FRI0106 RESULTS OF A SYSTEMATIC LITERATURE REVIEW OF PROGNOSTIC FACTORS IN RHEUMATOID ARTHRITIS AS A BASIS FOR A PROSPECTIVE RHEUMATOLOGISTS SURVEY

L. Carmona[1], T. Otón[1], A. Royo[2], J.L. Baquero[3], S. Luján[2], S. Muñoz-Fernández[4]. *[1]Instituto de Salud Musculoesquelética; [2]Medical Dpt., Bristol-Myers Squibb; [3]Departamento Científico, Scientia Salus; [4]Rheumatology, Hospital Universitario Infanta Sofía, Universidad Europea, Madrid, Spain*

Background: Selecting the most appropriate therapy for each patient with rheumatoid arthritis (RA) is crucial in order to prevent joint damage, particularly in patients with rapidly progressing disease. The literature on prognostic factors is tremendous, being practical to summarize which factors are most strongly associated with a particular outcome and what is the utility that rheumatologists assign to these factors.
Objectives: To identify well established factors predicting long-term outcomes in RA, as the basis for a survey.
Methods: The identification of the factors was performed via an overview of systematic reviews studying prognostic factors in RA, followed by scoping reviews for individual factors. All searches were conducted in PubMed. In order to be included in the overview, the study had to be a systematic review of prognostic factors of any of the following outcomes: disability, mortality, remission, response to treatment, or radiological damage. All factors identified, in positive or negative association with the selected outcomes, were compiled in a matrix of factors * outcomes. Subsequent scoping literature reviews were performed for each combination of the matrix.
Results: The overview of systematic reviews allowed the identification of 36 prognostic factors (see Table 1).

Table 1. Prognostic factors identified in the overview of systematic reviews

Outcomes	Prognostic factors	
Disability	Genetic markers	Genetic polymorphisms
	Quality of life index	HAQ
Mortality	Genetic markers	Shared epitope
	Medical history	Lung disease
No remission	Medical history	Clinical Presentation
		Advanced age
		Age at disease onset
		Duration of disease
		Tobacco
		Obesity
		Comorbidities
		Disease activity
		Monotherapy
		Biological treatment
		Response to treatment
	Biomarkers	RF
		ACPA
		RFA
		IL2
		RANKL
		Vitamin D
	Radiological data	Residual synovitis by US
		Scintigraphy
		MRI
	Treatment	Treat to target
		Remission
No response to treatment	Biomarkers	Calprotectin
		RF
	Treatment	Treatment Failure
Structural damage	Genetic markers	Shared epitope
		Polymorphisms
	Radiological data	Erosions
	Biomarkers	Calprotectin
		RF
		ACPA
		Composite activity indices
	Treatment	Minimum treatment
		Combination Therapy Effect
		Recruitment time in clinical trials

After a round of discussions, we decided to remove all factors depending on treatment or study methodology for the scoping reviews, considering that they could not properly be considered prognostic factors but modifiers. Following the scoping reviews, we obtained a list of studies of prognostic factors, with methodological characteristics and 27 reviews of specific prognostic factors and outcomes. With this information, a survey addressed to practicing rheumatologists was developed to test how often they use the various factors to make long-term predictions, and how strong they think the association with outcome is.
Conclusions: We have analyzed and compiled a summary of prognostic factors published in RA and their predictability of long-term outcomes. This may act as a reference for cross-factor comparison and evidence-based risk assimilation and serve as a basis of surveying the value of such factors.
Acknowledgements: This study was funded by Bristol-Myers Squibb.
Disclosure of Interest: L. Carmona Grant/research support from: BMS, T. Otón Grant/research support from: BMS, A. Royo Employee of: BMS, J. L. Baquero Grant/research support from: BMS, S. Luján: None declared, S. Muñoz-Fernández Grant/research support from: BMS
DOI: 10.1136/annrheumdis-2017-eular.4765

FRI0107 DEVELOPMENT OF A PREDICTIVE MODEL FOR RHEUMATOID ARTHRITIS MORTALITY USING RANDOM SURVIVAL FOREST

L. Rodriguez-Rodriguez[1,2], J.M. Lezcano[3], E. Soudah[4], J.Á. Jover[1], I. González-Álvarez[5,6], F. Salazar[4], L. Abásolo[1,2]. *[1]Rheumatology, Hospital Clínico San Carlos; [2]San Carlos Health Research Institute, Madrid, Spain; [3]Rheumatology, San Carlos Health Research Institute; [4]CIMNE-Madrid; [5]La Princesa Health Research Institute; [6]Rheumatology, Hospital de la Princesa, Madrid, Spain*

Background: Different machine learning methods have been used to develop predictive models of high quality and precision [1]. Among them, Random Survival Forests (RSF) has been proposed as an alternative to traditional survival models [2], being able to overcome most of the limitation of traditional survival techniques, such as Cox proportional hazards models.
Objectives: Our objective was to develop and internally validate a predictive model for rheumatoid arthritis (RA) mortality using Random Survival Forests (RSF).
Methods: Retrospective longitudinal study involving 1,461 patients diagnosed with RA between January 1994 and August 2011, and followed at the outpatient clinic of the Rheumatology Department of the Hospital Clínico San Carlos (Madrid, Spain) until death or September 2013. Demographic and clinical-related variables collected during the first two years after disease diagnosis were used. RSF models were developed, based on 1,000 trees. 100 iterations of each model were performed to measure the mean and standard deviation (SD) of the predictive error and the integrated Brier score (IBS). Missing values were imputed using the function implemented by the *randomForestSRC* package [3]. The predictive capacity of the variables was assessed using the "variable importance" (VIMP). Two models were constructed using the log-rank (M_{LG}) or log-rank score (M_{LGS}) splitting rules. The model with the lowest prediction error was selected. Next, those variables with negative VIMP were excluded and a final model developed.
Results: 148 patients died (10.1%). M_{LG} showed the lowest prediction error. All variables exhibited a positive VIMP. Final model showed a mean (SD) prediction error and IBS of 0.187 (0.002) and 0.150 (0.003) respectively. The most important predictor variables were age at diagnosis, median erythrocyte sedimentation rate and number of hospital admissions in the first 2 years after RA diagnosis.
Conclusions: We developed an accurate and precise model for RA mortality using RSF. Age and disease activity showed the highest influence in mortality.
References:
[1] Churpek MM, Yuen TC, Winslow C, Meltzer DO, Kattan MW, Edelson DP. Multicenter Comparison of Machine Learning Methods and Conventional Regression for Predicting Clinical Deterioration on the Wards. Crit Care Med. 2016;44: 368–74.
[2] Ishwaran H, Kogalur UB, Blackstone EH, Lauer MS. Random survival forests. Ann Appl Stat. 2008;2: 841–860.
[3] Ishwaran H, Kogalur U. Random Forests for Survival, Regression and Classification (RF-SRC) [Internet]. 2016 [cited 15 Dec 2016]. Available: https://cran.r-project.org/package=randomForestSRC.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6139

FRI0108 TIME TO FIRST TREATMENT IS ASSOCIATED WITH A REFRACTORY COURSE OF RHEUMATOID ARTHRITIS

M. Bécède[1], F. Alasti[1], L. Haupt[2], A. Kerschbaumer[1], U. Landesmann[1], G. Supp[1], J. Smolen[1], D. Aletaha[1]. *[1]Department of Internal Medicine 3, Division of Rheumatology, Medical University of Vienna; [2]Hietzing Hospital, Vienna, Austria*

Background: It is an ongoing matter of research, whether the natural course of rheumatoid arthritis (RA) can be altered by an early intervention, a concept historically referred to as the "window of opportunity" (1). So far, only short-term disease activity outcomes have been investigated (e.g. "remission off drugs"), which are, however, inherently affected by the unknown rate of underlying rate self-limiting disease. It is unclear, whether among those, who eventually develop RA, the disease course is really affected by the timing of their initial treatment.
Objectives: To explore whether the long-term course of RA is different according to the delay of initial treatment.
Methods: Based on a longitudinal observational dataset, we initially identified a group of patients with an observed refractory disease, we defined presenting with ongoing moderate or high disease activity (by the Simplified Disease Activity Index, SDAI), despite at least three courses of DMARDs, of which at least on course was a biological compound. To ensure that sufficient time had been allowed for the previous treatments to be exert their non-effects, we also required these patients to have total treatment time of at least 18 months in accordance with treat to target strategy (3 x 6 months).
We identified 399 patients with a treatment time of at least 18 months. 48 patients were excluded despite fulfilling the disease activity criteria, because they haven't experienced enough treatment courses, or had received a biological compound yet, to claim refractory disease as per our criteria above. We could include 69 refractory and 282 non-refractory patients in our analyses and then performed