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Development and external validation of prediction models for adverse health outcomes in rheumatoid arthritis: a multinational real-world cohort analysis

Cynthia Yang, Erasmus MC



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Development and external validation of prediction models for adverse health outcomes in rheumatoid arthritis: A multinational real-world cohort analysis

Cynthia Yang ^{a, 1}, Ross D. Williams ^{a, 1}, Joel N. Swerdel ^b, João Rafael Almeida ^c, Emily S. Brouwer ^b, Edward Burn ^{d, e}, Loreto Carmona ^f, Katerina Chatzidionysiou ^g, Talita Duarte-Salles ^e, Walid Fakhouri ^h, Antje Hottgenroth ⁱ, Meghna Jani ^j, Raivo Kolde ^k, Jan A. Kors ^a, Lembe Kullamaa ^{l, m, n}, Jennifer Lane ^d, Karine Marinier ^o, Alexander Michel ^p, Henry Morgan Stewart ^q, Albert Prats-Urbe ^d, Sulev Reisberg ^{k, r, s}, Anthony G. Sena ^{a, b}, Carmen O. Torre ^q, Katia Verhamme ^a, David Vizcaya ^t, James Weaver ^{b, u}, Patrick Ryan ^{b, u}, Daniel Prieto-Alhambra ^d, Peter R. Rijnbeek ^a





STUDY-A-THON ON RHEUMATOID ARTHRITIS

- The European Health Data Network (EHDEN) and OHDSI organized a **5-day study-a-thon** to get from **study design** to **study results**.
- A multidisciplinary team consisting of rheumatologists, clinicians, epidemiologists, data custodians, and data scientists.









Some of our team members, January 2020, Barcelona.



BACKGROUND

- EULAR guidelines recommend methotrexate (MTX) monotherapy.
- Which RA patients initiating MTX monotherapy are at high risk of adverse health outcomes?

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

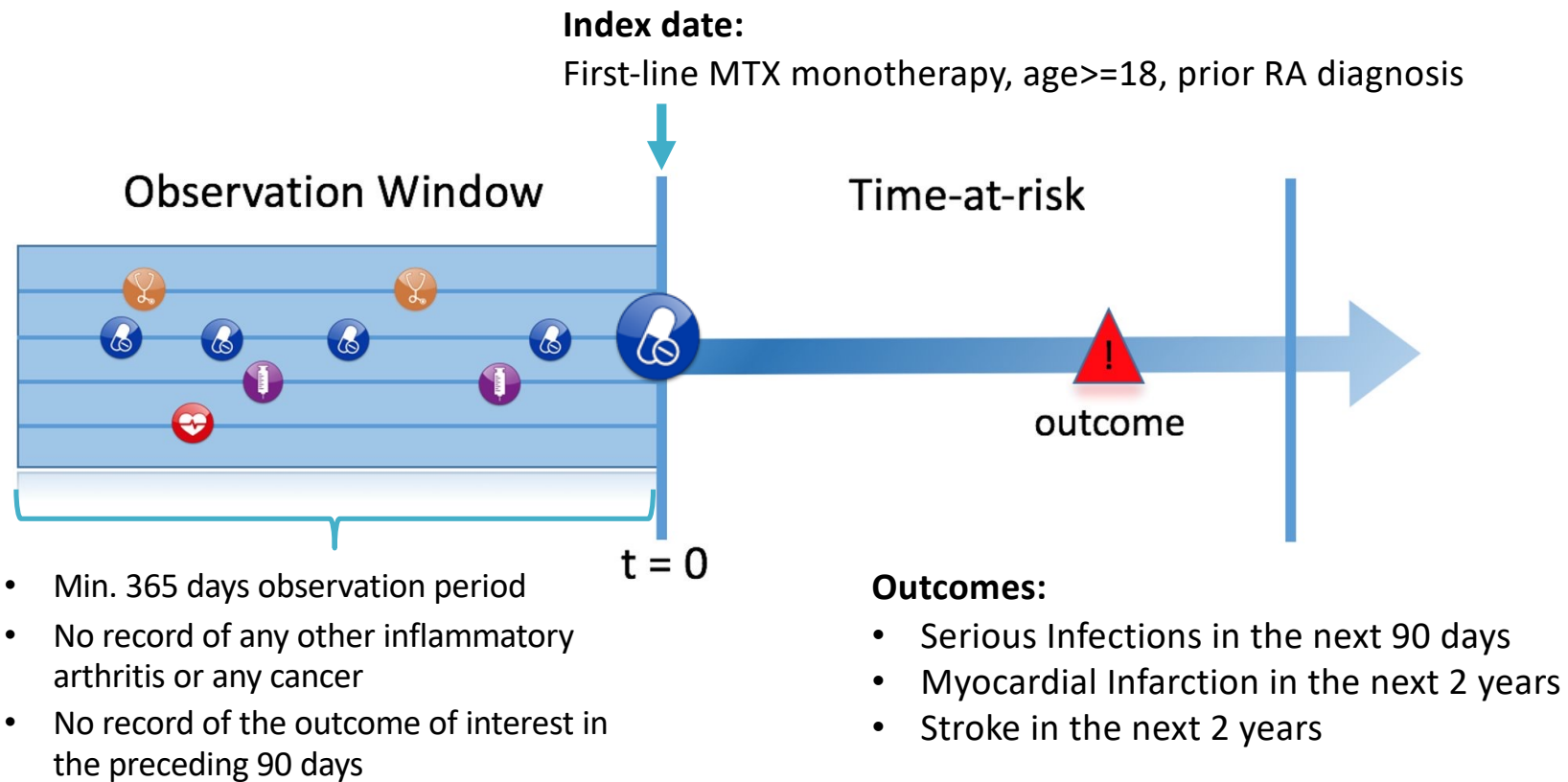
Josef S Smolen ¹, Robert B M Landewé,^{2,3} Johannes W J Bijlsma,⁴
Gerd R Burmester,⁵ Maxime Dougados,⁶ Andreas Kerschbaumer ¹, Iain B McInnes,⁷
Alexandre Sepiano ⁸, Ronald F van Vollenhoven,⁹ Maarten de Wit ¹⁰,
Daniel Aletaha,¹ Martin Aringer ¹¹, John Askling,¹² Alejandro Balsa,¹³
Maarten Boers,¹⁴ Alfons 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 a variety of adverse health outcomes in RA patients initiating first-line MTX monotherapy.



PROBLEM DEFINITION





DATASETS

- Health data from claims and electronic health records (EHR) were used from:
 - 6 European countries (Spain, Estonia, Netherlands, Germany, France, UK)
 - USA (7 databases)
 - Australia
 - Japan
- All data standardized to the OMOP CDM to enable common analytics.



MODEL DEVELOPMENT AND VALIDATION

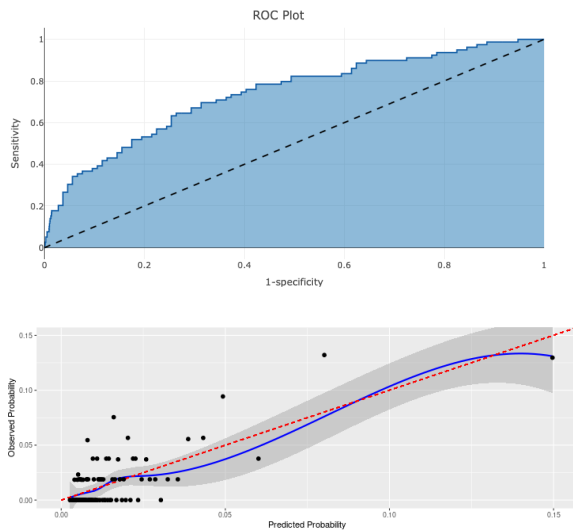
- Two LASSO logistic regression models per outcome:
 - Benchmark (age groups, sex)
 - Data-driven approach (age groups, sex, conditions, drugs)
- Model development on 21,547 patients from Optum® De-identified Clinformatics® Data Mart Database (USA claims, 87m patients, 2001-2020):
 - Model training on 75% of the patients
 - Internal validation on 25% of the patients
- External validation on 131,928 patients from 14 databases.



INTERNAL VALIDATION (OPTUM CLAIMS USA)

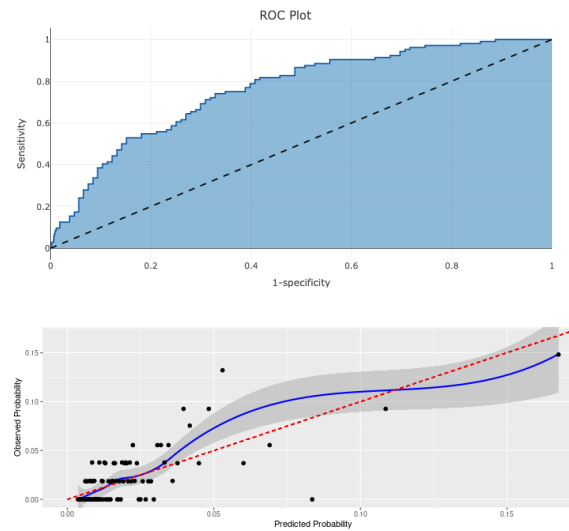
- Serious Infection:

- 21,267 patients
- 316 outcome events (1.5%)
- 87 predictors selected
- AUROC of 0.74



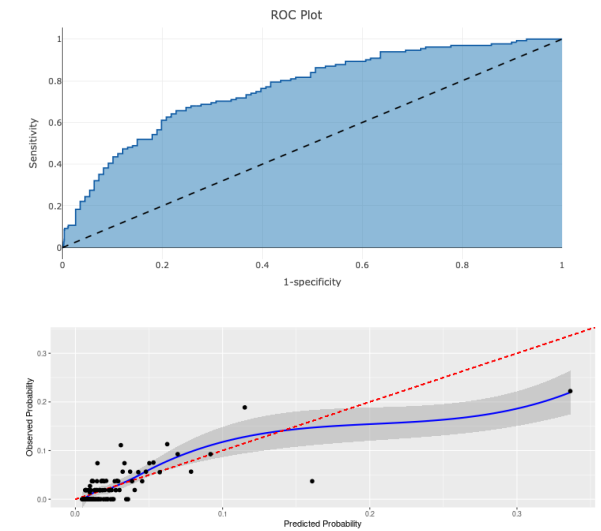
- Myocardial Infarction:

- 21,463 patients
- 417 outcome events (1.9%)
- 64 predictors selected
- AUROC of 0.76



- Stroke:

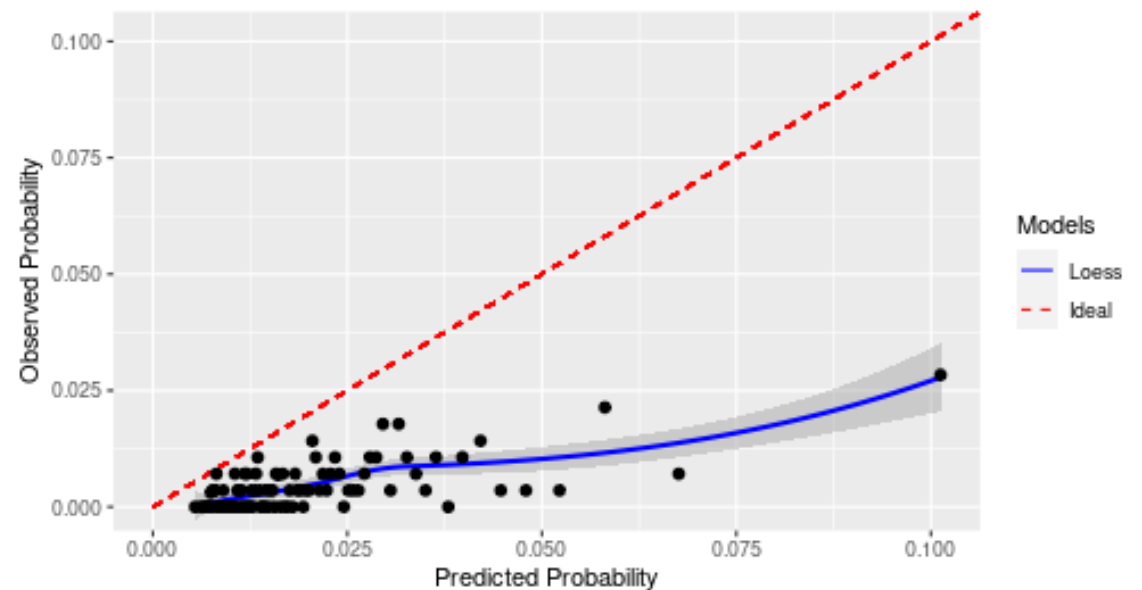
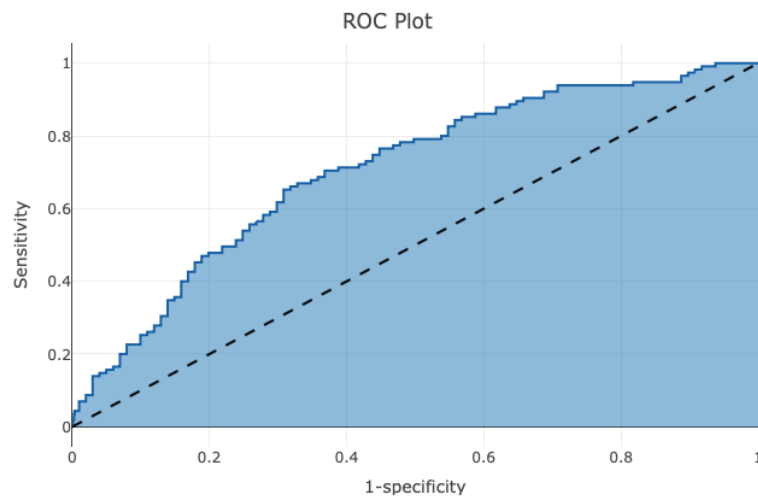
- 21,425 patients
- 527 outcome events (2.5%)
- 90 predictors selected
- AUROC of 0.77





EXTERNAL VALIDATION (IQVIA US AMBULATORY EHR)

- Stroke:
 - 28,163 patients
 - 100 outcome events (0.4%)
 - AUROC of 0.71





RESULTS DATA-DRIVEN APPROACH

Outcome	Internal AUROC	External AUROC median (min-max)
Serious Infection	0.74	0.70 (0.62-0.83)
Myocardial Infarction	0.76	0.68 (0.56-0.82)
Stroke	0.77	0.74 (0.63-0.95)

- 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 showed good performance across multiple databases, although for some databases, the models may benefit from recalibration.
- Research could be conducted to prove the value of the models as implemented in administrative or EHR software to generate automatic reminders.



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For more information:

c.yang@erasmusmc.nl



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