SPRING 21

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MASSACHUSETTS GENERAL HOSPITAL //
DISPATCHES FROM THE FRONTIERS OF MEDICINE

Will COVID-19 Change Medicine?

The past year has already reshaped how health care is practiced, perceived and paid for. Which of these shifts will endure? p10

A Reckoning for Cholesterol Deniers p22 • **The Pandemic Abroad** p30

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FEATURES

on the cover

A pandemic, a racial reckoning and a political shift have transformed medicine's landscape. How will these forces shape the profession in the decade to come? // Illustration by Kingsley Nebechi

proto: a prefix of progress, connoting first, novel, experimental. Alone, it conjures an entire world of the new: discoveries, directions, ideas. In taking **proto** as its name, this magazine stakes its ground on medicine's leading edge—exploring breakthroughs, dissecting controversies, opening a forum for informed debate.

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Founded in 1811, Massachusetts General Hospital is a 1,043-bed academic medical center located in Boston. It is a founding member of Mass General Brigham (formerly Partners HealthCare) and is the original and largest teaching affiliate of Harvard Medical School.

THIS HOSPITAL COMMUNITY—just like staff in hospitals across the nation—will always remember the year just past. We have all been, at times, pushed to our limits. We have all, I hope, felt pride in the service rendered to our patients and pride in the stunning research that moved along at record speed, propelled by urgency. I hold up our community's work as a personal reaffirmation of why I went into medicine and the honor I feel at being part of this incredible organization. For all of us, COVID-19 cannot help but leave an indelible and emotional impression.

This issue of *Proto* asks a related question—what mark will COVID-19 leave on us as practitioners? The changes in our routines were seismic even in the first days and weeks of the pandemic. We saw transformations in nearly every practice area, in supply lines and job descriptions, in the way we work, the places we work, in unexpected collaborations and in the newfound speed and agility of innovation. Which of these will endure?

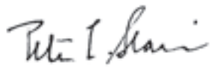
In these pages, 10 MGH clinicians and alumni offer their predictions. David Blumenthal, once the chief health information and innovation officer at the hospital and now president of the Commonwealth Fund, wonders what the extraordinary economic challenges posed by the pandemic might mean for smaller practices and national health care policy. Bruce Walker, founding director of the Ragon Institute of MGH, MIT and Harvard, sees new promise in the spirit of collaboration that was allowed to grow among institutions that normally compete in less dire times.

Several of the essayists reflect on how we will be shaped by this critical moment in the battle for racial and social justice—so inextricable from the inequalities laid bare by the pandemic. As telemedicine gains ground, can we ensure that all groups make equal use of it? How can we keep antiquated thoughts about race and disease from infiltrating algorithms that increasingly make up our diagnostic and treatment tools?

Personal lives of health care workers are also at an inflection point, as some writers note. MGH pediatrician Hemal Sampat observes the need for more of us to become full-time advocates for science, as the wide spread of misinformation has become a tragic, parallel "infodemic." The pandemic has been a flashpoint in the problem of clinician burnout, and we have seen the beginning of a national shift in the conversation about how institutions can protect their practitioners.

I personally believe that the changes coming out of our encounter with COVID-19 will be positive ones. We have all learned so much. In the name of those who have fought and those we have lost, we must use the lessons of this pandemic to become nimbler, more resilient and wiser in facing the challenges yet to come.

Peter Slavin notes that he is currently on the board of Amwell, a publicly traded telemedicine company.



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FOCUS

DAVE KASNIC

For this inmate at Chicago's Cook County Jail, a surgical mask and a closed cell door provide scant protection against COVID-19. In the first weeks of the pandemic, the virus sickened more than 1,000 prisoners and staff at the massive facility. With inmates held in dormitories or paired in 6-by-10-foot cells, the jail was at one point called the "top U.S. hot spot."

Nationally, at least one in three people held in prisons, jails or immigration detention facilities has been infected, as close quarters, unsanitary conditions and poor ventilation have fostered the spread of the disease. Death rates from COVID-19 have been more than three times the rate in the general population, and COVID-19 vaccine distribution has been uneven, with vaccination rates ranging from 69% in Virginia to just 3% in Idaho by April 2021.

From the earliest days of the pandemic, public health officials called for depopulating crowded prisons where possible, and a number of policy initiatives were put forward to allow for the early release of prisoners, especially those at risk of severe COVID-19 complications. But recent research from the Prison Policy Initiative shows that very few prisoners were released nationally, and in fact parole rates were lower in 2020 than they had been in 2019.

INTERVIEW

The Year of the Nurse

The World Health Organization gave Elizabeth Iro the job of advocating for nurses everywhere.

Before the pandemic hit, the World Health Organization had chosen 2020 as the International Year of the Nurse and Midwife. Instead of attending symposia and celebrations, however, most nurses faced the most brutal months of their careers. In large countries and small, nurses offered hands-on care in the face of a new virus, attending to the health of their patients even when it meant risking their own safety and that of their families.

Elizabeth Iro, who was named the first chief nursing officer of the WHO in 2017, is making sure that the importance of nurses is amplified, not overshadowed, by the encounter with COVID-19. Iro served for more than 25 years as a nurse and midwife in the Cook Islands before becoming that country's secretary of health. At the WHO, she immediately began working with a team on producing a State of the World's Nursing Report*, published last year, which lays out how the profession is changing and what must be done to support nurses in the years ahead.*

OPPOSITE PAGE: GUILLAUME MEGEVAND; THIS PAGE: THE NOUN PROJECT

Q: How did you find yourself taking on a series of leadership roles?

A: I've always kept my focus on my work, which is to look after people. That mission is a common thread among all nurses, I think. And like most nurses, I found myself running into certain frustrations. I started to look for ways to make a better argument, to advocate more convincingly for the people under my care.

That led me to read up on civil law and produce a few research papers, and then I did a master's degree in health science and also an MBA. All of that allowed me to see other sides of the problem. It also showed me how issues affecting nurses could be elevated by approaching ministers and other people in power with sound, evidence-based arguments.

Q: Can you elaborate on those "certain frustrations"?

A: One thing was not having enough staff. Nurses were being let go with no one coming in to replace them, yet we were expected to continue delivering the same care. But at the forefront of the response you come to understand how exhaustion becomes the norm, how absenteeism rises because of exhaustion and how work then doubles and quality drops.

This is also something we talk about in the context of the WHO's Year of the Nurse—that the world needs another 9 million nurses over the next 10 years if we're going to achieve adequate universal health coverage. Nurses are now responsible for so much and yet remain stretched thin.

Q: How have the responsibilities of nurses changed?

A: There has been a huge shift over the past 25 years. Nursing has evolved into a profession with rigorous academic requirements. There has been a proliferation of accreditations, and of course in many countries now, nurses have become autonomous and specialist practitioners.

Current global health crises have also shaped what we do. Noncommunicable diseases—I'm thinking particularly of obesity—are a primary challenge around the world. Nurses have been the ones responding to the lifestyle and health maintenance needs of patients with obesity in a major way. It is the same with other conditions.

With all of these changes, the profession is able to make a profound impact, especially in settings where health workers are limited. Nurses are often, de facto, primary caregivers. We know that if nurses are allowed to work to the full scope of their licenses, the benefits are enormous.

Q: What has the COVID-19 crisis meant for nurses?

A: The pandemic has exposed issues we have been trying to address. One is the shortage of nurses that I mentioned. We've seen nurses who have been overworked, overburdened and burnt out. We've seen them be stigmatized because of their work and hands-on proximity to the sick. We've seen them on the receiving end of shortages in equipment that jeopardize their health. These aren't new issues, but the pandemic brought them into sharp focus.

Going forward it is important that governments respond not just with applause and saying thank you. What's needed is for them to look seriously into the investment in health care workers. And one of the best ways is to incorporate nurses into decision-making. Health care systems around the world can be strengthened by having a nursing and midwifery perspective in their planning and in their policies.

BY THE NUMBERS

Short Staffed

16.5

Percentage of U.S. hospitals that expected critical staffing shortages in February 2021. Hospitals are scrambling to hire and retain physicians, nurses and support staff, but turnover is high—particularly among nurses. One hospital in rural Texas reported that its annual turnover rate for nurses had increased from 2% before the pandemic to 20%.

1:1

The ideal nurse-to-patient ratio in the ICU. Making nurses responsible for even one more patient can invite burnout and medical errors. But at the height of the pandemic, ICU nurses in California handled 1:3 ratios, while Utah nurses contended with ratios as high as 1:5.

$50.7

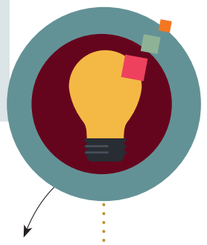
Billions in estimated monthly losses for America's hospitals and health care systems early in the pandemic. The Coronavirus Aid, Relief, and Economic Security (CARES) Act alleviated some of these financial woes.

8

Percentage of physicians who closed practices because of COVID-19. Another 43% have cut staff and 72% report reductions in income.

209

U.S. counties that had to implement crisis strategies to staff ICU units in April 2021. A dashboard from George Washington University updates this number weekly and serves as a new tool for an increasingly chronic problem.



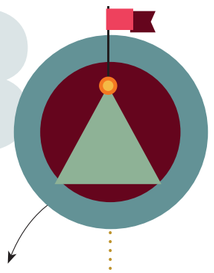
A COMMUNITY IS FOUNDED ...
In 2019, the **Alliance for Digital Pathology** was formed by pathologist **Jochen Lennerz**, medical director of MGH Center for Integrated Diagnostics; **Esther Abels**, now chief clinical and regulatory officer at the biotech firm Visiopharm; and imaging physicist **Brandon Gallas**, of the FDA's Office of Science and Engineering Laboratories. They were interested in promoting the use and acceptance of this relatively new specialty to improve patient care.

... RECRUITS MEMBERS ...
The group largely recruited through word of mouth, growing from 12 to more than 400.

Curious Professionals
Research Groups
Patient Groups
Clinicians
Private Industry

Membership is open and costs nothing, giving access to nontraditional participants, such as trainees from various disciplines, medical students or doctors from community hospitals.

Lennerz invited several patient advocates who have "helped us stay on course and steer in the right direction."



... WRITES A CHARTER ...
Following the FDA's Collaborative Communities Toolkit, the group drafted a charter and established rules of conduct, which include the admonition that members be "friendly, humble and patient."

CDRH

In late 2020, CDRH agreed to join the new group. That was a valuable addition, says Hetal Marble, a translational scientist at MGH's Center for Integrated Diagnostics, "because you can learn what the regulator is actually looking for."

No standard procedure for scanning tissue slides exists—a problem this group is working to address.

... MEETS OFTEN ...
The alliance formed working groups to address common concerns. Members often have strikingly different interests, so conversations can get lively. "Our diverse motivations actually help because it makes for a more robust discussion," says Laura Lasiter, director at the nonprofit Friends of Cancer Research.

Equitable Reimbursement
Data Standardization
Continuous Learning
Slide Protocols
Trainees Group

This group is working to ensure that payers recognize the value of digital pathology and reimburse for procedures accordingly.

... AND DELIVERS RESULTS.
Any member can submit a project idea, which is considered for a vote. If chosen, leadership decides what support to provide. While tools for regulation are one goal, many other projects take shape from the group.

Solid Tumor Diagnosis

One project is to develop a tool for evaluating machine-learning algorithms that diagnose solid tumor cancers. Such algorithms are "trained" by feeding them pathologists' evaluations, but a standard approach on how to ensure statistical accuracy is still lacking.

FLAVIO COELHO/GETTY IMAGES

GRAPHIC BY MSJONESNYC

INFOGRAPHIC

What Is a Collaborative Community?

An unconventional new model makes industry meetups a key part of medical device regulation.

BY TIMOTHY GOWER

Biopsies are still mostly read under a microscope by a human pathologist. The diagnostic process can be a painstaking endeavor and often renders an up-or-down opinion: cancer or no cancer, for example. Digitizing this work would not only speed up processing but, coupled with artificial intelligence, might give more accurate information—a 90% chance a tissue specimen is malignant and the patient will respond to a therapy, for example—that could affect treatment considerations.

But this frontier of digital pathology calls for new tools—scanners, viewers and software. And a lack of regulatory standards for these components has slowed their development and wider adoption. The same story is echoed across many new areas where device innovation moves quickly but expertise is limited to a small circle of specialists.

Enter the collaborative community (CC). The Center for Devices and Radiological Health (CDRH), which oversees regulation of medical devices for the U.S. Food and Drug Administration, launched the program. It encourages stakeholders—including those who make, sell, use and regulate medical devices—"to solve shared challenges in an environment of trust, respect, empathy and openness," says Michelle Tarver, deputy director of CDRH's Office of Strategic Partnerships and Technology Innovation.

These communities can help lay the groundwork for potential policy related to the devices, although the work that comes out of them is often much broader. While the CDRH has created a Collaborative Communities Toolkit, the FDA isn't in charge of any CC; rather, the agency is only one of many equal members. (The CDRH currently participates in 10 communities.) Collaborative communities work to find solutions to problems that affect a broad sector of the device industry. The experience of one group—the Pathology Innovation Collaborative Community (PIcc)—is shown above.

POLICY WATCH

The Doses Left Over

Is there any hope for saving wasted medications?

BY JOSHUA KRISCH

The good news from the early days of COVID-19 vaccination—that extra doses might be squeezed out of vials containing Pfizer's COVID-19 vaccine—shed light on a convention that clinicians know well. Drug vials often contain more than the indicated dose, whether to account for the range of possible dose sizes for patients of various weights, or as a simple contingency against minor spills.

But the practice of overstuffing vials has come under scrutiny, with one 2016 report estimating that the federal government and private insurers waste $2.8 billion each year by throwing away vials that contain leftover cancer medicine.

"I can assure you that payers are charged for the full cost of the vial, and patients may even pay out of pocket for their portion of the costs," says Edward Shortliffe, professor of biomedical informatics at Columbia University. "Yet a significant portion of the drug ends up discarded."

Shortliffe recently chaired a special committee from the National Academies of Sciences, Engineering, and Medicine to study the problem. Its report recommends exploring technologies to allow multiple patients to benefit safely from medicine in a single-dose vial, and to revisit potentially outdated guidelines for weight-based dosing. "We should expect drug developers to provide evidence that a drug needs to be weight-based," Shortliffe says. "If the same dose had the same impact on every patient, we could put the precise dose in each vial and very little would need to be discarded."

Crucially, however, the report is skeptical that money wasted at the bottoms of single-dose vials can be recovered. Because pharmaceutical companies price drugs based on the perceived value of the drug to the patient and the payer's willingness to pay, more patients benefiting from the content of a single-dose vial might only lead to the companies raising the price per bottle, the researchers note. Pfizer recently demonstrated this frustrating pricing philosophy with the announcement that it would send fewer vials of COVID-19 vaccine than initially expected, because clinicians managed to squeeze six doses out of five-dose vials.

"Pfizer has made it clear that drug pricing is based on treatment per patient, not the actual production cost of a vial," Shortliffe says.

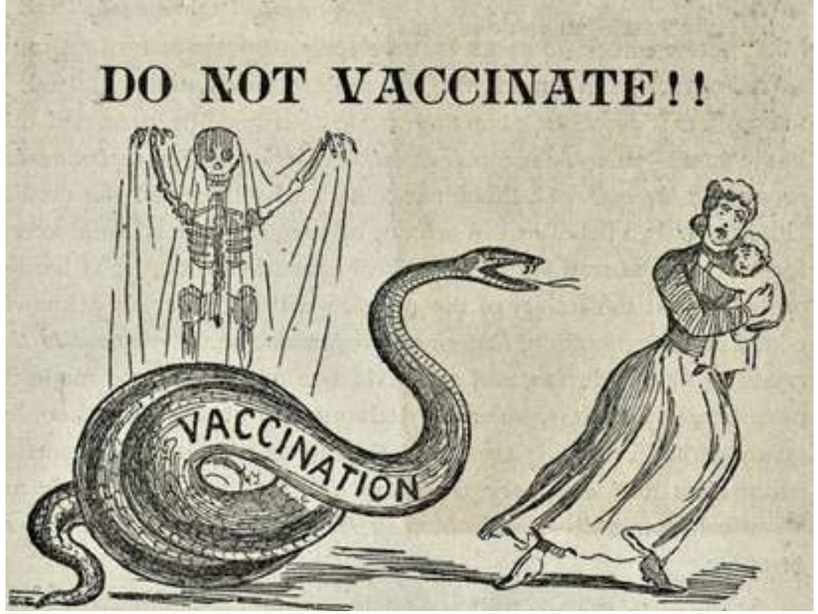
While medicine left behind in a vial may seem like liquid gold, "if we want to address the problem, we are going to need to look at the overall efficiency of how drugs are developed, manufactured, distributed and administered," Shortliffe says.

MILESTONE

Should We Insist on Shots?

Massachusetts broke ground on mandatory vaccination in 1905. History may repeat itself with COVID-19.

BY STEPHEN ORNES



THE ANTI-VAX MOVEMENT began more than a century ago, as this drawing from 1892 attests. While there had been skepticism about the effectiveness of vaccines, mandates from health authorities threw fuel on the fire, creating a backlash of organized societies that waged an early misinformation campaign about the harms and effectiveness of the drugs.

One spring morning in 1902, E. Edwin Spencer, the city physician of Cambridge, Massachusetts, visited the home of Henning Jacobson, a local Lutheran preacher. Spencer had the vaccination for smallpox. Jacobson refused it for both himself and his family. The standoff between the two men would lead to what historian Michael Willrich called "the seminal case in modern American public health law."

The Boston area was then experiencing what would be its last smallpox epidemic, which killed approximately 270 people over three years. At the time, smallpox—a highly contagious virus—was a leading cause of death around the world. Victims were diagnosed by telltale pustules, and during some outbreaks, as many as one in three infected people died.

The board of health in Cambridge, led by Spencer, had launched a citywide vaccination program that carried a financial ultimatum: Get vaccinated or face prosecution, including a $5 fine. The mandate applied to anyone who hadn't received a vaccine since 1897. (The smallpox inoculation protected a person for three to five years.)

A similar mandate in neighboring Boston had mobilized a growing anti-vaccination movement. At least 19 people in Boston refused and were prosecuted in court. In February 1902, "anti-vaccinationists" had lined up at the Massachusetts State House to vividly describe how vaccines had harmed them—one citing the loss of feeling in one arm, and another saying that a five-year-old child died of lockjaw after receiving the vaccine.

In Cambridge, Spencer was an improbable enforcer. Before attending medical school in Worcester, he had studied alternative medicine at the Eclectic Medical Institute in Cincinnati. He preferred botanical solutions to chemical cures. After the refusal from Jacobson—an imposing figure with thick eyebrows and a goatee—he notified the preacher of his fine and left.

But in late June, death counts began to surge again, with cases only blocks from Jacobson's home. City officials decreed that people who continued to refuse the vaccination would now be prosecuted, and on July 23, Jacobson became one of six refusers summoned to court.

As his case made its way through the courts, Jacobson preached to judge and jury with points borrowed from anti-vaccination societies. He said that his own childhood smallpox vaccination in Sweden caused "great and extreme suffering" and that vaccination led to "evil and dangerous effects." In ringing oration, he likened vaccination to a "barbarous ceremonial of blood-poisoning."

The U.S. Supreme Court, which decided the case in 1905, was not convinced. It ruled by a 7-2 margin that cities had the power and obligation to protect their citizens, through vaccination and other means, "as the safety of the general public may demand." Jacobson paid his fines.

During the COVID-19 pandemic, *Jacobson v. Massachusetts* has been cited to defend some public health measures. So far, however, those measures have not included mandatory vaccination. According to bioethicist Arthur Caplan at the New York University Grossman School of Medicine, one reason is that current vaccines are being administered under emergency use authorization from the U.S. Food and Drug Administration, and officials are unlikely to require people to take a drug that is still under investigation. But over the next few months, he expects the fights over mandatory vaccination to begin.

"You undoubtedly will see mandates as soon as licensure occurs, and the government could act even before licensure," Caplan says. "In the military, for example, if the Department of Defense says vaccination is necessary, the ability of a soldier to say, 'I don't want to do it' is nothing." A mandate for the armed forces would cover millions.

Immediately after the COVID-19 vaccines' full licensure—"within a day, day and a half," Caplan predicts—many more hospitals and nursing homes will most likely require vaccination among employees. These requirements will be similar to hospital mandates for workers to receive a flu vaccine. The future will probably also bring more vaccine mandates from airlines, cruise lines and other businesses.

"There will be lawsuits against any workforce mandates for health care workers, but we've already fought those out on the flu," Caplan says, adding that the courts have upheld the requirements. Other lawsuits may follow, but Caplan doesn't see those who press them having more luck than Henning Jacobson did. "You can't have a worldwide plague that has destroyed the economy, killed millions and caused such anguish, and end up with sympathy for people who don't want to vaccinate," Caplan says.

UPDATE

Clinician Violence Moves Online

As practice goes digital, so too does a brutal workplace hazard. BY LINDA KESLAR

Just before the pandemic began, a group from Northwestern University and the University of Chicago wrapped up one of the first major studies to describe physician experiences with online harassment. In the offline world, health care jobs are among the most dangerous, and hospital workers face four times the risk of violence as people in other industries ("When Healers Get Hurt," Winter 2019). The study, published in *JAMA Internal Medicine* early in 2021, found that this danger exists online as well, with one in four physicians reporting a personal attack on social media. Top reasons for attacks included the doctors' advocacy of vaccinations, gun control and access to abortion. But there were also personal attacks based on the poster's religion and race, and one in six female physicians faced online sexual harassment.

The problem has almost certainly escalated since the onset of COVID-19. The pandemic triggered a tide of medical misinformation, which health care workers have been on the front lines of correcting. In return, they have received threats of assault and death. The research team from the *JAMA* study expects to find that online violence against physicians has increased in a new, larger study it has launched. "These issues aren't going away," says Vineet Arora, a co-author of the study who is the assistant dean for scholarship and discovery at the University of Chicago Pritzker School of Medicine.

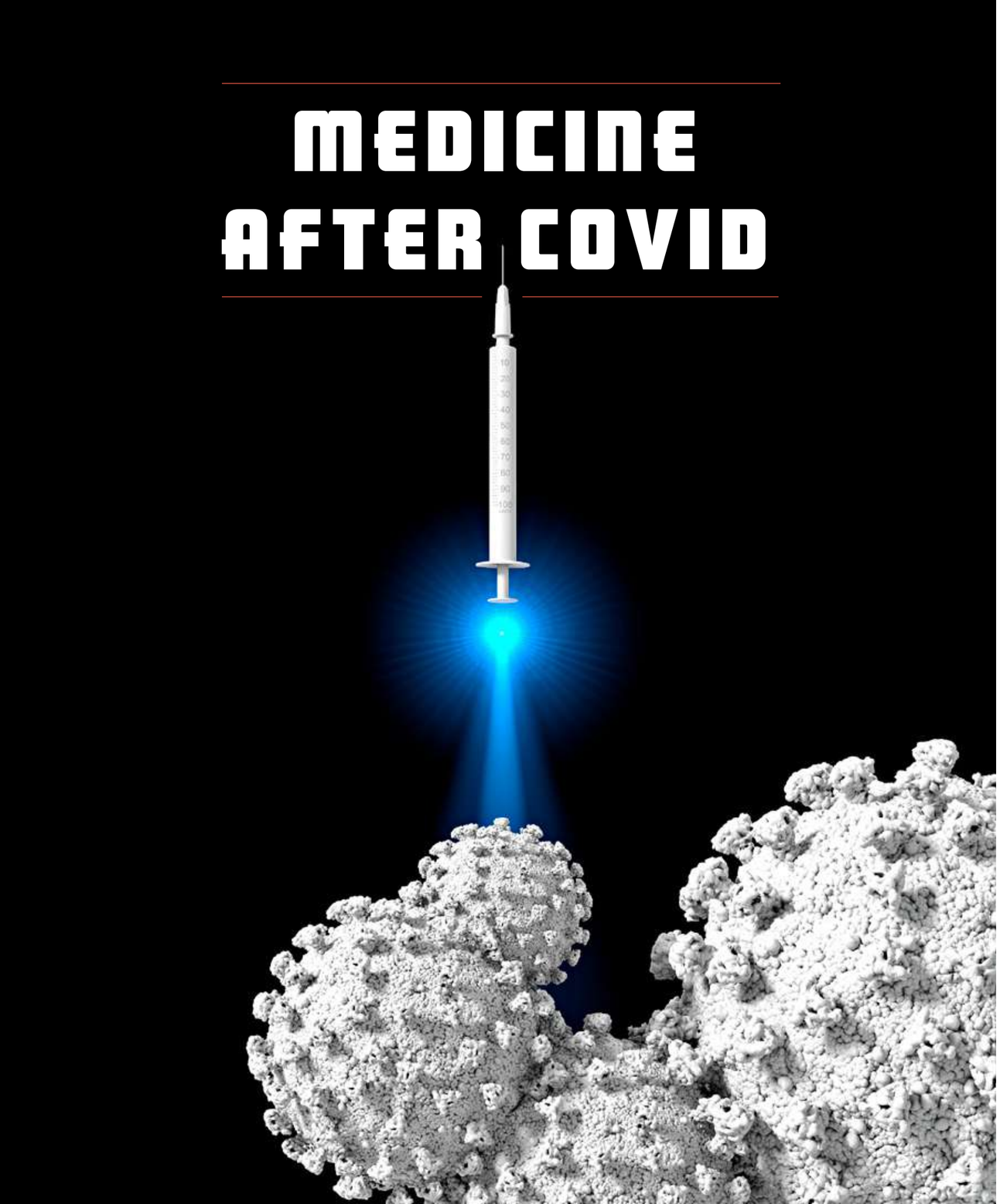
DANNY KIM/ORIGINAL IMAGE FROM GETTY IMAGES

What are the solutions? Ali Raja, a physician and executive vice chairman of the Department of Emergency Medicine at Massachusetts General Hospital, says he and many other health care workers have chosen a reduced social media presence. Raja says he only posts content on his Twitter account that is impersonal and professional and he uses a pseudonym on Facebook to limit the chances of becoming a target. "All it takes is one threat to be real," he says. "We deal with violent patients every day, and I'm definitely worried that people might find me or my family outside the emergency department."

Others are experimenting with ways to fight back. Todd Wolynn, a Pittsburgh-based pediatrician, was bullied online for his pro-vaccination views and saw his practice rating go down to one star online. In response, Wolynn co-founded Shots Heard Round the World, which now has 1,000 vetted volunteers who mobilize to combat anti-vaccine attacks. Participants are alerted by email to post supportive and factual content to drown out the misinformation. "We're the rapid response digital cavalry," Wolynn says. The network has been successful in countering more than 150 attacks against advocates so far.

Arora is a founding member of a similar effort, the Illinois Medical Professionals Action Collaborative Team, launched in 2020. Participants provide support to those on the receiving end of online attacks. "It's easier to advocate on social media as part of a group," Arora says. "We can be part of a louder voice that supports them."

MEDICINE AFTER COVID



It is slowly becoming possible, after a herculean public health effort, to imagine a post-pandemic world. What will health care look like on the other side? Ten voices offer their takes.

1.

AN EPOCHAL CHANGE IN CARE DELIVERY

During the Great Plague of the 17th century, nobles and the wealthy retreated to their villas in the hills while plague doctors roamed the streets and made house calls dressed in beaked masks to protect themselves, using a stick to "touch" the sick and dying. Today's plague of COVID-19 has had an equally profound effect on how we deliver medical care.

Social distancing forced many hospitals and clinics to close their doors, and only the sickest patients were treated in emergency departments and inpatient wards. The silver lining was that we had the technology to visit patients' homes virtually, in full view and unmasked, to ensure that they received the care they needed without interruption. We traded the beak and stick for the internet and Zoom, and opened a new chapter in medical history practically overnight.

Mass General Brigham, the hospital system of which Massachusetts General is a part, went from having 100 to 200 providers who made 10,000 virtual visits per year in 2019 to 10,000 providers making 1.38 million virtual visits from March through September 2020. Grandmothers who couldn't use a smartphone mastered videoconferencing for medical care—and then for just about everything else. My 86-year-old mother started doing Pilates on Zoom for her cardiovascular wellness, and my 90-year-old father now gets all of his medical care online.

At least 25% of the ambulatory care we provide at MGB is now virtual, and we are revolutionizing what it means to be hospitalized. Patients with COVID-19 are discharged early or not admitted in the first place and monitored safely at home via virtual care. Patients confined to hospital rooms can visit with family and friends via tablet computers brought to the bedside. When nurses, medical interpreters, disease specialists or others are needed, they can appear instantly at the touch of a button, as time and space no longer constrain how and where we practice medicine.

Perhaps most important of all, unlike our ancestors with the bubonic plague, patients with COVID-19 can see the faces of their caregivers. Without masks, gowns or gloves, we can speak with patients face-to-face over video

to understand their illnesses, help them make choices or just get to know one another. Before the pandemic, we worried that technology in medicine would increasingly come between providers and patients. Instead, it has opened the door to intimacy and connection.

With so many people cut off from seeing each other and making human connections, mental health has suffered greatly. Yet virtual care has made behavioral health specialists more available than ever before, while reducing the stigma of seeking care. It has also made it possible to offer services in communities that lack local providers.

While the massive adoption of virtual care during COVID-19 has shown us what is possible, many barriers still exist. With waivers of geographic, licensure and reimbursement restrictions expiring soon, it's likely there will be a retrenchment that shrinks the footprint of virtual care. We must all advocate together for much-needed legal and regulatory reforms to move forward with modern medicine rather than fall backward to old-fashioned methods.

Of course, not all medical care can be provided virtually, and decisions about when an in-person visit is needed must be driven by what is medically appropriate. Yet COVID-19 has finally shifted the axis of gravity toward a truly patient-centered reality. Value in health care will be transformed when we can monitor our patients remotely while they live their lives, helping us understand their patterns of behavior, identify when those patterns become aberrant and intervene before the next event, rather than after. That is the promise of virtual care. In this way, COVID-19 has changed medicine forever.

LEE SCHWAMM // ***director of the Center for TeleHealth at MGH and vice president for virtual care at MGB Digital Health***

2.

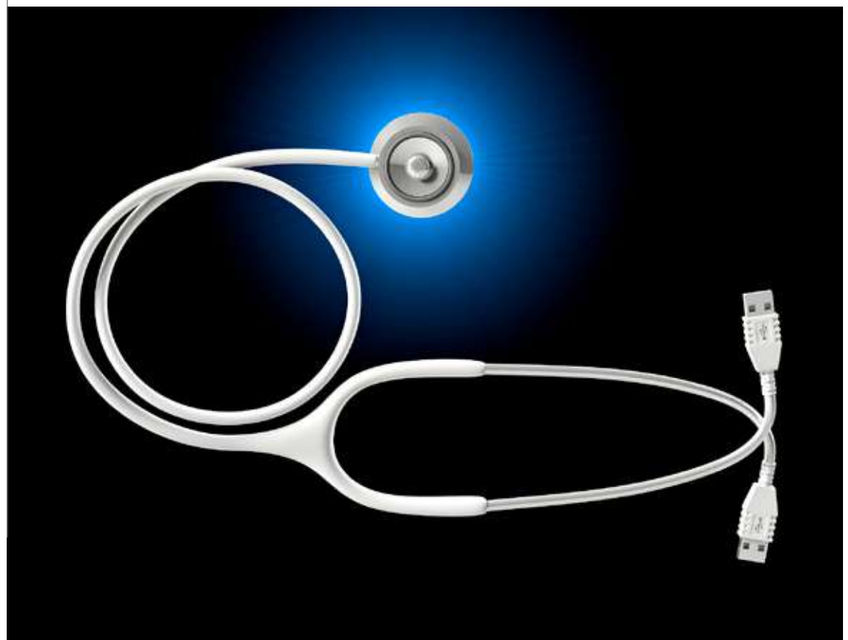
TELEMEDICINE AND ITS DISCONTENTS

The COVID-19 pandemic catalyzed a rapid uptake of telehealth, and most agree this change is here to stay. It does, however, raise a critical question: Will telehealth worsen health disparities, or can it be a tool to improve health equity? It all depends on how thoughtfully we adopt it.

The digital divide—the gulf between those with access to computers and high-speed internet and those without—has left a troubling mark in this pandemic. When in-person visits were largely unavailable, the digitally disconnected were unable to access any care. They have also been left behind in securing COVID-19 vaccine appointments distributed through online systems.

The ones affected are often vulnerable in other ways. One study published in *JAMA* last December showed that patients of older age, non-English language preference, Asian race and with Medicaid insurance were less likely to use telemedicine visits. Other studies have identified older patients, women and those in the Black and Latinx communities as less likely to participate in video visits. We cannot afford to shut these groups out.

And yet it's important to also recognize how telehealth can help with reaching vulnerable populations. I have had video chats with patients as they sat in parked cars or break rooms, using their break time to fit in a quick follow-up for high blood pressure. Many of my lower-income patients are more willing to pursue specialty consultation by telehealth as opposed to an in-person visit, which requires time-intensive transportation into the city and expensive parking. Recently, one of my patients with newly diagnosed metastatic cancer was able to receive a second opinion regarding his therapeutic options from the comfort of his home and in the presence of his two children.



The pandemic should teach us that we need to embrace telehealth in a way that promotes equity rather than worsens disparities. This will take work. We will need to track race, ethnicity, language and income so we can understand who is left behind, shift our strategies and monitor our improvements. Health care systems and providers must advocate for universal broadband access and recognize that access to computers, tablets and smartphones is a social determinant of health.

Our health systems can also employ multimodal technology streams, rather than constraining all communication to our user-unfriendly online portals. A program at Mass General Brigham, for instance, used a texting option to successfully communicate key COVID-19 messaging in multiple languages to its patients. This program improved access to important information for many, including those with low English proficiency, those without regular access to a computer or email and those without an account on our online portal.

Continued reimbursement for telephone visits in addition to video visits will be crucial to promote equity, given that accessing and navigating video platforms is not open to everyone. As telemedicine leaps ahead, let's remember to meet patients with the technology they have and know how to use today as we also work to expand everyone's digital tools and expertise.

SARAH MATATHIA // ***family medicine specialist with MGH Everett Family Care Center.***

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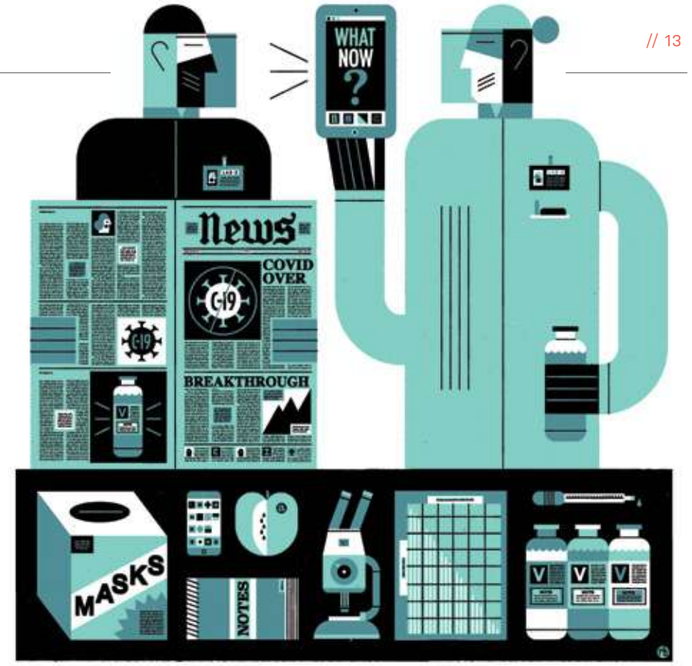


3.

THE CRACKS IN WALLS THAT DIVIDE US

On March 2, 2020, within days of the first reported cases of COVID-19 in the United States, a group of about 100 physicians and scientists gathered at Harvard Medical School to discuss the gathering storm.

The meeting was notable in that it reached beyond institutional walls. It included not only people from Harvard, but also from the University of Massachusetts, MIT, Boston University, Tufts and all the teaching hospitals. It included local biotechnology firms, including Moderna, and the Massachusetts Department of Public Health. Via video hookup, we had collaborators from the heart of the epidemic in China.

From this daylong meeting ensued a remarkable collaborative effort, the Massachusetts Consortium on Pathogen Readiness (MassCPR). Working groups were established that very day and centered around different aspects of the coming crisis: patient care, epidemiology, diagnostics, pathogenesis, treatment and vaccines. Within a month, sufficient philanthropic support had been raised to release funds for more than 60 separate support services and collaborative grants to benefit the more than 500 scientists and clinicians involved.

The past year has seen the worldwide biomedical community unite against a global health crisis with an unprecedented degree of data sharing and collaboration. This cannot

help but have an enduring, catalytic effect on confronting the challenges ahead. Collectively, MassCPR and the global web of similar efforts have created an enduring collaborative community. Humanity will be the better for it.

BRUCE WALKER *// founding director of the Ragon Institute of MGH, MIT and Harvard.*

4. HARD LESSONS IN HEALTH CARE ECONOMICS

The impact of the novel coronavirus pandemic on the U.S. health system won't be fully understood for years, but some of its implications are already becoming apparent.

Despite the heroic responses of health professionals and hospitals, we learned that our delivery system is not prepared for pandemics. In recent years, to improve efficiency, we have reduced hospitals' reserve capacity and streamlined supply chains. That leaves the hospital sector with very little ability to expand services rapidly to meet a surge in demand. For many hospitals, the only way to make room for COVID-19 patients was to stop elective care. That created economic problems for facilities and health problems for patients. Meanwhile, just-in-time supply protocols caused shortages in vital medicines and equipment.

A further problem is that our decentralized, competitive health care system lacks established mechanisms for collaboration during public health emergencies. Systems for sharing supplies, beds and personnel had to be created on the fly. The nation also lacks an electronic public health information system, so emergency data sharing had to go by fax.

COVID-19 also revealed that the way care is paid for leaves providers financially vulnerable during this kind of disruption. The great majority of hospitals and physicians survive on fee-for-service payments, and when the volume of services drops, so does provider revenue. Losing elective procedures, which are compensated more generously than other services, hit particularly hard.

At one point in April 2020, hospital admissions nationally dropped to 31% below expected levels, and from March through December, admissions lagged by 8.5%. Ambulatory visits plummeted 60% in March and April, and despite returning to normal levels by summer, visits for the full year remained considerably below what had been expected.

Financial losses have forced some hospitals and physician practices to close, especially in rural areas, and there have been widespread layoffs. Federal aid helped mitigate the damage, but the health care industry has emerged weakened. It has often proved itself to be recession proof, but it clearly is not pandemic proof.

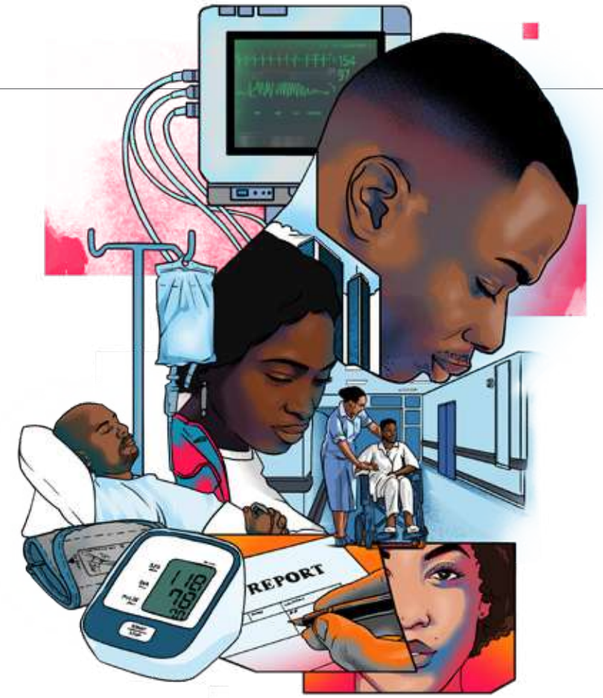
With strong public health leadership and the miracle of vaccines, we hope the worst of the pandemic will be behind us by late summer or fall. Humans being humans, most of us will then feel an overwhelming urge to return to "normal." For health care, that will probably mean pre-COVID business as usual, though perhaps with a couple of tweaks.

In the most likely scenario, our system will continue to rely on fee-for-service payment and remain unprepared to collaborate during public health emergencies. In addition, pre-pandemic trends toward consolidation in the health care sector are likely to accelerate, as providers severely weakened by the pandemic either go out of business or are acquired by stronger survivors.

An alternative, and perhaps less likely, scenario would see a thorough reevaluation of pandemic preparedness and require a public-private plan for pandemic resiliency. There would be financing of surge capacity for local health care facilities, protocols for sharing supplies and personnel during health crises—and regular drills to test these protocols—as well as changes in provider payment, with greater use of so-called "prospective payment," through which health care facilities are paid in advance for the number of patients they serve rather than the number of services they provide. Also critical: national and local electronic public health information systems that permit real-time data sharing to track the response to pandemic threats.

The recently enacted American Rescue Plan Act could support the reforms suggested above. But change will ultimately fall to leaders of our private health care institutions, which are on the front lines of preventing and combating illness in the United States. Let's hope we can prepare for future health threats to our national wellness as well as we do for military ones.

DAVID BLUMENTHAL *// president of the Commonwealth Fund, a foundation that promotes a better performing U.S. health care system.*



KINGSLEY NEBECHI

5. A TURNED PAGE ON RACIALIZED MEDICINE

≠ In the summer of 2020, physicians from Massachusetts General Hospital made their way to the State House in protest of the police killings of George Floyd and Breonna Taylor. As we look at the past year, we remember that it held a reckoning with what many have called "twin pandemics": COVID-19 and systemic racism. COVID-19 was new but it laid bare the long-standing, stark realities of racial injustice in our country.

In the medical field, this has partly meant revisiting fundamental questions about race and ethnicity. We commonly use race clinically, but our latest insights from population genetics have demonstrated convincingly that race is a poor proxy for genetic difference; studies have repeatedly shown that greater genetic variation exists within racial groups than between them. Race is a pervasive social construct, but biologically and medically it is less useful. Categories like "Black" or "white" are exceedingly unlikely to represent meaningful genetic differences between individual patients.

Medicine is still behind the curve in updating its practices to reflect this understanding. Our tools often use race as a proxy for true biological difference. Concerningly, many of these tools even use such variables in a way that can direct care or attention disproportionately toward white patients compared with patients of color. Calculators that predict lower chances of successful vaginal births for Black women may deter them from attempting such births. Risk scores that predict lower rates of fracture in Black patients could delay therapy for osteoporosis.

This year, critique of these practices gained new ground. Academic scholarship shed light on the widespread and often harmful practice of "race correction" in medical algorithms. Traction on this issue reached the federal level, and the chairman of the House Ways and Means Committee asked professional medical societies to account for their use, and many have assembled task forces.

In March, the American Society of Nephrology and National Kidney Foundation task force announced its official recommendation to end race adjustment in the widely used algorithm for kidney function called the estimated glomerular filtration rate (eGFR). The Maternal Fetal Medicine Unit Network also announced the development of a new tool for predicting successful vaginal birth after cesarean without race correction. This debate even reached the NFL, where a concussion lawsuit cast new light on a race correction used to interpret neurocognitive testing in football players. Different curves for Black and white players effectively lowered the chance of Black players earning concussion settlements compared with white players.

As medicine moves increasingly toward computerized models of risk assessment, the creation of best practices for the use of race becomes ever more urgent. It is crucial to understand that this does not suggest the adoption of race-blind medicine. Racism continues to have pernicious effects on health outcomes. But in the decade ahead, we must do the difficult work of recognizing those effects and addressing their causes, rather than defaulting to building these inequities into predictive tools. Once we see *racism* as the risk factor for poor health outcomes instead of *race*, our interventions can be designed to address root causes rather than risk perpetuating inequities.

DARSHALI VYAS *// clinical fellow in Medicine at MGH.*

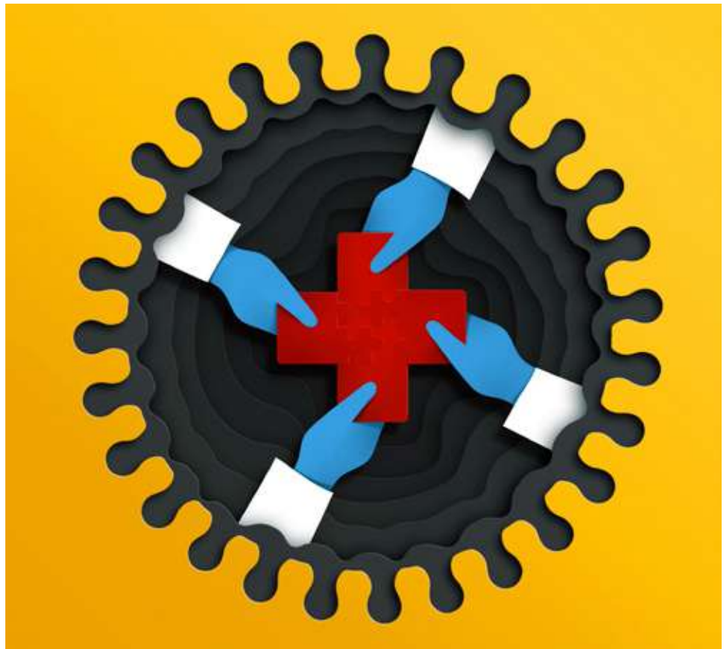
6.

A FUTURE INFORMED BY GENDER-AFFIRMING CARE

In 2020, systemic inequalities in health care and American life became so acute that they led millions to march and demand racial justice. An overlooked phenomenon is that the crisis has been transformative in the lives of transgender Americans as well.

When unemployment hit more than 21 million workers, transgender Americans were predicted to fare the worst, especially transgender people of color and those who live in rural areas. Because the U.S. Census doesn't specifically track LGBTQ+ Americans, the government could not measure and respond to the full impact of the pandemic on this population. We do know, however, that state legislatures used this time to forward bills that would make providing health care to transgender minors a felony.

Transgender Americans are not new to this kind of attack from the government, and we have learned only too well the connection between policy and health. We know that transgender rights are a patchwork across the United States and this means not everyone has equal access to care. We know that access to gender-affirming health care means access to our very identity, and that denying this health care results in terrible mental health outcomes. Over the past decade, we have advocated for—and seen—a profound expansion of services and education, so that our medications, surgeries and therapies are now considered medically necessary.



Our medical rights are at a crisis point—and, we hope, an inflection point. Despite hostile legislation, we have also seen an increased political will for expanded LGBTQ+ rights, such as the landmark Equality Act currently before Congress and moves to reverse discriminatory rule changes authorized by the Trump administration.

The pandemic has helped some doors open. The national explosion of telehealth offers new possibilities for helping those who live far from gender-affirming care centers. Before the pandemic, several new virtual care startups were created to meet the specific needs of transgender people. The largest, Folx, raised $25 million in funding in the thick of the COVID-19 crisis.

Our victories, if they come, can have effects that extend far beyond our own community. Gender-affirming care offers a model for all health care. It is an excellent expression of patient-centered care, one intimately based on patients' identity and values, and driven by the story of their lives. In this and other ways, transgender people have been on the frontier of exploration and expansion.

Transgender people have also had to learn, by necessity, to be active, informed and vocal patients—not only in their own care, but in the political and economic systems that govern it. In the coming year, the whole country will need to learn to follow our example: to become engaged in the shape of our health care system, to turn the challenges of the moment to our advantage. Transgender Americans, especially in the time of COVID-19, are showing what health care can be.

DALLAS DUCAR // *clinical lead for Mental Health Services at the MGH Transgender Health Program.*

TYLER COMRIE

DADU SHIN

7.

A RECKONING FOR NURSES AND NURSING

Nurses are no strangers to crisis. We dedicate ourselves to supporting people when they are at their most fragile and often sit with them in the last moment of their lives. The next day we come back, to offer our care and expertise for whoever comes through the door.

But this pandemic brought new levels of crisis and uncertainty. Many of us were working outside of our specialties. The number of clinicians who could interact with a COVID-19 patient in isolation was limited; more often than not, that clinician was one of us. We would enter a room filled with a new pathogen and be the hospital's lifeline to a patient. And we would also be that patient's lifeline to the world. We documented symptoms, administered experimental drugs and adjusted to unfamiliar equipment. But we also did our best to act as translators and go-betweens, to be IT consultants when a patient's phone or other digital lifeline got buggy. We became an all-too-rare source of touch and human contact. And when we could, we tried to answer the questions of why and how and how long.

As we think about future health crises, we need to remember those demands and their lessons. A study from late October found that one in four health care workers was experiencing PTSD, and in a separate survey, eight out of 10 nurses reported disturbances in mental health. Talking among ourselves, we know this experience has, in a profound way, made us reevaluate our attitudes toward stress and burnout. We've gotten more serious about self-care, both individually and as institutions. Together, we've become stronger and more confident. We are learning to take our pain seriously. We are learning to open up with colleagues, our second families.

But what we hope we've also learned—as a hospital, as a profession—is how important it is for all parts of the care team to listen to one another. From that vantage in the patient's room, nurses across the country and across the world became the eyes and ears and hands of hospital practice. When insights from nurses were heard and respected, patients benefited.

Historically, nurses have been underutilized in the decision-making of hospitals. This remains true despite studies in the United States and Sweden showing that nurse assessments of patient safety and quality of care correlated strongly with patient outcomes. Such findings underline what we already know—that nurses have a keen attention to the welfare of our patients, and when we are invited to identify problems and help find solutions, everyone benefits.

We all hope to never see another event like this, in our generation or the next. But if it happens, we will be ready to help, ready to listen, ready to share. Above all, we will be ready to stand with our teams and help our patients in the ways that serve them best.

KRISTIN EGAN // *nurse in the Surgical ICU department at MGH.* **ALYSSA MARCHANT** *and* **JESSICA O'NEIL** // *nurses in the Pediatric Surgical Unit at MGH.* **LISA MCNEIL** // *nurse in the Post-Surgical ICU at MGH.*

CHARLES WILLIAMS

8.

A TURNING POINT IN THE BURNOUT CRISIS

The COVID-19 pandemic has only exacerbated another public health crisis that had already reached epidemic proportions. Physician burnout is a syndrome characterized by depersonalization, emotional exhaustion and a low sense of personal accomplishment. It's extremely common, afflicting about one in two physicians in the United States. Burnout can compromise physicians' altruism, professionalism and the quality and safety of the care they provide. For individual physicians, burnout has been associated with cardiovascular disease, alcohol use, depression, suicide and a shorter life expectancy.

Prior to the pandemic, our efforts through the Massachusetts General Physicians Organization (MGPO) to mitigate burnout focused on three main areas—creating a culture of wellness, encouraging personal resilience and improving practice efficiency. In particular, our work attempted to home in on the systems issues that drive burnout, rather than focusing solely on the impact on individual physicians.

But COVID-19 changed everything. Not only were we suddenly facing incredible systemic challenges, but we also had to find ways to support a population of clinicians who were being stretched in ways they had never encountered before. Suddenly everyone was working long hours, often in unfamiliar clinical areas, on a disease no one had ever managed. Clinicians had to juggle work and home life more than ever, while also contending with a loss of personal connection on the job and the fear of becoming infected or transmitting COVID-19 to their families.

The MGPO's efforts centered on transparent communication, providing a leadership presence in clinical units, ensuring adequate supplies of personal protective equipment and facilitating active listening to identify needs. In practice, that meant several daily, organization-wide communications with the latest information about the hospital's evolving COVID-19 response. To support personal resilience, we helped make sure clinicians' basic needs—for food, shelter, safety, child care, transportation—were met while also providing up-to-date education on the virus, training and guidance on using PPE, instruction on how to protect yourself and your family, and strategies for connecting to others. We offered space for reflection and processing as well as mindfulness and stress-reduction programs and expanded access to mental health services. Virtual care platforms helped enhance practice efficiencies as we also supported new COVID-related workflows and clinician training to provide care outside usual practice spaces.

The impact of the COVID-19 pandemic on clinician burnout will continue to be felt for years to come, and we'll have to do even more to understand and meet needs that existed pre-pandemic, have arisen because of it and are yet be identified. But we have learned how important it is to focus on burnout not only among physicians but also to include clinicians of all kinds. The challenges have been undeniable, and defeating burnout won't come easily. Yet the innovations we have witnessed—efforts that transcend ordinary divisions among generations and kinds of providers—offer hope for the future.

MARCELA DEL CARMEN // *interim president of the Massachusetts General Physicians Organization.* **KERRI PALAMARA MCGRATH** // *leads the Center for Physician Well-Being for the Department of Medicine at MGH.*

9.

MEDICAL EDUCATION WILL BE TRANSFORMED

After all of the disruptions that the COVID-19 pandemic forced on traditional medical school and graduate medical education in the past year, can anything be gained? We now have a unique opportunity to transform medical education and ensure that we equip the next generation of physicians with the tools to fulfill the social compact of medicine.

In March 2020, the Association of American Medical Colleges and the Accreditation Council for Graduate Medical Education both called a halt to in-person educational and clinical activities for medical students, residents and fellows. With a sense of urgency brought by the pandemic, educators rapidly deconstructed traditional models of medical education that required physical contact, replacing them with alternatives that could prepare trainees to graduate on time without compromising standards of education and care.

As challenging as it was, the necessity of this change led to many innovations. Residents and fellows benefited not only from observing local clinicians; they could also watch lecturers from across the nation via video-based platforms. Virtual chalkboards, which let remote users collaborate digitally, and other technologies provided a canvas for innovative, engaging ways of teaching. Asynchronous learning experiences meant lectures and presentations could be prerecorded, supplemented with other digital materials, and then viewed and responded to when it fit students' schedules.

All of these changes came at the cost of social interaction and personal contact among teachers and learners. Yet much was gained, especially for digitally native

JASON HOLLEY

trainees, who embraced the ability to make virtual visits to patients' homes, network virtually with master clinicians and learn from "flipped classrooms," an educational method in which students complete readings before class and work on problem-solving during class time. Centralizing resources reduced duplication of efforts. Tight timelines enabled educators to bypass burdensome bureaucratic processes.

During these uncertain times, medical education has remained robust and grounded in the values of compassion, professionalism and excellence in patient care. The pandemic has taught us to embrace change and to be agile and adaptable. We are finding ways to incorporate novel technology to meet the needs of learners and to engage in scholarly work that informs and enhances the delivery of care to all patients equitably and without barriers. Curricular changes that incorporate health care disparities and structural racism increase trainees' awareness of these urgent problems that need rapid solutions. Lectures now incorporate clinical photos and findings representing racially diverse patients; highlight disparities in health care access, quality and outcomes by race or socioeconomic status; and show how current clinical decision tools, metrics and guidelines may perpetuate racism.

As we emerge from the COVID-19 pandemic, we must remain committed to the ongoing redesign of educational programs that benefit students and trainees while putting the patient in the center of these efforts. We must learn the lessons of this past year and move forward with the same flexibility, freedom and creativity that helped us adapt on the fly, yielding continuous quality improvement of medical education throughout the spectrum of training.

JATIN VYAS // *Internal Medicine Residency Program Director at MGH.* **ALBERTO PUIG** // *director of the Clinician Educator Service in the Department of Medicine at MGH*

NICOLAS ORTEGA

10.

OUR CALL TO COMMUNICATE THE TRUTH

A high school acquaintance recently asked if I would speak to the staff of a small company about the COVID-19 vaccine. They had questions, and the only vetting I needed was that someone had vouched for me. I agreed, because this was a chance to provide correct information that they'd share with their friends and families. I believe this role of scientific evangelist will become more and more a part of our job descriptions in the years to come.

In the first months of COVID-19, the World Health Organization had already called out the alarming threat of misinformation—the "infodemic." We all saw false statements spread rapidly, aided at times by top-level politicians. The findings of scientists became a topic for political debate, and trust in national medical experts such as Anthony Fauci often split along partisan lines.

Misinformation costs lives. It has led, in the past year, to flouted safety protocols, to people using ineffective or dangerous treatments and to hesitancy around vaccines. How will we stop the spread?

While the traditional gatekeepers against misinformation—public health authorities, watchdogs of social media and policymakers—are all distilling lessons from the infodemic, it will not fall to them to stop it. It will fall to grassroots-level health care professionals, who must become the trusted voices in our communities once again.

People place enormous trust in their community. That roomful of office workers could have read a statement from the CDC. But they wanted to hear the truth from the friend of a friend. A 2017 study from the American Press Institute found that people were more likely to believe a news story shared on social media by someone they trust, irrespective of the news source itself.

Whether we realize it or not, we in health care think the same way. To be sure, we spend years training our brains to be skeptical of our "gut feelings" and to trust evidence-based medicine, but we're not data-driven computers. We "trust the evidence" because we trust the people and processes we know.

We should learn from the current moment and each commit to being more vocal in our communities. We all need to be out there—on social media, on the local news, in op-eds. People may not trust the voice of a public health official they've never met, but the community doctor they know can change minds and, in the process, save lives.

To make sure we're communicating effectively, we absolutely must enhance communication education. It is a skill that needs to be systematically taught—in medical school, in residency and in continuing medical education. Effective communication with patients and the public should not just be a gift that some health professionals have and some don't. It is, now more than ever, our duty to society.

Our patients are going to be hearing information from somebody. We need to make sure they trust what they hear from us.

HEMAL SAMPAT // *internist and pediatrician at MGH.*

DOSSIER

"COVID-19—Implications for the Health Care System," by David Blumenthal et al., *The New England Journal of Medicine*, October 2020. The paper explores four intertwined health care crises that came into play over the course of the pandemic, and outlines a number of policy ideas that could begin to address them.

"Hidden in Plain Sight—Reconsidering the Use of Race Correction in Clinical Algorithms," by Darshali Vyas et al., *The New England Journal of Medicine*, August 2020. The authors outline a number of diagnostic and predictive algorithms that use race as a factor, sometimes to the detriment of minority patients, and call for a reevaluation of such practices.

TRAVIS RATHBONE/TRUNK ARCHIVE

The Cholesterol Deniers

For decades, a tiny encampment of researchers has held that statin treatment is a hoax. In a time when contrarian views roar to life on social media, how can medicine keep minority opinions from doing irreparable harm?

By Anita Slomski //

Cardiologist Steven Nissen, chief academic officer of the Heart and Vascular Institute at the Cleveland Clinic, delights in the reputation he has earned among his critics. One prized possession is a photograph digitally doctored to show him wearing a tinfoil dunce cap, with the headline, "Steven Nissen goes full quack." The image appeared on the home page of *Natural News*, a website that promotes fringe theories about vaccines and other practices of conventional medicine. "Those guys call me the statinator," Nissen says, a testament to his passionate advocacy of statin drugs—a tool to prevent heart attacks and strokes by reducing high levels of low-density lipoprotein cholesterol (LDL-C).

Nissen certainly isn't alone in advocating statins. They are one of the most prescribed drugs in the United States and the best available tool to fight heart disease, the country's leading cause of death. But Natural News isn't the only statin detractor, either. The International Network of Cholesterol Skeptics (THINCS) has, since 2003, been a gathering place for clinicians, researchers and science writers who question the accepted theory on cholesterol—that it contributes to heart disease, and that statins can help prevent heart attacks and strokes. Even some prominent mainstream physicians—including, perhaps most notably, cardiologist and *JAMA Internal Medicine* editor Rita Redberg—question the science that has established high cholesterol as a medical problem that must be treated. "We are telling people to take a daily drug for 20 to 30 years, and we have no trial that follows people for more than five years," Redberg says.

Longstanding debates in medicine are nothing new, and sometimes outsider theories have led to valuable insights. Such camps can trade volleys for decades—many arguments from the "cholesterol deniers" are variations on themes from 10 or 20 years ago. What has changed, perhaps dangerously, is the degree to which these views can catch on in the public media landscape and exist, unchallenged, in the walled-off information silos of the 21st century.

Indeed, minority viewpoints have always been more likely to be reported than mainstream views, and the same is true for the cholesterol debate. Journal articles from cholesterol contrarians make their way into the press far more often than those that extol statins' virtues. One study found that news stories about statins in the British press were twice as likely to be negative as positive. "The media publish articles that people will click on, and it's intriguing to read an article that says you don't have to take a very common medication or that you can live a less healthy lifestyle," says Ann Marie Navar, associate professor of cardiology at the University of Texas Southwestern Medical Center, who serves as associate editor of *JAMA Cardiology* and as a board member of the American Society for Preventive Cardiology.

That reporting comes to rest in digital media, where the majority of Americans now read their news, and where misinformation can spread unchecked. Nissen, who finds the views of statin deniers radical and dangerous, says their studies frequently reach the public through "cult-like messaging" on social media and websites such as Natural News. He worries that these studies dissuade patients from taking a drug that may save their lives. Indeed, about 40% of those at highest risk for cardiovascular disease who are prescribed statins stop taking them or don't take them as prescribed after three months.

One response has been to point fingers at online places where inaccurate stories are disseminated. In 2019, the editors of nearly 30 cardiovascular medical journals wrote a letter blaming the media for the "wanton spread of medical misinformation" about statins. "Misinformation travels faster through social networks than truth," they wrote, and they called on the media and social channels to act responsibly and to refrain from giving "rogue" voices the same weight as the views of mainstream science.

These views can catch on in the public media landscape and exist unchallenged.

But it is perhaps naïve to think that disagreements among researchers will not be politicized by the general public. The problem of minority viewpoints spreading virally became critically dangerous during the COVID-19 crisis and its concurrent "infodemic"—the spread of fake news and the promotion of unorthodox theories. Former Stanford University radiologist Scott Atlas, who served on the White House coronavirus task force during the Trump administration, challenged the use of masks to prevent the spread of COVID-19. Physician Jane Orient, executive director of the Association of American Physicians and Surgeons, was one of many prominent figures to promote the antimalarial drug hydroxychloroquine to treat COVID-19; clinical trials ultimately showed the medication to be ineffective and sometimes harmful. Both ideas still echo in online communities, hindering efforts to control the pandemic.

For statins, with so many lives on the line, is it time to stop ignoring the dangerous views of a small-but-vocal group of cholesterol deniers? "The whole point of science is to refute accepted theories and hypotheses," says Donald Lloyd-Jones, chair of the Department of Preventive Medicine at the Northwestern University Feinberg School of Medicine and president-elect of the American Heart Association. "But there comes a point—and I think cholesterol reached that point long ago—where this kind of debate creates harm and does not advance the knowledge of science."

PHOTO EUPHORIA/GETTY IMAGES

At about the time the famed Framingham Heart Study commenced in 1948, researchers began to pay serious attention to cholesterol and its effect on arteries. Along with other epidemiological studies, Framingham established high cholesterol as a risk factor for cardiovascular disease, adding to a list that also includes hypertension, smoking, obesity, diabetes and lack of exercise. By 1984, the National Institutes of Health had asserted that "it has been established beyond a reasonable doubt that lowering ... blood levels of low-density lipoprotein cholesterol will reduce the risk of heart attacks due to coronary heart disease." People with high cholesterol were advised to modify their diets, and it was recommended that all Americans reduce the amount of fat they consumed. Yet dietary changes usually resulted in only minor improvements, and the few drugs available then to reduce LDL cholesterol weren't very effective, says cardiologist Christopher Labos, an associate in the Office for Science and Society at McGill University in Montreal.

The following year, Michael Brown and Joseph Goldstein won a Nobel Prize for their discovery that familial hypercholesterolemia—a condition in which people are born with extremely high levels of LDL-C and have an elevated risk of premature heart attacks—is caused by mutations in the gene that encodes the LDL receptor responsible for clearing LDL-C from the blood. "That discovery confirmed that LDL cholesterol is a key target for reducing future cardiovascular disease," says Pradeep Natarajan, director of preventive cardiology at Massachusetts General Hospital.

Lloyd-Jones considers it indisputable that LDL-C is the primary culprit in creating atherosclerotic plaques. "That is simply the biology," he says. "Under the microscope, you can see LDL particles eliciting an inflammatory response from the body and doing direct damage to artery walls." Humans need only a small amount of

LDL cholesterol to make hormones and for cellular repair, and any excess creates arterial plaques, Lloyd-Jones says. "LDL cholesterol meets all of the criteria for a causal risk factor, and if the LDL level is high enough, it causes atherosclerosis," he says.

The vast majority of cardiologists and primary care clinicians agree with that assessment. "Only a few completely deny the role of cholesterol in causing cardiovascular disease," estimates Salim Virani, chair of the prevention of cardiovascular disease section of the American College of Cardiology and professor of cardiology and cardiovascular research at Baylor College of Medicine.

Statins' effectiveness in treating LDL-C is also not in dispute, according to most physicians. "Statins reduce the risk of cardiovascular disease by 15% to 30%, and they've greatly contributed to the dramatic drop in deaths from atherosclerotic vascular disease," says Mason Freeman, chief of the Lipid Metabolism Unit at MGH. He estimates that the vast majority of interventional cardiologists over age 40 who work in cardiac catheterization labs take statins themselves. "I don't think there is a higher endorsement for the benefits of statins than that the doctors who understand most about the ravages of a disease personally take the preventive medicine," he says. "The science is crystal clear that statins reduce cardiovascular risk, but individuals on statin therapy can still have atherosclerotic vascular events, such as a heart attack or stroke."

One response has been to point fingers at online places where the stories live.

It's that last fact that opens the door to critics, Freeman says, with many attacks based on a supposedly weak connection between statin use and reduced incidence of heart problems and strokes. Yet those criticisms, according to mainstream researchers who have looked into them, are based on questionable studies or don't reflect the biology of atherosclerosis. "They use data in a very selective way, focusing on one data point instead of looking at the evidence of the entire study," Virani says. "Or they use observational data to build a case for their theories and disregard large randomized trials or epidemiological studies. That leads to misinterpretation of the evidence."

One tactic, according to UT Southwestern's Navar, is to cite evidence from short-term trials in which no participants taking statins died and few had heart attacks or strokes. This is misleading, Navar says. While not all statin trials show a reduction in deaths, a five-year trial can't reflect statins' true power. "We aren't trying to prevent cardiovascular events in the next five years with a statin," she says. "The goal is to provide protection over the next 15 to 30 years. The longer you take a statin, the more benefit you get by preventing plaque from building up in your arteries."

In addition, not dying after a heart attack isn't the only outcome that matters to patients, Virani says. Many people today survive heart attacks and strokes but may face significant disability and poor quality of life.

Physicians who doubt the conventional wisdom about cholesterol and statins hold a range of views, but those from THINCS members tend to be the most extreme. In recent medical journal articles, THINCS director Uffe Ravnskov, a nonpracticing Danish physician and independent researcher, and David Diamond, a cognitive neuroscientist at the University of South Florida, dismissed almost all of what the medical mainstream believes about cholesterol and statins. They concluded, from a multi-study review, that elderly people with high LDL-C live just as long as or, in most cases, longer than those with normal or low LDL-C. Ravnskov also argued that infections are a common cause of cardiovascular disease and that LDL-C plays an important role in the body's immune response against harmful pathogens. In line with these claims, they find fault with European guidelines on managing heart disease and diabetes, which recommend prescribing statins as part of treatment to cut levels of LDL-C. Diamond says he believes statins may have a small benefit in preventing heart attacks and strokes, but he ascribes that result to the drugs' ability to reduce inflammation and blood clotting.

Retired cardiologist Robert DuBroff, who taught at the University of New Mexico, says some patients with high LDL-C may benefit from statins. But he thinks it's time for physicians to acknowledge that randomized controlled trials have at times produced inconsistent and contradictory evidence about the benefits of cholesterol reduction. His analysis of 35 cholesterol-lowering drug trials, published in *BMJ Evidence-Based Medicine* in 2020, found that there was no mortality benefit in roughly three-fourths of the trials, and nearly half reported no significant reduction in cardiovascular events. According to his analysis, some of the trials that reported the greatest drop in LDL-C among participants demonstrated no accompanying cardiovascular benefit. But in other trials where LDL-C levels dropped only modestly, there was a robust reduction in cardiovascular risk. "The cause of atherosclerosis is far more complex than we originally thought," DuBroff says. "But our LDL-centric approach to preventing cardiovascular disease may have distracted us from investigating other mechanisms and treatments."

Cardiologists have ready rebuttals for cholesterol deniers' claims. In some people, low LDL-C is a marker of significant systemic disease, such as severe infection or sepsis—and it's that underlying systemic disease, rather than low LDL-C by itself, that causes people in some clinical studies to die.

Another false argument—that people with high cholesterol tend to outlive those with normal cholesterol levels—illustrates the problem of selection bias, Labos says. "If your study includes only people who died from a heart attack, for example, you can make dangerous things such as smoking and high cholesterol seem protective if you don't properly adjust for them statistically," he says. The likely reason that some people with no apparent risk factors may die of a heart attack is that their genetic makeup led to the development of heart disease.

A 2016 meta-analysis examining 25 statin trials showed that the more you reduce cholesterol, the greater the cardiovascular benefit. And Labos's own study that analyzed data from recent randomized trials of statins found conclusively that statins' cardiovascular benefit is directly related to their LDL-C-lowering properties rather than to any other effects.

Redberg has long disputed the majority view of cholesterol and statins. "I believe there is an association between LDL cholesterol and heart disease, but it's very weak and it's certainly not causal," says Redberg, professor of medicine at University of California, San Francisco. She declines to treat patients with statins to prevent a first heart attack or stroke regardless of LDL-C levels. Although current clinical guidelines call for giving statins to anyone who has LDL-C of at least 190 milligrams per deciliter, Redberg advised her mother, who had high total cholesterol, not to take any statins. Redberg attributes the longevity of her mother, who lived to age 94, to a good diet and exercise. "Mine is a minority opinion among physicians, but it should be mainstream," says Redberg, who launched a "Less is More" series of articles in *JAMA Internal Medicine* that focuses on what she considers the overmedicalization of Americans.

Redberg says she believes there are minimal benefits in taking a statin to prevent a heart attack or stroke for someone who hasn't already had one. "If 100 people take statins for primary prevention, only two will avoid a heart attack, which means that 98 won't get any benefit from the statins, but up to 20% will have adverse effects and none will live longer," she says.

But Redberg's advice about statins is different for those who have already had a heart attack or stroke. For so-called secondary prevention, taking a statin may be worthwhile because the cardiovascular risk is so much higher, she says. "Everyone who has had a heart attack gets a statin, regardless of their cholesterol level, because you are much more likely to have a second heart attack after your first one," Redberg says. "If your risk of having a second heart attack is 20%, a statin may cut that risk by 2%." In contrast, a healthy person with high cholesterol may have a 1% chance of having a heart attack, and taking a statin reduces that risk by a mere 0.1%, she says. This is accurate, according to Labos. "The higher your risk, the more you benefit from treatment, which is pretty standard in all fields of medicine," he says.

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Some of those who question the evidence of statins' benefits point to the lack of transparency in the way much of statin research is conducted and analyzed. For instance, the Cholesterol Treatment Trialists' (CTT) Collaboration, a division at the University of Oxford in the United Kingdom that has received significant financial support from the pharmaceutical industry, keeps patient-level trial data secret. "Virtually everything we and the experts who write clinical guidelines know about statins comes from the CTT Collaboration," says John Abramson, a lecturer on health care policy at Harvard Medical School and author of *Overdosed America*. "Individual patient-level data from the trials remains sealed, which means we have no confidence that the published data

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Statins and the Nocebo Effect

Some patients are scared of the side effects—which often may be a byproduct of those fears.

Patients often report intolerable side effects from taking statins, a fact that has continued to perplex physicians. Although clinical trials point to a few adverse effects, many patients say they are debilitated by severe muscle pain and other symptoms. A new study shows that many of these may stem from the "nocebo effect"—a product of a patient's negative expectations rather than the drugs themselves.

The SAMSON study, published in *The New England Journal of Medicine* in 2020, recruited people who had tried statins but stopped taking them because of severe side effects. Each participant received 12 bottles—four containing a statin, four with a placebo and four that were empty—and rotated through them monthly, recording daily symptoms. (The months with empty bottles provided a baseline of everyday aches and pains.)

Investigators found that 90% of the adverse symptoms occurred during the months that patients weren't taking a statin. These symptoms were so severe that participants stopped taking the placebo pills on 71 occasions. The investigators then showed participants their own symptom data. Many were astonished to learn they had felt fine during the statin months and agreed to resume taking statins. "Only 18 of the original 60—less than one-third—told us they weren't restarting because they still believed they caused side effects," says lead investigator James Howard, cardiologist and clinical research fellow at Imperial College London.

"SAMSON demonstrates that the nocebo effect dominates in a majority of patients. The real side effects are much rarer than we thought," Howard says.

SAM KAPLAN/TRUNK ARCHIVE

are a fair and complete representation of the trials' results."

The CTT Collaboration was formed to bring together participant data from big, long-term randomized controlled trials of statin therapy. Having information about a larger, more diverse population of study participants enables the companies that voluntarily participate in the CTT to report on the effectiveness of statins versus placebo in women, for example, or in people over age 75 or those with a low risk of developing heart disease. Those finer distinctions may enable drugmakers to show that statins as a class are safe and effective for more diverse groups of people. But in return for participating in the CTT, companies were assured that their raw patient data would be kept under wraps.

The CTT Collaboration confirms that it doesn't routinely share data about individual participants in statin trials. But responding to Abramson's claims in a letter to *The Lancet*, the group said that it employs an independent panel to provide "external oversight, and the collaboration responds to external requests for analysis."

Clinicians will have to make their case person by person, engaging in detailed discussions.

Editorials in *JAMA* and *The BMJ* have criticized the CTT Collaboration for refusing to make all trial data available to other researchers. The editors of *The BMJ* say they have made multiple requests over several years to the CTT to release the data, but only a handful of collaboration members who conduct statin trials have complied. Secrecy about statin trial results underscores the "deep flaws in our current system for evaluating medicines and guiding clinical decisions," *The BMJ* editors wrote recently.

But Baylor's Salim Virani thinks the focus on the CTT Collaboration is just one more conspiracy theory promoted by anti-statin clinicians. He notes that most of the thousands of researchers who have worked on statin trials over the years are not members of the CTT, and those researchers do make their data available to other scientists. In addition, Virani says, the U.S. Food and Drug Administration reviews all relevant trial data before approving a statin, and if statin makers were attempting to cover up dangerous side effects, it would be discovered during those regulatory reviews. "These conspiracy theories have definitely cost lives by convincing patients not to take statins," he says.

Statin use doesn't begin when it's prescribed but rather when a patient decides to take it. The lopsided coverage of the cholesterol debate outside of medical journals can play into that patient decision in a potentially deadly way, Labos says. "There is a real danger that misinformation causes people to stop taking their medications"—or not to start in the first place. In Australia, for example, statin prescriptions dropped by 14,000 per week following a 2013 television special about the dangers of that class of drugs. The collateral damage, according to a group of researchers, was that more than 60,000 people were affected, and that 1,500 to 3,000 potentially avoidable heart attacks and strokes would occur if those patients remained off statin therapy for the next five years. In Denmark, researchers attributed a 2% rise in heart attacks and a 1% increase in cardiovascular deaths to people abandoning their statins after watching negative news reports about the drug.

How to keep the public informed about the actual state of the debate among physicians is tricky. On one hand, physicians have an obligation to protect patients by keeping scientifically unsound articles about cholesterol out of medical journals, says Nissen of the Cleveland Clinic. "If medical misinformation is out there and we just shrug, we have shirked our responsibility," he says. "Journals need reviewers who are scientifically strong and can take apart a meta-analysis and say, 'This isn't right.' What disturbs me is that some pretty good journals seem to allow these contrarian views about cholesterol and statins into their pages," he says, referring in particular to Redberg's *JAMA Internal Medicine* and *The BMJ*.

But until there are changes in the process through which journals select and review the articles they decide to publish, clinicians will have to make their case person by person, engaging in detailed discussions with their patients about the existing evidence around statins. Some patients, looking at the evidence, may decide their risk doesn't merit taking a daily statin for years. "It's a fair argument for a healthy person with high cholesterol to decline a statin, which isn't going to prevent that many heart attacks or strokes if the patient's only risk factor is high LDL-C," Labos says. "But if you have high cholesterol, have a family history of heart disease and have hypertension or other risk factors, then taking a statin will have a much larger preventive benefit. And as you age, your risk of heart disease increases, which also makes taking a statin beneficial."

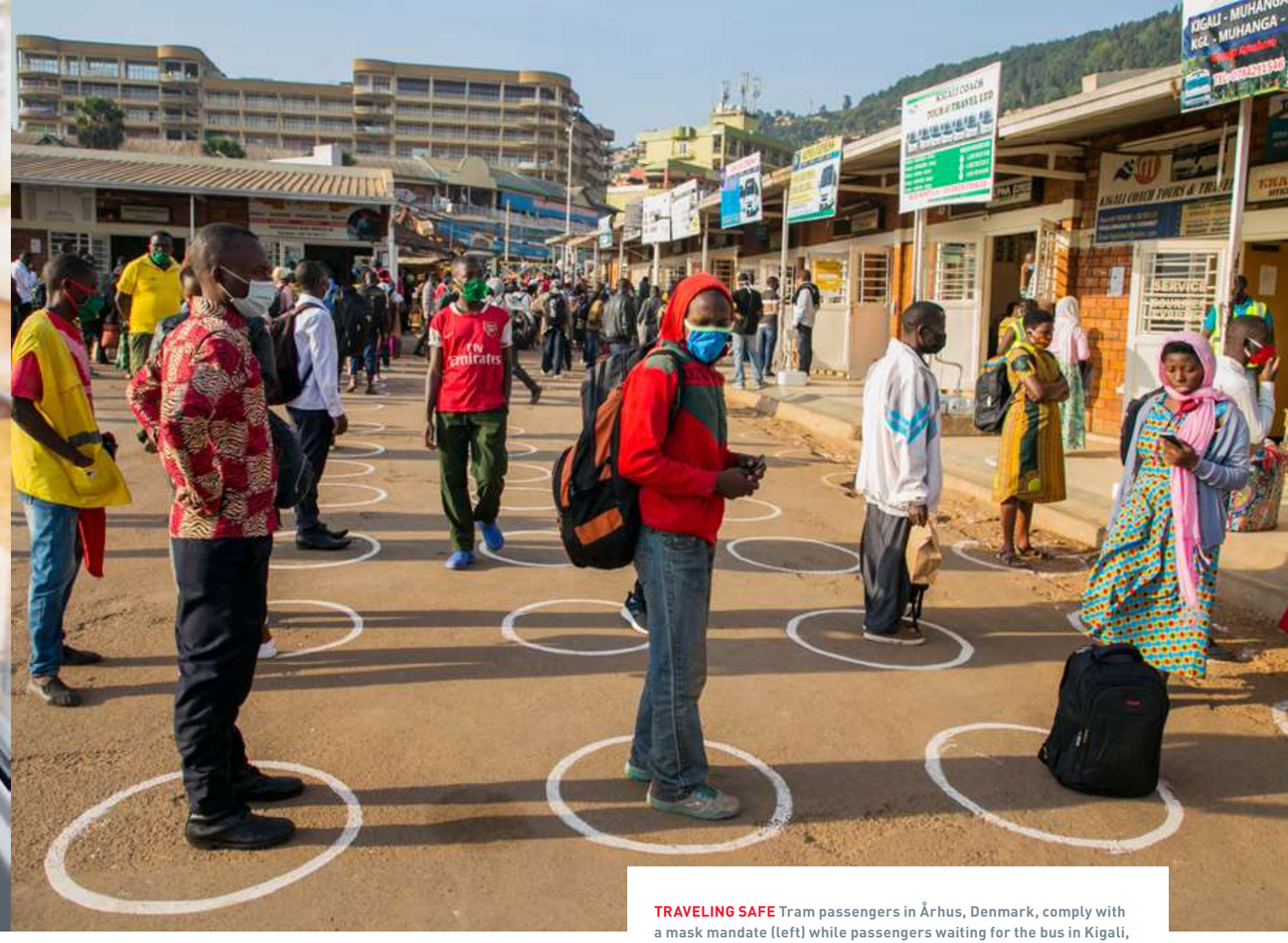
"The way to deal with misinformation is to provide the right information, one patient at a time," Virani says. "When patients express concerns about taking a statin, the worst thing clinicians can do is be dismissive. Hear them out, provide the evidence and direct them to resources such as clinical guidelines and reputable sites. Then let patients be the judge of whether they want to take a statin."

Although statins have been a treatment mainstay for several decades, it could take even longer to extinguish dangerous misinformation about cholesterol and statins. "Eventually there will be a new generation of doctors who can't believe there ever was an argument about whether reducing cholesterol was a good thing," Labos says. "No one remembers the time when prominent cardiologists believed that lowering blood pressure was dangerous." Labos quotes John Hay, writing in *The British Medical Journal* in 1931: "There is some truth in the saying that the greatest danger to a man with a high blood pressure lies in its discovery, because 'then some fool is certain to try and reduce it.'"

DOSSIER

"Popular Media and Cardiovascular Medicine: 'With Great Power There Must Also Come Great Responsibility,'" by Anandita Agarwala et al., *Current Atherosclerosis Reports*, October 2019. The authors analyze how social media perpetuates medical falsehoods and discuss how clinicians can address their patients' misconceptions.

"Interpretation of the Evidence for the Efficacy and Safety of Statin Therapy," by Rory Collins et al., *The Lancet*, September 2016. This exhaustive review examines evidence from clinical trials of statins, outlining their proven benefits, adverse effects—proven and claimed—and the public health consequences of the spread of misinformation about the safety of statins.



TRAVELING SAFE Tram passengers in Århus, Denmark, comply with a mask mandate (left) while passengers waiting for the bus in Kigali, Rwanda, stand in white circles to maintain social distance.

TWO TAKES ON A PANDEMIC

Every nation has had its own experience of COVID-19. The stories of Denmark, a model of socialized care, and Rwanda, a bright spot among developing nations, both hold wider lessons for the world.

BO AMSTRUP/GETTY IMAGES

XINHUA NEWS AGENCY/GETTY IMAGES

In spring 2020, when the COVID-19 pandemic was first raging through sub-Saharan Africa, Hassan Nsabimana was among countless truck drivers who continued to work transporting essential cargo to Rwanda from neighboring countries. In a phone conversation last May from Tanzania, Nsabimana told his eldest son, Faycal Hassan Tuyishime, that he wasn't feeling well and was heading home. "In his voice, you could tell he was critically ill," Tuyishime says.

It was their last conversation. Nsabimana, 65, was tested for the virus at a border checkpoint, then rushed by ambulance to Rwanda's main COVID-19 treatment center in Kigali, the capital. By then, he was having trouble breathing and was put on a ventilator in intensive care. He died two days later and was the country's first fatality linked to the virus. His death was widely reported in Rwanda—in part because at the time, COVID-19 was still relatively rare in the nation of some 13 million people. In late May, the country had fewer than 400 confirmed cases.

That Rwanda has continued to fare relatively well by the grim statistical measures used to gauge the impact of COVID-19 most likely came as a surprise to much of the global public health community. Most of Africa, which had been ravaged by AIDS, Ebola and other contagions, was thought to be ill prepared for a pandemic. In the 2019 Global Health Security Index, which assessed 195 nations' preparations for the kind of global outbreak that would begin a year later, the United States ranked highest, followed closely by the United Kingdom and other developed countries. China ranked 51st, and most African countries were at the bottom.

Rwanda is one of the world's poorest countries, with annual per capita income, adjusted for cost of living, of just $2,000 in

2020. A high population density of 525 people per square kilometer—more than 14 times the density of the United States—also seemed likely to encourage the spread of an extremely infectious disease.

Denmark, in contrast, ranks among the wealthiest nations, with a 2019 per capita annual income of $65,147. Its pandemic preparedness ranked eighth in the Global Health Security Index, just behind Sweden and ahead of South Korea. The population in 2021 was just 5.8 million, and there were only 135 people per square kilometer. So Denmark's relative success in confronting the pandemic is perhaps less surprising. At the end of the pandemic's first year, the country had seen a much heavier toll than Rwanda, with 2,385 deaths compared with the African country's 273. But the impact of the disease in Denmark has been only about a third as high as in Switzerland, for example, a slightly more populous European country of comparable geographic size.

The pandemic responses in both Denmark and Rwanda have been vastly more effective than those of the United States and many other much larger global powers. While very different from each other, the two nations have both benefited from having trusted, government-run health care systems, consistent public health messaging and smart use of the technology available to them. Having the courage to tell the truth about COVID-19 and impose often unpopular restrictions has also played a central role in their still unfolding strategies. But it's in the finer details of what they've done that there are lessons, perhaps, for other health care systems.

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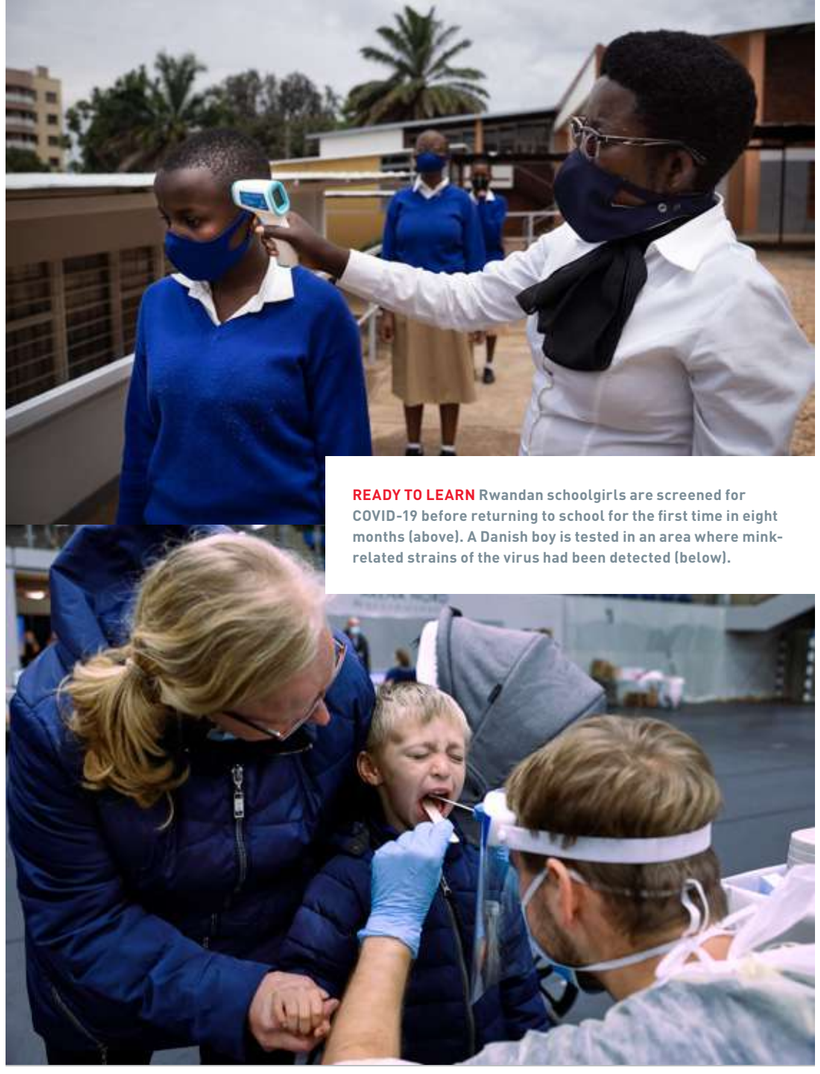
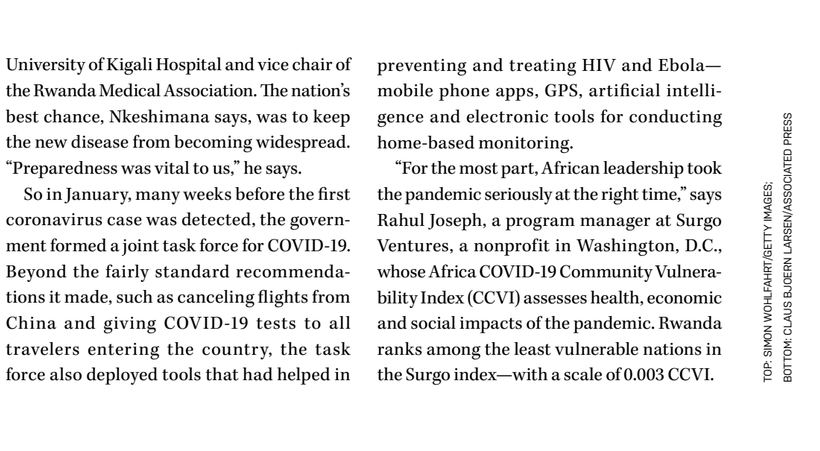
In much of Africa, medical resources are limited, health systems are fragile and even before the pandemic, half of the continent's deaths were caused by infectious diseases. And in Rwanda, mathematical models created in January to predict the likely consequences of COVID-19 showed a health care system almost sure to be overwhelmed, says Menelas Nkeshimana, a physician at the University of Kigali Hospital and vice chair of the Rwanda Medical Association. The nation's best chance, Nkeshimana says, was to keep the new disease from becoming widespread. "Preparedness was vital to us," he says.



READY TO LEARN Rwandan schoolgirls are screened for COVID-19 before returning to school for the first time in eight months (above). A Danish boy is tested in an area where mink-related strains of the virus had been detected (below).



TOP: SIMON WOHLFAHRT/GETTY IMAGES; BOTTOM: CLAUS BJOERN LARSEN/ASSOCIATED PRESS

So in January, many weeks before the first coronavirus case was detected, the government formed a joint task force for COVID-19. Beyond the fairly standard recommendations it made, such as canceling flights from China and giving COVID-19 tests to all travelers entering the country, the task force also deployed tools that had helped in preventing and treating HIV and Ebola—mobile phone apps, GPS, artificial intelligence and electronic tools for conducting home-based monitoring.

"For the most part, African leadership took the pandemic seriously at the right time," says Rahul Joseph, a program manager at Surgo Ventures, a nonprofit in Washington, D.C., whose Africa COVID-19 Community Vulnerability Index (CCVI) assesses health, economic and social impacts of the pandemic. Rwanda ranks among the least vulnerable nations in the Surgo index—with a scale of 0.003 CCVI.

Rwanda's decentralized health care system was built from the ground up after the 1994 genocide that left the country in ruins. Although there is only about one physician per 10,000 people, the system provides universal coverage while granting considerable autonomy to community health workers spread across the country. The system is also extremely popular. In a pre-pandemic study from the Wellcome Trust in 2019, 97% of Rwandans expressed confidence in their health sector—a higher approval rating than anywhere else in the world—which proved to be a powerful benefit in facing down a global viral onslaught. "People know the system is not against them and that public health guidance is based on science and not politically motivated," says Agnes Binagwaho, vice chancellor of the University of Global Health Equity in Rwanda, a former health minister and a key architect of the modernized system. "If the health minister says something is good for you, people will do it because of trust."

As the pandemic found its way into Africa, Rwanda mounted a public awareness campaign to inform Rwandans about how the new coronavirus was transmitted and urging them to take measures to slow its spread. Later, everyone was required to wear face masks in public and encouraged to submit to testing and contact tracing. These messages were disseminated on social media platforms, radio, television and newspapers and broadcast from vans driving through neighborhoods.

On March 14, Rwanda announced its first confirmed COVID-19 case. A week later, the government instituted a national stay-at-home order, closed borders to all but essential goods and cargo and suspended commercial air travel. It was one of the first lockdowns in Africa.

From the beginning, testing was widespread, and health authorities didn't wait for people to come to them. Instead, medics in protective gear stopped people randomly on the streets to offer tests, then sent samples to labs that in many cases repurposed equipment designed to detect HIV infection. Researchers at the University of Rwanda devised a system for pool testing, which enabled two dozen tests to be processed in one batch. If infection was detected, technicians went back and tested each sample. Pool testing proved faster and cheaper, and by August, Rwanda was conducting 10,000 tests a day.

As the outbreak escalated, a small army of newly trained contact tracers was deployed, and anyone who had come into contact with an infected person was called or visited and had to quarantine until a COVID-19 test could be administered. At the COVID-19 task force command post, computer dashboards displayed real-time data pinpointing geographic areas where cases were spiking.

Other technology also boosted Rwanda's response. Drones, already used to deliver blood and medical supplies to remote regions, now were deployed to distribute COVID-19 tests, personal protective equipment and other pandemic-related items. Drones have also been used by police for surveillance, to spot large groups gathered in violation of government edicts.

Drones, already used to deliver blood and medical supplies to remote regions, now were deployed to distribute COVID-19 tests.

Then there were the robots. On May 19, at the COVID-19 Treatment Centre in Kanyinya, Health Ministry officials introduced five human-sized robots manufactured by a Belgian company that were designed to reduce human interactions and the risk of viral transmission. They could screen more than 50 people per minute for common virus symptoms—fevers, dry coughs—as well as deliver food and medication to patient rooms. One robot was deployed at Kigali International Airport to screen incoming passengers, and the others were sent to treatment centers and out onto the streets, where they could detect people without masks or who were wearing them incorrectly and instruct them in proper usage. At treatment centers in Gatenga and Kanyinya, the availability of the robots has cut the exposure of human providers to infected patients almost in half.

All of these efforts seemed to pay off, and by late spring, with case counts stable or falling, the government began easing the lockdown in phases. There was still a nightly curfew, but by early June, the country was open for domestic travel and tourists from outside the country were allowed in. Then, when infection surges were detected—at the borders, in markets, in prisons and elsewhere—more restrictive measures were put back in place. "Localized testing and lockdowns are two measures that Rwanda has done well," Joseph says.

In late October, the World Health Organization applauded Rwanda "for instituting a strong system" that enabled the country to "effectively confront" the COVID-19 pandemic. And in January 2021, Rwanda's response ranked sixth globally and first among countries in Africa in the COVID-19 Performance Index compiled by the Lowy Institute, an Australian think tank.

Still, human rights groups have criticized the authoritarian government's tactics in enforcing public health measures. Not wearing masks or breaching social distancing rules can result in fines, or jail for multiple offenses, and anyone who tests positive for the virus but still mingles with the public could be subject to a two-year imprisonment. Citizens detained by security forces

for violating curfews have reportedly been forced to spend the night in a stadium listening to public health broadcasts blaring from loudspeakers.

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One of Denmark's main advantages in confronting the pandemic is the country's social cohesion. According to the European Values Study, which maps attitudes, beliefs and behaviors in European countries, Danes have the continent's highest level of social trust in one another. They also believe in Denmark's government-run health care system, which is free for everyone and is considered one of the best in the world. There's high regard for science, and some Danish habits, such as not typically hugging in greeting, have amounted to a kind of natural social distancing.

Perhaps Denmark's biggest edge comes from being one of the most digitized countries in the world.

But perhaps Denmark's biggest edge comes from being one of the most digitized countries in the world. Every citizen has a 10-digit personal identification number linked to a central national registry, and that electronic infrastructure proved crucial in supporting the country's COVID-19 testing and detection strategies and enabling detailed epidemiological research throughout the pandemic.

As with other countries, Denmark also closed its borders, shuttered schools and other public institutions and banned gatherings of more than 10 people. But the government didn't restrict travel inside the country or issue curfews or stay-at-home orders, and there was no government-enforced contact tracing. "While Danes are very trusting and law obeying, people are very much against unnecessary supervision by the state," says Trine Mogensen, a physician and researcher at Århus University Hospital and co-author of an online medical journal article that analyzed the country's pandemic response.

A central pillar of Denmark's containment strategy has been free COVID-19 testing available to everyone, and whenever someone tested positive for COVID-19, that anonymized result was recorded in the national system, with information about where and when it occurred. "We can detect what COVID transmission patterns look like in real time," says Jens Lundgren, professor of infectious disease at the University of Copenhagen and Rigshospitalet.

Users of mobile apps also contributed to the well of data available to the government and to medical researchers. Smittestop, which means "halt infection," notifies people when they come near someone infected with the virus and was downloaded by 12% of Danes in the first two weeks it was available. Moreover, the Danish population has long been accustomed to digital communications from government authorities, and in spring 2020, a text alert to every mobile user in the country announced a new fine for failing to observe social distancing guidelines. When the Danish Patient Safety Authority announced it was setting up a secure email system to allow the anonymous reporting of anyone suspected of having COVID-19, however, public backlash led to a quick reversal.

The first wave of infections peaked the first week of April, when 535 patients in Denmark were hospitalized and 146 were in intensive care. The government then began a phased removal of restrictions. As a small economy dependent on foreign trade, the nation had taken a big economic hit when it shut down, and reopening was a political priority. Denmark was the first in the European Union to reopen primary schools, day care centers and some small businesses, and a month later, retailers, restaurants and secondary schools also opened and cultural activities were allowed to resume. Limits on public gatherings were eased, and border crossings resumed.

During the summer, as infection numbers continued to fall, health authorities settled on an approach they called "the green curve." They would take actions to suppress the pandemic as needed to minimize the strain on hospital capacity but would otherwise let infection levels peak and decline naturally as immunity in the overall population increased. "We looked to the testing infrastructure to manage the fluctuations," Lundgren says.

That strategy worked during the summer months, when several small local outbreaks were identified and contained. But in early August, infections surged in Århus, Denmark's second-largest city. Hundreds of new infections were detected, particularly within the Somali community, with contact tracing linking many of those cases to a large funeral. Testing through the fall, in Århus and much of the rest of the country, revealed a second wave of the pandemic.

During that second wave, the Danish tracking system showed a surprising source of new infections. It was discovered that mink could become ill with COVID-19 and could spread the virus to humans. When mink-linked human infections climbed to more than 200 cases by November, health authorities quarantined workers and conducted extensive testing of more than 280,000 people. In late November, the government dictated that all of the mink on 289 farms where infections had been documented, as well as those on other nearby farms, would be killed. That added up to 17 million animals.

Lundgren believes mink-sourced infections contributed to the fall surge of the disease. But a far larger factor behind Denmark's second wave was public complacency, he says: "People just stopped paying attention to advice." In early December, with new infections running at about 3,000 a day, partial lockdowns were rolled out in areas covering about two-thirds of the country.

But this time, hospitalized COVID-19 patients benefited from a growing arsenal of treatments. Danish physicians and patients continue to participate in many international trials of experimental drugs and vaccines. In addition, data from widespread testing in Denmark—more than 10 million tests of 4 million people, covering 70% of the population—facilitated the world's first large-scale study of COVID-19 reinfection rates. The findings confirmed that most people who have had COVID-19 are protected from catching it again for at least six months, although older patients are more prone to reinfection.

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Denmark has been a pioneer in tracking COVID-19 mutations through genomic sequencing of positive tests, and concerns about virus variants, including the B.1.1.7 variant first detected in the U.K., have risen. Moreover, a renewed lockdown implemented at the end of 2020 was only starting to be eased four months into the new year. But the rollout of COVID-19 vaccinations was proceeding, and the government hoped to have the entire population inoculated by July.

Rwanda, experiencing its own wave of infections in early 2021, imposed another lockdown in the capital, banned movement among regional districts and lengthened curfew hours. But as numbers of new cases and deaths fell by half, some restrictions were eased. By early April, just under 400,000 vaccine doses had arrived, and the government said it hoped to provide shots to about a third of Rwanda's population by the end of the year, with the remaining two-thirds getting vaccinated in 2022.

In both of these countries, like everywhere else in the world, the battle against COVID-19 has not quite ended. Yet even now, as the United States, under a new administration, looks at home and abroad for insights into what did and didn't work in combating this pandemic—and how to better prepare for future viral onslaughts—the experiences of Rwanda and Denmark may offer strategies disproportionate to their small geographic footprints.

SAFER SPACES Medical staff await patients in a new Copenhagen rapid test center (above). Rwandans arrested for violating COVID-19 restrictions sit in a stadium to hear speeches about disease prevention (below).

TOP: LISELOTTE SABROE/GETTY IMAGES; BOTTOM: STR/GETTY IMAGES

DOSSIER

"Rwanda's Secret Weapon Against COVID-19: Trust," by Eli Cahan, *The BMJ*, December 2020. In this interview, Agnes Binagwaho, an architect of Rwanda's health system, describes how the country managed the first wave of the virus despite lacking certain resources.

"The COVID-19 Pandemic in Denmark: Big Lessons From a Small Country," by David Olagnier and Trine Mogensen, *Cytokine Growth Factor Review*, June 2020. Researchers examine how Denmark weathered the COVID-19 crisis with a relatively low rate of infection.

Lowy Institute COVID Performance Index. This interactive website measures how certain factors are impacting the COVID-19 response in more than 100 countries.

FIRST PERSON

The Rage Room

BY CHRISTINE BARBA

I couldn't scream because I knew it would hurt my throat. But there was something in the sound of things shattering—a white dinner plate, a salt shaker—that was like language for me. I put down the baseball bat and picked up a sledgehammer. It was surprisingly heavy, but hefting it up felt as if a weight had been lifted off my shoulders. "This is my toast to you, 2020," I said, and I smashed a wine glass.

Rage rooms have been around for several years, but it took the pandemic for me to find one. The name tells you all you need to know. Sign a waiver, and you're allowed to go into a metal cage and demolish objects to your heart's desire. That might be figurines, coffee mugs or, for the big spenders, entire cars. While you let loose, you can blast your favorite music over the Bluetooth speakers. I went with '90s pop-rock.

Of course, you have to wear protective gear. But the black coveralls, face shield and sneakers they had me put on were a nice change. For the past few years, I'd too often been in hospital gowns, masks and surgical booties.

Three years ago, an upper respiratory infection took a bad turn and became an irritating tingling sensation. By April 2019, the tingling turned to nerve pain. I was unable to speak, eat or laugh without pain—a burning coupled with the feeling of 1,000 knives stabbing every inch of tissue. If you've ever had strep throat, imagine that in a super mega size that never goes away.

The next few years had me seeing scores of doctors. Eventually a team of otolaryngologists, gastrointestinal specialists and neurologists gave me a diagnosis: atypical glossopharyngeal and vagal neuropathy. Glossopharyngeal neuropathy is sometimes nicknamed the suicide disease because it is unrelenting and difficult to treat. I had never been depressed, but for months after my diagnoses, I called the suicide hotline and begged my parents to end my suffering if I couldn't somehow manage it.

I stayed focused on ways to feel better. I received ketamine infusions, nerve blocks, three procedures that used pulsed radiofrequency and tried having exosomes injected into the glossopharyngeal and vagus nerves. Relief was hard to come by, and frankly, the medical journey was exhausting in itself. While some doctors were empathetic, one "top" neurosurgeon asked if I'd tried throat lozenges or weed yet. Another doctor mentioned euthanasia. After a visit, I'd often feel like a brittle and disposable object—the kind I was now beating to pieces.

At the start of 2020, I got the bright idea of trying to improve my mental health through adrenaline. I tried activities like skiing and parasailing. In some way they helped, allowing me to get out of my skin for a minute. But then COVID hit, a week after my 28th birthday. The isolation was another source of pain, as it was for so many people with chronic conditions, who were kept from the simple joys and connections so vital to our mental health. That felt like another door slammed shut.

Sweating, standing in the middle of the chaos, I realized that the rage room had been a eureka moment. Throughout my treatment journey, why hadn't I thought of just getting angry? I was safely distanced from anyone—who would get near a 5'3" brunette woman with a sledgehammer?—and I let it swing as Meredith Brooks wailed, "I've been numb, I'm revived, can't say I'm not alive."

I can't say that the moment washed everything away, but it was freeing. For a second, I could let go of the frustration, fear and sadness. Seconds are so important to me now. For years now I've had to hold it all together. This was a place to let loose.

The rest of the night I couldn't stop smiling, but I can't say I found the answer in rage. Not long after, though, I did find a course on retraining the brain's responses. I spent 15-hour days learning about neuroplasticity and how to use my mind differently. I went from breaking inanimate objects to, finally, a kind of breakthrough: laughing and taking deep breaths without pain.

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