Combination prevention for COVID-19

The coronavirus disease 2019 (COVID-19) pandemic has produced the fear and disorder inevitably provoked by emerging pathogens. As such, it should also inspire consideration of our experience with HIV over the past 40 years. As with HIV, the road to reducing infections with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, the cause of COVID-19), and attendant morbidity and mortality, requires medical and nonmedical strategies. The most important lesson learned from tackling HIV is to use a combination of prevention strategies.

The first step to stopping the spread of SARS-CoV-2 has already been taken—behavioral changes. This reflects a rapid but imperfect understanding of the transmission of this virus. At the beginning of the AIDS epidemic, changes in sexual behavior, condom promotion, and government interventions (closing "hotspots" of HIV transmission such as bathhouses) made a difference. For SARS-CoV-2, masks and gloves, hand hygiene, and "shelter in place" mandates have already demonstrated benefits. More efficient behavioral intervention requires better understanding of the rules governing SARS-CoV-2 transmission. What are the risks from exposure to respiratory droplets, airborne virus, and surface contamination? What concentration of SARS-CoV-2 is required for transmission? Evidence suggests that SARS-CoV-2 transmission is greatest very early in infection prior to development of symptoms—the same lessons learned from HIV. Given this rule of transmission, biomedical prevention strategies that provide reliable protection become essential. And as has proven true for HIV, directing prevention to people at the highest risk for SARS-CoV-2 infection or the worst disease outcomes will be an important consideration.

Historically, antiviral therapies that reduce the severity of infection have preceded the development of biomedical approaches to prevent onward transmission (although interruption of viral replication also offers a prevention benefit). The first HIV treatment, azidothymidine (AZT), extended life by up to 18 months, providing hope that HIV infection could be transformed from a death sentence to a treatable disease. Reduced risk of mother-to-child transmission by AZT was the first biomedical prevention against HIV transmission. This success was the precursor to "pre-exposure prophylaxis." AZT also launched research focused on "treatment as prevention" where antiviral agents reduce the HIV viral load to a point where infected people no longer transmit. This approach, which uses combinations of powerful antiretroviral agents, is now the mainstay of HIV prevention worldwide.

For SARS-CoV-2, we have leapt into a cacophony of clinical trials of drug candidates with differing degrees of plausibility. Preliminary results from a large randomized controlled trial show that the antiviral drug remdesivir substantially reduced the duration of hospitalization for COVID-19. To date, COVID-19 testing results have been used primarily for patient isolation, contact tracing, and quarantine. But effective therapies will lend great urgency for the universal availability of rapid and reliable testing for SARS-CoV-2 infection, so that treatment can be provided when indicated.

Long-acting antiviral agents and monoclonal antibodies that neutralize SARS-CoV-2 may become important nonvaccine pharmacologic tools for prevention. Antiviral agents that prevent replication of SARS-CoV-2 could be used as pre-, peri-, or postexposure prophylaxis. Several different potent monoclonal antibody combinations designed to treat and prevent SARS-CoV-2 will enter clinical trials in June 2020.

Ultimately, a safe and effective vaccine is crucial for preventing COVID-19. Vaccine efforts started immediately after the discovery of SARS-CoV-2. Numerous vaccine candidates have been identified, and early-phase vaccine studies of several are underway. Proof of vaccine efficacy will require large trials with 6000 to 12,000 participants or more in each study. Because SARS-CoV-2 is moving around the planet, clinical research teams must prepare for trials where incident infections occur (a sufficient "attack rate"). We cannot predict the time of availability or degree of efficacy of a SARS-CoV-2 vaccine with precision, but most trials in development are designed to demonstrate 60 or 70% prevention efficacy, not 100% protection.

HIV has taught us that multiple concomitant prevention strategies are essential. Behavioral changes to reduce SARS-CoV-2 spread must be accepted as the "new normal." The COVID-19 toolbox must include safe and effective interventions whose values have been proven through robust scientific methods honed over decades. Ongoing research in each prevention domain must be sustained. We simply cannot depend on any single "magic bullet."

–Myron S. Cohen and Lawrence Corey

Myron S. Cohen is a professor in the Department of Medicine, Division of Infectious Diseases, and The Institute for Global Health and Infectious Diseases at the University of North Carolina at Chapel Hill, Chapel Hill, NC, USA. mscohen@med.unc.edu

Lawrence Corey is a professor in the Vaccine and Infectious Disease Division at the Fred Hutchinson Cancer Research Center, Seattle, WA, and a Professor of Laboratory Medicine and Medicine at the University of Washington, Seattle, WA, USA. lcorey@fredhutch.org