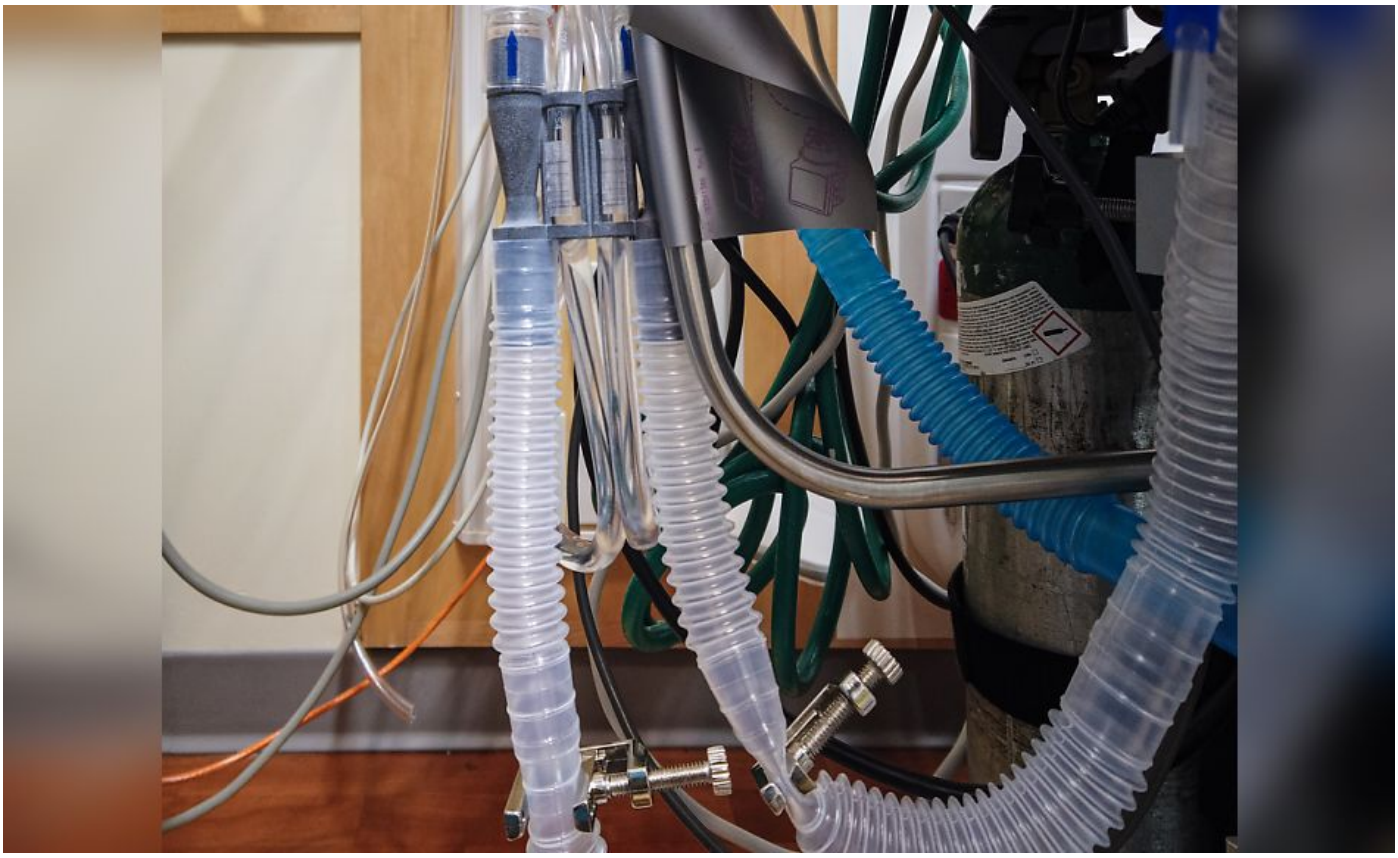
Sharing a Ventilator, Sparing a Life: Two Yale Groups Create Different Ways To Maximize Ventilator Capacity in a Crisis < Yale School of Medicine



The Vent Multiplexor

Peter Kahn, Brian Beitler, and Timothy Foldy-Porto worked around the clock to design, build, and test the Vent Multiplexor, a device that regulates the tidal volume of air available to patients' lungs. Most recently, the device was approved for use by the U.S. Food and Drug Administration (FDA) April 15.

Photo by Andrew Osborne

The worldwide shortage of ventilators for COVID-19 patients has been widely covered in both scientific and popular media, as has the difficulty in getting companies to produce enough of them to ensure everyone who needs one has access to the lifesaving equipment. One solution has been to hasten the manufacturing process. Another solution, preferred by entrepreneurs like Elon Musk, is to retrofit other devices to provide the same service.

But possible solutions can be found elsewhere, too. For instance, two groups at Yale, working independently of one another, developed strategies that have the potential to make a real difference in the national ventilator shortage. Laura Niklason, MD, PhD, the Nicholas Greene Professor of Anesthesiology and professor of biomedical engineering, is working with members of her lab on splitting one ventilator for use with two patients, a concept they call the Pressure Regulated Ventilator Splitting response paradigm or "PReVentS." Meanwhile Yale New Haven Hospital (YNHH) Resident Peter Kahn, MD, MPH, is leading a team to develop a splitter device known as the "Vent Multiplexor," with assistance and input from Elaine Fajardo, MD, assistant professor of medicine (pulmonary) and Jonathan Siner, MD, associate professor of medicine in the Section of Pulmonary, Critical Care and Sleep Medicine.

The projects have connections to a university-wide initiative, the Coalition for Health Innovation in Medical Emergencies (CHIME). A multidisciplinary group that came together in March to address innovations related to COVID-19, CHIME is working to rapidly develop devices and procedures to help treat COVID-19 patients more effectively. PReVentS and the Vent Multiplexor provide complementary solutions to different aspects of the same challenge: how does one treat multiple patients at the same time using a single ventilator?

Both groups developed devices that allow a single ventilator to treat two patients simultaneously, and, critically, individually. "The main problem with using one ventilator to ventilate two patients," said Fajardo, who is also the medical director of respiratory therapy, the unit in charge of ventilator support at YNHH, "is that the patients are different, they require individual volumes and individual pressures." Current ventilator splitters require patients to be nearly identical, which make the solution very hard. Working separately and unaware of one another's efforts, the two groups independently created two separate solutions, one that focused mainly on individualizing the volume for each patient and one that allowed individualization of the pressures. "Their approaches are very complementary," said Fajardo. "Together, they addressed the major limitations associated with ventilator splitting."

Vent Multiplexor: Creative Energy by Collaborative Medical Students

Kahn is swift to assign credit for the creative energy behind Vent Multiplexor to his teammates, Brian Beitler, a Yale College graduate in his second year of pursuing an MD at Yale School of Medicine, and Timothy Foldy-Porto, a Yale College senior studying physics. "After Brian reached out to me, I brought the device to the hospital for testing, and have been helping operationalize it ever since," Kahn said. Their latest coup: the Vent Multiplexor received FDA approval April 15.

Beitler and Foldy-Porto met as undergraduates two years ago during an independent study in mechanical engineering at Yale's Center for Engineering, Innovation, and Design (CEID). "Tim was working on a project involving our student ID cards, which I found very interesting," Beitler recalled. "After talking for a bit, we realized there was a potentially cool correlary to his project. It was 5 p.m. on a Tuesday, and we decided to just get after it. Eight hours later we had a working prototype."

That serendipitous meeting and collaboration blossomed over time, so by the time the two found themselves at a CHIME meeting in late March about ways to tackle the problems posed by COVID they were used to working together. Organized by Joseph Zinter, PhD, research scientist in Mechanical Engineering and Materials Science, the meeting brought people with different forms of expertise together into a brainstorming session. Beitler had an idea during the meeting—the short-term problem of too few ventilators might be partly absorbed by improving existing ventilator splitting technology. After the meeting, Foldy-Porto called him. The issue, he thought, could be solved using Venturi tubes to measure flow and regulate the tidal volume of air (the amount of air displaced between inhalation and exhalation) entering patients' lungs. Foldy-Porto owned a 3D printer, and dove into designing and building a working prototype. In short order, they had something they felt was ready to test.

What they didn't have was access to the type of expertise or training capacity they needed to prove or test concepts. In stepped Kahn, who had been introduced to Beitler by a classmate at Yale School of Medicine in mid-March. Kahn made introductions to pulmonologists within the hospital, Fajardo and Siner, and secured the technical and legal expertise necessary to bring the idea into reality.

The first week in April, as the crisis intensified here in New Haven, the group got very focused on developing a model that could be tested on real patients. "It was a wild week of constant work, with everyone focused on getting a working device tested as quickly as possible," said Kahn. "Everyone was doing something to contribute. We had this sense that lives were on the line."

With "integral" contributions from Fajardo, Siner, and respiratory therapists, Kahn, Beitler, and Foldy-Porto were able to successfully test the Vent

Multiplexor at YNHH on Tuesday, April 8. According to Fajardo, this was only the third such ventilation of two patients in the United States, and could not have come at a more important time: "New technologies like the Vent Multiplexor are a critical part of the path forward as we work to save as many lives as possible."

Siner who, in his role as the director of the Medical Intensive Care Units, oversees the expanded COVID-19 critical care deployment at YNHH, expressed hope that the Vent Multiplexor would not be necessary, though he was glad it was ready: "While we continue to hope for lower than predicted volumes of COVID-19 patients, we have to be prepared for worst-case projections. We invested so much time and effort to allow both groups to develop and test their devices. We needed to know if we have a ready solution in the case of ventilator shortage."

A 'Pulmonary Architect' Designs a Nuanced Solution

Meanwhile, across campus, Niklason and her team were pursuing the solution of how to split ventilator modules among multiple patients from the perspective of regulating air pressure, rather than volume. An informal group dedicated to researching ventilator splitters had reached out to Niklason, and with her lab closed to abide by social distancing restrictions and a background in pulmonary architecture (Niklason focuses on growing lungs from scratch), she decided to look at what could be done.

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"A lot of companies were volunteering to build ventilators, and that's the safest way to go, one ventilator per patient, so building more of those was our first impulse," said Sam Brickman Raredon, MS, a member of the

Niklason lab in Yale School of Medicine's MD-PhD program. "But reengineering and approving a ventilator from scratch is really difficult and time-consuming. We needed another, more accessible solution."

Of particular interest was a paper co-authored by Charlene Babcock, MD, and Greg Nyman, MD, which had been published in 2006 about the possibility of using ventilators to treat up to four patients simultaneously.

According to Clark Fisher, MD, PhD, a resident in the Department of Anesthesiology who had worked with Niklason in the past, Babcock and Nyman's hypothetical procedure was put into practice at least once, out of desperation, after the Las Vegas shooting of 2017. There, local hospitals had been briefly overwhelmed by patients from the mass casualty event.

Reading through the literature, Niklason's team identified a problem. In Las Vegas, concert-goers had mostly been young, healthy people without underlying conditions. The improvised ventilator splitters were employed for hours, no more than a day at a time, for people who had been shot but were otherwise in good shape.

"Intubating someone with a healthy pair of lungs, even one that has been injured through trauma, is very different from what we're seeing with COVID-19," Fisher said.

Patients of COVID-19 require ventilators for much longer, and have wildly varying physiological and immunological profiles. This means that simply dividing a ventilator's capacity between two patients may not be sufficient—a setting that stabilizes one patient could make another patient far worse. In a life-and-death situation, hospitals across the world wagered that a chance at life was better than no chance at all, and that the risks were worthwhile.

Niklason's team hit upon PReVentS, which is a nuanced system that

regulates air pressure in order to oxygenate COVID-19 patients' lungs.

Both the Vent Multiplexor and PReVentS allow a single ventilator to treat two patients simultaneously, and, critically, individually. According to Raredon, although the ventilator splitters coming out of Yale have been created with two patients in mind, Babcock's paper establishes that it should be possible to use a single ventilator for up to four patients. Everyone in the Vent Multiplexor and PReVentS groups took pains to stress that ventilator splitting was for emergencies only; the ideal ratio for treating patients with ventilators being 1:1.

From its inception as an idea at the end of March, it took about two weeks of working with engineers, clinicians, and other specialist consultants to develop the prototype, a video of which was posted to Twitter on Tuesday, April 7.

Before posting the video, the team shared their work on MedRxiv, an open-source repository developed by Yale, the British Medical Journal, and the Cold Spring Harbor Laboratory, of research that has not yet been published. The group's goal in sharing their work with other teams working along similar lines, is to accelerate the procurement of effective quality ventilator splitters in ICUs before they are overwhelmed by ventilator need.

Niklason and her team are motivated to finish work on PReVentS. "There's a tremendous feeling of urgency and immediacy," said Niklason. "Our lab has operated at the intersection of lung medicine and bioengineering for a long time—we were a natural to work on the problem. Now it's a matter of finishing it; not just for this illness, but for any future similar illness, too."

Naftali Kaminski, MD, chief of pulmonary, critical care, and sleep medicine at Yale School of Medicine, said the progress made by both groups in such a short time has been tremendous.

"These two initiatives are amazing," he said. "One is called Vent Multiplexor and the other PReVentS, but in my mind they should both be called the Yale Ventilator Solution."