Since the outbreak of COVID-19, many randomized controlled trials have been launched to test the efficacy of promising treatments. These trials will offer great promise for future treatment. However, a public health emergency calls for a balance between gathering sound evidence and granting therapeutic access to promising trial drugs as widely as possible. In an electronic survey, we found that 3.9% of the participants preferred to receive an unproven trial drug directly in the hypothetical scenario of mild COVID-19 infection. This percentage increased drastically to 31.1% and 54.2% in the hypothetical scenario of severe and extremely severe infection, respectively. Our survey indicates a likelihood of substantial receptivity of trial drugs among actual patients in severe conditions. From the perspective of deontological ethics, a trial can only be approved when potential benefits of the investigational treatment are presumed to outweigh risks, so compassionate or off-label use of investigational therapies merits evaluation.

By the end of June 2020, the cumulated number of patients affected by the global pandemic of coronavirus disease 2019 (COVID-19) exceeded 10 million.1 The pathogen of COVID-19 is similar in structure to those causing severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).2,3 Total infections and deaths from COVID-19, however, have far exceeded those from SARS and MERS.

To date, there is no widespread consensus on any treatment of COVID-19, and the state of the art of treatment is still supportive care. In late January 2020, compassionate use of remdesivir in a patient in the United States showed a therapeutic effect without recognized adverse events,4 and later France news media reported a similar case.5 Since early February 2020, several randomized controlled trials (RCTs) have been launched focusing on remdesivir (results of two placebo-controlled RCTs are available now and are discussed later). In addition to RCTs on remdesivir, hundreds of other RCTs have also been registered, covering a wide range of treatments such as chloroquine phosphate and convalescent plasma.

These RCTs will offer great promise for future treatment. However, it has been argued that a public health emergency calls for a balance between gathering sound evidence and granting therapeutic access to an unproven drug (i.e., likely effective but being tested by RCTs) as widely as possible.6 Emergency use of unproven drugs has also been advocated by the World Health Organization (WHO) for ethical considerations.7 In modern clinical settings, patients’ values and preferences are core for shared decision making. This may be particularly important for patients with severe infectious diseases, who often live with anxiety, fear, and even panic. It is possible that a significant number of COVID-19 patients would prefer to use an unproven drug after becoming aware of its potential benefits and risks. We therefore conducted an electronic survey to explore this matter among Chinese-speaking adults during February 26–27, 2020, when the epidemic of COVID-19 was severe in China.

Our survey was conducted via WeChat by snowball sampling, a popular and free messaging and social application in China. Four authors of this study (all are members of the faculty or post-graduate students at Peking University Health Science Center; mean age, 27.5 years) initially distributed invitations via their private chat groups (including classmates, colleagues, friends, and family members) as well as WeChat Moments, inviting people to answer the questionnaire, and meanwhile, encouraging participation and urging recipients to distribute invitations to their own chat groups and WeChat Moments. This explains why our study participants were relatively young and had a high proportion of medical backgrounds (see below). The survey questionnaire included eight brief questions. The first three questions placed the respondents in hypothetical scenarios of choosing a course of treatment when having COVID-19 with three degrees of severity: mild, severe, and extremely severe. Respondents were asked to choose one course of treatment: (1) receive usual care; (2) join an RCT which offers a 50% probability of receiving an unproven drug versus receiving placebo, in addition to usual care; and (3) receive the unproven drug directly in addition to usual care. We provided some brief information about potential risks and benefits of the unproven drug (simulating remdesivir). We noted the importance of testing the efficacy and safety of the unproven drug using RCTs, and the equal probability and blindness of receiving the unproven drug and placebo for participants joining the RCT. Information on disease prognosis that may also affect participants making choices was incorporated into the stem of the first three questions. Questions 4–7 collected data on participants’ gender, age, education, and whether participants’ major or occupation was related to medicine. The last question asked participants how avidly they had followed the progress of the COVID-19 epidemic. More detailed information can be found in the questionnaire (see the Supplemental Information). This online survey was deemed to be exempt from review by the Peking University Health Science Center’s Institutional Review Board because it did not involve any sensitive personally identifiable information.

We recruited 1,110 participants who were based in 183 cities of China and nine cities abroad; approximately 60% were females and 40% were males. The majority of participants were aged between 18 and 40 years (83.7%) and had a college education or higher (92.9%). Slightly more than half of the participants had a medicine-related major or occupation, and 95.7% of participants reported paying close attention to the progress of the COVID-19 epidemic.

We found that 3.9% of the participants preferred to receive the unproven drug in the hypothetical scenario of mild COVID-19 infection. This percentage increased drastically to 31.1% and 54.2% in the hypothetical scenario of severe and extremely severe infection, respectively. In contrast, participants...
who chose to receive usual care decreased from 55.1% to 5.7% with increasing hypothetical disease severity. The percentage of participants who preferred to participate in an RCT fluctuated between 40.1% and 54.7% (Table 1). Choices made by participants with and without a medical background were rather consistent (Table 1). Some other factors affected participants’ choices, such as age and education. Their effects, however, were much more modest compared with those of disease severity (data not shown).

Our survey has limitations. First, respondents were making choices in a hypothetical scenario when they were presumably well, and “choices” made while well may not translate into preferences later. Second, we did not provide the kind of detailed information about potential risks and benefits that would presumably be given to patients and families at the time of illness. More detailed information could certainly change preferences. Third, our sampling began with young, educated people who had a medicine-related occupation or major, and so unsurprisingly yielded a sample that differs substantially from the overall Chinese population, as well as the population at risk for severe COVID-19. This could have biased our estimates in either direction.

Nevertheless, our survey indicates that the receptivity of a potentially effective unproven drug is likely to be substantial among actual patients in severe conditions. More recently, results of two placebo-controlled trials on remdesivir have become available. Although their findings on efficacy are not consistent, both showed acceptable safety of remdesivir for treating severe COVID-19 patients and one trial showed a rate ratio of 1.32 (95% confidence interval, 1.12–1.55) for recovery and a hazard ratio of 0.70 (95% confidence interval, 0.47–1.04) for death in 14 days for remdesivir compared with the remdesivir-placebo. This evidence may lead to increased preference for compassionate use of remdesivir, and possibly to compassionate or off-label use of other promising therapies.

From the perspective of deontological ethics, an RCT can only be approved by an ethical committee when potential benefits of the investigational treatment are presumed to outweigh its risks, so compassionate use or off-label use of investigational therapies may have its rationality. This would inevitably delay the generation of sound evidence, and from the perspective of utilitarianism, may harm the interests of more patients. Receiving usual care only or off-label use of investigational therapies may have its rationality. This perspective of utilitarianism, may harm the interests of more patients. This evidence may lead to increased preference for compassionate use of remdesivir, and possibly to compassionate or off-label use of other promising therapies.

Table 1. Percentage of Participants Choosing Each Treatment Option, Overall Results, and Stratified by Medical Background (%)

| Hypothetical COVID-19 Disease Severity | Overall Results (N = 1,110) | Stratified Results With and Without a Medical Background (N = 603) | Without a Medical Background (N = 507) |
|--------------------------------------|-----------------------------|-----------------------------------------------------------------|--------------------------------------|
|                                      | Usual Carea | RCTb | Unproven Drugc | Usual Carea | RCTb | Unproven Drugc | Usual Carea | RCTb | Unproven Drugc | p Value* |
| Mild                                 | 55.1        | 40.9 | 3.9           | 52.4        | 44.1 | 3.5            | 53.1        | 42.4 | 4.5            | 0.61     |
| Severe                               | 14.2        | 54.7 | 31.1          | 13.6        | 58.4 | 28.0           | 15.2        | 53.8 | 31.0           | 0.32     |
| Extremely severe                     | 5.7         | 40.1 | 54.2          | 5.6         | 43.9 | 50.4           | 8.9         | 43.4 | 47.7           | 0.11     |

Percentages may not add up to 100% due to rounding.
aReceiving usual care only.
bJoining the unproven drug RCT in addition to usual care.
cUsing the unproven drug directly in addition to usual care.
dMedical background refers to a medicine-related major or occupation.
*eDerived from chi-squared tests between participants with and without a medical background.

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