



ScienceDirect

Contents lists available at sciencedirect.com
Journal homepage: www.elsevier.com/locate/jval

The Economic and Public Health Imperatives Around Making Potential Coronavirus Disease–2019 Treatments Available and Affordable

Steven Forsythe, PhD, MBA,^{1,*} Joshua Cohen, PhD, MA,² Peter Neumann, ScD,³ Stefano M. Bertozzi, MD, PhD,^{4,5,6}
Anthony Kinghorn, MBBCh, MA⁷

¹Avenir Health, Glastonbury, CT, USA; ²Joshua P. Cohen Healthcare Analytics, Boston, MA, USA; ³Tufts Medical Center, Boston, MA, USA; ⁴University of California Berkeley School of Public Health, Berkeley, CA, USA; ⁵Instituto Nacional de Salud Pública, Cuernavaca, México; ⁶University of Washington, Seattle, WA, USA; ⁷Perinatal HIV Research Unit, University of the Witwatersrand, Soweto, South Africa.

Keywords: COVID-19.

VALUE HEALTH. 2020; ■(■):■–■

Estimates of the global economic costs of coronavirus disease 2019 (COVID-19) vary from \$77 billion to as high as \$2.7 trillion.¹ As of this writing, there have been over 4.3 million infections and 300 000 deaths globally. There is currently no cure for patients with COVID-19, but there are more than 300 different trials launched to discover a drug that would minimize both morbidity and mortality.² Although the availability of a proven treatment for COVID-19 would be met with extreme enthusiasm, the successful testing of any drug will only be the first step in determining how to provide access on a global level. Any treatment must be widely available and affordable to address this global pandemic.

Given the magnitude and pace of the worldwide spread of the novel coronavirus, it is important to preemptively develop strategies for making a treatment available affordably, rapidly, and at scale. Appropriate strategies could avoid delays and inefficient policy decisions and ensure that stakeholders are incentivized to develop and roll out effective products. Organizations such as the Bill and Melinda Gates Foundation, Wellcome Trust, and Mastercard have already committed \$125 million not only to accelerate the development of a COVID-19 therapeutic, but also to accelerate manufacturing and distribution of any such treatment. As stated by Bill Gates, any treatment for COVID-19 must be “available and affordable for people who are at the heart of the outbreak and in greatest need. Not only is such distribution the right thing to do, it’s also the right strategy for short-circuiting transmission and preventing future pandemics.”³

In this commentary, we define affordability in terms of “being relevant if paying for all patients [who are] potentially eligible for a new treatment would force either an overrun of the payer’s planned budget or a displacement of other treatments regarding as being cost-effective.”⁴ In the context of developing countries, affordability would be a particularly acute issue if a COVID-19 medication was very effective and would be required by a large

patient population. Given the limited and short-term health budgets of most developing countries, any such new COVID-19 treatment would require that the country (1) forgo the opportunity to access the new COVID-19 treatment (as occurred in the early days of antiretroviral therapy for HIV in most developing countries), (2) discontinue offering other cost-effective treatment program to access the new COVID-19 treatment, or (3) identify external sources of funding that could pay for the new COVID-19 treatment.

A variety of drugs are currently being tested as potential treatments, including Gilead’s remdesivir, AbbVie’s lopinavir/ritonavir (Kaletra), Fujifilm Toyama Chemicals’ anti-influenza drug favipiravir (Avigan), and generic antimalarials. Remdesivir had apparent success in treating a 35-year-old COVID-19 patient with pneumonia in Washington state.⁵ An analysis of 53 patients receiving remdesivir for compassionate use showed that 36 of them (68%) had clinical improvements, although the results are difficult to generalize given the lack of a control population.⁶ A subsequent trial conducted by the National Institutes of Health found that remdesivir was effective in reducing the length of hospitalization and might decrease the mortality of patients with COVID-19. Lopinavir/ritonavir also seemed to be successful in treating a 62-year-old in Spain with COVID-19,⁷ but a recently published trial suggests the drug may not be effective.⁸ An early trial of favipiravir tablets among 340 patients found that the drug shortened the period to recovery while also improving the lung function of patients.⁹ In the meantime, a range of other medications is being explored, including chloroquine and hydroxychloroquine.¹⁰

Another treatment approach entering trials is the use of antibodies (convalescent sera) from people who have recovered from COVID-19. This approach has been used previously, as long ago as the 1918 influenza pandemic and as recently as the 2014 Ebola

* Address correspondence to: Steven Forsythe, PhD, MBA, Avenir Health, 655 Winding Brook Dr, Suite 400, Glastonbury, CT 06033, USA Email: sforsythe@avenirhealth.org

epidemic.¹¹ The use of convalescent sera is dependent on local availability of sophisticated blood banks with apheresis capacity. Countries that have experienced early epidemics could possibly scale up production, but it will always be a high-cost product. Even the production of monoclonal antibodies is inherently more expensive and more difficult to replicate, typically, than synthesis of small-molecule drugs.

A key question raised by national and international public health officials, as well as companies manufacturing these drugs, relates to the price(s) for a COVID-19 treatment that would be considered just, affordable, reasonable, and fair.¹² Proactive consideration of the question could affect the speed, scale, and effectiveness of decisions and responses, as well as factors such as willingness to invest in research and development. An ideal approach would maximize value globally, assure equity in access to treatment, and focus on those who are worse off.¹³

The example of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) medications illustrates the challenges when a new treatment is discovered and launched, but there is no strategy for making it affordable in the countries most in need. Antiretroviral therapy was found to be a highly effective treatment for people living with HIV in 1996. Nevertheless, at prices of \$10 000 to \$15 000 per patient per year, it was unaffordable in African countries, where most infections were occurring. Antiretroviral therapy only became available in most African countries in 2002 (the launch of the Global Fund to Fight AIDS, Tuberculosis and Malaria) and 2003 (the start of the President's Emergency Plan for AIDS Relief). As a result, more than 5 years were lost because treatment was largely limited to developed countries.¹⁴ Millions died as a result of an inability to provide affordable treatment during this time. This tragic lesson could be sadly relevant for any COVID-19 medication if affordability is not addressed immediately.

In the case of COVID-19, there is great uncertainty about the potential pricing of any treatment. Oppenheimer analyst Hartaj Singh has projected a price of \$50 to \$100 per patient if remdesivir is successful.¹⁵ Financial analysts from Morgan Stanley estimated that remdesivir could be sold for \$260 per patient.¹⁶ RBC Capital Markets has indicated that Gilead could charge between \$900 and \$1000 per patient treated if remdesivir is proven to be effective.¹⁷ Michael Yee from Jefferies' has proposed that Gilead could charge between \$1000 and \$5000 for a round of treatment, again assuming that the drug is effective.¹⁸ These estimates are willingness-to-pay estimates, based on a relatively free market, such as the United States. They are unlikely to be acceptable for most markets outside the United States where prices are often negotiated with a national health authority.

Any manufacturer of an effective COVID-19 therapeutic is likely to adopt a differentiated pricing model, both to maximize their reach as well as profits, though some drug makers may launch treatments on a not-for-profit basis. The lowest prices would presumably be charged to low- and middle-income countries (eg, Ethiopia, Malaysia, Pakistan, South Africa, Guatemala, and Kenya). Moderate prices would be charged in higher-income countries with strictly regulated markets (eg, Japan, South Korea, United Kingdom, France, and Germany). The highest prices would probably be charged in high-income countries with relatively unregulated markets (eg, United States).

Ultimately defining what the value of any treatment is will depend on several factors (Table 1). The first and most critical factor relates to the drug's effectiveness and safety. Even if the drug is effective, it may turn out to be effective only for certain subgroups of patients (eg, the most severely ill), and not recommended for all infected individuals. In addition, a drug may not only be useful for treating an individual infected with COVID-19,

but also in preventing new infections. By reducing viral levels in body fluids, treatment may prevent secondary COVID-19 infections. In addition, it might be feasible to use the drug prophylactically to prevent new infections. This would make treatment especially desirable from a public health perspective.

Price will also be influenced by the manufacturer's market power. There is already a highly competitive race for an effective treatment, with each manufacturer trying to be the first to demonstrate effectiveness and to have their product widely available and patented. If multiple manufacturers can demonstrate successful treatments, there will be a downward pressure on prices, while if there is only 1 successful candidate, the resulting price will likely remain high. There is also the potential for alternatives to treatment such as a vaccine, which could limit the need, and thus the value, of any treatment.

The type of treatment will also play a role in how much countries are able and willing to pay and how much producers will charge. For example, a medication only available as an intravenous injection and requiring hospitalization is likely to be priced differently than an outpatient oral medication. The price of any medication will also be influenced by the cost of manufacturing, including the cost of creating production capacity at scale, the investment in research and development, and the ability of any company to develop the supply chain needed for wide distribution (if that company does not already have such a supply chain) across countries, as well as opportunities for licensing drugs.

From a public health perspective, there will be a large demand for any effective treatment, for both immediate care and for the purpose of stockpiling medications for future outbreaks. Despite the significant public pressure to access any effective treatment, all countries have limits in their ability to purchase any single treatment. Most African countries, for example, have very constrained healthcare budgets. Thus far, they have suffered relatively limited impact from COVID-19. Nevertheless, this could change rapidly with particularly disastrous consequences.

It will also be important to analyze the cost-effectiveness of any new drug from a longer-term and societal perspective. Compared to competing health interventions, the drug might have high costs relative to its effectiveness, making it difficult to prioritize allocating scarce health budgets to the drug, if its price does not fall.

It is also important to distinguish between the price a drug may command on the open market and the out-of-pocket costs of insured patients (or uninsured patients who get subsidies from the government). In the United States, Health and Human Services Secretary Alex Azar has indicated there would not be any price controls per se.¹⁹ Nevertheless, the government may ensure affordability by subsidizing costs (for both insured and uninsured patients), particularly if use of the treatment by more individuals creates externalities in broader social benefits from reducing the spread or impact of illness.

In the event of a very severe, sustained epidemic, there will be pressure for the government, insurers, and manufacturers to agree on volumes, prices, and licenses to other manufacturers, including generic formulations, to create more certainty and capacity for rapidly scaling up access to the drug. In several low- and middle-income countries, marginal cost pricing is used, which sets prices close to the cost of production. Furthermore, countries such as Brazil have already established a precedent by using the threat of compulsory licensing of antiretroviral drugs for treating patients with HIV to increase affordable access.²⁰

The United Kingdom's experience with oseltamivir (Tamiflu) illustrates that governments need to carefully consider factors in making large-scale procurement decisions. Between 2006 and

Table 1. Factors influencing the value of any potential treatment.

Factor	Public health perspective	Manufacturer perspective
Drug characteristics		
Treatment effectiveness	A therapeutic with significant health benefits, in reduced morbidity and mortality, will have greater value for consumers and for the countries purchasing them.	Manufacturers will be able to charge more for a product with significant health benefits.
Speed to market	The speed at which a treatment becomes available is essential, because the costs of illness can increase rapidly as the infectious disease spreads.	Manufacturers will also want to deliver their product quickly to become the standard of care and to make it more difficult for competitors to take market share.
Economies of scale	Countries will want to benefit from economies of scale, especially those countries with a large population and/or a high prevalence of COVID-19. Similarly, if there was pooled purchasing at a global or intercountry level, countries could negotiate a lower price.	Initially rapid scale-up can be costly, resulting in lower margins. Nevertheless, as production expands, the cost of producing the treatment should decline.
Drug route	There may be less demand for a drug that requires injection rather than oral administration, if there are health system capacity constraints.	Manufacturers will prefer a product that could be administered to the largest number of people possible.
Epidemiology		
Severity	Medications that are used to treat more severe illnesses would have greater value than a medication that addresses more mild illnesses.	Manufacturers who treat diseases that are more severe are likely to be able to charge more for the medication.
Infectivity	A more infectious or more pathogenic organism makes it more important to have widespread, rapid access to treatment. A treatment that also reduces infectivity will also have a higher value to society.	A manufacturer is likely to be able to charge higher unit costs for a therapeutic agent that provides preventive as well as therapeutic characteristics.
Scale of demand	Larger-scale demand will pose more challenges of affordability. As the number of people needing treatment increases, the overall price tag becomes higher.	Manufacturers are likely to be willing to negotiate lower prices as countries commit to larger and longer-term purchases, including the purchase of stockpiles of the drug.
Likelihood of multiyear outbreaks	Countries may wish to negotiate lower prices and possibly longer contracts if they are planning to purchase stockpiles of medications for future use.	Manufacturers may have less need to recoup their investment costs immediately if the demand is going to continue in the future, especially if herd immunity effects are limited.
Potential for a vaccine or alternative treatments	Countries may not be willing to pay higher unit prices for treatment in the short run if a vaccine or alternative is imminent or already available.	Manufacturers may try to increase short-term prices if they do not expect long-term demand for their products.
Economic parameters		
Market share	As countries can choose from alternative treatment approaches, they will have greater ability to negotiate lower prices.	Manufacturers will be limited in their ability to charge higher prices if multiple products are approved at the same time.
Cost-effectiveness and cost-benefit of treatment	The greater the cost-effectiveness of any treatment (including benefits from reductions in both morbidity and mortality), the more a country may value that treatment.	A manufacturer with a highly cost-effective product will be able to charge more for that product. On the other hand, products with smaller benefits will not be priced as highly.
Health financing system	Larger countries and those with strictly regulated or centralized purchasing mechanisms would have greater negotiating power to reduce the price of any therapeutic.	Manufacturers may target their sales, at least initially, to countries where purchases tend to be less regulated and ability and willingness to pay is higher (eg, United States).
Economic status of countries	Lower-income countries are likely to have less ability to pay for a treatment, particularly if it also requires other significant healthcare costs. Thus, lower-income countries will require discounted prices of products.	Manufacturers can benefit from differential pricing, charging higher prices in high-income countries and lower prices in low-income countries.

continued on next page

Table 1. Continued

Factor	Public health perspective	Manufacturer perspective
Social and political imperatives		
Disease burden	As total mortality and morbidity rise in a country, the ability of the country to pay per course of treatment would decline, since the number of people needing the treatment would represent a significant commitment by the government.	Suppliers will face political pressure to deliver as quickly and affordably as possible, particularly as potential patients go untreated. Increased volume may compensate for reduced margins per dose or course.
Public relations/advocacy	Countries may encourage advocacy to laud suppliers who are viewed as prioritizing the public good while shaming suppliers who are viewed as taking advantage of a global crisis.	A manufacturer may view the launch of a new drug as perilous given the potential positive or negative perception of that company. Any perception of price gouging could significantly damage their reputation.

COVID-19 indicates coronavirus disease 2019.

2013, the government bought large volumes of oseltamivir at a total negotiated price of \$685 million, in preparation for a flu pandemic.²¹ Nevertheless, the procurement of oseltamivir generated some controversy, because much of the large stockpile was never used, and it was unclear if the effectiveness and cost-effectiveness of oseltamivir was adequate to justify the cost.

Ideally, there would be a global mechanism that would simultaneously incentivize rapid development of treatments for COVID-19 and ensure very rapid and affordable access for the world's population. This will require compensating successful innovation and simultaneously unleashing global generic manufacturing capacity. Much has been written about these types of mechanisms. They typically resemble a large prize that is awarded to the innovator in exchange for the intellectual property rights (at least for low- and middle-income countries). For a pandemic of this sort, it might well be more efficient for the access to be universal, with set global prices (that would presumably be different depending on the wealth of the country) obviating the need for country-specific negotiations. There would be a clear role for a multilateral agency such as the World Health Organization or the World Bank to play.

The complexity of such approaches lies in who is eligible for the prize and how the terms are set. For example, if the prize defines eligibility as a COVID-19 therapeutic that reduces mortality by 50% or more and costs less than \$200 per course of treatment and company A is the first to produce and demonstrate the efficacy of such a product, it would win the prize. If a month later company B introduces a second drug that reduces mortality by 80%, would it also be eligible for the prize? What about company C that produces a drug that is also 50% effective, but costs 1/10th of the cost of company A's drug to produce? Now is the time to contemplate and define these parameters and for countries to immediately commit to a fund that would administer the prizes and negotiate global prices for any treatment.

In conclusion, it is imperative to develop economic scenarios and to assess now how best to assure sustainability, analogous to the way epidemiologists are creating epidemiologic scenarios based on various assumptions about the future. Economic scenarios must consider the characteristics of the potential therapeutics. In each scenario, economists should evaluate methods to incentivize or require manufacturers and donors to invest in developing and providing equitable and affordable access to treatments. Economists should also assess the cost-effectiveness associated with different therapeutics, to inform decision making by national and international policy makers regarding allocation of scarce resources. At the same time, policy makers should

be informed of various ways to make treatments more affordable, including methods for using compulsory licensing, generics, and consolidated national/regional/global purchasing.

Ultimately, the world cannot repeat the mistakes that were made in the early years of HIV/AIDS treatment. Having heavily affected countries excluded de facto from acquiring treatment due to unaffordable price structures is not an acceptable outcome. Economic planning is required to understand incentives, prices, willingness to pay, and cost-effectiveness so that decisions can be made that benefit the entire world when and if a treatment becomes available.

REFERENCES

- Evans D, Over M. The economic impact of COVID-19 in low- and middle-income countries. Center for Global Development. <https://www.cgdev.org/blog/economic-impact-covid-19-low-and-middle-income-countries>. Accessed March 12, 2020.
- Devlin H, Sample I. Hopes rise over experimental drug's effectiveness against coronavirus. *The Guardian*. <https://www.theguardian.com/world/2020/mar/10/hopes-rise-over-experimental-drugs-effectiveness-against-coronavirus>. Accessed March 11, 2020.
- Gates B. Responding to Covid-19 — a once-in-a-century pandemic? *N Engl J Med*. 2020;382(18):1677–1679.
- Danzon PM, Drummond MF, Towse A, Pauly MV. Objectives, budgets, thresholds, and opportunity costs—a health economics approach: an ISPOR Special Task Force Report [4]. *Value Health*. 2018;21(2):140–145.
- Holshue ML, DeBolt C, Lindquist S, et al. First case of 2019 novel coronavirus in the United States. *N Engl J Med*. 2020;382(10):929–936.
- Grein J, Ohmagari N, Shin D, et al. Compassionate use of remdesivir for patients with severe Covid-19 [published online ahead of print April 10, 2020]. *N Engl J Med*. <https://doi.org/10.1056/NEJMoa2007016>.
- Guell O. Un farmaco contra el sida tiene éxito en la cura del primer contagio por coronavirus. *El País*. <https://elpais.com/sociedad/2020-02-28/un-farmaco-contra-el-sida-tiene-exito-en-la-cura-del-primer-contagio-por-coronavirus.html>. Accessed March 18, 2020.
- Cao B, Wang Y, Wen D, et al. A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. *N Engl J Med*. 2020;382(19):1787–1799.
- Inagaki K. Flu drug Avigan speeds up coronavirus recovery in early trials. *Financial Times*. <https://www.ft.com/content/1c6cbefc-6925-11ea-800d-da70cffe4d3>. Accessed March 18, 2020.
- Touret F, de Lamballerie X. Of chloroquine and COVID-19. *Antiviral Res*. 2020;177:104762.
- Casadevall A, Pirofski L. The convalescent sera option for containing COVID-19. *J Clinical Investigation*. 2020;130(4):1545–1548.
- Emanuel EJ. When is the price of a drug unjust? The average lifetime earnings standard. *Health Aff (Millwood)*. 2019;38(4):604–612.
- Emanuel EJ, Persad G, Upshur R, et al. Fair allocation of scarce medical resources in the time of Covid-19 [published online ahead of print March 23, 2020]. *N Engl J Med*. <https://doi.org/10.1056/NEJMs2005114>.
- Forsythe SS, McGreevey W, Whiteside A, et al. Twenty years of antiretroviral therapy for people living with HIV: global costs, health achievements, economic benefits. *Health Aff (Millwood)*. 2019;38(7):1163–1172.
- Sozzi B. Coronavirus vaccine could add billions in value to this one stock. Yahoo Finance. <https://finance.yahoo.com/news/coronavirus-vaccine-could-add-billions-in-value-to-gilead-161233464.html>. Accessed March 4, 2020.

16. Prvulovic M. Will Gilead Sciences make a fortune off its coronavirus drug? The Motley Fool. <https://www.fool.com/investing/2020/03/09/will-gilead-sciences-make-a-fortune-off-its-corona.aspx>. Accessed March 9, 2020.
17. Pagliarulo N. A closer look at the Ebola drug that's become the top hope for a coronavirus treatment. BioPharmaDive. <https://www.biopharmadive.com/news/coronavirus-remdesivir-gilead-antiviral-drug-covid-19/573261/>. Accessed March 5, 2020.
18. Shtrubel M. Gilead Sciences could be the first to beat the coronavirus. Nasdaq. <https://www.nasdaq.com/articles/gilead-sciences-could-be-the-first-to-beat-the-coronavirus-2020-03-08>. Accessed March 8, 2020.
19. Togoh I. Health secretary Alex Azar refuses to guarantee coronavirus vaccine would be affordable for all. *Forbes*. <https://www.forbes.com/sites/isabeltogoh/2020/02/27/health-secretary-alex-azar-refuses-to-guarantee-coronavirus-vaccine-would-be-affordable-for-all/#4385256f490c>. Accessed February 27, 2020; 2020.
20. Guennif S. Evaluating the usefulness of compulsory licensing in developing countries: a comparative study of Thai and Brazilian experiences regarding access to AIDS treatments. *Dev World Bioeth*. 2017;17(2):90–99.
21. O'Dowd A. Government says it would stockpile Tamiflu again. *BMJ*. 2014;349:g6386.