### Title
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### Authors
Strathdee, Steffanie A
Martin, Natasha K
Pitpitan, Eileen V
et al.



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What the HIV Pandemic Experience can Teach the U.S. about the COVID-19 Response

Steffanie A. Strathdee, PhD[a], Natasha K Martin, DPhil[a], Eileen V. Pitpitan, PhD[b], Jamila K. Stockman, PhD[a], Davey M. Smith, MD[a]

[a]Division of Infectious Diseases and Global Public Health, Department of Medicine, University of California San Diego, 9500 Gilman Drive, MC0507, La Jolla CA 92093

[b]San Diego State University, School of Social Work, 5500 Campanile Drive, San Diego, CA 92182-4119

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Corresponding Author: Steffanie A. Strathdee, PhD, Division of Infectious Diseases and Global Public Health, Department of Medicine, University of California San Diego, 9500 Gilman Drive MC0507 La Jolla CA 92093, P: (858) 822-1952, F: (858) 534-4642

**Running Head**: Lessons from HIV/AIDS applied to COVID-19

**Abstract**

**Background**: The novel coronavirus, SARS-CoV-2, which was first recognized in December 2019, is responsible for the COVID-19 pandemic that is having a devastating impact on human health, society and the global economy.

**Methods**: We summarize lessons learned from the HIV epidemic that offer insights about how the response to COVID-19 can be improved, especially in the United States which has incurred one quarter of world's infections to date.

**Results**: Lessons learned include: the need to develop and deploy valid tests for point-of-care diagnosis and surveillance; the importance of considering HIV and COVID-19 in the context of syndemics; the potential role of structural interventions that address drivers of disparities; how existing research infrastructure can be leveraged to accelerate development of therapeutics and vaccines; and how modeling that is tailored to regional epidemics can inform policy.

**Conclusions**: The window of opportunity to prevent a widespread COVID-19 epidemic in the United States has already closed, but it is not too late to implement a mitigation strategy that can save thousands of lives. Decisive leadership that develops policies grounded in scientific evidence is key to charting a path forward. The question is whether the United States is prepared to learn from its past successes and mistakes with the HIV epidemic to develop a nation-wide plan that puts politics aside and prioritizes saving lives.

Keywords: HIV; pandemic; epidemic; COVID-19; SARSCoV-2

## Introduction

The COVID-19 epidemic that first began in China in early 2020 has quickly become a pandemic that is having a tremendous impact on the physical and mental health of populations and how they live, work and socialize. The last time a respiratory virus caused a pandemic with such far-reaching consequences was in 1918, when H1N1 influenza killed nearly fifty million people worldwide.[1] However, since the early 1980's, the world has been dealing with another devastating pandemic, when the virus first known as Human T-cell Lymphotrophic Virus III (HTLV-III) -- and later Human Immunodeficiency Virus (HIV) -- was first identified as the causative agent responsible for Acquired Immune Deficiency Syndrome (AIDS).

By the end of 2018, 75 million people had been infected with HIV, of whom 32 million hav died and 1.7 million people were newly infected that year.[2] The number of reported HIV cases in the U.S. overall is relatively low (1.2 million) and has been relatively stable for the last several years (13.3 per 100,000) relative to many low and middle income countries, especially those in Africa, Central and Southeast Asia and Eastern Europe. However, national HIV surveillance data masks disproportionate incidence among Blacks and Latinx, especially young MSM, and those living in southern states[3], as well as people who inject drugs (PWID) in many rural and semi-urban areas.[4] For over thirty years, researchers, civil society and policymakers have worked to prevent HIV transmission by developing and scaling up interventions aimed at individual and community-level behavior change. International teams and networks of researchers, philanthropists, non-governmental organizations (NGOs) and pharmaceutical companies have also strived to develop efficacious antiviral treatments and ensure equitable access, and are still pursuing efficacious preventive and therapeutic HIV vaccines.

For those on the frontlines of the HIV pandemic, the early days of the COVID-19 pandemic has brought a surreal sense of déjà vu. While HIV and SARS-CoV-2 have different viral lineages and their transmission routes differ, the world's experience with the HIV pandemic can still offer insights about how we can improve our response to COVID-19. In their recent commentary, Hargreaves and colleagues offered three lessons that the HIV epidemic has taught us to anticipate and address inequalities, create an enabling environment for behavior change and launch a multidisciplinary effort to design and evaluate interventions that promote behavior change.[5] We agree and offer additional lessons from the HIV epidemic that can help chart a path to reduce morbidity and mortality associated with COVID-19. We focus our discussion primarily on the U.S., which has borne the greatest burden of reported COVID-19 cases to date.

**The Importance of Surveillance and Diagnostic Testing**

Although the history of the HIV pandemic is well known to most *JAIDS* readers, it is helpful to review hallmarks of its epidemiology to compare to the recent COVID-19 pandemic. In 1981, it was first reported that young gay men were dying of rare illnesses associated with immune suppression in cities like Los Angeles and New York,[6] followed by similar observations among blood transfusion recipients and PWID. Health officials recognized that they were dealing with a new infectious disease that eventually spread to every continent through infected body fluids, predominantly infected blood and semen. However, it wasn't until 1984 that its etiology was linked to a novel virus: HIV.[7,8]

Although it was determined years later that HIV had jumped from chimpanzees to humans in the 1950's and subsequently spread widely in the U.S. gay male community in the 1970's,[9] numerous conspiracy theories persisted that HIV was invented by the U.S. government or the pharmaceutical industry, which at times has significantly hampered efforts to promote HIV prevention and treatment.[10,11] Once the syndrome was described, scientists started work on identifying the etiology and developing a diagnostic test. Yet it took almost four years from the first report of AIDS in the literature to the time when a HIV antibody test was available, and another twelve to develop a viral detection assay to diagnose acute HIV infection.[12]

In contrast to HIV, SARS-CoV-2 was detected relatively quickly. Astute health officials and epidemiologists identified new respiratory infections and deaths from an unknown cause in Wuhan, China between November and December 2019, although some speculate it may have first appeared months earlier.[13] Using next generation amplification and sequencing technologies that were not available in the 1980's, scientists worked quickly to identify the pathogen as a novel coronavirus that was eventually designated as SARS-CoV-2.[14] Teams investigating the infection benefited from lessons learned from the relatively recent epidemics of related coronaviruses, sudden acute respiratory virus (SARS-CoV-1) that emerged in 2003[15] and Middle-Eastern Respiratory Syndrome (MERS) in 2012.[16] Despite rumors that SARS-CoV-2 was genetically engineered in Wuhan or the U.S, sequencing of the SARS-CoV-2 genome confirmed that it was not derived or purposefully manipulated in a laboratory.[17] All three coronaviruses have been found to originate in animals, with SARS-CoV-1 being found in civets and MERS being traced to camels.[18] SARS-CoV-2's genetic composition closely resembles that of bats, although some studies have implicated an intermediate host such as a pangolin.[16,18]

With the sequence of the pathogen known, scientists quickly turned to develop PCR-based methods for the detection of SARS-CoV-2 RNA. Since HIV is a chronic viral infection and

SARS-CoV-2 is limited to an acute infection, their testing strategies are different. In general, any test that identifies the presence of HIV RNA or past infection with HIV via serology reflects that the person has been HIV-infected, while only a test that can detect the presence of virus, such as a nucleic acid or antigen test is useful for identifying active (i.e. acute) infection with SARS-CoV-2. The main advantage of serological testing for SARS-CoV-2 is epidemiologic surveillance, but since SARS-CoV-2 infection may cause disease long after active infection is resolved, antibody testing may be helpful in identifying the cause of associated symptoms, although specific treatment for such sequalae is currently lacking. Given strides in technology that were first developed for HIV, molecular SARS-CoV-2 assays were rapidly deployed around the world. Although the validity of many tests were initially suboptimal, they were sufficient for diagnosing most people who had become infected and provided alarming evidence that the scope of the epidemic was quickly expanding.[19,20]

The first tests for HIV usually took weeks for results to return and if the test was positive, confirmatory tests such as the Western Blot were required. This not only delayed diagnosis of persons with HIV, but also implementation of contact tracing. New tests were eventually developed to reliably diagnose a person at point-of-care (POC), within minutes of testing.[12] These next generation POC tests allowed persons with HIV to immediately initiate life-saving antiretroviral treatment (ART).[21]

A similar testing process is happening with the COVID-19 pandemic, albeit at a faster pace. Encouraged by diagnostic companies, next-generation diagnostics are materializing, including POC viral nucleic acid or antigen tests and serologies. Once available, POC tests can be rapidly deployed to diagnose persons with SARS-CoV-2, enabling people to learn when they should self-isolate, and allowing health officials to employ rapid contact tracing. Such procedures would greatly enhancement prevention measures.[19] Due to ongoing delays in the scale up of SARS-CoV-2 testing in the U.S., health officials are also turning to pooling approaches that proved to be cost-effective and scalable earlier in the HIV epidemic and in resource-limited settings.[22-24]

## HIV and COVID-19 disproportionately affect Disadvantaged Populations and Communities of Color

Since the beginning of the HIV epidemic, communities of color and disadvantaged populations have been disproportionately affected. As of 2018, Black and Latinx populations in the U.S. accounted for 69% of new HIV infections.[3] Compared to Whites, Blacks and Latinx have an 8.2 and 3.4 times greater HIV incidence, respectively. HIV mortality is also higher for Blacks and Latinx with rates being 6.5 and 1.8 times greater than Whites,[3] respectively. Globally, other populations that have disproportionately high burdens of HIV infection are those with unequal opportunities and/or social exclusion, including sex workers,[25] MSM,[26] PWID,[27] prisoners,[28] and transgender persons.[29] Racial and ethnic minorities and disadvantaged populations also have poor outcomes along the HIV care continuum, including lower rates of linkage and retention in care, later initiation of ART and lower adherence leading to sub-optimal viral suppression.[30,31]

Existing surveillance data on COVID-19 similarly indicates a disproportionate burden of morbidity and mortality is borne among communities of color.[32,33] Racial/ethnic minorities are more likely to test positive for SARS-CoV-2 than Whites.[34] Blacks account for 22% of infections, yet comprise 13% of the U.S. population; Latinx account for 33% of infections but 18% of the population.[35] Blacks are almost 3 times more likely to be hospitalized for COVID-19 than Whites.[36] Across the U.S., COVID-19 mortality rates are 80% higher for Blacks and over 50% higher for Latinx relative to Whites.[37] COVID-19 data for disadvantaged populations is currently limited to outbreaks in concentrated settings, but these highlight emerging disparities among people who are incarcerated and unstably housed or homeless.[38-40]

**Social and Structural Factors are Potent Epidemic Drivers**

Social and structural determinants are those that are exogenous to the individual which can fuel disparities in viral transmission and disease among communities of color and disadvantaged populations. For example, stigma and discrimination can increase HIV risk and undermine HIV prevention and treatment, especially among racial and ethnic minorities and socially marginalized populations. HIV-stigma is grounded in the intersectionality of HIV infection, racism, homophobia, and sexism[41,42]; stigmatization often manifests into fear of and experience of discrimination in health care settings.[43]

In the beginning of the HIV epidemic, MSM were singled out for abuse as they were blamed for spreading HIV.  AIDS was initially referred to as “Gay-Related Infectious Disease” (GRID),[44] a label that was seized upon by sensational media outlets that published headlines referring to the ‘gay plague’”. Human rights violations, stigma and discrimination perpetuated against sexual minorities and PWID continue to be major barriers to accessing HIV prevention interventions, testing and ART.[45,46] Mistrust in the health care system consistently translates to reduced engagement in HIV prevention behaviors[47,48] and poor retention in HIV care and medication adherence.[49,50] Fear of discrimination due to testing positive has been documented among people living with HIV (PLWH) who delay testing.

Comparable stigmatization in communities of color stemming from systemic racism and discrimination has already influenced the COVID-19 pandemic. When the origin of the outbreak was reported in China, Asians and Asian Americans were targeted and labelled by key figures including the President of the United States who referred to SARS-COV-2 as the "Chinese virus" and COVID-19 as "Kung Flu." People of Chinese and other Asian descent became victims of physical and verbal abuse. Whereas HIV was used as justification to uphold homophobic legislation, COVID-19 is being used as an excuse to promote racism and social exclusion, further inciting racial tensions.[51,52] When repercussions exist for testing positive for SARS-CoV-2, such as lost wages or being shunned by peers, it should be anticipated that some people will delay testing and/or hide their positive test results.

The physical environment in which people live, work, and spend time can confer HIV risk or protection. For example, among PWID, physical HIV risks include drug injecting locations, jails and prisons as well as drug trafficking routes.[46] Among sex workers, establishments such as brothels and bars sometimes offer free access to condoms and therefore pose a lower risk of HIV transmission than sex work that occurs in the street.[53,54] Racial and ethnic minorities are also burdened by increased risk of HIV due to their living conditions, including racial residential segregation, whereas residing in densely populated areas and multi-generational households[55] can increase the risk of exposure to SARS-CoV-2. Residing in homeless shelters, overcrowding, poor ventilation, close habitation or dormitory-style housing and poor personal hygiene due to restrictions on soap, cleaning supplies and hand sanitizer[56] pose additional risks. Residing in high-poverty areas where there is limited access to health care likely contributes to delayed COVID-19 testing and presenting with more advanced disease.

Economic factors, policies and politics are also potent drivers underlying infectious disease transmission. During government-mandated stay-at-home orders, the majority of critical essential workers (e.g., service industry, agriculture, nursing, correctional staff) are racial and ethnic minorities, rendering them more likely to interact with someone infected with SARS-CoV-2.[55] Racial and ethnic minorities are more likely to be employed in minimum wage jobs where they lack paid sick leave and experience unsafe or limited workplace protections,[57] which creates pressure to work while sick or to avoid advocating for a safer workplace.

In the early 1980's, then U.S. President Ronald Reagan was criticized for his silence on the HIV/AIDS epidemic; he did not publicly refer to AIDS or use the word 'condom' until 1985. During the COVID-19 epidemic, President Donald Trump derided face masks and until recently, refused to wear one. As a result of these leadership failures, both diseases and the prevention strategies needed to mitigate them have been undermined because they have become intensely politicized.

**Syndemics Exacerbate Poor Health Outcomes**

People who are at risk for or are living with HIV often live in the margins of society. It is in these margins that individuals are more likely to experience a multitude of negative conditions that interact to produce and sustain poor health.[58] This phenomenon has been termed, "syndemics," a combination of the words "synergy" and "epidemics".[59] Many marginalized and disadvantaged individuals experience high rates of substance use (e.g., alcohol and drug use),[60] adverse mental health (e.g., depression, PTSD),[61] and violence (e.g., police, community, and intimate partner violence)[62,63]. The factors described above contribute towards a multitude of negative syndemic conditions that co-occur and that are additively associated with increased risks for acquiring HIV, such as condomless sex, multi-person use of syringes among PWID, and poor engagement in HIV care.[59,64-66] These conditions give rise to a number of other over-lapping epidemics, such as those caused by hepatitis B and C viruses, sexually transmitted infections and tuberculosis.[67]

The same syndemic conditions that fuel HIV transmission and their root causes have played a role in the COVID-19 pandemic. For example, just as food insecurity can be a potent driver of survival sex work in low and high income settings,[68,69] it is also one reason why some people in low and middle income countries seek out bush-meat in jungles or wet-markets, which can spark zoonotic infections like HIV, SARS-Co-V1 and SARS-CoV-2.[70,71]

Structural and individual factors contribute to syndemics among disadvantaged and marginalized communities, particularly communities of color, and will exacerbate the likelihood of experiencing the negative and serious health consequences of COVID-19, as well as "deaths of despair"[72,73] from substance use (e.g., drug overdose, alcohol-related liver disease and suicide). Systemic or structural factors contributing to syndemics include residential segregation, which is associated with a shortage of mental health professionals available to provide support.[74] and higher rates of substance use.[75,76] At an individual level, people of color experience everyday violence and discrimination that can proliferate stress, affect immune function, and increase susceptibility to illness and poor health outcomes.[77,78] Alcohol and/or drugs may be used as a coping mechanism for discrimination and the stress that culminates from poor life circumstances.[79] As a result, top-down processes (i.e., from broader institutional and social structures down to individual level outcomes and behavior) may function to produce higher rates of comorbidities. The process is likely cyclical, with bottom-up processes functioning to sustain the (inequitable) status quo. For instance, Black and Hispanic youth who engage in substance use and experience poor mental health may face worse academic outcomes, contributing further to economic racial/ethnic disparities.[80,81]

## The Importance of Structural Interventions

Early in the HIV epidemic, prevention scientists focused on understanding and changing individual-level determinants of poor health behavior and HIV.[82,83] This approach neglected root causes. Now that scientists have begun to recognize the importance of social determinants, they are turning to multilevel approaches and those directed at HIV and accompanying syndemics (e.g., mental health disorders, addiction, gender-based violence, homelessness, food insecurity).[84-90]

Some HIV prevention programs have successfully used community mobilization by enlisting stakeholders in their development and implementation. For example, to counter stigma and discrimination among MSM in the early 1980s, gay communities created non-governmental organizations (NGOs) such as ACT-UP, the Treatment Action Group and Gay Men's Health Crisis to provide prevention advice, HIV care and advocacy to promote compassionate access to experimental treatments.[91] The American Foundation for AIDS Research was founded in 1983, followed by the International AIDS Society in 1988, which promoted advocacy, networking and sharing of scientific data.  Elsewhere, community mobilization and advocacy was responsible for monumental victories among disadvantaged populations such as the provision of ART to all people living with HIV in Brazil,[92] approvals for generic nevirapine for HIV-positive pregnant women[93] and expansion of voluntary medical male circumcision among primarily Black men in sub-Saharan Africa.[94,95]

Although it is early in the COVID-19 pandemic, some survivors have begun to organize. Such grassroots efforts may be needed not just for social support, but to advocate for health care reforms, since millions of people who have become unemployed during the epidemic have lost employer-subsidized health insurance. COVID-19 patients who suffer long-term health sequelae could also be excluded from health insurance programs on the basis of having 'pre-existing conditions'.[96,97] To reduce morbidity and mortality related to COVID-19, community leaders should be enlisted to disseminate education, promote testing and public health prevention strategies (e.g., social distancing and facemasks) through social networking shown to be successful in HIV prevention efforts in communities of color.[98,99] Since the ongoing Black Lives Matters protests have highlighted broader social and structural inequalities, there is due diligence to leverage community involvement to support collaborative public health responses that will ultimately bridge access to adequate health care. By demanding equity in the Black community, it may be possible to leverage Black Lives Matter protests as an opportunity to *reduce* racial health disparities. For example, at a time when SARS-CoV-2 is surging in many U.S. states, a federal mandate requiring facemasks in public could reduce stigma, backlash and violence against Black men who continue to be disproportionately targeted by police. Reports of increases in police arrests of homeless people who cannot adhere to shelter-in-place orders could be addressed by police education programs that bundle occupational safety with harm reduction, as has been done for HIV.[100]

Historically, the disease-specific response and resources dedicated to addressing the HIV epidemic was known as AIDS exceptionalism.[101] This concept began as a Western response to HIV and its disproportionate impact on specific groups, in which HIV was positioned as not only a health condition, but also a social issue that required a political, as well as a medical, response.[101] Through AIDS exceptionalism, vertical programming for HIV care and treatment was established; however, horizontal programming efforts – community-based or patient-centered paradigms of care - have evolved as an optimal solution to addressing HIV prevention and treatment and co-morbidities among disproportionately affected populations.[102,103] At the beginning of the COVID-19 epidemic, vertical programming was initiated whereby a significant proportion of resources were directed towards testing and treatment. However, there is a critical need for the integration of surveillance, testing, and treatment of COVID-19 into programming efforts for other syndemics that affect the same communities. Integrated programming efforts that are community-based and patient-centered are essential given scarce allocation of medical resources during the COVID-19 epidemic,[104] especially those that address underlying social and structural drivers among disproportionately affected populations.

Structural interventions also include policy changes. In 1990, the U.S. Congress passed a bill enacting the Ryan White AIDS program that became the largest federal funded program in the U.S. for PLWH, increasing access to ART for disadvantaged populations.[105] On the other hand, the U.S. was much slower than the United Kingdom, Canada, Australia and Western Europe in adopting legislation to allow federal support for needle exchange programs that can significantly reduce the risk of needle sharing and HIV incidence among PWID. Yet when the U.S. Congressional ban on the use of federal funds to support needle exchange programs was finally overturned in December 2015 following an HIV outbreak among PWID in rural Indiana, it had bipartisan support.[106]

In U.S. states that did not endorse the Affordable Care Act (ACA), low-income people without health insurance may lack access to COVID-19 testing and care. However, by intervening at a macro-level, structural interventions may not only reduce incidence and deaths from HIV and COVID-19, but also "deaths of despair." By integrating free testing and contact tracing programs for multiple infections of public health importance (e.g., HIV, HCV, STIs and SARS-CoV-2), it could be possible to simultaneously test for all infections and coordinate contact tracing when necessary, which would also reduce costs and stigma. Macro-level policy changes (expanding access to ACA marketplaces) can provide more immediate critical assistance with COVID-19 testing and care to individuals who have lost their jobs and health insurance.[97] Beyond COVID-19, the ACA was shown to improve timely diagnosis and care in HIV and chronic conditions, medication adherence, and overall health for low-income individuals.[107-109] Other structural approaches that could have a more immediate impact on curbing SARS-Co-V2 community transmission include ensuring paid sick leave, extending moratoriums on rental and mortgage payments, providing housing for individuals who are homeless and providing hand-washing stations in areas with higher concentration of people experiencing homelessness.[97,110-114]

**Accelerating the Pace of Experimental Treatments and Vaccines**

When faced with a new infectious disease that has both high incidence and mortality, scientists face dual pressure to develop treatments to reduce morbidity, as well as vaccines that can prevent infection. With the AIDS death toll mounting in the 1980's and activists placing pressure on governments, scientists needed substantial infrastructure and funding. The first drug that showed efficacy against HIV, zidovudine (AZT), was a re-purposed cancer drug.[115] When it was clear that AZT would not be enough, a large clinical trials group was established by the National Institute of Health (NIH) in 1987 to partner with pharmaceutical companies to assist in the development and validation of new antiretroviral agents specifically developed for HIV, the AIDS Clinical Trials Group (ACTG). This group has pioneered the rigorous evaluation of all currently available HIV medications, culminating in the one-pill once-a-day regimens we have now.[116] The ACTG was later followed by the HIV Prevention Trials Network (HPTN) and the HIV Vaccine Trials Network (HVTN), and Centers for AIDS Research at multiple U.S. universities which were also funded by the NIH.[117]

Similar efforts are taking place for COVID-19, with a drug initially developed for SARS-CoV1 and MERS, remdesivir, being re-purposed to treat SARS-CoV-2.[118] Other drugs used to treat a variety of other diseases that had potential activity against SARS-CoV-2 were also tested, including hydroxychloroquine, azithromycin, ritonavir, and lopinavir.[119,120] Initially, only remdesivir has showed efficacy for the treatment of COVID-19,[118] but in June, 2020, a clinical trial reported that a relatively inexpensive steroid, dexamethasone, reduced mortality among severely ill COVID-19 patients, but not in patients with milder infections.[121] The next generation of anti-SARS-CoV-2 agents are already being developed and tested, including viral enzyme inhibitors, small interfering RNA agents, and monoclonal antibodies. These classes of agents also have a history in the treatment of HIV.[122] Similarly, they are being rigorously tested in clinical trials groups with partnerships from pharmaceutical companies, including the ACTG.[123] These trials have benefited from the existing infrastructure developed to respond to the HIV pandemic, as well as adaptive study designs that allow multi-site clinical trials to nimbly test numerous therapies using the same control group.

Like HIV, there is no vaccine available for SARS-CoV-2. It was widely touted in 1982 by Margaret Heckler that there would be an HIV vaccine within a year,[124] and yet after almost four decades, the world is still waiting. Similar remarks are being made about a vaccine for SARS-CoV-2.[125] Soon after SARS-CoV-2 was discovered, open source sequences for numerous isolates were shared on the internet, enabling unprecedented collaborations between scientists around the world that is accelerating the pace of innovation.[126] Although it is remarkable that thirty-eight SARS-CoV-2 vaccines were undergoing evaluation in human clinical trials by September 2020, three of which had entered Phase III, SARS-CoV-2 vaccines face considerable challenges, suggesting that expectations should be tempered. Even in the absence of an HIV vaccine, great strides have been made in our understanding of the immune responses needed to protect against HIV infection, and such knowledge will greatly assist in the development of a vaccine for SARS-CoV-2. Efforts are needed now to address growing levels of vaccine hesitancy and mistrust associated with the anti-vaxx movement, which is already unraveling decades' worth of public health efforts to achieve herd immunity for other infectious diseases, such as measles, pertussis and diptheria.[127] Social media is an under-utilized tool that could be harnessed to promote science communication and to counteract mis-information about vaccines (i.e., 'infodemics').[128]

**The Importance of Epidemiologic Data to Inform Policy**

Epidemic and economic modeling are critical tools to inform policy responses and resource allocation during the HIV and COVID-19 pandemics. At best, models can help understand epidemic drivers, predict and assess intervention impact, and optimally allocate funding.[129,130] However, they can also be inaccurate, which can lead to erroneous policy decisions. An analysis of ten HIV models for South Africa[131] found that all projected lower prevalence compared to a subsequent household survey in 2012, and may have been overly optimistic about the impact of ART on HIV transmission. This led to an underestimation of resources needed for HIV treatment and prevention in South Africa, which continues to experience some of the highest HIV incidence rates in the world. Compared to previous models, however, the models performed better at capturing the overall magnitude and age distribution of the epidemic, as well as mortality changes, which was attributed to investments in surveillance data informing the models' assumptions.

Three key lessons emerge from these and other modeling successes and mis-steps. First, good data are essential; good models cannot compensate for bad or missing data. Especially for emerging infectious diseases, rigorous population-based epidemiological studies are required to obtain unbiased estimates of critical parameters such as prevalence, rates of asymptomatic disease, hospitalization and mortality. In India, sentinel surveillance among pregnant women and high-risk groups led to estimations that India had the highest burden of HIV in the world, but subsequent general population surveys found previous estimates were overestimated by 2-3 fold.[132]

In the U.S., lack of widespread SARS-CoV-2 testing and the failure to quickly establish population-based and sentinel surveillance systems and reporting requirements led to a major failure in case ascertainment and contact tracing and undermined the ability to obtain rigorous epidemiological data. Some counties and states delayed reporting key data, such as hospitalizations and deaths, hampering monitoring and modeling based on these key metrics. Meaningful investments in surveillance and epidemiological data collection are essential and are urgently needed to understand the epidemic and inform modeling. It is also imperative to maintain transparency in SARS-CoV-2 testing, hospitalization and mortality data to enable timely epidemiologic analysis and modeling to inform policy. When data are uncertain or unavailable, sensitivity analyses are critical to understanding how different assumptions may change model outcomes, and can help prioritize data collection.

Second, models need to be validated against real data to verify predictive performance, and iteratively refined with new data. For example, modeling groups in the U.S. and elsewhere developed online interactive 'dashboards' as part of the public health resource. In some cases, however, these models relied on data from settings not generalizable to the U.S. or made incorrect assumptions[133] about the impact of social distancing interventions and led to frustration, confusion and inappropriate messaging around the importance of social distancing and likelihood of resurgence after relaxation of stay-at-home orders.

Third, models incorporating historical context, structural drivers, and disparities are essential to informing the tailored prevention responses needed. A 'one size fits all' response ignores local complexity in structural risks and drivers, population heterogeneity in risk and behavior, disparities, and differential epidemic stages. Strategies required for ending the HIV epidemic in

Atlanta where the most vulnerable to HIV infection are young Black MSM will differ from rural U.S. counties hard hit by rising rates of injecting drug use and HIV.[129,134] Disparities in health care access by race will continue to fuel disparities in HIV incidence unless directly addressed.[129] Decentralized and integrated HIV prevention and care can increase access to services among underserved populations and provide synergistic benefits.[135]

Similarly, the surge of COVID-19 in rural U.S. settings following a decline in New York and other northeastern cities,[136] and the disparate approaches to social distancing across states[137] emphasize the need for local perspectives. The disproportionate number of racial and ethnic minorities living in densely populated housing areas (due to historical housing segregation and regulation) which confer higher risk of SARS-CoV-2 transmission should be considered in a local context. Further, the over-representation of Blacks in essential worker occupations and resulting higher risk of SARS-CoV-2 infection and mortality[138] should be incorporated into models which examine how to reduce disparities. Explicit consideration of these structural factors and disparities which shape risk and outcomes, informed by data, is needed for models to accurately inform effective local strategies.

**Conclusions**

At the time of writing in September, 2020, the U.S. accounted for nearly one quarter of the world's reported COVID-19 cases, SARS-CoV-2 incidence was still increasing in thirteen states and there were approximately 40,000 new infections and 1,000 COVID-19 deaths daily across the nation. Despite this, there is still no national mandate for basic prevention precautions such as facemasks or social distancing. Although the U.S. response to the HIV epidemic has had its flaws, HIV/AIDS prevention and treatment improved following the implementation of national AIDS strategies and the President's Emergency Plan for AIDS Research (PEPFAR) became known as a global leader in scaling up HIV treatment in lower and middle income countries. In contrast, the U.S. response to COVID-19 has been an unmitigated disaster mired in testing delays, shortages of personal protective equipment (PPE), uneven reporting, highly politicized public health recommendations and a continued lack of a national plan to mitigate ongoing transmission.

Decisive leadership that develops policies grounded in scientific evidence is key to charting a path forward. The proposed U.S. withdrawal from the World Health Organization will only weaken attempts for a coordinated, multi-lateral response to this pandemic and could have a ripple effect on others, like antimicrobial resistance. Already it is anticipated that COVID-19 will erase 20 years' worth of prevention gains for HIV, TB and malaria.[139] In July, 2020, the U.S. bought the world stockpile of remdesivir, one of the only drugs shown to have antiviral activity against SARS-CoV-2, leaving the rest of the world reeling. Experts fear that the U.S. federal government's plan to select promising SARS-CoV-2 vaccine candidates and bring them to scale by the end of 2020 ("Operation Warp Speed") are intended only for Americans and may overlook promising candidates since the operation excludes those developed in China.[125] The COVID-19 pandemic will not end if the U.S. or other countries take an ethnocentric approach by stockpiling essential medicines, vaccines or personal protective equipment. Instead, all countries need to recognize that the sustainability of civilization is inexorably linked to that of inequitable and unsustainable resource utilization, a core tenet of planetary health.[140] Decisions about access to future life-saving treatments and vaccines should be made jointly and with transparency through a process that includes representatives from affected communities, and based on ethical principles such as health as a human right.

COVID-19 has exposed the ‘fault lines’ in our society.[141] It is a national tragedy that the window of opportunity to prevent a widespread COVID-19 epidemic in the U.S. has already closed, but it is not too late to implement a mitigation strategy that can save thousands of lives. The question is whether the country is prepared to learn from its past successes and mistakes with the HIV epidemic, and develops a nation-wide plan that puts politics aside and prioritizes saving lives.


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