Most prescribed blood pressure drugs may be less effective than others

October 24 2019

Credit: CC0 Public Domain

A new multinational study shows that the most popular first-line treatment for hypertension is less effective and has more side effects than an alternative that's prescribed much less often.

The researchers, including Columbia's George Hripcsak, MD, and

Patrick Ryan, Ph.D., analyzed electronic health records and claims data from nearly 5 million patients who had begun drug treatment for hypertension. They found that patients who were first prescribed thiazide diuretics had 15% fewer heart attacks, strokes, and hospitalizations for heart failure, compared to those who were prescribed ACE inhibitors. Patients who began with thiazides also experienced fewer side effects.

The researchers estimated that approximately 3,100 major cardiovascular events among the patients who first took ACE inhibitors could have been avoided had they first been treated with a thiazide diuretic.

The study—the most comprehensive to compare outcomes in newly treated patients with hypertension—was published in *The Lancet*.

Little Evidence to Guide Drug Selection

Current guidelines from the American College of Cardiology and the American Heart Association recommend starting antihypertensive therapy with any drug from five different classes of medications, including thiazide diuretics, ACE inhibitors, angiotensin II receptor blockers (ARBs), dihydropyridine calcium channel blockers, and non-dihydropyridine calcium channel blockers.

But there is little evidence to help physicians decide which drug class to start with: the literature contains data from randomized, controlled clinical trials encompassing just 31,000 patients—and none of them were just beginning antihypertensive treatment. As a result, most clinical guidelines are based on expert opinion rather than data.

"Randomized clinical trials demonstrate a drug's effectiveness and safety in a highly defined patient population," says George Hripcsak, MD, chair

of biomedical informatics at Columbia University Vagelos College of Physicians and Surgeons and an author of the study. "But they're not good at making comparisons among multiple drug classes in a diverse group of patients that you would encounter in the real world."

Observational studies can be used to detect effects that might not have been apparent in randomized trials. But many are too small to draw meaningful conclusions or suffer from other types of distortion.

"Unintentionally or not, journals and authors tend to publish studies that have exciting results, and researchers may even select analytical methods that are best suited to getting the results that fit their hypotheses," says Hripcsak. "It comes down to a cherry-picking exercise, which makes the results less reliable."

Read this article to learn more about bias in observational studies.

Solution: Big Data

To address these limitations, the researchers analyze data from millions of patient health records and account for tens of thousands of different variables—critical to eliminating confounding factors. The method, known as Large-Scale Evidence Generation and Evaluation across a Network of Databases, or LEGEND, was pioneered by a consortium of scientists participating in the Observational Health Data Science Initiative (OHDSI, pronounced 'odyssey') network. Using LEGEND, the researchers are able to share their methodology and standardize the data, minimizing bias.

"LEGEND provides a systematic framework that can reproducibly generate evidence by applying advanced analytics across a network of disparate databases for a wide array of exposures and outcomes," says Patrick Ryan, Ph.D., adjunct assistant professor of biomedical

informatics at Columbia University Vagelos College of Physicians and Surgeons and vice president, Observational Health Data Analytics, Janssen Research and Development. "Not only does LEGEND offer a path to scale to the real needs of the healthcare community, it also provides the complementary diagnostics to help us understand how much we can trust the evidence we've produced."

The current study analyzed insurance claims and electronic health records from 4.9 million patients in four countries who were starting antihypertensive therapy with a single drug. The researchers used a complex algorithm to identify the number of heart attacks, hospitalizations for heart failure, strokes, and nearly 50 medication side effects occurring in patients taking any of the first-line antihypertensive drugs. They also employed a number of techniques designed to minimize bias—and account for about 60,000 different variables.

The study found that ACE inhibitors were the first antihypertensive drug prescribed to 48% of patients, compared with 17% of patients who were first prescribed thiazide diuretics. Yet patients who were first treated with thiazide diuretics had 15% fewer heart attacks, hospitalizations for heart failure, and strokes compared with those treated with other first-line therapies. In addition, patients first treated with ACE inhibitors had higher rates of 19 side effects compared with thiazide users.

The study also found that non-dihydropyridine calcium channel blockers were less effective than all of the other first-line drug classes.

"With LEGEND, we have found a way to fill in the gaps left by randomized, controlled trials and help guide physicians in their clinical decision making," says Hripcsak.

The paper, "Comprehensive comparative effectiveness and safety of first-line antihypertensive drug classes: a systematic, multinational, large-

scale analysis," was published in *The Lancet*.

Provided by Columbia University Irving Medical Center