

Clinical Research
FORUM
Analysis. Advocacy. Action.

Stories of Success
in Clinical Research



Clinical Research (CR) Forum was formed in 1996 to discuss and address the unique and complex challenges to clinical research in academic health centers. Our members are medical school deans, academic and medical center leaders, and top clinical researchers—all committed to support research that, as rapidly as possible, leads to better diagnostics, treatments and cures that improve human health and well-being. Every year, CR Forum recognizes outstanding clinical research through its Top Ten Clinical Research Achievement Awards. These awards honor groundbreaking, clinical and translational research advances that benefit the health and welfare of all Americans and reflect the influential work being conducted by investigators at nearly 60 research institutions and hospitals across the United States, as well as at partner institutions from around the world.



Introduction

The examination room in the doctor's office today is not furnished for difficult news. The side chairs are never very comfortable, and more often than not you sit on a padded, elevated table that is covered with white paper. Sometimes you're in your clothes, sometimes in a drafty, awkward hospital gown.

You sit there with your feet dangling because something is not right. And when you receive the diagnosis, your only thought is, "How can we treat this?" But lurking in the back of mind is the nagging fear that there might not be any treatment, much less one that is both available and affordable.

We know more about keeping people healthy than we've ever known before. It feels like medical breakthroughs get announced more often than new problems arise. And yet, the hard work doesn't stop with the "Aha!" moments in the science lab. Clinical and translational research—the work done to bring the breakthroughs to the patients—has to keep up with the pace of both the problems and the solutions.

In these pages, we'll talk through some of the most important clinical and translational research studies over the last few years. These include innovations that bring the best strategies for:

- ▶ Reducing hypertension in the people and communities that experience higher rates and yet have limited access to treatment and other resources to address it;
- ▶ Changes in breast cancer surgery guidelines that reduce the chance of recurrence;
- ▶ Interventions that dramatically improve opioid addiction treatment; and
- ▶ New approaches for doctors to understand diseases that have eluded diagnosis and have left patients untreated and suffering for far too long.

This is the hard work that helps make those doctor visits reassuring and impactful, not difficult. Modern medicine relies on the insights and practical applications provided by clinical and translational research so that patients can get diagnosed and treated, minimizing the amount of time spent waiting and wondering what type of news they'll receive. This is the research that needs volunteer patients, labs, outreach staff, and an infrastructure and sufficient resources to keep the study running until conclusion.

At Clinical Research Forum, this is our work—and we are proud to put a spotlight on it. Since 1996, we have advocated for broader support of clinical research from the federal government—along with its translation to improve health outcomes—and we have promoted the "best practices" that have led to some of the most important treatment breakthroughs in our lifetime.

Clinical research shapes and changes treatment directions and cures—and this is its story.



Improving breast cancer surgery

For many types of breast cancer, partial mastectomies have long been a preferred treatment, reflecting the goal to do as little cosmetic harm as possible to patients facing a potentially lethal disease. But, in the impetus to preserve as much of the breast as possible, how much tissue should be removed?

This is the question that Anees B. Chagpar, MD, MPH, and colleagues tackled. They conducted a randomized controlled study on “cavity shave margins”—looking at how much tissue surgeons should remove around the edges of tumors targeted in partial mastectomies. In many cases, oncologists found that their patients needed additional surgeries, as not enough cancerous or pre-cancerous tissue was removed initially.

All patients in the study were operated on according to standard guidelines, with surgeons removing all the identified tumor. But in half of the operations, the surgeon went further, removing a little bit more of the surrounding tissue—not enough to make a difference cosmetically.

Dr. Chagpar found that removing a little more tissue than what was called for diagnostically helped reduce the need for additional surgeries by more than 50 percent. This significant gain in precision—which came at a very limited cost and did not significantly impact the patient cosmetically—reshaped the conversation around breast cancer surgery guidelines.

The study that was honored by the Clinical Research Forum and published in the *New England Journal of Medicine* had a profound impact nationally and globally. ASCO, the world’s largest oncology professional organization, lauded this work as one of the key cancer advances for 2016. For many, it changed practice, with surgeons adopting routine cavity shave margins as a standard practice to reduce re-excision rates.



Project Title

A Randomized Controlled Trial of Cavity Shave Margins in Breast Cancer

Publication

N Engl J Med. 2015; 373:503-510.
<https://www.nejm.org/doi/full/10.1056/NEJMoa1504473>

Lead Author

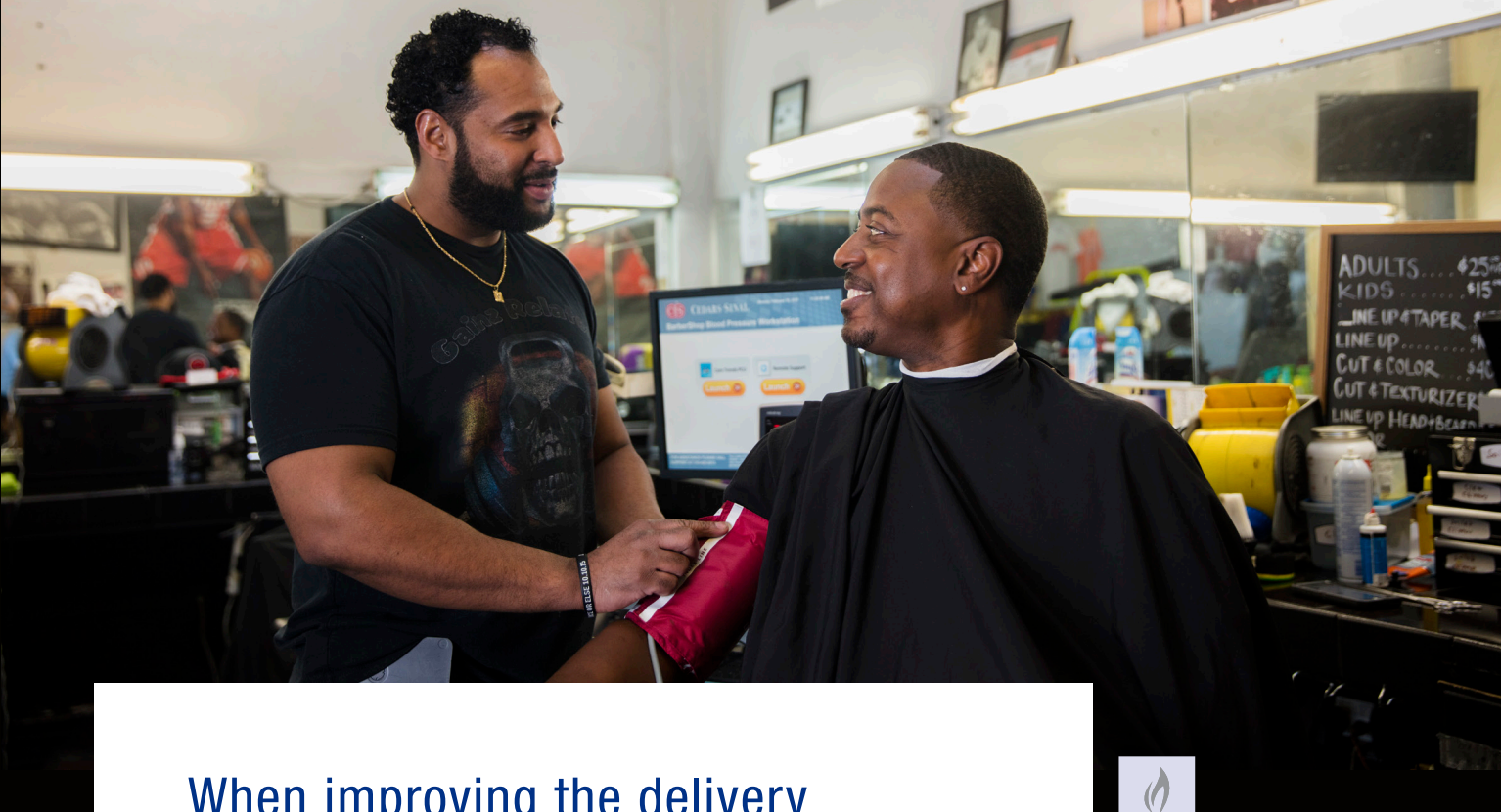
Anees B. Chagpar, MD, MPH

Institutions

- Yale University School of Medicine
- Yale Cancer Center
- Thomas Jefferson University

Funding

Yale Cancer Center



Cedars-Sinai Medical Center

When improving the delivery improves the treatment

Studies show that black men from low-income families are one of the least likely groups to see a doctor on a regular basis. Hypertension rates are climbing in this population even though there is a treatment for this condition that has been proven effective. So, the impetus became clear—medicine would have to seek them out, if they wouldn't seek medical diagnosis and treatment on their own.

To make this happen, researchers in public health have identified the community barbershop, a social hub where African American men are loyal patrons who trust their barbers, as one of the best opportunities to provide medical treatment and health interventions.

Ronald G. Victor, MD, and colleagues at Cedars-Sinai Medical Center conducted an experiment in medical outreach by working with 52 black-owned barbershops to recruit 319 black male patrons whose blood pressure was high—their systolic blood pressure was greater than 140 mm Hg. Half of the participants were encouraged by their barbers to talk to a pharmacist who could prescribe medication, in collaboration with physicians, and follow up periodically, while the other half received advice from their barber about lifestyle changes and were encouraged to make appointments with their doctor.

Both approaches were effective in lowering the blood pressure of participants, but the pharmacist-led intervention had greater impact, lowering blood pressure to almost normal levels in six months. This can be attributed to the effectiveness of the medicines that the patients received. But only by bringing the diagnosis and treatment to the patients, in a setting where they enjoyed significant peer support, did the patients actually use the services.

As the nation continues to grapple with the direction and cost of healthcare, this simple and effective lesson can inform many other prevention initiatives.



Project Title

A Cluster-Randomized Trial of Blood-Pressure Reduction in Black Barbershops

Publication

N Engl J Med. 2018; 378:1291-1301
<https://www.nejm.org/doi/full/10.1056/NEJMoa1717250>

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Funding

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Preparing emergency departments to intervene and treat opioid addiction

Opioid addiction and abuse have been called the deadliest drug epidemic in US history. According to the US Centers for Disease Control and Prevention, the past eight years saw almost 400,000 people die from an overdose involving an opioid drug.

Many people with addictions visit the emergency departments of nearby hospitals because of overdoses or other problems related to their troubles, or for other healthcare needs. All of these visits are an opportunity for intervention and treatment—but which solution works best for this opportunity?

Gail D’Onofrio and colleagues at Yale New Haven Hospital arranged for three approaches for managing opioid-addicted patients who came through their doors: 1) a referral for treatment services; 2) a more direct intervention that provided a motivational speech and then connected the patient with treatment services provided; and 3) the administration of medicine to treat the addiction, directly followed by treatment services through the hospital’s primary care center.

The study found that seizing the opportunity to treat immediately worked best. Patients who received medicine—buprenorphine, a commonly used addiction therapy—were far more likely to continue treatment after one month than those whose treatment depended on patient initiative after leaving the emergency department.

Dozens of emergency departments—in the Northeast and across the US—are now starting to embrace emergency department visits as opportune moments to begin addiction treatment. To expand this mode of treatment to more facilities, emergency departments need training for the administration of treatment and medication, and follow-up care is essential. But the results underscore that, to stop the continued growth of the opioid epidemic, we need to take advantage of every opportunity for intervention.



Project Title

Emergency Department–Initiated Buprenorphine/Naloxone Treatment for Opioid Dependence

Publication

N Engl J Med. 2015;313(16):1636-1644
<https://jamanetwork.com/journals/jama/fullarticle/2279713>

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Funding

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The Undiagnosed Diseases Network

Figuring out what's wrong when it's not in the textbook

About 6 percent of the 6,000 people annually seeking assistance from the Office of Rare Diseases Research at the National Institutes of Health (NIH) suffer from an “undiagnosed disease,” a medical condition without a known cause. Without knowing the cause, doctors can only treat the symptoms, often unsuccessfully—and the condition continues, unresolved.

With the advent of inexpensive genetic sequencing and shared data, it has become much easier to identify rare diseases. But even with the ability to pinpoint the organisms causing the vast majority of disease, outliers still slipped past the medical system. In 2014, to facilitate this identification process, NIH established the Undiagnosed Diseases Network, a partnership of clinical sites, genetic sequencing labs and screening centers.

Patients now have an easier process to navigate, and the mystery cases are all genetically sequenced—less than one third of accepted patients had previously undergone sequencing for treatment. In the first 20 months of the Network's existence, 31 new syndromes were identified. The clinical diagnosis of the program was 35 percent, substantially trimming the number of patients stuck in medical diagnosis limbo.

Researchers also noticed a significant cost savings in the diagnostic process. For those patients whose financial information was available and who received a diagnosis through the Network, the average cost of care before evaluation was more than \$300,000—compared to the cost of the Network evaluation, which was under \$20,000.

The Undiagnosed Diseases Network has not been able to help every patient who reaches out for services, but in creating a system for genetic sequencing and sharing results, specimens and other data, the Network has the potential to make the correct medical treatment less of a mystery for doctors and patients alike.



Project Title

Effect of Genetic Diagnosis on Patients with Previously Undiagnosed Disease

Publication

N Engl J Med. 2018; 379:2131-2139
<https://www.nejm.org/doi/full/10.1056/NEJMoa1714458>

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- University of Maryland
- Baylor College of Medicine
- Stanford University
- University of California, Los Angeles
- Vanderbilt University
- HudsonAlpha Institute for Biotechnology
- Oregon Health and Science University
- Pacific Northwest National Laboratory, University of Oregon
- Duke University

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More Resources Bring More Cures

Despite all of the progress in medicine, there are still many problems that need solutions. While breast cancer treatment has seen many advances, pancreatic cancer treatment hasn't. People with this cancer, Parkinson's, Alzheimer's, diabetes, and many other diseases do not have years to wait for treatments to evolve.

Only 5 cents of each dollar spent on healthcare in the US is spent on research to prevent, cure and treat disease and disability. The cost of these health threats is much higher in the number of lives cut short and lost productivity.¹ We have come so far in treating disease, and yet have so much further to travel.

To increase funding for clinical research, we need to increase the size and scope of the National Institutes of Health (NIH), Patient-Centered Outcomes Research Institutes (PCORI), and the Agency for Healthcare Research and Quality (AHRQ).

Investments in clinical research are investments in quality of life and the economic health of our communities. With additional funding, we can find treatments and cures for life-threatening and chronic diseases. It takes years and great dedication to achieve results. We need to make it easier for researchers to figure out how patients can have the treatments they need, when they need them, and then move on with their lives.

This is the focus of Clinical Research Forum, and we welcome your support on this mission.

¹ https://www.researchamerica.org/sites/default/files/RA-2017_InvestmentReport.pdf

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