

**Arthritis Australia 2024 National Research Program
Project Grant**

Lay summary

Machine learning to predict and prevent rheumatoid arthritis

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Lay Summary:

Rheumatoid arthritis (RA) is a debilitating disorder, where the body's own defences (the immune system) attack the tissues lining the joints. It is not currently possible to prevent RA as we don't know what causes it, however, we do know that both our genes and some lifestyle factors can increase or lower the risk. To address these gaps in knowledge, we conducted a study at the University of South Australia which used artificial intelligence to discover new risk factors for RA and predict whether these factors increase or lower the risk of disease.

We looked at information from nearly 450,000 individuals who did not have RA or any related diseases at the start of the study. We had access to detailed information on their health, genes, lifestyles, diets, environments, blood markers, medical history, physical measurements and sex-specific factors. The information, comprising around 3,000 characteristics, was fed into a machine learning model (a form of artificial intelligence) that determined which characteristics were most important for predicting who will develop RA within the next 5-10 years.

The model suggested 200 characteristics that were potentially important for predicting RA; 113 of which were confirmed as potential risk factors of RA in further analyses. We learnt that characteristics related to low socioeconomic status, indicators of poor general health, physical inactivity, and history of other joint disorders or lung disease may increase the risk of RA. We also discovered that blood markers involved in inflammation and altered function of the liver and kidneys are important in predicting RA, which presents the opportunity to develop and refine blood tests that check for risk of RA. Our study highlights the need for earlier diagnosis of RA, as our findings showed that individuals experienced symptoms of RA several years before their formal diagnosis.

Next, we looked closely at the genetic risk factors of RA. We identified 24 risk factors that could be modified by lifestyle changes and investigated whether action on these risk factors can reduce risk for those that are genetically predisposed to RA. We found that rheumatoid factor may be a stronger predictor of RA in those who are at high genetic risk of RA, however the effect of other biomarkers and lifestyle factors did not differ notably by genetic susceptibility. This suggests that the key modifiable risk factors of RA apply regardless of genetic susceptibility.

This is the first and largest study of its kind, exploiting large-scale data and newly developed machine learning methods. The findings have added to our understanding of what increases and decreases risk of RA, and will support efforts to improve screening and prevention strategies for RA. Our study was conducted in a UK population, which shares many similarities with the Australian population and will help to guide current guidelines and future research projects in Australia.