

Machine learning predicts response to drug for arthritis in children

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Credit: Pavel Danilyuk from Pexels

Doctors might one day be able to target children and young people with arthritis most likely to be helped by its first-line treatment, thanks to the application of machine learning by University of Manchester scientists.



Though methotrexate is the first-line drug to be given for Juvenile idiopathic arthritis (JIA), it is only effective or tolerated in half of the children and <u>young people</u> who receive it.

Those patients not helped by the drug have to wait longer to receive second-line therapies, potentially prolonging the severe joint pain and other symptoms which often have a devastating impact on children and their families.

The study, <u>published</u> in the journal *eBioMedicine*, could facilitate more precise research into the identification of response predictors to methotrexate, such as biomarkers, and lead to better forecasting of likely outcomes following drug initiation.

It confirms that one in eight children and young people starting methotrexate will demonstrate improvements in inflammatory features of disease yet have some symptoms.

They also showed that in 16 percent of children taking methotrexate, improvements in disease activity could be slower than in others over time.

Lead author Dr. Stephanie Shoop-Worrall said, "Giving methotrexate to children who it will not help wastes time, money and effort for health care services- as well as unnecessarily exposing them to potential side effects.

"But now <u>machine learning</u> has opened the door made it possible to predicting which aspects of a child's disease would be helped by the drug and so which children should start other therapies either alongside or instead of methotrexate straight away.

"In addition, this work shows how <u>clinical trials</u> are missing the mark in



only looking at drug 'response' or 'non-response' for childhood-onset arthritis.

"This oversimplification could lead to a drug being labeled as 'effective' when key symptoms such as pain remain, or 'ineffective' where a significant improvement is seen in one aspect of this complex disease."

The research team accessed data from four nationwide cohorts of children and young people who began their <u>treatment</u> before January 2018.

Juvenile arthritis <u>disease activity</u> score components (including how many swollen joints, a doctor's perception of disease, a patient/parent report of well-being, results of a blood test for inflammation) were recorded at the start of treatment and over the following year.

They used machine learning identify clusters of patients with distinct disease patterns following methotrexate treatment, predict clusters; and compare clusters to existing treatment response measures.

From 657 children and young people verified in 1,241 patients they identified Fast Improvers (11%), Slow Improvers (16%), Improve-Relapse (7%), Persistent Disease (44%).

Two other clusters they called Persistent physician global assessment (8%) and Persistent parental global assessment (13%), were characterized by improvement in all activity score features except one.

Dr. Shoop-Worrall added, "The longer-term impact of this slower disease control needs further investigation. Our study also demonstrates the utility of machine learning methods to uncover clusters of <u>children</u> as a basis for stratified treatment decisions.



"This work builds on existing studies of methotrexate treatment response, confirming that response is not bivariate but can be highly variable across different features of disease within individuals.

"At the moment trials of <u>methotrexate</u> in JIA categorize patients into responders and non-responders.

"That misclassification can compromise studies looking to identify predictors of response, such as biomarkers."

More information: Stephanie J.W. Shoop-Worrall et al, Towards stratified treatment of JIA: machine learning identifies subtypes in response to methotrexate from four UK cohorts, *eBioMedicine* (2024). DOI: 10.1016/j.ebiom.2023.104946

Provided by University of Manchester

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