Development and validation of patient-level prediction models for adverse health outcomes amongst adult RA patients initiating first-line treatment of methotrexate monotherapy

a multinational real-world cohort analysis including 164,734 subjects

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on behalf of European Health Data and Evidence Network (EHDEN) RA Research Group
• Joel Swerdel and Patrick Ryan are full-time employees of Janssen Research & Development, a pharmaceutical company of Johnson & Johnson, and shareholders in Johnson & Johnson.

• Katerina Chatzidionysiou is a consultant of AbbVie, Pfizer and Lilly.

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• Peter Rijnbeek reports research grants from Janssen Research & Development.

• Cynthia Yang, Ross Williams, Meghna Jani, Talita Duarte-Salles have nothing to disclose.
The objective of this study was to develop and validate prediction models for adverse health outcomes in RA patients initiating first-line MTX monotherapy.
The European Health Data Network (EHDEN) and Observational Health Data Sciences and Informatics (OHDSI) initiatives organized a 5-day study-a-thon to get from study design to study results.

A multi-disciplinary team consisting of 40 clinical, academic, and data partners joined forces.

Some of our team members, January 2020, Barcelona.
PROBLEM DEFINITION

Index date:
First-line MTX monotherapy, age>=18, prior RA diagnosis

Observation Window

- Min. 365 days observation period
- No record of any other inflammatory arthritis or any cancer
- No record of the outcome of interest in the preceding 90 days

Time-at-risk

Outcomes:
- Serious Infections in the next 90 days
- Myocardial Infarction in the next 2 years
- Stroke in the next 2 years
• Health data from claims and electronic health records were used from:
  – 6 European countries (Spain, Estonia, Netherlands, Germany, France, UK)
  – USA (7 databases)
  – Australia
  – Japan

• All data standardized to the **OMOP Common Data Model** to enable common analytics.
MODEL DEVELOPMENT AND VALIDATION

• Model development on 21,307 patients from OPTUM (USA claims, 88m patients, 2001-2019).

• Large-scale data-driven approach using logistic regression with LASSO regularisation (12,011 potential predictors):
  – Model training on 75% of the patients
  – Internal validation on 25% of the patients

• External validation (AUROC, calibration) on 143,427 patients from 14 databases.
**INTERNAL VALIDATION (OPTUM USA)**

- **Serious Infection:**
  - 5,251 patients
  - 79 outcome events (1.5%)
  - 92 predictors included
  - AUROC of 0.75

- **Myocardial Infarction:**
  - 5,308 patients
  - 98 outcome events (1.8%)
  - 78 predictors included
  - AUROC of 0.77

- **Stroke:**
  - 5,301 patients
  - 127 outcome events (2.4%)
  - 70 predictors included
  - AUROC of 0.78
EXTERNAL VALIDATION (CCAE USA)

- **Serious Infection:**
  - 27,877 patients
  - 216 outcome events (0.8%)
  - AUROC of 0.66

- **Myocardial Infarction:**
  - 28,084 patients
  - 173 outcome events (0.6%)
  - AUROC of 0.73

- **Stroke:**
  - 28,082 patients
  - 243 outcome events (0.9%)
  - AUROC of 0.73
EXTERNAL VALIDATION (IQVIA EHR GERMANY)

• Stroke:
  – 7,416 patients
  – 37 outcome events (0.5%)
  – AUROC of 0.70
### RESULTS

<table>
<thead>
<tr>
<th>Model</th>
<th>Internal AUROC</th>
<th>External AUROC median (min-max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious Infection</td>
<td>0.75</td>
<td>0.67 (0.61-0.82)</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>0.77</td>
<td>0.68 (0.49-0.76)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.78</td>
<td>0.73 (0.63-0.79)</td>
</tr>
</tbody>
</table>

- Online results at: [https://data.ohdsi.org/ehdenRaPrediction/](https://data.ohdsi.org/ehdenRaPrediction/)
CONCLUSIONS

• Models were developed that identify RA patients at risk of serious infection, myocardial infarction, and stroke at the initiation of first-line MTX monotherapy.

• The developed models generally had good transportability to other databases.

• These models would allow clinicians to provide more personalized care.

• Future work: development of parsimonious models.
We like to thank all the participants of the RA Study-a-thon, OHDSI, and EHDEN.

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