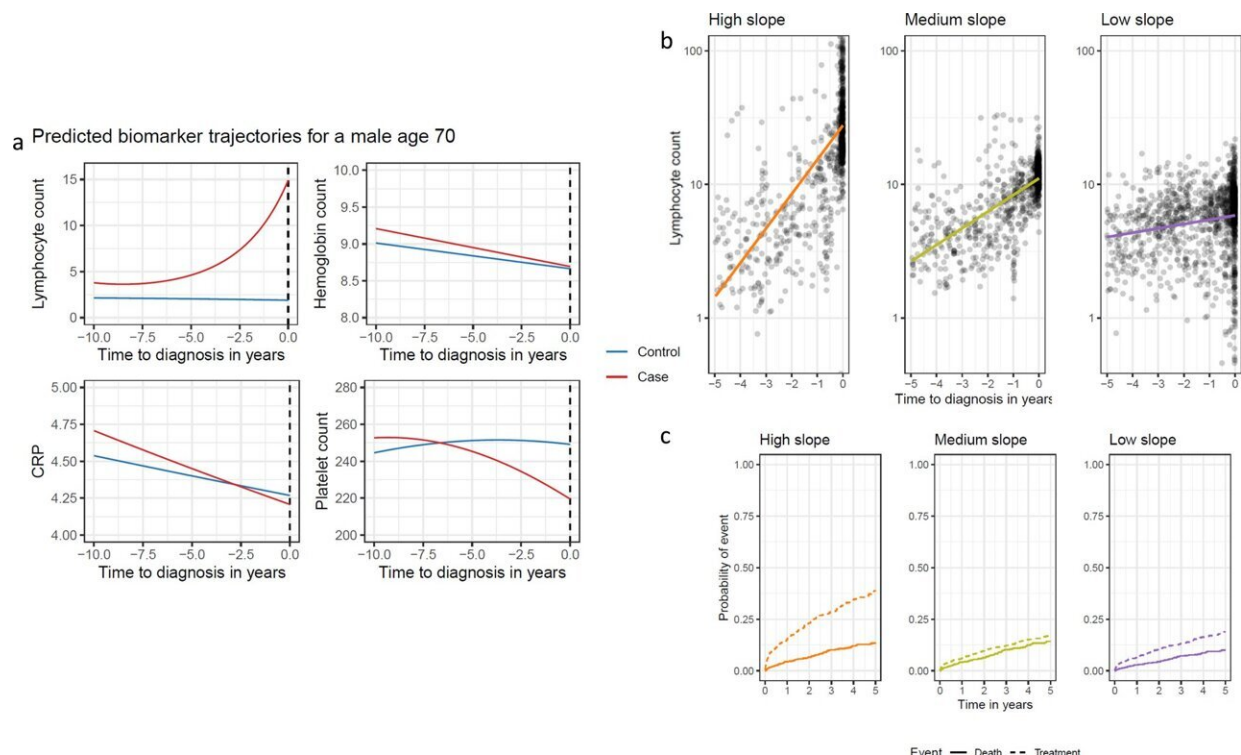# An app to help doctors help patients with leukemia

June 24 2022

Model predictions for a 70-year-old person. **a** Predictions for a 70-year-old male based on the linear regression model for absolute lymphocyte count (ALC), hemoglobin count, CRP, and platelet count. **b** Observed ALC for the three slope groups. The colored line is a linear smoother. **c** The graphs show the cumulative incidence of time to first treatment or death from time of diagnosis for the three pre-diagnostic slope groups for a male with CLL-IPI 1. CRP C-reactive protein, CLL-IPI international prognostic index for chronic lymphocytic leukemia. Credit: *Communications Medicine* (2022). DOI: 10.1038/s43856-022-00117-4

Within five years, 25% of patients suffering from chronic Lymphocytic leukemia (CLL) will develop a serious infection or need early treatment for CL: 10% of these risk dying within a month.

In order to help these patients, doctors would like to be able to identify those at risk of developing infections immediately after they have been diagnosed with CLL.

A team of researchers from the University of Copenhagen and Rigshospitalet has made this their mission, and this has led to the development of an app.

Chief physician and Clinical Associate Professor Carsten Niemann, who is part of the team responsible for the new study, explains:

"It has improved our chances of identifying those patients, once diagnosed, who will require treatment and close follow-up. We have developed an app that allows doctors to enter previous and current blood test results and thus receive data on the individual patient's risk of a severe course of illness," says Carsen Niemann from the Department of Clinical Medicine at the University of Copenhagen and the Department of Haematology at Rigshospitalet, Denmark's leading hospital.

If a patient is considered to be in the risk group, they may benefit from starting treatment earlier. A new study seeks to determine whether this is indeed the case.

And even though the researchers still do not know whether patients would benefit from starting treatment earlier, the new knowledge will be able to ease pressure on the healthcare system and patients, Carsten Niemann explains:

"Instead of practicing the same frequency of monitoring and hospital

follow-up for all patients, we are able to target efforts to those at high risk of a severe course of illness."

The app is currently in its pilot phase and still has not been approved as an official aid. Nevertheless, it can be used, even though it does not save the data entered.

"We are working on a new project which aims to make another version of the app interact with the medical records system. This requires a series of authorizations, which means that for the time being only the pilot version of the app is available," says Carsten Niemann.

Blood tests from 1.3 million Danes

As part of the study, the researchers analyzed a data set containing 112 million blood tests from 1.3 million Danes, 1,123 of whom suffer from CLL.

A main aim was to study the change over time in lymphocyte count, which is the concentration of a specific white blood cell in the blood.

"We knew that in the years leading up to diagnosis, CLL patients exhibited a high number of these white blood cells. But we did not know how or precisely when the number started to increase. It is these numbers, among others, that we have analyzed in order to predict who is at risk of developing CLL and who is at risk of suffering from an infection," explains first author of the study medical doctor Michael Asger Andersen from the Department of Clinical Pharmacology at Rigshospitalet.

Patients were also monitored via the Danish CLL register, which gave the researchers access to data on prognosis, treatment and course of illness as well as patients' unique mutations in the CLL cells.

"Another important parameter has been the connection between the development in white blood cell numbers and mutations in the genes responsible for the cells' transformation into cancer cells. This is referred to as patients' IGHV mutation status, and driver mutations," says Michael Asger Andersen.

"We were able to demonstrate that those patients experiencing rapid growth in white blood cells—the lymphocyte count—also appear to harbor more mutations which help make the cancer cells more aggressive. And vice versa: Those experiencing a more modest increase in white blood cell numbers, harbor fewer mutations, but mutated IGHV status. That is, the growth pattern is closely connected to patients' IGHV mutation status and pattern of driver mutations."

The Danish health records offer a unique advantage

The researchers subsequently inserted these findings into the CLL-PLY app.

"A lot of studies have been unable to merge genetic data with routine blood test results; here the Danish health records provide us with a unique advantage," says co-author of the study Clinical Professor and chief physician Christen Lykkegaard Andersen from the Department of Public Health at the University of Copenhagen and the Department of Haematology at Rigshospitalet.

In particular, the researchers have benefited from the Copenhagen Primary Care Laboratory (CopLab) database, which constitutes general practitioners' laboratory data from around 2000 till 2016.

Parallel with this study, the researchers have been involved in a major European collaboration compiling information about mutations and clinical data from a lot of different patients.

"We are constantly seeking to expand the dataset in order to strengthen the association between routine blood test results and genetic data and thus improve results in the future," Christen Lykkegaard Andersen concludes.

The research was published in *Communications Medicine*.

More information: Michael Asger Andersen et al, Pre-diagnostic trajectories of lymphocytosis predict time to treatment and death in patients with chronic lymphocytic leukemia, *Communications Medicine* (2022). DOI: 10.1038/s43856-022-00117-4

Get the app: clllab.shinyapps.io/cllprognosis/

Provided by University of Copenhagen

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