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Five Ways that COVID-19 Diagnostics Can Save Lives: Prioritizing Uses of Tests to Maximize Cost-Effectiveness

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Supplies of tests to diagnose the virus that causes COVID-19 (SARS-CoV-2) are still limited in many countries, and there is uncertainty about how to allocate the scarce supply across alternative types of testing to support diagnosis and disease control in the most cost-effective way. This Research & Policy Brief quantifies the cost-effectiveness of five types of interventions in terms of tests required per death averted. Across the five types, a single death can be averted by administering 940 to 8,838 tests, implying a large and positive return on investment in all five types—even assuming a very low value for loss of life. That is, all five types pay for themselves many times over. When prevalence of SARS-CoV-2 is high, the most cost-effective uses of SARS-CoV-2 diagnostics seem to be clinical triage of patients, at-risk worker screening, and population surveillance. Test-trace-isolate programs and border screening are also worthwhile, although they are more resource intensive per death averted if done comprehensively. These latter two interventions become relatively more cost effective when prevalence is low, and can stop the virus from entering a community completely. While governments should seek widespread deployment of tests in all five types of interventions, prioritizing them in this way is likely to maximize the cost-effectiveness of their use. As more contagious strains emerge, each type will become more valuable than ever.

Introduction

SARS-CoV-2, like many infectious diseases, can be transmitted from persons who are not obviously ill. This presents a major challenge because it means that a public health response cannot rely upon symptoms to track and control its spread (Fraser et al. 2004). Indeed, even if everyone immediately self-isolated upon the onset of symptoms, and the self-isolation eliminated any risk, this would reduce transmission by, at most, 50 percent (Grassly et al. 2020)—and that is not enough to avert an epidemic of SARS-CoV-2.

Because vaccinating enough of the population to reach herd immunity will take time, in both high-income countries (where a majority are hesitant to get the vaccine immediately) (Galewitz 2021) and in middle-income and low-income countries (where supplies could be constrained until 2024, according to a risk-assessment by COVAX (Beaumont 2020), a global facility to provide universal vaccine access), countries continue to implement nonpharmaceutical interventions, including social distancing and full or partial lockdowns. Lockdowns can arrest epidemic spread in many settings (Flaxman et al. 2020) but carry enormous economic costs—perhaps 0.25 to 0.86 percent of GDP per week (see Acemoglu et al. 2020; Alon et al. 2020; de Walque et al. 2020; Eichenbaum, Rebelo, and Trabandt 2020). Notably, China's GDP declined by 0.86 percent per week in the first quarter of 2020. In settings where households lack buffer stocks of food and savings, and must leave their homes for their livelihoods in the absence of social protection, lockdowns may not be feasible and there may be greater reliance on a set of "social distancing" measures. Such measures may have an important effect, but the available evidence does not suggest they would be sufficient to avert an epidemic (Flaxman et al. 2020), especially as contagiousness rises with new strains.

Fortunately, diagnostics can be used to test persons for the presence of current infection. This opens new approaches to control transmission and ease the trade-off between economic and health concerns with targeted rather than general containment measures. In combination with a range of other concerted activities (self-isolation and nonpharmaceutical interventions), they could contribute enormously to saving lives and minimizing costly lockdowns.

This Brief considers five types of intervention (among many) to pinpoint the means by which testing for SARS-CoV-2 can contribute to saving lives during the COVID-19 pandemic (table 1). These cases are provided as quantitative illustrations of what may be possible. The precise way in which tests can be best put to use in any particular setting, and the actual benefits derived, are highly sensitive to many factors specific to the setting and mode of use. The Brief considers

Table 1. Summary of Diagnostic Cost-Effectiveness by Type of Intervention

	Intervention	Tests per death averted	COVID-19 deaths averted	Tests required	Testing population
1	Clinical triage and cohorting	940	106	100,000	100,000 patients upon admission
2	At-risk worker screening	1,042– 5,208	19–96	100,000	100,000 workers for one week
3	Population surveillance to trigger or avoid lockdown	1,611	175	281,884	Regular samples per 100,000 for one year
4	Test-trace-isolate	4,459	392	1,763,485	Regular samples per 100,000 for one year
5	Border screening	8,838	11+	100,000	100,000 border crossers

Source: Authors' calculations.
Note: Tests per death averted may not match ratio of tests required to COVID-19 deaths averted due to rounding. All scenarios consider the incremental value of testing, compared to a scenario where individuals are isolated based on symptoms alone. The major effect of border screening is in minimizing the introduction of virus to the country and so contributes to making all the other aspects of mitigating epidemic more likely to work. " + " indicates that the estimate of deaths averted refers only to the number of infections among those quarantined, who were not already infected.

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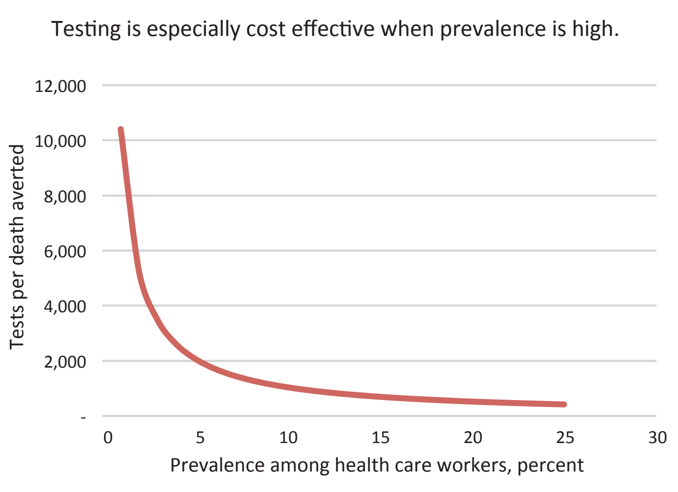
those tests that detect infection 90 percent of the time (test sensitivity), and correctly identify negative cases 97 percent of the time (test specificity), in line with available antigen-based rapid diagnostic tests. The details of each type are considered in turn in the discussion that follows, although it is important to note that these cases do in fact interlock and depend upon one another.

The analysis also computes the cost-effectiveness of each type, as measured by "tests per death averted" (see results in table 1). The incremental impacts of diagnostics are considered, over and above self-isolation and social distancing. Given the low cost of a single test, the results suggest benefits that substantially exceed costs: a death can be averted for the cost of $4,700 to $44,190, depending on type, or the cost of 940 tests to 8,838 tests at $5 each. Following others who have quantified a return on investment (ROI) with respect to the recommended value of a statistical life, the ROI of one test ranges between 3.5 (for border screening) and 41.6 (for clinical triage and cohorting) when assuming a low value of statistical life of only $200,000— which is 2 percent (1/50) of the estimate for the United States derived by Robinson et al. (2019). Higher valuations would lead to even higher returns.

In certain circumstances (described in the discussion that follows), these returns are in addition to other major benefits, such as avoiding lockdowns and increasing confidence among consumers and workers.

These estimates tend to be conservative, as they do not incorporate several factors that are likely to be important. First, several of the calculations consider only the effect of the intervention on reducing transmission from a single person, and do not account for the effect that this may have in stemming a whole chain of transmission. The analysis focuses only on deaths, whereas SARS-CoV-2 also causes substantial illness, and long stays in hospital for many patients are costly and may overwhelm the health system, increasing the risk of death overall. The benefits of controlling hospital-acquired (nosocomial) infections— by placing patients known to be infected with SARS-CoV-2 in isolation wards together and screening health care workers may have the additional benefit of lessening disruption of other services and freeing up staff to attend to other forms of care; this could help avoid knock-on consequences of the COVID-19 epidemic (Hogan et al. 2020). Other economic benefits may not be reflected in these calculations: for instance, screening of key workers may enable more business to continue operating, and screening haulers at the border (rather than closing borders) helps international trade to continue.

Figure 1. How the Prevalence of SARS-CoV-2 among Health Workers Influences the Number of Tests Needed to Avert One Death



Source: Authors' calculations.
Note: Calculation assumes 100,000 health care workers, a case fatality rate of 1 percent, and a basic reproduction number of 3, consistent with a high degree of interaction in the clinical setting.

Five Types of Interventions

1. Clinical Triage and Cohorting

In a clinical setting, diagnostic tests may be used to confirm patients' infection so that infected patients may be grouped together and isolated from other patients, a policy known as cohorting. Without a test for SARS-CoV-2, this may be done instead based on symptoms, whereby hospitals group all patients without symptoms together. As a result, those who are not infected may be grouped with those who are infected with SARS-CoV-2 but are asymptomatic.

Authors' calculation shows that cohorting using a diagnostic test rather than symptoms alone can reduce infections originating from the hospital by 87 percent, resulting in 106 fewer deaths per 100,000 patients at the peak of the epidemic. It is assumed that 50 percent of patients entering the hospital have SARS-CoV-2 at the peak of an epidemic. To account for risk of in-hospital infection, it is assumed that the potential for transmission (i.e., R_0, the basic reproduction number) is 2.5 in the hospital setting (meaning that each infection leads to 2.5 more infections), but this does not affect the proportionate reduction in transmission risk that is provided by the use of testing (see Excel spreadsheet for calculation).

2. At-Risk Worker Screening

The risk of any group of workers contributing to onward transmission can be reduced by screening them for SARS-CoV-2. Screening enables those persons who are infected but not symptomatic to self-isolate (in addition to those who have symptoms) (Grassly et al.2020). The impact depends on how often they are screened and the delay until they self-isolate (if the test is positive). If screening is done weekly and test results are provided before they risk infecting others, this could reduce the risk of onward transmission by about 32 percent.

The cost of at-risk worker screening depends on the number of tests needed to find one person who is currently infected who would not self-isolate without screening: that is, the prevalence of SARS-CoV-2 among those without symptoms in that group. Thus, screening is more cost effective when it is done on higher-risk groups, such as health care workers, and those in public-facing roles. This prevalence will depend on the epidemic stage and other factors: for example, it was found to be as high as 10 percent among health workers in London at the peak of the epidemic (see, for example, Treibel et al. 2020), and 20 percent among those on COVID-19 wards in an Oxford hospital (Eyre et al. 2020), but 2 percent in frontline workers in the United Kingdom overall some weeks later (see, for example, the 2020 ONS survey in the United Kingdom). Between these high and low extremes, the number of tests per death averted ranges between 1042 and 5208, respectively (figure 1). Thus, when deployed among a group at very high risk, this would appear to be one of the most cost-effective and widely applicable types of interventions.

3. Population Surveillance to Trigger or Avoid Lockdown

If the policy is to implement a lockdown in an area (such as a large city) if there is a chance that the prevalence of SARS-CoV-2 infection is more than 2 percent, random samples could be drawn from the population to inform that decision. This trigger value of prevalence is chosen somewhat arbitrarily. Smaller trigger values would require larger sample sizes but lead to longer periods of lockdown. It is an open question (not addressed here) as to the optimal triggers to use in this regard.

As an example, a daily random sample of 772 persons (or an equivalent) could be used to check if it can be ruled out (with 99 percent certainty) that prevalence exceeds 2 percent (see online appendix A for derivation) To have the same certainty that the prevalence is below 0.1 percent would require a random sample of 15,745 persons. The same-size sample is required to measure prevalence (with a given level of certainty) in any population, if the sampling is representative.

Using the epidemiological model described in online appendix B, this analysis calculates lives saved from a lockdown policy that triggers when more than 2 percent of tests are positive, and is released when less than 1 percent of tests are positive. The lockdown is calibrated to reduce interpersonal contact such that the Reproduction Number (R) falls below 1. If implemented for one year, the lockdown policy guided by random sampling is expected to avert 175 deaths per 100,000 people at the cost 281,884 tests per year (that is, 772 tests per day), leading to a cost-efficiency of 1,611 tests per death averted.

By the same token, because lockdown can be released quickly (or avoided altogether when unnecessary), days of unnecessary lockdown are avoided, and this would minimize disruptions to the economy. Box 1 describes how such an approach may have contributed to imposing and relieving lockdowns in Italy.

Box 1. Population Surveillance to Guide a Response in Practice

Italy was the country second worst affected by COVID-19 after China by March 2020. When the country suffered its first death on February 22 in the small town of Vo (3,000 inhabitants) in Veneto, the whole town was put in quarantine and every inhabitant was tested. During the first round of testing, 89 people tested positive. During the second round, 9 days later, only 6 were infected. Interestingly, the Italian authorities found that at the time of the first symptomatic case, about 3 percent of the population had already been infected and most of them were completely asymptomatic. Through mass testing and isolation of those infected, the virus was eradicated from the town rapidly. At least 60 percent of all people infected by the virus were asymptomatic. Mass testing can give a clear picture of how many people are carrying the virus and can transmit it to others.

Source: Crisanti and Cassone 2020.

4. Test-Trace-Isolate

Again using the epidemiological model outlined in online Appendix B, the analysis considers a "test-trace-isolate" (TTI) intervention being rolled out, whereby an index person who has had symptoms (who is self-isolating) receives a test. If the test is positive, their recent contacts are instructed to self-isolate, and they, in turn, are tested. If their test is negative, they will cease self-isolating. If the test is positive, a new round of contact tracing occurs whereby their own recent contacts are instructed to self-isolate and then are tested. TTI is the most targeted form of lockdown; it is applied only to those who are infectious. Box 2 presents a the case study of this intervention in practice.

Box 2. Test-Trace-Isolate in Practice

The Republic of Korea experienced a steep growth in COVID-19 cases early in the pandemic, but it quickly reduced rates of infection and maintained low numbers of daily new cases. Korea did not implement strict lockdown measures, but focused on case-based contact tracing and cluster testing and isolating. The country expanded testing capacity from 3000/day on February 7, 2020 to 15,000/day to 20,000/day, with a turnaround time of 6 hours to 24 hours by the end of March. All suspected cases and patients under investigation are tested. Contact-tracing is performed through a mix of patient interviews and analysis of mobile phone location, credit card transactions, and health data.

Source: Dighe et al. 2020.

The analysis focuses on a highly effective testing and tracing system whereby tests are provided quickly (90 percent within 48 hours) to those who are self-isolating; the message to self-isolate is conveyed to all contacts rapidly (90 percent within 48 hours); and the intervention begins from a point when incidence is low (0.01 percent of the population infected). It considers a city of 100,000 people in which other available interventions have already been used. The analysis assumes that the R_0 is 1.5, having been reduced through effective social distancing measures, and further assumes that 25 percent of persons self-isolate effectively upon the onset of symptoms that could be caused by COVID-19. In addition, persons may have symptoms that are caused by another pathogen but that are mistaken as being those of COVID-19, and this leads to unnecessary periods of isolation for some.

Compared to a scenario without it, the test-trace-isolate intervention could help avoid a wave of the epidemic, preventing 392 deaths per 100,000. If a more general lockdown would have been ordered (as per the same criteria), the intervention would also help avoid that lockdown. This would spare the economy a loss of 12 percent of GDP, assuming productivity under lockdown is 70 percent lower than normal.

The distinctive contribution of the testing component (as opposed to the tracing and isolating components) is to allow persons who are not actually infected to avoid the period of isolation (which they would endure if there were no testing and they had symptoms or were in recent contact with someone who did and were traced). An intervention that includes testing leads to 29 percent fewer person-days spent in isolation than one that does not include testing.

These calculations are sensitive to many assumptions but are broadly consistent with other independent analyses of the impact of contact tracing (Ferretti et al. 2020; Grassly et al. 2020; Kucharski et al. 2020). The assumption used here that half the people infected with SARS-CoV-2 have no symptoms but have the same risk of transmission as others makes our estimates of the impact of the "test-trace-isolate" intervention conservative. However, the intervention would be substantially less effective if it was slower to test and trace persons than assumed here, or started from a point of a higher number of cases. The intrinsic value of testing per se would also be lower if the frequency of symptoms not caused by SARS-CoV-2 (but rather by influenza) was lower, or adherence to self-isolation did not increase even if those tested received a positive test result.

5. Border Screening

The number of infected persons entering a country can be reduced through testing and quarantine of those testing positive. Again, this approach is more effective than solely quarantining persons who have symptoms. The proportional reduction in the number of persons with SARS-CoV-2 who enter the country following screening is equal to the sensitivity of the test: so, a 90 percent sensitivity test implies 90 percent fewer introductions of infection to the country, compared to screening with symptoms alone. The fewer persons who enter a country with infection, the less likely it is that the infection will spread widely and the more likely it is that effective measures can be put in place to control it. Of course, the effectiveness of border screening also depends on what coverage of border-crossers can be achieved.

There is further risk that, without testing, quarantine of persons with symptoms crossing the border can result in additional infections, if those quarantined are housed in the same location as those without SARS-CoV-2 (for example, Zimbabwe reports new infections at quarantine facilities, ACF 2020). Authors' calculations show that "border screening" could achieve 11 fewer deaths per 100,000 people crossing the border. Here, it is assumed that 1 percent of the population crossing the border has SARS-CoV-2, and that R_0 is 3.0, to account for the fact that social distancing may not be adhered to at border crossings. A lower R_0 would imply fewer deaths averted per test (see Excel spreadsheet with the calculation).

Economic Considerations

This Brief has illustrated five ways that SARS-CoV-2 diagnostics can save lives, and has estimated the cost-effectiveness of each type of intervention using a standard epidemiological approach. There is a large and positive return on investment in diagnostics in all five types, even for a very low value of a statistical life. Clinical triage and cohorting; population surveillance to trigger or avoid lockdown; and at-risk worker screening appear to be the most cost effective, followed by test-trace-and-isolate programs and border screening. While governments should seek supplies to deploy diagnostics in all five types, prioritizing them in this order is likely to maximize the cost-effectiveness of their use.

To arrive at these results, the analysis has assumed that disease prevalence is very high—that is, the pandemic is out of control—as is the case in many countries. A caveat demonstrated in figure 1 is that deaths averted per test falls as disease prevalence falls, because with lower prevalence more tests will be used on those who are not infected. For countries with very low prevalence and where very few cases would be detected in a clinical setting, border screening may be more cost effective than either clinical triage and cohorting or screening of at-risk workers. Readers may use our Excel tool to compare cost-effectiveness under alternative levels of prevalence.

Additional considerations concern how transmissibility and virulence affect the calculations. New, more contagious strains imply that any single social interaction is more likely to lead to infection, which will only make testing more valuable. Differences in the age distribution and obesity rates across communities may affect the case fatality rate (Goldberg and Reed 2020) and thus deaths averted per test, though such differences will not materially affect the ranking of the five types of interventions by cost-effectiveness within a community. Moreover, even with a lower case fatality rate, each type will still have an ROI greater than 1, even for a very low value of a statistical life.

The effectiveness of testing is linked to how much societies invest in it. If countries invest more in the research and development of more accurate and rapid tests and in the complementary skills required for delivery and tracing, this investment can help save even more lives and livelihoods.

Finally, social returns from testing are higher than individual returns. Indeed, contagion implies a negative externality (a cost to others that is not internalized by the contagious individual), while testing implies a positive externality (a benefit that extends to society beyond the contagious individuals' benefit). This wedge between private and social benefits is particularly high for asymptomatic but infectious people because they have no incentive to get tested or to isolate themselves. To solve this externality, governments should think about using incentives for people to get tested. Such incentives for testing have been used in the past for tuberculosis (TB) and HIV (Geffen 2011; Keating 2013).

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