



## BETTER HEALTH CARE WITH LESS HEALTH SPENDING

The Stanford Clinical Excellence Research Center (CERC) is discovering new care delivery methods to solve our nation's persisting crisis in the affordability of excellent care.

### REVEALING PERSISTENT CARCINOGENS IN U.S. MEDICATIONS CATALYZES GOVERNMENT ACTION

CERC Director Arnold Milstein, MD, challenged colleague Kevin Schulman, MD, to repeat in the United States his prior study in Nigeria of dangerous drug impurities. Taking on the challenge, Dr. Schulman selected the generic drug metformin, America's most widely consumed oral diabetes medication.

CERC's research team tested multiple metformin samples from large factories in East and South Asia that dominate the U.S. market. Since the FDA recalled generic metformin as recently as 2020 due to the presence of the carcinogen NDMA, the research team did not expect to find persistent carcinogens. Counterbalancing this was an awareness that congressional underfunding of the FDA had shielded many offshore factories from onsite FDA inspections for more than five years.

Testing revealed the persistence of NDMA in 7% of our samples, as well as DMF, a carcinogen recently banned by the European Medicines Agency, the EU's drug regulatory agency. CERC's findings were released in October 2023 in the *American Journal of Managed Care*. The persistence of carcinogens in 2022 suggests a fundamental failure of U.S. systems to ensure safely manufactured drugs.

CERC and its independent lab contractor presented their findings to the U.S. Department of Defense (DOD) and FDA. The DOD rapidly committed to routine independent testing of generic drugs. The FDA's response is pending.

Routine independent testing of generic drug batches would add 1% to 3% to the very low cost of U.S. generic drugs. In exchange, it would prevent thousands of downstream U.S. cancer deaths and substantial cancer treatment costs. CERC continues to advocate for such testing with the FDA, White House, congressional committees, and large employer-sponsored health plans affiliated with the Purchaser Business Group on Health (PBGH).

A parallel CERC study is underway with generic methylphenidate, the most widely prescribed drug for American children with attention deficit hyperactivity disorder (ADHD). Funding for CERC research on low-value drugs was drawn from philanthropic contributions from the Sandler, Moore, Freidenrich, and Bowes family foundations.



## AI RESEARCH TO PROTECT ICU PATIENTS FROM COSTLY ERRORS

CERC's Partnership in AI-Assisted Care (PAC) with the engineering school's Department of Computer Science is rapidly accelerating at Stanford Health Care (SHC). The team completed the installation mid-pandemic of eight high-definition video cameras in ICU rooms at 500P and collected more than 800 terabytes of bedside video data. An additional 36 ICU rooms will be equipped during the next several months. Equally important, the team is taking care to respect the privacy and dignity of ICU patients and staff.

Co-directed by Dr. Milstein and Fei-Fei Li, PhD, co-director of the Stanford Institute for Human-Centered Artificial Intelligence (HAI) and professor of computer science, PAC is pursuing diverse applications of computer vision to profoundly improve bedside care of seriously ill ICU and surgery patients and reduce "soul-sucking" medical record documentation burden imposed on nurses and other bedside clinicians worldwide. CERC faculty and student ICU 500P research teams are led by CERC faculty members Ehsan Adeli, PhD, and Kevin Schulman, MD. 500P ICU nurses and CERC faculty physicians Amit Kaushal, MD, PhD, Paul Tang, MD, PhD, Swati DiDonato, MD, and Dev Dash, MD, are vital research partners and teachers of PAC's computer science students.



If successful, CERC will also create an opportunity for Stanford's Office of Technology Licensing to attract a commercial partner to enable the university to "do good at scale and do well." Funding for PAC research at Stanford hospitals is drawn from pooled philanthropic contributions to SHC, Stanford Medicine Children's Health, and by the Gunn and Schmidt family foundations.

## EARLY SIGNS THAT 2016 LEGISLATION TO ACCELERATE NEW DRUG APPROVALS MAY UNDERMINE VALUE

The 2016 21<sup>st</sup> Century Cures Act was intended to accelerate the flow of valuable new drugs to the market. Heavily lobbied by pharmaceutical companies, a new CERC study reveals that the Cures Act is also creating unintended risks to clinical value.

CERC faculty member and former NIH Assistant Director Robert M. Kaplan, PhD, led this freshly published research. Before the new law, the majority of approvals were based on three or more clinical trials. Multiple trials help ensure clinical value because trials may differ in their conclusions about a new drug's effectiveness and safety.

Dr. Kaplan found that 65% of new drugs are now being approved based on a single clinical trial. Before the new law, 41% of new drug approvals were based on a single study.

His research also highlighted a striking decline in industry public reporting of clinical trial results. Dr. Kaplan found that only one in four trial findings are being made public prior to gaining approval. By withholding unfavorable trial results, pharmaceutical companies prevent consumers and their clinicians from weighing in during the FDA's approval deliberations and from making results-informed treatment decisions after FDA approval.

Existing laws to ensure prompt public reporting of all trial results appear insufficient: Almost never deployed by the FDA is the authority to fine drug companies up to \$10,000 a day for late disclosure of trial results. The CERC study team will now collaborate with CERC's Washington, DC-based senior scholar, Barak Richman, PhD, to engage the FDA and relevant congressional committees to correct these unintended threats to the value of novel drugs to patients.

