

**Table 1. Sensitivity, Specificity, PPV and NPV are computed on the ABIRISK validation cohort for each strategy**

| Drug                           | AUC<br>(ESPOIR)     | AUC<br>(ABIRA)        | STRATEGY 1 (high confidence in response) |                                   |                                   |                  | STRATEGY 2 (high confidence in non-response) |                  |                  |                                   |
|--------------------------------|---------------------|-----------------------|--|-----------------------------------|-----------------------------------|------------------|--|------------------|------------------|-----------------------------------|
|                                |                     |                       | Sensitivity                              | Specificity                       | PPV                               | NPV              | Sensitivity                                  | Specificity      | PPV              | NPV                               |
| Overall TNFi                   | 0.72<br>(0.68-0.73) | 0.65<br>(0.54 - 0.75) | 18%<br>(10%-27%)                         | <b>91%</b><br>( <b>82%-98%</b> )  | <b>76%</b><br>( <b>54%-95%</b> )  | 42%<br>(32%-51%) | <b>90%</b><br>( <b>83%-96%</b> )             | 30%<br>(18%-44%) | 67%<br>(58%-76%) | <b>67%</b><br>( <b>45%-86%</b> )  |
| Etanercept                     | 0.74<br>(0.68-0.75) | 0.70<br>(0.57- 0.82)  | 60%<br>(44%-74%)                         | <b>73%</b><br>( <b>55%-89%</b> )  | <b>78%</b><br>( <b>63%-92%</b> )  | 53%<br>(36%-69%) | <b>95%</b><br>( <b>88%-100%</b> )            | 15%<br>(4%-30%)  | 64%<br>(52%-76%) | <b>67%</b><br>( <b>20%-100%</b> ) |
| Monoclonal anti-TNF antibodies | 0.74<br>(0.69-0.77) | 0.71<br>(0.55-0.86)   | 37%<br>(20%-55%)                         | <b>95%</b><br>( <b>83%-100%</b> ) | <b>92%</b><br>( <b>73%-100%</b> ) | 50%<br>(35%-66%) | <b>90%</b><br>( <b>78%-100%</b> )            | 40%<br>(19%-62%) | 69%<br>(54%-84%) | <b>73%</b><br>( <b>44%-100%</b> ) |

[2] Anon. ABIRISK Anti-Biopharmaceutical Immunization: Prediction and Analysis of Clinical Relevance to Minimize the RISK. 2019.

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#### MACHINE LEARNING PREDICTS RESPONSE TO METHOTREXATE IN RHEUMATOID ARTHRITIS: RESULTS ON THE ESPOIR, T-REACH AND LEIDEN COHORTS

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**Background:** Methotrexate (MTX) is the first line of treatment for rheumatoid arthritis (RA) patients. Unfortunately, 30% to 40% of RA patients do not respond to MTX, resulting in uncontrolled joint pain and potential joints destruction. At the same time, many efficient second-line treatments exist and can be given to the inadequate responder patients. Predicting patient response to MTX before prescribing the treatment is therefore a major goal and could enable physicians to directly prescribe second-line treatments if inadequate response to MTX is predicted.

**Objectives:** We aimed to build machine learning models based on simple clinical and biological data to predict patient response to MTX.

**Methods:** We used data from the ESPOIR early arthritis (1) and Leiden cohorts (2) to train the models, and the tREACH cohort to validate the results. We included patients that fulfilled the EULAR/ACR 2010 criteria and that were treated with MTX in monotherapy as their first treatment for RA. The models take as inputs patient's characteristics at treatment initiation and predict the therapeutic response, defined as the EULAR response 3 to 12 months after treatment initiation. We evaluated four missing data imputation methods (median, mean, MICE, KNN); we used the backward feature selection algorithm to select the most relevant variables; and compared the performances of four models (Linear Regression, Random Forest, XGBoost, and Catboost) on the training set by cross-validated them using the Area Under the ROC Curve (AUCROC). The best model was then evaluated on the validation dataset.

**Table 1. Sensitivity, Specificity, PPV and NPV are computed on the T-REACH validation cohort for each strategy**

| AUC<br>(ESPOIR, LEIDEN) | AUC<br>(T-REACH)    | STRATEGY 1 (High confidence in responders) |                                   |                                   |                  | STRATEGY 2 (high confidence in non-responDeRS) |                  |                  |                                  |
|-------------------------|---------------------|--|-----------------------------------|-----------------------------------|------------------|--|------------------|------------------|----------------------------------|
|                         |                     | Sensitivity                                | Specificity                       | PPV                               | NPV              | Sensitivity                                    | Specificity      | PPV              | NPV                              |
| 0.72<br>(0.70-0.73)     | 0.73<br>(0.64-0.81) | 20%<br>(12%-28%)                           | <b>98%</b><br>( <b>83%-100%</b> ) | <b>95%</b><br>( <b>82%-100%</b> ) | 40%<br>(32%-49%) | <b>91%</b><br>( <b>85%-97%</b> )               | 33%<br>(20%-47%) | 71%<br>(63%-79%) | <b>68%</b><br>( <b>48%-86%</b> ) |

**Results:** We included 435 patients from the ESPOIR cohort, 243 patients from the Leiden cohort and 143 patients from the t-REACH cohort. Results of the model are displayed in Table 1. The variables automatically selected to perform prediction were Sex, DAS28, White blood cells, AST, ALT and lymphocytes. Our model performs well on unseen data, this result comes from the fact that we included two different cohorts in our training set which reduces the overfitting of our model and helps him generalize. Our model predicts a probability for a patient to respond to MTX. This probability is compared to a decision threshold to obtain the final binary outcome. Two decision thresholds were tested. The first prioritizes a high confidence when identifying responders (Strategy 1) while the second prioritizes a high confidence when identifying non-responders (Strategy 2). This second strategy would enable physicians to identify highly probable inadequate responders to methotrexate and propose them directly a targeted DMARD such as TNF inhibitors, while still treating more than 70% of patients with MTX as first-line treatment.

**Conclusion:** The machine learning models developed in this study can predict RA patients' response to methotrexate with a good accuracy exclusively using data available in clinical routine. It paves the way for personalized therapeutic strategies in rheumatoid arthritis.

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#### REMOTE MONITORING TOOLS IN RA PATIENTS: FACIT-FATIGUE AND HAQ

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**Background:** The need to avoid the transmission of COVID19 infection has forced to promote teleconsultations for rheumatic diseases follow-up. However, remote monitoring for rheumatic diseases which require clinical examination, as rheumatoid arthritis (RA), may affect to the evaluation of clinical activity, including the biological therapies follow-up. Due to that, count on tools as Patient Reported Outcomes (PROs) could help the remote monitoring of patients when it is not advisable their physical presence in health centers, being a great help in RA control.

**Objectives:** We aim to assess the association among the tiredness, disability and pain perception with the clinical activity in RA patients.

**Methods:** We performed a prospective observational study of three months of follow-up in RA patients (ACR/EULAR 2010) who are newly on biological or anti-JAK therapy. A basal visit and 1, 3 months follow-up visits were conducted. We analyzed changes during follow-up in the PROs parameters reported by patients through FACIT-fatigue and HAQ questionnaires, as well as pain VAS (0-10). Moreover we measured clinical activity through Das28, Das28-CRP, SDAI and CDAI index.

**Results:** We included 60 patients (83.3% female), with a mean age of 55 (13) and mean disease evolution of 13 (11) years. At the basal visit, 55% of them exhibited increased levels of CRP and the 48.3% of ESR, showing moderate or high clinical activity the 83.3% of the total patients.