Moving the diagosis of rheumatic diseases into the era of precision medicine

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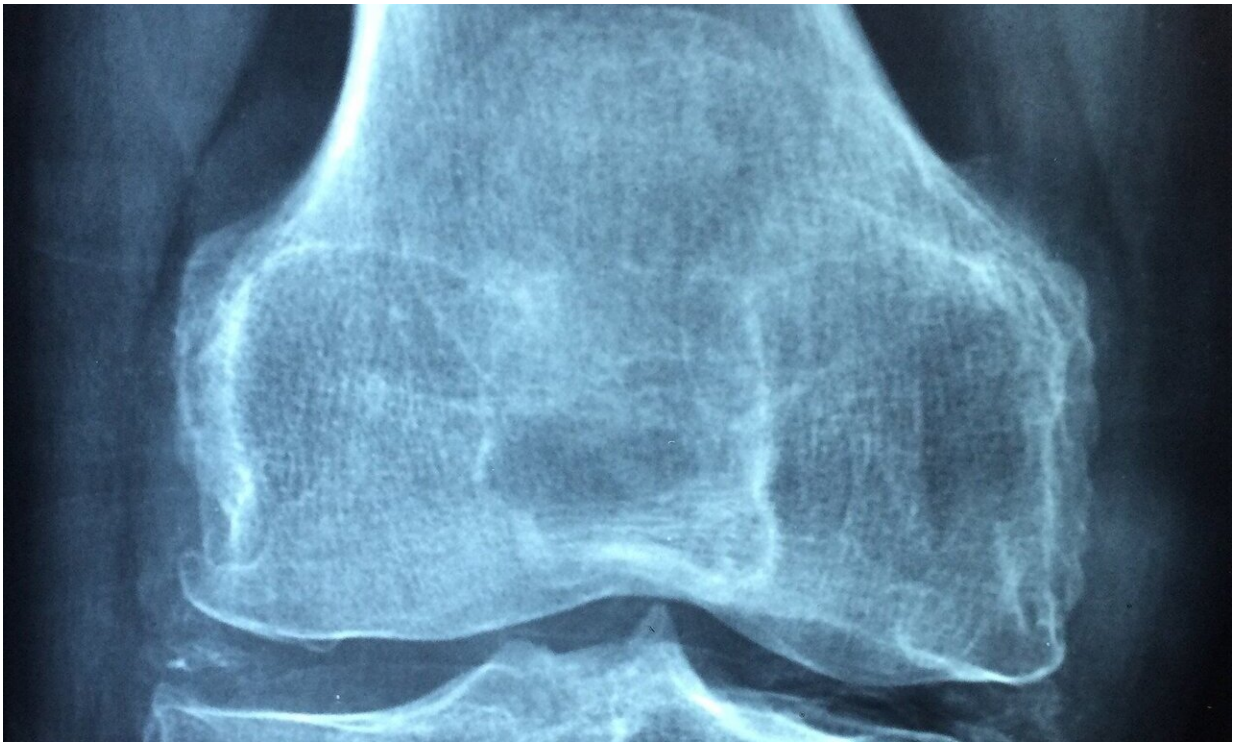

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Many rheumatic conditions develop slowly and initially have inflammatory arthritis as the first sign that something is amiss. The trouble with such close similarity is the difficulty that clinicians have differentiating one condition from another in the early stages of the disease process.

Dr. Rachel Knevel and colleagues at Brigham and Women's Hospital in Boston and Leiden University in the Netherlands have developed a gene-based algorithm called G-PROB, an acronym that stands for genetic probability tool. The new diagnostic has allowed the team to discriminate among gout, lupus, rheumatoid arthritis, psoriatic arthritis and spondyloarthropathy.

Reporting in *Science Translational Medicine*, Knevel and her team describe the new diagnostic tool and note that it combines a patient's genetic data with genetic risk scores. This double-barreled approach allowed them to home in on the most probable diagnosis among five rheumatic diseases.

The team used G-PROB with roughly 1,700 patients whose genetic and clinical data were accessible through the eMERGE or Partners biobanks. Each patient had been diagnosed with at least one type of rheumatic disease or had presented with early inflammatory arthritis in their first visit to an outpatient clinic. The new approach, according to Knevel and her team, allowed them to rely on genotype information to make precise, early diagnoses of rheumatic disorders.

"Pre-existing genetic data could be considered part of a patient's medical history, given its potential to improve precision medicine in the modern outpatient clinic," Knevel and her collaborators wrote in the journal.

Testing their new platform on this large collection of patients' genetic samples, the team was able to rule out at least one disease in all patients, identify a likely diagnosis in 45 percent of the patients, and catch incorrect clinical diagnoses in 35 percent of cases.

Adding genetic risk score calculations to clinical data improved G-PROB's diagnostic accuracy to 51 percent compared with 39 percent resulting from interpretation of clinical data alone.

Rheumatic diseases comprise a broad spectrum of disorders, and a misunderstanding of what they are is still clouded by the long-outdated but still commonly used term "rheumatism," which means joint pain. Doctors say rheumatic conditions not only include those that cause joint pain, but also autoimmune disorders—the inflammatory diseases typified by turncoat cells and proteins—that wage war on everything from the joints to the skin and vital organs.

The American College of Rheumatology notes that while most people think of rheumatic diseases as rare, the disorders are strikingly common throughout the U.S. population.

An estimated one in four adults in the United States has been diagnosed with arthritis or another rheumatic condition. The Centers for Disease Control and Prevention has predicted that the number of affected people will continue to rise. By 2040, according to the CDC, a vast swath of the population—approximately 78 million adults—will have been diagnosed with a rheumatic disease.

Among rheumatic disorders, osteoarthritis is the most common, affecting about 26 million adults in the United States, followed by fibromyalgia, which is estimated to afflict an estimated 10 million people, and gout, which affects 8.3 million.

Although autoimmune disorders are considered rare, they afflict a significant portion of the population—about 1.3 million U.S. adults have been diagnosed have rheumatoid arthritis and anywhere from 200,000 to 300,000 have lupus, figures from the American College of Rheumatology show.

Knevel and colleagues, meanwhile, will have to further refine the algorithm's precision before it is ready for wide use in outpatient treatment centers. However, they have been able to demonstrate that

genotype data can aid individual diagnoses by keenly discriminating among related but profoundly different rheumatic conditions.

More information: Rachel Knevel et al. Using genetics to prioritize diagnoses for rheumatology outpatients with inflammatory arthritis, *Science Translational Medicine* (2020). DOI: 10.1126/scitranslmed.aay1548