FEATURE

CORONAVIRUS

Covid-19's impact on US medical research—shifting money, easing rules

In the US, basic research has largely shut down. But **Mara Kardas-Nelson** reports that some clinical research is continuing—and some is being repurposed in the fight against covid-19

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The only time that Denis Wirtz, vice provost for research at Johns Hopkins University in Baltimore, can find to talk to me is on a Sunday. He's blunt when I ask how he's doing. "I've never worked so hard in my life," he says. "But, thinking of frontline healthcare workers, I'll shut up about it."

Over the past several weeks Wirtz has overseen the university's transition from everyday research—when hundreds of studies are conducted on things such as swallowing dysfunction and caffeine addiction—to the reality of physically distanced science in the midst of a global pandemic. To help keep people at home and to shift towards covid-19 related research, Johns Hopkins University has essentially scaled down almost all of its everyday work, save for experiments that have a clear benefit for human participants, such as cancer fighting drugs. "For anything short of that very high standard, studies have been stopped a long time ago," he says.

The Johns Hopkins scale-down mirrors efforts throughout the country, as university laboratories and medical schools have put most ongoing clinical and basic research on hold and started no new efforts. Most have made these decisions case by case, with guidance from their administrations, institutional review boards, and clinical trial guidance from the National Institutes of Health (NIH). With physical distancing in place, most labs have taken a similar approach to Hopkins: if a clinical study can be stopped without seriously harming its outcomes or the patients in it, then stop it.

This halt has affected everyone from scientists studying *Escherichia coli* to those considering early treatments for dementia. Many are doing what they can at home—writing up results and submitting them to academic journals that are willing to publish early, as well as reviewing papers and speaking to colleagues across the country they don't regularly have time to touch base with. But even with these attempts to stay busy, says Ben Ewen-Campen, "I think this is going to be devastating on academic research."

Ewen-Campen, a postdoctoral fellow studying genetics under Norbert Perrimon at Harvard University, works with fruit flies—a long way from clinical research but a key first step to understanding basic genetics. Some flies have been saved and are supported by a small team that feeds them regularly. But others were thrown out overnight to minimize the in-person footprint at the lab. "Flies that I've been working on four or five years, I just watched them go to waste in one fell swoop," he says.

Clinical trials disrupted

Clinical trials have also been affected. Charbel Moussa is a researcher at the Georgetown University Medical Center in Washington, DC, where he studies dementia, Alzheimer's, and Parkinson's. He's stopped recruiting for new trials, and, although most ongoing studies can continue, his patients are in the high risk category, where in-person visits are both feared and ill advised. This isn't always a problem—telemedicine works for some check-ins, and some trials are nearing their end anyway—but others may require in-person tests, blood draws, or electrocardiograms. Moussa expects that these will experience a "severe hemorrhage of data." He explains, "If patients don't come in and you can't collect data on safety and clinical outcomes, you can't include those patients in the final study." Already, a handful of patients have stopped coming to in-person visits, reducing one trial size by 30%.

Moussa's team has tried to shift quickly, allowing local clinics to collect some samples rather than requiring patients to come to the hospital. But this works for only some patients and some trials. All told, he says, "We have to double the time and double the effort for these studies. When you think a clinical trial should finish in three years, now it won't finish for five years."

Back at Johns Hopkins, Wirtz has no doubt that "there will be a slowdown for new drugs. It's a terrible by-product of this pandemic." The slowdown has financial implications, too. He notes that the university is receiving no new money from its

pharmaceutical sponsors of clinical trials, as payment is based on the number of patients newly enrolled.

Michael Lauer, deputy director for extramural research at the NIH, expects “at least three months of complete disruption, then at least two to three months of recovery, if not longer. So, we’re talking about six to 12 months of lost productivity.”

The NIH will spend about \$41bn (£32.8bn; €37.7bn) this year on medical research,¹ with more than 80% going to research institutions around the country. It’s being flexible with funding, allowing researchers to note little progress without fear of reprimand, as well as accepting late applications, allowing grants to run for longer, and letting institutions continue to charge salary and stipends even if the everyday work has stopped.

Lauer says, “We’ve talked to leaders at various research institutions around the country, and their thinking is that as much as possible they want to keep their teams together, even if they are unproductive right now, so that when the country does reopen they’re going to be able to get things started quite quickly.”

Drug companies have recently overtaken the NIH on total biomedical research funding, and they’ve quickly jumped into coronavirus research. The US pharmaceutical companies trade group PhRMA says that more than half of its members have committed research and development money towards treatments and vaccines.² The major research foundations have all also jumped in.

Labs switching over

Johns Hopkins is now working on nine different coronavirus related areas, including a convalescent blood study considering whether a “120 year old treatment with a modern flavor,” in the words of Wirtz, could help covid-19 patients. The university is also working on developing better personal protective equipment (PPE) and studying the potential for coronavirus reinfection.

Other labs, such as those at University of California San Francisco and University of California Berkeley, have shifted towards testing coronavirus samples. Jennifer Doudna, who helped to discover the gene editing technique CRISPR-Cas9, helped Berkeley’s Innovative Genomics Institute to create a pop-up testing lab within three weeks. It now works with the university’s healthcare center, the city of Berkeley, and a local health center to provide free testing to students, city employees such as firefighters, and homeless people who are vulnerable and unable to be tested through conventional channels.

Primate research in the US has also seen a significant shift in work. The California National Primate Research Center at University of California Davis has asked researchers not to initiate new non-covid-19 work and is also scaling down some ongoing research on Alzheimer’s, tuberculosis, and influenza. At the same time the researchers have begun studying how monkeys respond to coronavirus, before testing potential treatments such as convalescent plasma and repurposed drugs—and then, finally, vaccine candidates.

The center is in regular contact with the Tulane National Primate Research Center in Louisiana, which made the decision to shift much of its work towards covid-19 in January and is also

working on diagnostics, treatments, and vaccines. Both are speaking weekly with other researchers, the NIH, and the private sector.

Cooperation becoming the norm

Speaking of the collaboration, “I’ve never seen anything quite like it,” says John Morrison, director of the California National Primate Research Center. “Science is very competitive, everyone wants to get that first paper out there, and people can be secretive. But I haven’t seen any of that. Every center is completely open with their data. There’s a sense of urgency in the clinic that’s permeated to science, as well.”

Working together has fueled “warp speed” efforts throughout the scientific community, says the NIH’s Lauer. “We are seeing research efforts that would typically take months or longer happening in days or weeks,” he explains.

Many US scientists are eager to help, reaching out beyond their institution’s walls. Berkeley’s Doudna has created a Slack communication channel, with about 400 researchers sharing best practices on coronavirus testing. Michael Wells, a postdoctoral fellow at the Broad Institute of MIT and Harvard, has put together a database that allows scientists from around the country “who are eager to volunteer time, expertise, equipment, and consumables to help respond to the covid-19 crisis.” Thus far, 9000 researchers from all 50 states—plus DC, Puerto Rico, and Guam—have signed on, and the database has been shared with agencies and institutions that may need an extra set of hands, including the Federal Emergency Management Agency and state health departments.

Another database, Crowdfunder Covid-19, allows researchers to come together to share ideas, collaborate on projects, ask for help on specific tasks, and ask and answer specific questions. Some 43 000 volunteers have signed up, 25 requests have been solved, and 140 are ongoing.

For Wirtz, the pandemic presents another silver lining. In normal circumstances, he says, “Connections between both basic science and academic research in general and people’s everyday lives can be lost. But this crisis has crystalized the central importance of research.

“Science has never been so important, and clearly everyone is seeing it. People know that until we get treatments in the short term and vaccines in the long term, the economy is not going to be taking off.”

bmj.com Feature: Covid-19 makes the future of UK clinical research uncertain (BMJ 2020;369:m1619, doi:10.1136/bmj.m1619)

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- 1 National Institutes of Health. Budget. <https://www.nih.gov/about-nih/what-we-do/budget>.
- 2 PhRMA. The latest on the biopharmaceutical industry’s efforts to beat coronavirus. <https://phrma.org/Coronavirus>.

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