Picture a patient in the intensive care unit, strapped to various machines and monitors, which beep and blink with different data points at any given moment of the day. How helpful is that data to the patient’s doctor? And where does it go?

The answers, historically, have been “somewhat” and “into the ether,” respectively.

Modern medicine gathers astronomical amounts of information on patients, but has had little sense of how to store, process, or apply it. But now doctors and researchers at the University of Michigan are working across disciplines and in multiple areas of medicine to harness individuals’ stats to develop more precise approaches to care.

Precisely individualized treatment offers hope for a range of ailments — including cancer, whose basis in gene mutations make it ripe for therapies targeted to a particular alteration.

“Medicine creates a lot of data, but a lot of it is not utilized,” says Ashwin Belle, a research investigator in the University of Michigan’s Department of Emergency Medicine and analytics architect at the Michigan Center for Integrative Research in Critical Care (MCIRCC). “When it is utilized, it’s sometimes misinterpreted because of variability.”

MCIRCC is helping critical care specialty areas learn from each other by sharing information and expertise, and developing ways to apply that data across specialties.

Belle and his colleagues — experts in computer science, data science, and engineering — have joined forces with physicians to figure out how to effectively gather, interpret, and apply medical figures in ways that can do everything from assess a patient’s true condition to getting a sense of how they might fare with a given course of treatment.

Their efforts, part of what is known as precision medicine, are distinctive for both their breadth and sophistication.
"We would define precision medicine as the right care for the right patient at the right time," says Dr. Kevin Ward, director of the MCIRCC and a professor of emergency medicine. "For us, if you can't use the data to make better decisions for an individual patient at any moment, you haven't achieved your goal. It's all about clinical decision support. Data scientists and engineers know how to look at information differently than traditional clinicians do. I want data that will help me manage 20 incredibly sick people and help me know who I need to go to, who's getting better, and who's getting worse."

Targeting Public Enemy No. 1

Precision medicine grew out of cancer research and treatment, as scientists identified not only specific gene mutations that correlated with specific cancers, but sub-genes that could differentiate two patients with the same type of cancer.

U-M was one of the first places to carry out comprehensive gene sequencing efforts in cancer patients.

"Non-genetic factors come into play, but cancer is primarily a genetic disease," says Dr. Arul Chinnaiyan, professor of pathology and urology at U-M and director of the Michigan Center for Translational Pathology. "The person's own genome and the genome for the tumor and how it differs from the person — that's the essence of precision medicine as it relates to cancer. Patients should be treated differently based on the molecular make-up driving their cancer."

Cancer researchers identifying those molecular make-ups saw early successes with drugs that precisely targeted them with laser-like focus, like Gleevec, for patients with chronic myeloid leukemia.

"Before the drug, patients were all dying; now they often live long lives," Chinnaiyan says. "Researchers identified the key gene fusion in that case and found all the [patients with chronic myeloid leukemia] have it, and matched it precisely with the drug. The drug has no real effect in other leukemias."

Similarly, for breast cancer patients with the HER2 gene, the drug Herceptin has been effective — but not for those with non-HER2 breast cancer.

So far, university researchers have sequenced more than 2,500 patients with metastatic cancer, which leads to death 90 percent of the time; a coauthored paper that landed on the cover of Nature in August describes the first 500 patients of that group, focusing on the genomic architecture of their metastatic tumors and the sort of trials that could be appropriate for each patient.

"Metastatic is the form of cancer we really do need to understand, because those are the patients that are at the end of the line," Chinnaiyan says.

"The bottom line is all cancer patients shouldn't be treated the same," he adds. "It's an exciting time to be in cancer research because the technology has matured to the point where we can get this comprehensive assessment.

"We're seeing some light in terms of matching single alterations and pathways with therapies, but we're also looking at the successes with HIV and AIDS, where combination treatments have had a major impact. We're hoping to have a similar effect."

Sorting Through Options

Some medical advice applies to everyone: Don’t smoke. Eat a diet rich in fresh fruits and vegetables. Get enough sleep.

In many instances, though, two individuals with the same condition will be given the exact same treatment even though they might be quite different from one another.

"There's been a sense for a long time that we're taking care of people based on the averages," says Dr. Brahmajee Nallamothu, an interventional cardiologist, professor of internal medicine, and faculty lead for the university's Michigan Integrated Center for Health Analytics and Medical Prediction (MiCHAMP), which he created. "You'll have a study where half the people get a treatment, even though we know the risk-benefit balance is unlikely to be the same across a swath of people."

MiCHAMP includes faculty from the fields of medicine, engineering, nursing, public health, statistics, and pharmacy, and utilizes health care data sets to develop prediction models. In January, MiCHAMP landed a $1.25 million grant from the Michigan Institute for Data Science to improve those models, especially in the areas of acute respiratory distress syndrome and chronic hepatitis C infection.

"My colleague and lead of the hepatitis C project, Akbar Waljee, is working to take a disease that is really tough to treat and make it much easier with very few side effects; the challenge is there are a lot of patients with hepatitis C, and the path in which it progresses varies substantially across individuals," Nallamothu says. "There are also a lot of comorbidities (presence of other diseases or conditions) that are super important in determining who might be easier to treat — some are medical, but others are socioeconomic, like substance abuse. We're trying to help physicians who see these patients recognize them through the utilization of specific tools, and then guide them toward treatments."

Using precision medicine to make effective, individualized clinical decisions requires broadening the definition of the types of material necessary to make any medical decisions at all, says Dr. Sachin Kheretpal, associate professor of anesthesiology at U-M and a member of the National Institutes of Health’s All of Us advisory panel.

In the past, a patient's medical records and, if available, their gene sequence, were largely considered to be sufficient.

"That's completely been shown to be wrong," Kheretpal says. "Your ZIP code is probably just as important as your genetic code. We need broader sources — we need to know where you live, what insurance you have, what support structure you have. When you go home from the hospital after a cardiac event, the right drug for you might be dependent on whether you have someone at home to help you take it three times a day."
Taking Stock of the Data

Knowing which data is relevant to assessing a patient and predicting how they’ll fare in the coming hours and days often isn’t a straightforward matter, and gathering the facts correctly is more complicated still.

Belle, Ward, and their colleagues at MCIRCC regularly sit down to hash out which patient data they should track, and how much weight to give those points relative to others.

“There’s no gene that predisposes you to a car accident,” Ward says. “If you’re in the ICU and you’re hooked up to a bunch of monitors, it can be up to 100,000 data points per second.

“You can’t track it all in real time,” he says. “We’re hemorrhaging data [and] missing patterns. With precision medicine, we’re harnessing data, whether it’s lab work, imaging, the beeping machines in the hospital room. We trying to recognize patterns in all this data that tells us whether you’re going to get worse or better.”

A lot of this is finding the valuable needles in a haystack, Ward adds. “But you have to have the whole haystack.”

Belle and his colleagues have built a dazzling series of algorithms and programs that take patient data, sort and analyze it, and make it easily searchable and usable by clinicians. ICU patients’ data is fed into MCIRCC’s various programs, which offer increasingly sophisticated pattern recognition as time goes on, pulling out patterns that are invisible to the human eye.

“The tool tells us what your future state is going to be like, so we can intervene sooner,” Ward says. “We would call this approach data-in-motion phenotyping. It’s real time — telling you what your current and future phenotype will be. Otherwise, this is why we haven’t made improvements, because we treat every patient the same way. We’re reactive instead of proactive.

“We keep getting beat again and again by the disease because we can’t predict how you’re doing,” Ward says.

Spreading the Data Wealth

For precision medicine to flourish, physicians’ relationship with patients must shift. “We need a different level of transparency in terms of why we ask you to do what we ask you to do,” Khertepal says. “We need more ‘share-too-much’ doctors and nurses and health care providers. We need to actually tell patients, ‘Here’s why I’m recommending this.’ Precision health doesn’t mean getting the perfect answer. It means getting a more informed answer with more transparency.”

As U-M teams and others around the country develop better means for gathering and interpreting information, the challenge becomes helping health care providers around the country do the same. The university’s infrastructure is unmatched and doctors who see patients at small community hospitals currently have little access to such tools.

“How do you actually get these things into routine practice in the real world?” Nallamothu says. “There’s a tendency to keep doing the same old, same old. You have these discoveries and can build these algorithms, but how will they impact a life?”

Making precise care broadly available requires new equipment. To that end, Ward directs Fast Forward Medical Innovation, a university hub that helps faculty develop ideas for everything from new diagnostic and therapeutic devices to software applications, then partner with industry professionals to bring them to market.

“I don’t have much more to work with in the ICU to help save your life than I did 25 years ago,” Ward says. “Part of it is we haven’t engaged these other disciplines like engineering and computer science. Doing that has allowed us to develop this huge technology portfolio. Now we’re making big advances, spinning off companies.”
Making precision medicine work will not only take new discoveries and new technologies, it will also take a change in how they’re applied in routine practice, Nallamothu says. “How are we going to take this information and push it out there? It’s not going to take a cool algorithm, but really thinking about how the system is designed and how we make it so this is a default rather than an exception.”

That’s what’s really exciting about having people at Michigan like Kevin Ward, he adds. “They don’t just want to build an algorithm or discover something, they want to make a human life better. That last part is extraordinarily rare these days. That it’s actually impacted a human life.”

IT REALLY IS ROCKET SCIENCE …

Some of the MCIRCC’s algorithms lean on those utilized by Wall Street and by the space program to use past trends and real-time data to predict the future. They’re deployed and tested repeatedly, using data from hundreds of thousands of patients simultaneously. And they can spot patterns doctors might miss.