

lic health policies and clinical decisions by different avenues, in both domains we must often make choices with less-than-perfect evidence.

Many U.S. governors are opening up workplaces now without requiring evidence of immunity or prior infection. Is this policy better than a more nuanced policy of requiring less virologic testing and mitigation for people who obtain a positive result from a serologic test — even an imperfect one — based on the unproven but likely premise that there is some immunity conferred by the presence of antibodies? We don't give penicillin to everyone with a sore throat; a throat culture is usually a prerequisite. Even though throat cultures have false positives and false negatives, they are still useful.

Demands for guarantees are both particularly appealing and especially dangerous in times of crisis. The Covid-19 pandemic throws the risk–benefit trade-off into relief so stark that many of us would rather turn away than confront it. By soft-pedaling the less tangible, less emotionally salient considerations that figure into a decision, insisting on certainty permits policymakers to speak with persuasive, decisive clarity in the space of a tweet. No need for “on the other hand” equivocation. Those who believe that no economic benefit justifies the risk of spreading Covid-19 can find shelter in the solution of not reopening the economy until the entire population is covered by a completely effective vaccine or until a highly effective treatment is widely available. At the other extreme is the solution arrived at by those who would reopen the economy without regard for the

risks that individual workers would incur and impose on others.

A more reasoned, humane position is to take explicit stock of the benefits and harms. Four independent pieces of information need to be weighed against one another in assessing serologic testing as a basis for returning people to work.

First is our understanding of the presence of SARS-CoV-2 antibodies in the population (prevalence). Second is our understanding of the performance of serologic testing — both its ability to detect the presence of antibodies (test sensitivity) and its ability to confirm the absence of SARS-CoV-2 antibodies when they are truly absent (test specificity). Third is our beliefs about whether and how antibodies confer immunity; if they do, what do we assume about the relationship between antibody level (titer) and the resultant degree and persistence of any immunity that is conferred? Fourth is our belief about the relative magnitude of the two different kinds of harm that we could cause: the net harm of mistakenly releasing a susceptible, and potentially infectious, person into the workforce with minimal mitigation (false positive cost) and the net cost of failing to certify a truly immune person to rejoin the workforce (false negative cost).

The delicate balance to be struck among these four considerations can be described mathematically, but the bottom line is this: we have enough evidence and expert opinion to make an informed decision today. And we can put the monitoring systems in place to learn from that decision so that we can make even better choices tomorrow.

In the world of randomized clinical trials, statisticians test scientific hypotheses by requiring a probability of less than 5% that the observed result could have occurred by chance. This so-called type I error — and the associated mistake of approving a truly ineffective (or even dangerous) drug — is the enemy of the truth. But reducing the risk of type I error places us unavoidably at greater risk of committing a type II error and failing to approve a truly effective drug. In times of crisis, when the consequences of both action and inaction are so serious, it makes sense to take into account the benefits and harms of all possible errors and to be prepared to commit some type I errors in exchange for fewer type II errors and the opportunity to learn something important.

To be sure, there are problems with serologic testing. Tests with poor quality control and unacceptably high error rates need to be culled out, as the Food and Drug Administration has begun to do.³ Persons receiving false positive test results may be mistakenly reassured that they are safe and may pay less attention to basic prevention (e.g., social distancing). Tests with nontrivial false positive rates should not be used when the prevalence of the condition being tested for is too low, as it remains in most communities. First-generation antibody tests for HIV had specificities in the range we currently see for Covid-19 antibody tests, but today HIV antibody tests are 99.5% specific.⁴ Soon, Covid-19 antibody tests could reach that level of accuracy.⁵

Important ethical questions need to be addressed regarding

the implications of restricting work on the basis of health status. Any public policy that distinguishes among citizens according to their Covid-19 serologic status has the potential to threaten rights of equal access to paid employment, undermine freedom to socialize and to travel, violate expectations of privacy, and exacerbate enforcement practices that discriminate against vulnerable groups.

The risks of reopening workplaces and the economy to individuals and communities are real; steps in that direction should be taken cautiously. Antibody testing, made available to those in the workforce, will soon offer a scientifically valid way to better determine workplace access and mitigation strategies based on the

risk that individuals may transmit the virus to or acquire the virus from coworkers. But the costs of delaying any reopening until we are certain that no one returning to work will transmit Covid-19 are also real. There is no such thing as a 100% safe bet. Let's not permit an unattainable ideal to be the enemy of a very good option that we currently have.

Disclosure forms provided by the authors are available at NEJM.org.

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This article was published on June 5, 2020, at NEJM.org.

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DOI: 10.1056/NEJMp2017739

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