

Seek COVER: Development and validation of a personalized risk calculator for COVID-

19 outcomes in an international network

Ross D. Williams^{1,†} MSc, Aniek F. Markus^{1,†} MSc, Cynthia Yang¹ MSc, Talita Duarte Salles² PhD, Scott L. DuVall³ PhD, Thomas Falconer⁴ MS, Jitendra Jonnagaddala⁵ PhD, Chungsoo Kim⁶ PharmD, Dr. Yeunsook Rho⁷ PhD, Andrew Williams⁸ PhD, Amanda Alberga⁹, MPH, Min Ho An¹⁰ MD, María Aragón² PhD, Carlos Areia¹¹ MSc, Edward Burn^{2,12} PhD, Young Hwa Choi¹³ MD PhD, Iannis Drakos¹⁴ PhD, Maria Tereza Fernandes Abrahão¹⁵ PhD, Sergio Fernández-Bertolín² MSc, George Hripcsak⁴ MD, Benjamin Skov Kaas-Hansen^{16,17} MD, Prasanna L Kandukuri¹⁸ MS, Jan A. Kors PhD¹, Kristin Kostka¹⁹ MPH, Siaw-Teng Liaw⁵ MBBS PhD, Kristine E. Lynch, PhD³, Gerardo Machnicki²⁰ PhD, Michael E. Matheny²¹, MD, Daniel Morales²² PhD, Fredrik Nyberg²³ MD PhD, Rae Woong Park²⁴ MD, PhD, Albert Prats-Urbe¹² MPH, Nicole Pratt²⁵ PhD, Gowtham Rao²⁶ PhD MD PhD, Christian G. Reich¹⁹ MD PhD, Marcela Rivera²⁷ PhD, Tom Seinen¹ MSc, Azza Shoaibi²⁶ MPH PhD, Matthew E Spotnitz⁴ MD, Ewout W. Steyerberg^{28,29} PhD, Marc A. Suchard³⁰ MD PhD, Seng Chan You²⁴ MD, Lin Zhang^{31,32} MD PhD, Lili Zhou¹⁸ PhD, Patrick B. Ryan²⁶ PhD, Daniel Prieto-Alhambra¹² MD PhD, Jenna M. Reys^{26,&} PhD, Peter R. Rijnbeek^{1,&,*} PhD

¹Department of Medical Informatics, Erasmus University Medical Center, Rotterdam, The Netherlands

²Fundacio Institut Universitari per a la recerca a l'Atencio Primaria de Salut Jordi Gol i Gurina (IDIAPJGol)

³Department of Veterans Affairs, University of Utah, Salt Lake City, UT, US,

⁴Department of Biomedical Informatics, Columbia University, New York, NY

⁵School of Public Health and Community Medicine, UNSW Sydney

⁶Department of Biomedical Sciences, Ajou University Graduate School of Medicine, Suwon, Republic of Korea

⁷Department of Bigdata, Health Insurance Review & Assessment Service, Republic of Korea

⁸Tufts Institute for Clinical Research and Health Policy Studies, Boston, MA, 02111, USA

⁹Independent Epidemiologist, OHDSI

¹⁰So Ahn Public Health Center, Wando County Health Center and Hospital, Wando, Republic of Korea

¹¹Nuffield Department of Clinical Neurosciences, University of Oxford

¹²Centre for Statistics in Medicine, NDORMS, University of Oxford

¹³Department of Infectious Diseases, Ajou University School of Medicine, Suwon, Republic of Korea

¹⁴Center for Surgical Science, Koege, Denmark

¹⁵Faculty of Medicine, University of Sao Paulo, Sao Paulo, Brazil

¹⁶Clinical Pharmacology Unit, Zealand University Hospital, Roskilde, Denmark

¹⁷NNF Centre for Protein Research, University of Copenhagen, Denmark

¹⁸Abbvie, Chicago, United States

¹⁹Real World Solutions, IQVIA, Cambridge, MA, United States

²⁰Janssen Latin America, Buenos Aires, Argentina

²¹Department of Veterans Affairs, USA; Vanderbilt University, USA

²²Division of Population Health and Genomics, University of Dundee, UK

**²³School of Public Health and Community Medicine, Institute of Medicine, Sahlgrenska Academy,
University of Gothenburg Gothenburg, Sweden**

**²⁴Department of Biomedical Informatics, Ajou University School of Medicine, Suwon, Republic of
Korea**

**²⁵Quality Use of Medicines and Pharmacy Research Centre, University of South Australia, Adelaide,
Australia**

²⁶Janssen Research & Development, Titusville, NJ, USA

²⁷Bayer Pharmaceuticals, Bayer Hispania, S.L., Barcelona, Spain

²⁸Department of Public Health, Erasmus University Medical Center, Rotterdam, The Netherlands

**²⁹Department of Biomedical Data Sciences, Leiden University Medical Center, Leiden, The
Netherlands ³⁰Department of Biostatistics, UCLA Fielding School of Public Health, University of
California, Los Angeles, CA, USA**

³¹School of Public Health, Peking Union Medical College, Beijing, China;

³²Melbourne School of Public Health, The University of Melbourne, Victoria, Australia.

†These authors contributed equally as co-first authors.

&These authors contributed equally as co-last authors.

Abstract

Abstract text goes here, justified and in italics and be no more than 250 words. All submission types have the same format and length requirements. Use a minimum of 11pt font when writing all sections of this abstract.

Research Category (please highlight or circle which category best describes your research)

patient-level prediction

Introduction

COVID-19 is causing high mortality worldwide. Quantifying the risk of poor outcomes in COVID-19 infected patients could help develop strategies to shield the vulnerable during de-confinement¹.

Methods

We analyzed a federated network of electronic medical records and administrative claims data from 14 data sources and 6 countries, mapped to a common data model.

Participants

Model development used a patient population consisting of >2 million patients with a general practice (GP), emergency room (ER), or outpatient (OP) visit with diagnosed influenza or flu-like symptoms any time prior to 2020. The model was validated on patients with a confirmed COVID-19 diagnosis across five databases from South Korea, Spain and the United States.

Predictors and outcomes

Age, sex, historical conditions, and drug use prior to index date were considered as candidate predictors.

Outcomes included i) hospitalization with pneumonia, ii) hospitalization with pneumonia requiring

intensive services or death, and iii) death in the 30 days after index date.

Results

Overall, 44,507 COVID-19 patients were included for model validation, after initial model development and validation using 6,869,127 patients with influenza or flu-like symptoms. We identified 7 predictors (history of cancer, chronic obstructive pulmonary disease, diabetes, heart disease, hypertension, hyperlipidemia, and kidney disease) which combined with age and sex could discriminate which patients would experience any of our three outcomes. The models achieved high performance in influenza. When transported to COVID-19 cohorts, the AUC ranges were, COVER-H: 0.69-0.81, COVER-I: 0.73-0.91, and COVER-F: 0.72-0.90. Calibration was overall acceptable, with overestimated risk in the most elderly and highest risk strata.

Conclusion

Three 9-predictor models perform well for COVID-19 patients for predicting hospitalization, intensive services and fatality. The models could aid in reassurance of low risk patients and shield high risk patients from COVID-19 during de-confinement.

References

1. Smith George Davey, Spiegelhalter David. Shielding from covid-19 should be stratified by risk *BMJ* 2020; 369 :m2063