection rates have been controlled in the most advanced countries, it will be crucial to do the same in the developing ones and achieve the same success in more-difficult ‘socio-sanitary’ settings.

For this reason, it will be in humanity’s own interest to not be greedy and instead provide vaccines at an affordable price to all mankind: history has in fact taught that

when dealing with the global control of an infectious disease, the most effective way to be selfish is to be generous. □

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Competing interests

The authors declare no competing interests.



Choosing Wisely for COVID-19: ten evidence-based recommendations for patients and physicians

To the Editor—The COVID-19 pandemic has produced devastating effects worldwide, with the causative coronavirus SARS-CoV-2 infecting over 170 million patients and causing more than 3.5 million deaths as of 1 June 2021. The resultant fear and anxiety among the public and treating physicians has frequently resulted in rapid changes to clinical practices and hospital triage decisions, many of which are not evidence based and are often detrimental. There have been wide variations at global and regional levels on guidance related to mask usage, testing protocols, vaccination and patient triage (both hospital admission and escalation to an intensive care unit), as well as the use of various pharmaceutical interventions in treating patients with COVID-19. Many of these deviations from evidence-based healthcare result in substantial harm, as they divert efforts and

resources from outcome-based, data-driven best practices toward those that are of doubtful efficacy and are even harmful. As many countries continue to experience repeated waves of COVID-19, it is important to identify practical approaches that are evidence based and implementable in the real world to optimize the use of resources and improve outcomes. Although these are important all over the world, they are crucial in low- and middle-income countries, where resources are scarce.

The Choosing Wisely initiative was begun to promote conversations between patients and physicians about avoiding unnecessary medical interventions. The mission of Choosing Wisely is to help patients and physicians choose care that is evidence based, not duplicative, free from harm, and truly necessary¹. It works by creating lists of ‘things clinicians and

patients should question’, something that is particularly appropriate to public-health responses and management decisions in the current pandemic. In response to the widespread use of non-evidence-based practices, we initiated Choosing Wisely for COVID-19 to identify ‘best buys’ for the general public, patients and physicians.

We created an 18-member Choosing Wisely for COVID-19 Task Force in April 2021 with multi-stakeholder involvement. Members were drawn from the fields of public health, epidemiology, general practice, primary care, infectious disease, virology, critical care, internal medicine, pulmonology, pediatrics, oncology, health economics, clinical research, implementation science, and health policy. We also had patient and civil-society representatives to ensure that their views and voices were given due importance. Advisors

Table 1 | The ten Choosing Wisely for COVID-19 recommendations

Recommendation	Comments	Refs.
For the general public		
1 Do use well-fitting masks appropriately, whenever in public	A systematic review and meta-analysis of 10 adjusted ($n = 2,647$) and 29 unadjusted ($n = 10,170$) observational studies showed that the risk of infection was significantly reduced with facemasks (adjusted odds ratio (aOR), 0.15, and 95% confidence interval (CI), 0.07–0.34, for adjusted studies; odds ratio (OR), 0.34, and 95% CI, 0.26–0.45, for unadjusted studies). N95 masks were associated with greater reductions in risk than were surgical or other masks. Double masking is preferable to single masking unless the masks are N95.	4
2 Do avoid crowded places, especially while indoors	A systematic review and meta-analysis of 9 adjusted ($n = 7,782$) and 29 unadjusted ($n = 10,736$) observational studies showed that the risk of infection was significantly reduced with physical distancing of >1 meter (aOR, 0.18, and 95% CI, 0.09–0.38, for adjusted studies; OR, 0.30, and 95% CI, 0.20–0.44, for unadjusted studies). The more the physical distancing was, the lower the chance of infection was. Maintaining adequate ventilation by opening doors and windows is an important measure for decreasing the spread of infection.	4
3 Do get tested if you have symptoms of COVID-19, and isolate yourself at home if symptoms are mild	Early testing and isolation at home are advisable if someone has symptoms of COVID-19, such as fever, sore throat, cough, loss of smell and/or taste. Testing enables a test-trace-isolate strategy, which is effective in controlling further spread. If someone has these symptoms and does not have access to reliable test facilities, syndromic diagnosis can be done. Most patients can be managed at home and recover well with regular monitoring of temperature and oxygen saturation. The only interventions required are maintaining hydration (plenty of oral fluids) and acetaminophen (paracetamol) for fever and body aches.	5,6
4 Do seek medical help if you have difficulty breathing, or your oxygen saturation drops to less than 92%	Patients who are breathless at rest or after exercise, or those with oxygen saturation of <92% or those with a drop of >4% in oxygen saturation after an exercise test ^a should seek medical help and should be appropriately triaged for medical treatment in hospital and non-hospital settings. Lying down in a prone position will help to improve oxygen saturation.	6,7
5 Do get vaccinated as soon as you are eligible, and even if you have had COVID-19 in the past	Several randomized trials have demonstrated the efficacy of various approved vaccines in preventing infection with SARS-CoV-2 and serious illness and mortality due to COVID-19. Vaccination remains an extremely effective population-level strategy for the prevention and mitigation of COVID-19. This recommendation applies even if someone has had COVID-19 in the past.	8
For healthcare workers		
6 Do not prescribe unproven or ineffective therapies for COVID-19	There are no data at present to support the use of favipiravir, ivermectin, azithromycin, doxycycline, oseltamivir, lopinavir-ritonavir, hydroxychloroquine, itolizumab, bevacizumab, IFN- α 2b, fluvoxamine, convalescent plasma or herbal preparations in the treatment of COVID-19. None of these are currently recommended by the WHO. This list will need to be revised as new evidence emerges.	6,7,9
7 Do not use drugs like remdesivir and tocilizumab except in specific circumstances where they may be of use	Tocilizumab is useful only in patients who are severely ill, are receiving steroids, have signs of inflammation, and have rapidly increasing requirements for oxygen. Use in other clinical situations is not beneficial and is probably harmful. Remdesivir has marginal efficacy in shortening the time to recovery in adults when given early to patients requiring oxygen in some trials, but not in others. It does not decrease mortality and is not indicated in other clinical situations.	6,7,9
8 Do use steroids prudently only in patients with hypoxia, and monitor blood sugar levels to keep them in the normal range	Randomized trials have shown benefit with a short-duration (5- to 10-day) use of steroids such as Dexamethasone (6 mg per day) in patients with COVID-19 who require oxygen. The sicker the patient is, the greater the benefit is. Other steroid equivalents such as methylprednisolone (16 mg twice daily) or prednisolone (20 mg twice daily) may be used. Steroids do not benefit and might harm patients who do not require oxygen. There are no data to support the use of steroids for a longer duration (>10 days) or a higher dose of steroids. It is important to maintain glycemic control in patients on steroids to reduce the risk of secondary fungal infections such as mucormycosis. There is no need to taper steroids after use for 5–10 days.	6,7,9
9 Do not routinely perform investigations that do not guide treatment, such as CT scans and inflammatory biomarkers	There are no data to support the routine use of CT chest scans, CT scores or inflammatory biomarkers such as ferritin, IL-6, LDH and procalcitonin to grade the severity of COVID-19 or to guide treatment protocols.	6,7
10 Do not ignore the management of critical non-COVID-19 diseases during the pandemic	Several studies have shown that the care of illnesses such as cancer, tuberculosis and cardiac and renal disease, and conditions such as mental health, childbirth, perinatal care and childhood immunization, has suffered during the pandemic. This has serious implications on their outcomes. Essential healthcare services should continue to be provided during any pandemic. For example, it is estimated that suspension of cancer services will result in more deaths than those due to COVID-19 during the pandemic.	10

IFN, interferon; WHO, World Health Organization; CT, computed tomography; IL, interleukin; LDH, lactate dehydrogenase. ^aExamples of an exercise test include a 1-minute sit-and-stand test or a 6-minute walk test.

to the group included leaders of the World Health Organization and senior government officials. Task Force members contributed to an initial 'long list' of 47 recommendations based on available evidence, including 9 recommendations from a Choosing Wisely initiative undertaken in 2020 (ref. ²). The members undertook two rounds of a modified Delphi process (described elsewhere³) to assign scores to the recommendations, and voted for their inclusion using the following criteria: evidence to support the recommendation, extent to which it is practiced, cost associated (including opportunity cost), clarity of the recommendation, feasibility of measurement, and relevance to the current situation.

We provide here the ten recommendations with explanations (Table 1): the first five are directed toward the general public, whereas the remaining five are meant for physicians managing COVID-19. The final recommendations are related to the following (recommendation numbers from Table 1 in parentheses): precautionary practices to decrease the risk of being infected (1 and 2); measures to be taken if someone has symptoms or has been diagnosed with COVID-19 (3 and 4); vaccination (5); judicious use of drugs (6, 7 and 8) and investigations (9) in managing COVID-19; and health systems and policies (10). The first two recommendations are most relevant in regions of high community spread and low vaccine coverage, whereas the remaining eight are relevant regardless of the setting.

The Choosing Wisely recommendations for the prevention, care and control of COVID-19 include the best evidence available at present, and address practices that are common, inefficacious, of low value or harmful in the response to COVID-19 in several countries. All recommendations are based on robust evidence and can improve outcomes for pandemic control globally. These are especially relevant in low- and middle-income countries, where resources are scarce, government expenditure on public healthcare is low, and optimum utilization is crucial. We emphasize that these recommendations are not meant to replace treatment protocols; instead, they are intended to promote shared decision-making by patients and physicians, and to provide guidance to treating physicians and the general public.

Our consensus list of recommendations for COVID-19 control has several implications. First, it provides guidance to the general public on simple measures that could decrease their risk of contracting COVID-19—we emphasize

the importance of appropriate mask usage, avoiding crowded places (including social mixing) and encouraging adequate ventilation indoors, on the basis of growing understanding of the transmission of SARS-CoV-2. Second, this consensus list provides practical guidance to patients on what to do when they develop symptoms of or test positive for COVID-19, including recognition of symptoms and signs that warrant medical attention. Guidance for patients is important, as healthcare systems should also adopt a hospital triage system in which patients with mild to moderate illness are not admitted to the hospital, so precious hospital beds are reserved for patients with more-severe disease. Third, the consensus list provides clear recommendations to the general public on vaccination, as vaccines provide the most important path to control of the pandemic. Fourth, the consensus list encourages physicians to make evidence-based, outcomes-driven treatment decisions that will optimize resources and avoid wastage. By disseminating these recommendations, we are also discouraging defensive medical practice by physicians who fear litigation or criticism if they did not treat patients with unproven therapies. Finally, we emphasize the importance of maintaining essential non-COVID-19 healthcare areas such as cancer, tuberculosis, renal and cardiac disease, mental health and reproductive health even during major pandemics, as the consequences of not doing so are dire. During subsequent waves of the pandemic, policy decisions should ensure that while care for COVID-19 is maintained, other essential healthcare delivery continues uninterrupted.

Our Choosing Wisely for COVID-19 initiative has some strengths and limitations. The Task Force and advisors comprised diverse experts and representatives from all possible stakeholders involved in the management of COVID-19, including patient representatives and policymakers. This ensures that all stakeholders' viewpoints are considered and makes our list of recommendations generalizable, widely applicable and implementable. All the recommendations have high-quality evidence to support them. Nevertheless, data on COVID-19 are rapidly evolving, and it is possible that these recommendations may change as new evidence is available. We reiterate that these recommendations are context specific, and that some of them (mask usage and physical distancing) may be most relevant in settings of widespread community transmission and limited vaccine access. Globally, vaccine access is highly inequitable, and many parts of the

world are unlikely to have adequate vaccines for their populations within the next 2 years. In summary, the Choosing Wisely for COVID-19 initiative has identified ten key recommendations for the control of COVID-19 through inputs and systematic development process from diverse stakeholders. Adopting and implementing this list will promote more evidence-based implementation of policy and practices in managing the COVID-19 pandemic in various parts of the world. Most importantly, this list emphasizes the critical role that evidence-based medicine should serve, even during a raging pandemic. □

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Author contributions

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Competing interests

G.K. is vice-chair of the board for the Coalition for Epidemic Preparedness Innovations, director of MSD Wellcome Trust Hilleman Laboratories, director of the Ignite Life Science Foundation, a member of the scientific advisory board of Mynvax, a member of the scientific advisory board for mRNA vaccines at Cipla (all of which are honorary, except Hilleman Laboratories, where G.K. is a Wellcome Trust–nominated Director and receives an honorarium that is transferred to her institution). M. Pai receives funding from the Bill & Melinda Gates Foundation for tuberculosis research.