

# **Largest study of osteoarthritis to date discovers new genetic risk factors and identifies drug targets**

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The Genetic Burden of Osteoarthritis. Credit: Cindy Boer

Osteoarthritis is a disease of the joints and affects over 300 million individuals worldwide. It is characterized by a gradually increasing degeneration of the cartilage on the joint surface. This results in chronic pain and stiffness in the joints and is a leading cause of disability. Until today, no curative treatments have been available. An improved understanding of what causes the disease and the development of novel treatments are therefore urgently needed and eagerly anticipated by patients.

In the largest study of osteoarthritis to date (across over 825,000 individuals from nine populations), an international team of researchers led by Helmholtz Zentrum München discovered new genetic risk factors for the [disease](#) and identified high-value drug targets. This study provides a stepping stone for translating genetic discoveries into osteoarthritis drug development, ultimately helping to catalyze an improvement in the lives of patients suffering from osteoarthritis. "This is a major step forward in understanding this debilitating disease and could not have been achieved without this international team effort," said Eleftheria Zeggini, Director of the Institute of Translational Genomics at Helmholtz Zentrum München and professor at the Technical University of Munich.

The researchers also found previously unknown differences in disease risk for weight-bearing and non-weight-bearing joints, the first ever female-specific risk factors for developing disease, and the first risk factors for early-onset disease. For the first time, they found genetic links between osteoarthritis and its main symptom, pain.

"Because we have investigated osteoarthritis in multiple joints, we have also identified specific genetic changes that underpin the risk for all forms of osteoarthritis. Some of these genes may prove to be validated as therapeutic targets for osteoarthritis, regardless of the joint affected," says Cindy Boer from Erasmus MC University Medical Center in the

Netherlands, co-first author of the article.

## Identifying new drug targets

By combining multiple lines of evidence, the researchers pinpointed likely causal genes for [osteoarthritis](#) that constitute potential drug targets for the disease. Many of the implicated genes code for molecules that are the targets of approved (licensed) drugs and drugs in clinical development. These findings substantially strengthen the evidence for these potential therapeutics and provide novel [drug](#) repositioning opportunities.

This work provides a robust springboard for follow-up functional and clinical studies. These are necessary to elucidate how to target the implicated genes and proteins, and ultimately, how these interventions will affect disease outcome in the patient.

**More information:** Boer, Hatzikotoulas, Southam et al., 2021: Deciphering Osteoarthritis genetics across 826,690 individuals from 9 populations. *Cell*, [DOI: 10.1016/j.cell.2021.07.038](https://doi.org/10.1016/j.cell.2021.07.038)

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