

**Predicting Clinical Remission of Chronic Urticaria Using Random Survival Forests:
Machine Learning Applied to Real-World Data**

Pivneva, Irina¹, PhD, Balp, Maria-Magdalena², PhD, Geissbühler, Yvonne², PhD, Smeets, Serge², Signorovitch, James³, PhD, Royer, Jimmy¹, PhD, Liang, Yawen¹, PhD, Cornwall, Tom¹, PhD, Pan, Jutong¹, PhD, Danyliv, Andrii², PhD, McKenna, Sarah Jane⁴, MSc, Marsland, Alexander M.^{5*}, MD, Soong, Weily^{6*}, MD

¹ Analysis Group, Inc., Montréal, QC, Canada

² Novartis Pharma AG, Basel, Switzerland

³ Analysis Group, Inc., Boston, MA, United States

⁴ Novartis Business Services, Dublin, Ireland

⁵ Salford Royal NHS Foundation Trust & University of Manchester, Salford, United Kingdom

⁶ AllerVie Health-Alabama Allergy & Asthma Center, Clinical Research Center of Alabama, Birmingham, AL, United States

**Joint senior authors*

Corresponding author: Dr. Irina Pivneva

Manager, Analysis Group, Inc.

1190 avenue des Canadiens-de-Montréal

Tour Deloitte, Suite 1500

Montréal, QC H3B 0G7

Tel: 1+514-394-4458

Email: irina.pivneva@analysisgroup.com

Table E1. Diagnosis codes for urticaria

ICD-9	ICD-10	Description
<u>CSU</u>		
708.1	L50.1	Idiopathic urticaria
708.8	L50.8	Other specified urticaria
708.9	L50.9	Urticaria, unspecified
995.1	T783	Angioneurotic edema (secondary)*
<u>CIndU</u>		
708.0	L50.0	Allergic urticaria (secondary)*
708.2	L50.2	Urticaria due to cold and heat
708.3	L50.3	Dermatographic urticaria
708.4	L50.4	Vibratory urticaria
708.5	L50.5	Cholinergic urticaria
—	L50.6	Contact urticaria
—	L56.3	Solar urticaria

* Secondary code was considered only when a patient had ≥ 1 non-secondary diagnosis code

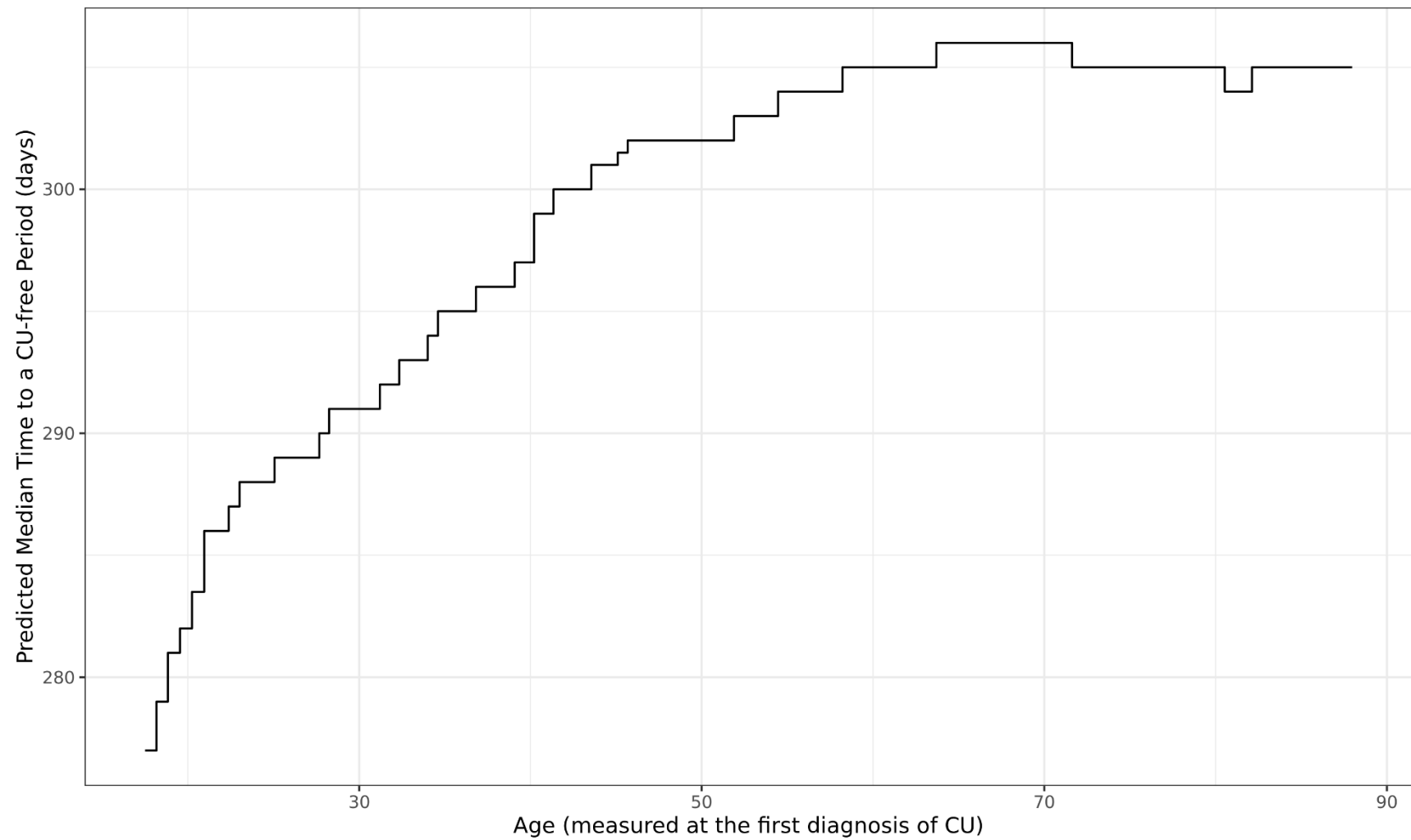
Abbreviations: CIndU = chronic inducible urticaria; CSU = chronic spontaneous urticaria; CU = chronic urticaria; ICD-9/10 = International Classification of Diseases, 9th/10th edition.

Table E2. Urticaria-related treatments

Class	Treatment(s) included
Antidepressants	Doxepin
Antihistamines*	Acrivastine, Astemizole, Azelastine, Bepotastine, Bilastine, Brompheniramine, Carbinoxamine, Cetirizine, Chlorphenamin/chlorpheniramine, Cimetidine, Clemastine, Cyproheptadine, Desloratadine, Dexbrompheniramine, Dexchlorpheniramine, Diphenhydramine, Ebastine, Emadastine, Fexofenadine, Hydroxyzine (atarax), Ketotifen, Levocetirizine, Loratadine, Mizolastine, Pramoxine, Promethazine, Pyrilamine, Quifenadine, Ranitidine, Rupatadine, Terfenadine, Trimeprazine, Triprolidine
Colchicine	Colchicine
Cyclosporine*	Cyclosporine
Dapsone	Dapsone
Hydroxychloroquine	Hydroxychloroquine
Immunosuppressants	Azathioprine, Mycophenolate, Methotrexate, Tacrolimus
Leukotriene receptor antagonists*	Montelukast, Zafirlukast
Levamisole	Levamisole
Narrowband	Narrowband
Mesalazine	Mesalazine
Nifedipine	Nifedipine
Oral corticosteroids	Methylprednisone, Prednisolone, Prednisone
Omalizumab*	Omalizumab
Sulfasalazine	Sulfasalazine
Stanozolol	Stanozolol
Thyroid hormone	Levothyroxine
Warfarin	Warfarin

* Indicates treatments specified for urticaria in the AAAAI and ACAAI guideline *The diagnosis and management of acute and chronic urticaria: 2014 update* [14]. Treatments that are not specified in the guidelines were required to be accompanied by a CU diagnosis on the same day as the treatment. All types of antihistamines are listed here independent of their subclass.

Figure E1. Partial dependence plot of time to clinical remission as a function of age



Abbreviation: CU = chronic urticaria.