unlikely, in my view right now sitting here, that anything’s going to change,” he says.

Another hope for hydroxychloroquine, that it might prevent people exposed to the virus from getting sick, also faded last week when David Boulware of the University of Minnesota, Twin Cities, and colleagues published the results of the largest study to date of this strategy, called post-exposure prophylaxis (PEP). The researchers sent either hydroxychloroquine or a placebo by mail to 821 people who had been in close contact with a COVID-19 patient for more than 10 minutes without proper protection. They reported in The New England Journal of Medicine that 12% of the people who took the drug went on to develop COVID-19 symptoms, versus 14% in a placebo group, a difference that was not statistically significant.

A second large PEP trial has come up empty as well, its leader tells Science. Carried out in Barcelona, Spain, that study randomized more than 2300 people exposed to the virus to either hydroxychloroquine or the usual care. There was no significant difference between the number of people in each group who developed COVID-19, says Oriol Mitjà of the Germans Trias i Pujol University Hospital. Mitjà says he has submitted the results for publication.

The data are important because they come from large randomized trials. So far, most data came from small trials or case series. A meta-analysis of 24 such studies published in the Annals of Internal Medicine concluded there was “insufficient and often conflicting evidence on the benefits and harms of using hydroxychloroquine or chloroquine to treat COVID-19.”

The new findings raise questions about whether to stop other trials. Most are much smaller than Recovery, and thus less powerful; their outcomes are unlikely to change many minds. And continuing the trials may prevent researchers from testing drugs with a better chance of working and robs patients of the chance to try those. Landray says the World Health Organization (WHO) is now likely to end the hydroxychloroquine arm of its large COVID-19 treatment trial, named Solidarity. “I think the decision is pretty obvious,” he says. WHO says it is considering the issue.

There is one exception. Many researchers agree that a good case can be made for continuing to test whether hydroxychloroquine can prevent infection if given to people just in case they get exposed to the virus, for instance on the job at a hospital—a strategy called pre-exposure prophylaxis (PrEP). “You have a much better chance of preventing something with a weak drug than you have of curing a fully established infection,” says White, who runs one of the largest PrEP trials. He notes that doxycycline, an antibiotic, has long been used in malaria prophylaxis. “We would never treat anybody with it, it’s too weak. But it’s a very good prophylactic.”

Landray, however, is on the fence about continuing prophylaxis trials: “I suspect it’s one of these decisions where there isn’t a right or wrong.” It’s an important question, Bhadelia says, because an effective PrEP drug could have a major impact on the pandemic. Hydroxychloroquine, a cheap and widely available drug, is one of the few compounds that could fit the bill.

But the Lancet paper, despite its retraction, will make it more difficult to continue current trials, White laments. Published on 22 May, the study claimed, supposedly based on data from 96,000 patients around the world, that hydroxychloroquine and chloroquine, whether given alone or in combination with another drug, caused a steep increase in deaths. That led many regulatory agencies to ask scientists to halt their trials and make sure they were not harming their patients. Recovery and Solidarity were temporarily halted but resumed after a safety committee took a look at the data.

Many other trials are still on pause. U.K. regulators, for instance, have asked for a raft of additional safeguards, says Joseph Cheriyan, a clinical pharmacologist at Cambridge University Hospital and principal investigator of a PrEP trial in health care workers. That study already excluded patients who take any one of several dozens of drugs, but Cheriyan says regulators have asked for more changes, which will set the trial back weeks. And despite the Lancet retraction, the alarming headlines about the drug’s risks have made it much more difficult to convince people to participate in a trial, White says. “I just think these trials have been really badly damaged and some of them may never restart.”

The problem for scientists is that there’s such a rush to find treatments for the rapidly spreading virus, Mitjà says: “The pressure is immense.” Yet that shouldn’t stop researchers from properly analyzing data and making carefully considered decisions, White says. “We don’t always have to act today,” he says. “Let’s not panic.”

COVID-19

Authors, elite journals under fire after major retractions

Editors, co-authors missed warning signs, critics say

By Charles Piller and John Travis

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ast month, Mandeep Mehra, Amit N. Patel, and Sapan Desai were riding high, with shared co-authorships on major new papers in The Lancet and The New England Journal of Medicine (NEJM) and an influential preprint. Drawing on what appeared to be a vast patient data trove from hospitals around the world, the papers delivered seemingly definitive news about whether already approved drugs were safe for COVID-19 patients, or effective against the disease.

Now, the two journal papers have been retracted, the preprint taken down, and Patel’s academic affiliation severed. The three physician-scientists are under the microscope as a shocked scientific community evaluates what may be the first major episode of research fraud in the pandemic. The journals are receiving withering criticism for what some call a failure of editorial processes and peer review. The retractions are “unnerving and disturbing,” says Leigh Turner, a bioethicist at the University of Minnesota, Twin Cities. The rush to publish on COVID-19 has exposed a lack of rigor that has reached “elite journals at the top of the academic pyramid,” he says.

The retracted NEJM paper “had external peer review and statistical review, as well as scientific and manuscript editing,” an NEJM spokesperson says. The Lancet did not comment on its review process. Neither journal notes submission or acceptance dates for papers, but a spokesperson for Mehra says reviews for each paper took about 1 month.

By publishing only author retraction statements, the journals “didn’t show any self-reflection, any introspection,” Turner says. To him, the case also raises a bigger question about how much access to key data each journal should require—and whether all co-authors should have full access to a data set. “The less access they have, the greater the chances that there will be
errors, data fabrication, or outright fraud.”

Publication of the *Lancet* paper abruptly halted many trials of hydroxychloroquine, the antimalarial touted by President Donald Trump, because of its finding that COVID-19 patients receiving the drug had a greater death rate than a control group (see p. 1166). The *NEJM* paper exonerated blood pressure drugs that some thought might worsen CO-

VID-19, and the preprint found that mortality was dramatically reduced in COVID-19 patients receiving the parasite drug ivermectin, which drove huge demand for the medicine in Latin America (*Science*, 5 June, p. 1044).

Mehra, Patel, and Desai were the only scientists on more than one of the three papers, and all of the other co-authors are linked to at least one of the trio. After critics discovered anomalies in the data and wondered how Surgisphere, Desai’s small company, could have amassed and analyzed tens of thousands of hospital records from around the world, the core authors promised independent data audits. But Surgisphere declined to make the firm’s database and hospital agreements available, prompting the journal retractions. “We can no longer vouch for the veracity of the primary data sources,” Mehra, Patel, and a third author wrote in the *Lancet* retraction.

The ivermectin study quietly vanished from the SSRN preprint server. “There’s no retraction letter. But its ghost lives on in Latin America,” says tropical disease physician Carlos Chaccour of the Barcelona Institute for Global Health, who, with colleagues, raised questions about the preprint. (African physicians who developed a COVID-19 severity rating system with Surgisphere’s help withdrew the tool last week.)

Desai, Mehra, and Patel had never before published together, and that should have been a red flag to any journal, says Jerome Kassirer, editor-in-chief of *NEJM* during the 1990s. Co-authors of high-profile papers normally share subject area expertise or have clear professional ties, he says, calling the collaboration of the apparently disparate individuals “completely bizarre.”

Prior to the retractions, Desai, a science-fiction writer, entrepreneur, and vascular surgeon, had defended Surgisphere and its database. Neither Mehra, a highly respected scientist at Harvard University and Brigham & Women’s Hospital, nor Patel, a little known cardiac surgeon who recently resigned from an unpaid adjunct position at the University of Utah, has talked to the press. But Mehra apologized in a statement. “I did not do enough to ensure that the data source was appropriate for this use. For that, and for all the disclusions—both directly and indirectly—I am truly sorry.”

As CEO of Surgisphere, Desai has received the most scrutiny. He started the company in 2007 as a medical resident at Duke University. It initially produced medical guides. In 2010, under the firm’s auspices, he founded the *Journal of Surgical Radiology*, which folded in 2013. Its articles have been cited only 29 times, according to Scimago, a journal rating service. Yet an undated Surgisphere webpage, no longer accessible, said the online-only publication had 50,000 subscribers and nearly 1 million page views monthly.

Surgisphere also claimed to have gathered and analyzed data on nearly 100,000 patients at some 700 hospitals worldwide. But no hospitals have acknowledged giving data to the firm. National Health Service Scotland, noted in a case study on the company’s website, tells *Science* that none of its hospitals worked with Surgisphere. It will ask the firm to remove a website image of a Glasgow hospital.

While he was CEO of Surgisphere, Desai practiced at U.S. hospitals; Illinois court records show he is facing two malpractice suits filed last year. He spoke often at medical conferences, impressing more senior researchers. In a conference talk last year on “millennials” in vascular surgery, Gilbert Upchurch, chair of the University of Florida’s surgery department, brought up Desai, saying he had never worked with him, but had mentored him remotely and they had an online friendship. Upchurch placed Desai in a group of “amazing and talented young vascular surgeons.”

But another physician scientist who worked closely with Desai several years ago says the more time people spent with him, the greater their doubts. “Just about everyone who knew him would say: ‘I just didn’t have a good feeling about him.’ … After they’d been with him, most people dissociated themselves from him,” says the person, who declined to be named to avoid personal and institutional embarrassment.

Patel started as a full-time faculty member at the University of Utah in 2008, gained tenure in 2013, and in late 2016 moved to University of Miami’s Miller School of Medicine as head of cardiac surgery. Recently, he returned to the University of Utah. Patel is also an unpaid collaborator on a trial using stem cells from umbilical cord blood to treat COVID-19, according to Camillo Ricordi, chief of cellular transplantation at the University of Miami and a principal investigator on that trial. Ricordi praises Patel’s work in regenerative medicine.

Much of Patel’s decades-long research career has involved experimental stem cell therapies purported to, for example, treat or cure heart disease and sexual dysfunction, or reverse aging. The therapies were sometimes sold with limited evidence of efficacy. Patel has never received National Institutes of Health funding, according to the agency’s database. And of more than 100 publications listed on his University of Utah online profile—which the school removed last week upon his leaving—nearly two-thirds were actually co-authored by other scientists who share Patel’s surname, *Science* found.

Patel recently tweeted that he is “related to Dr. Desai by marriage,” but added that he remains in the dark about the Surgisphere data. Mehra, author of more than 200 scholarly articles and editor of a transplantation journal, enjoys considerable support even after the retractions. “I’ve never had any indication whatsoever that he would do anything unethical,” says Keith Aaronson, a cardiologist at the University of Michigan, Ann Arbor, who has collaborated with Mehra.

Mehra says he met Patel in “academic and medical circles” and that Patel connected him to Desai. In journal papers, including the retracted ones, Mehra also acknowledged receiving consulting fees from Triple-Gene, a gene therapy company Patel co-founded. “I think [Mehra] just fell into this—perhaps a little naïvely,” says another collaborator, surgeon Daniel Goldstein of the Albert Einstein College of Medicine.

But Kassirer faults Mehra for apparently letting ambition get the best of him. “If you’re a scientist and you’re going to sign on to a project, by God you should know what the data are,” Kassirer says.

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Authors, elite journals under fire after major retractions
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