EHDEN

EUROPEAN HEALTH DATA & EVIDENCE NETWORK

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

Cynthia Yang, Ross Williams, Joel Swerdel, Meghna Jani, Talita Duarte-Salles, Katerina Chatzidionysiou, Daniel Prieto-Alhambra, Patrick Ryan, Peter Rijnbeek

on behalf of European Health Data and Evidence Network (EHDEN) RA Research Group

imi innovative medicines initiative

efpia

OHDSI OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

DISCLOSURES

- 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.
- Daniel Prieto-Alhambra reports research grants from AMGEN, UCB Biopharma and Les Laboratoires Servier.
- Peter Rijnbeek reports research grants from Janssen Research & Development.
- Cynthia Yang, Ross Williams, Meghna Jani, Talita Duarte-Salles have nothing to disclose.

BACKGROUND

- EULAR guidelines recommend the initiation of methotrexate (MTX) monotherapy as soon as possible after the diagnosis of RA.
- Evaluating patient-level risks for adverse health outcomes after MTX initiation would allow clinicians to provide more personalised care.

EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update

Josef S Smolen ,[1] Robert B M Landewé,[2,3] Johannes W J Bijlsma,[4] Gerd R Burmester,[5] Maxime Dougados,[6] Andreas Kerschbaumer ,[1] Iain B McInnes,[7] Alexandre Sepriano ,[8] Ronald F van Vollenhoven,[9] Maarten de Wit ,[10] Daniel Aletaha,[1] Martin Aringer ,[11] John Askling,[12] Alejandro Balsa,[13] Maarten Boers,[14] Alfons A den Broeder,[15] Maya H Buch ,[16] Frank Buttgereit,[5]

https://ard.bmj.com/content/annrheumdis/early/2020/01/22/annrheumdis-2019-216655.full.pdf

The objective of this study was to develop and validate prediction models for adverse health outcomes in RA patients initiating first-line MTX monotherapy.

STUDY-A-THON ON RHEUMATOID ARTHRITIS

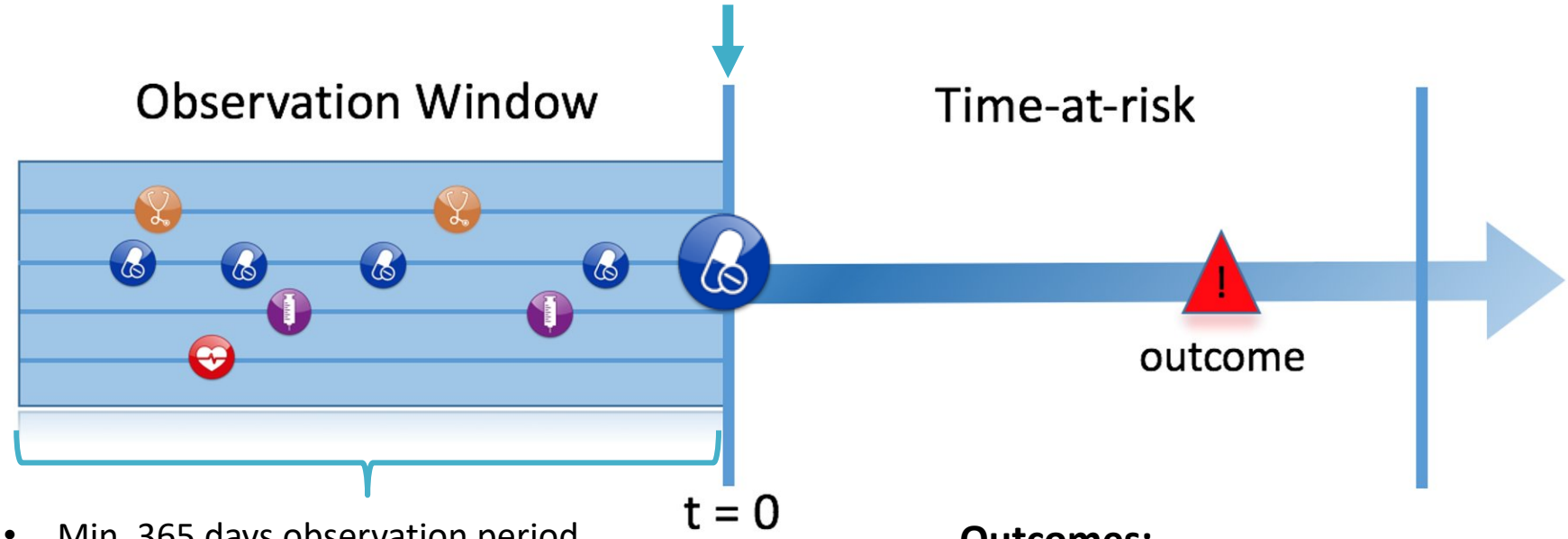
- The European Health Data Network (EHDEN) and Observational Health Data Sciences and Informatics (OHDSI) initiatives organized a **5-day study-a-thon** to get from **study design** to **study results.**

- 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



- 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

Outcomes:
- Serious Infections in the next 90 days
- Myocardial Infarction in the next 2 years
- Stroke in the next 2 years

DATASETS

- 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

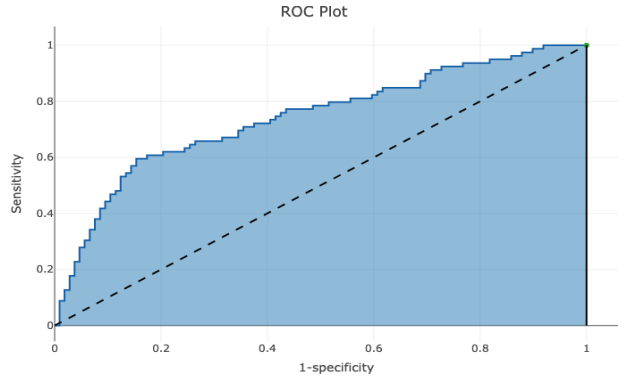
- Model development on 21,307 patients from OPTUM (USA claims, 88m patients, 2001-2019).

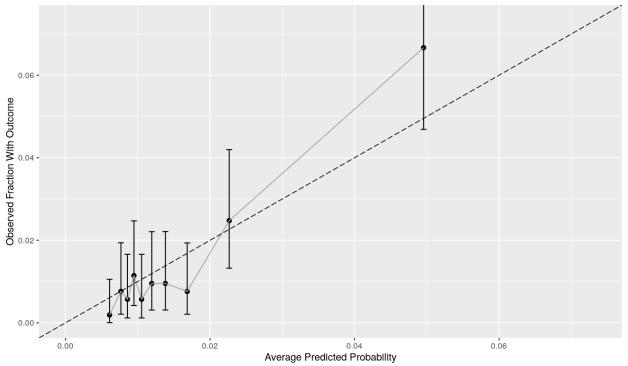
- Large-scale data-driven approach using logistic regression with LASSO regularisation (12,011 potential predictors):
  - Model training on 75% of the patients
  - Internal validation on 25% of the patients

- External validation (AUROC, calibration) on 143,427 patients from 14 databases.

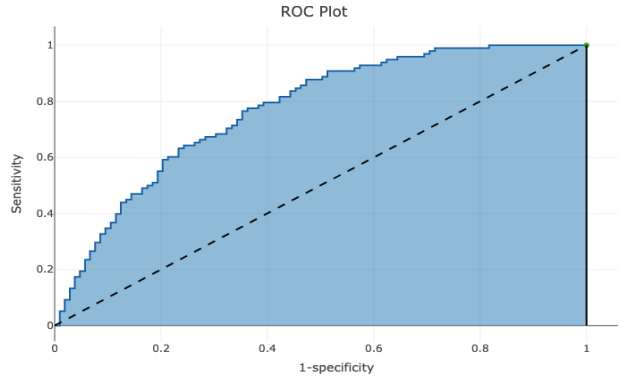
INTERNAL VALIDATION (OPTUM USA)

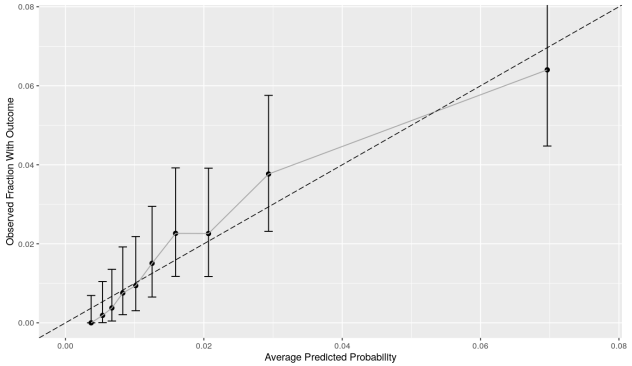
- Serious Infection:
  - 5,251 patients
  - 79 outcome events (1.5%)
  - 92 predictors included
  - AUROC of 0.75



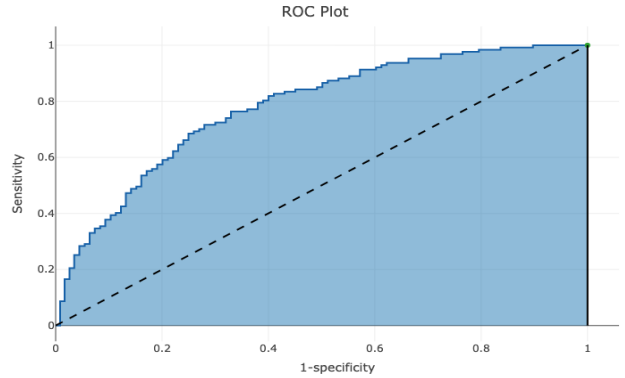


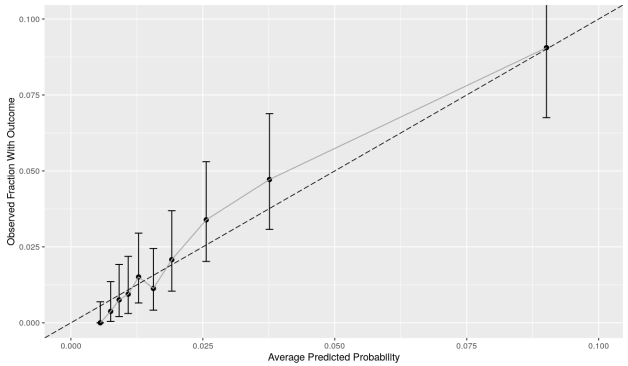
- Myocardial Infarction:
  - 5,308 patients
  - 98 outcome events (1.8%)
  - 78 predictors included
  - AUROC of 0.77





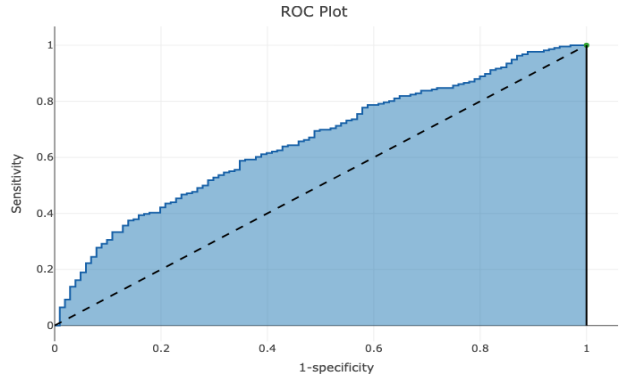
- Stroke:
  - 5,301 patients
  - 127 outcome events (2.4%)
  - 70 predictors included
  - AUROC of 0.78

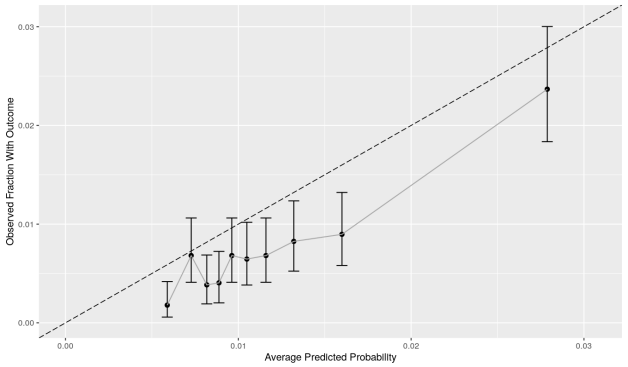




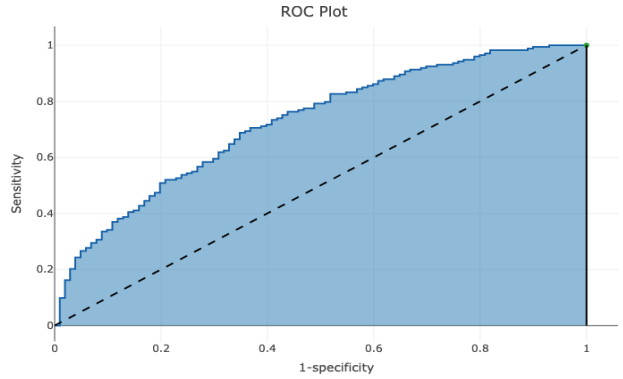
EXTERNAL VALIDATION (CCAE USA)

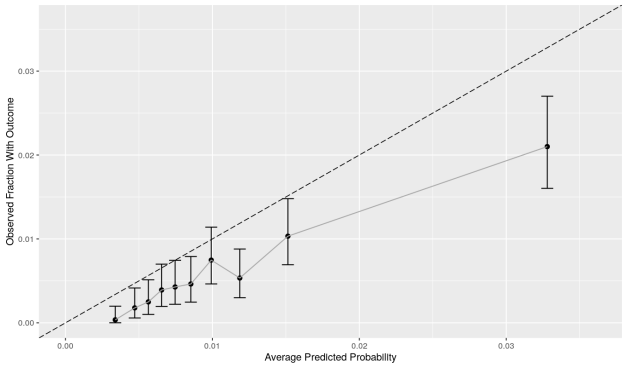
- Serious Infection:
  - 27,877 patients
  - 216 outcome events (0.8%)
  - AUROC of 0.66



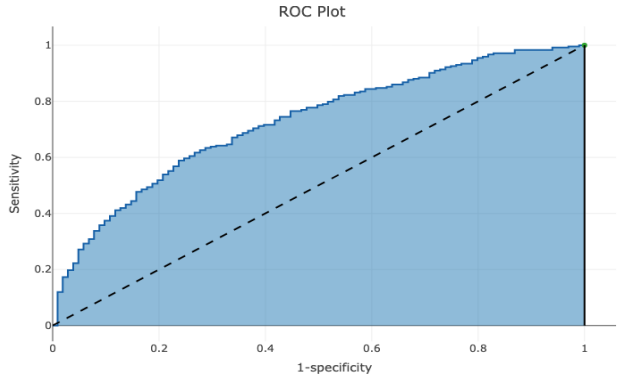


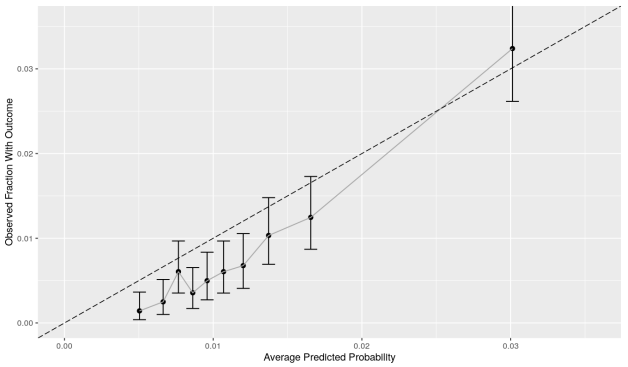
- Myocardial Infarction:
  - 28,084 patients
  - 173 outcome events (0.6%)
  - AUROC of 0.73





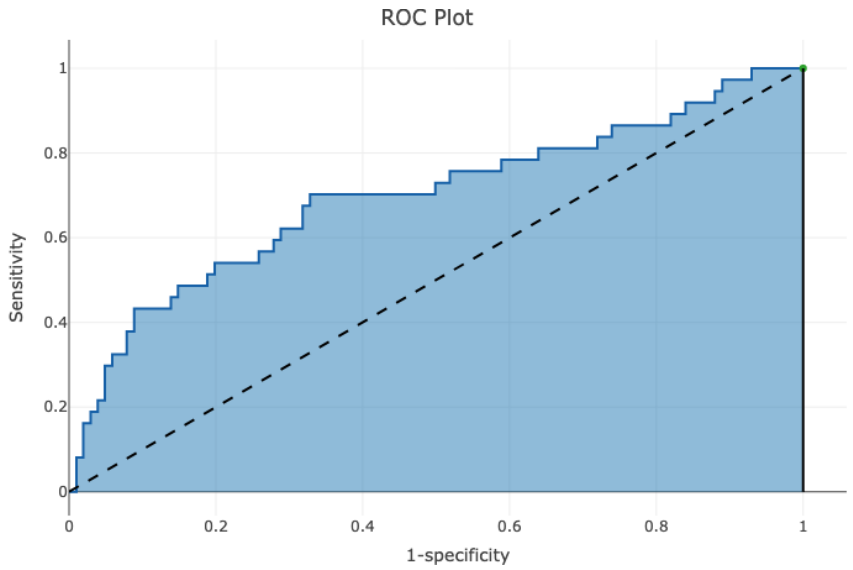
- Stroke:
  - 28,082 patients
  - 243 outcome events (0.9%)
  - AUROC of 0.73

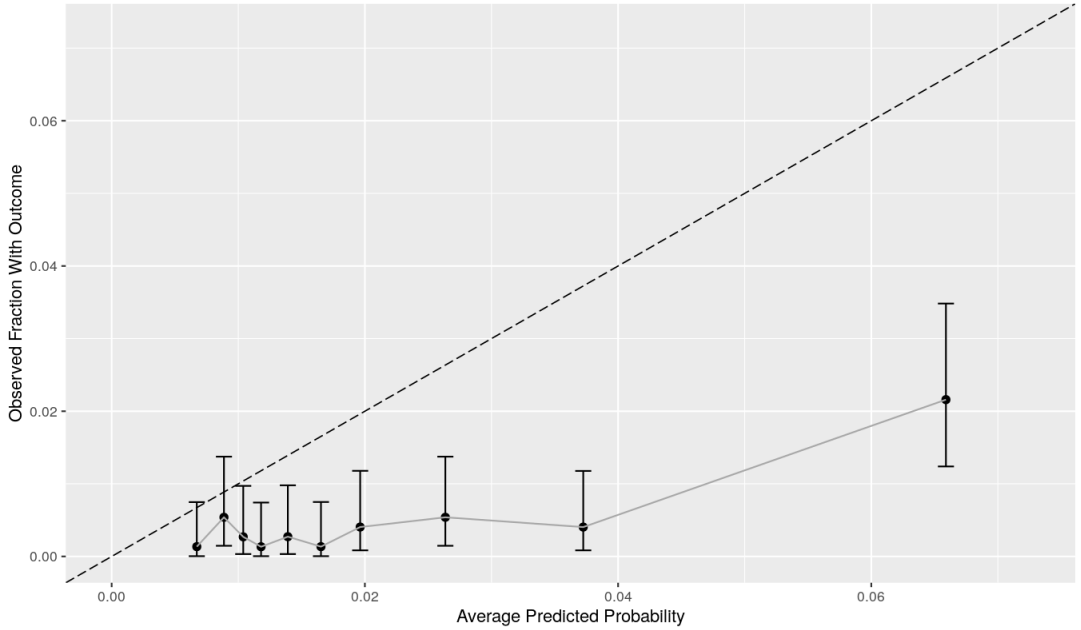




External validation (IQVIA EHR Germany)

- Stroke:
  - 7,416 patients
  - 37 outcome events (0.5%)
  - AUROC of 0.70





RESULTS

Model	Internal AUROC	External AUROC median (min-max)
Serious Infection	0.75	0.67 (0.61-0.82)
Myocardial Infarction	0.77	0.68 (0.49-0.76)
Stroke	0.78	0.73 (0.63-0.79)

- Online results at: 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.

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For more information:

c.yang@erasmusmc.nl

www.ehden.eu

@IMI_EHDEN

IMI_EHDEN

github.com/EHDEN

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