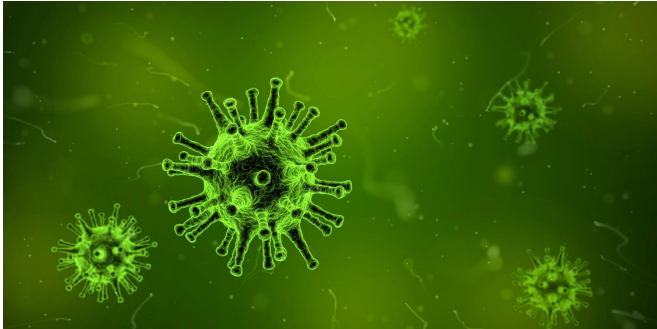


Flu forecasting tool uses evolution to make earlier predictions

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Each year, public health officials monitor the spread of influenza to identify which flu strains need to go into that year's vaccines and where outbreaks will occur. But it can be difficult to predict how bad a particular flu season will be until people actually start getting sick.

A new flu forecasting tool built by scientists at the University of Chicago aims to make better predictions by combining data about how the virus spreads with an estimate of how much the current virus evolved compared to recent years. Using historical data as a test, the new [model](#) accurately predicted the total number of cases for each [season](#) in the U.S. from 2002 to 2016, and produced an accurate, real-time prediction for the 2016-17 season before it started last year.

The researchers say the new model, described this week in *Science Translational Medicine*, can be used to complement existing forecasting tools that track flu outbreaks in real time by providing an early warning before the season starts.

"Combining information about the evolution of the virus with epidemiological data will generate disease forecasts before the season begins, significantly earlier than what is currently possible,"

said Mercedes Pascual, PhD, professor of ecology and evolution at UChicago and senior author of the study. "You could imagine using our model to make an early prediction about overall severity of the season, and then use other methods to forecast the timing of the outbreak once it begins."

Each year, four influenza strains circulate in the human population: H3N2, H1N1, and two B variants. These viruses spread seasonally each year because of a phenomenon known as antigenic drift. They evolve just enough to evade human immune systems, but not enough to develop into completely new versions of the virus.

If the virus changed a lot, more people get sick because they haven't been exposed to that particular variation. But most flu forecasting models don't factor in this change. Instead, they are based on mathematical calculations of how quickly the virus is spreading—and these projections can't be made until the current season is already underway.

For the new model, Pascual and Xiangjun Du, PhD, a postdoctoral fellow at UChicago who led the study, analyzed genetic sequences from previous years of the H3N2 virus. They then compared them to early samples of the current virus that were collected before the season started each year. This allowed them to create an evolutionary index for the current virus, or a measure of how much it changed. Adding this crucial piece of information to the [new model](#) generates an early estimate of the overall severity of the coming [flu season](#), because they can make a projection as soon as current year's variation of the virus starts to emerge in the spring and summer.

"Every two or three years, there is a big genetic change in the virus, which can make many more people sick," Du said. "Without factoring evolution into the model, you cannot capture these peaks in the number of cases."

The model was built with historical data about the H3N2 virus, although it could be adapted for other strains of flu. The researchers tested its accuracy by seeing how well it predicted past seasons from 2002-2016, including years that weren't used to initially calibrate the tool (the final five from 2011-2016). It generated accurate estimates of the overall number of cases in the U.S. for each year, and produced an accurate forecast for the 2016-17 season before it started last fall.

So, what's in store for this flu season?

"That's the million-dollar question," Pascual said. "Our analysis for this year showed that the [virus](#) is already changing in a significant way. We predict an outbreak that is above average but moderate, not severe, because last year was such a bad season."

The study, "Evolution-informed forecasting of seasonal influenza A (H3N2)," was supported by the University of Chicago. Additional authors include Aaron A. King and Robert J. Woods from the University of Michigan, who were supported by the National Institutes of Health, the National Institute of General Medical Sciences and the National Institute of Allergy and Infectious Diseases.

More information: X. Du et al., "Evolution-informed forecasting of seasonal influenza A (H3N2)," *Science Translational Medicine* (2017). [stm.sciencemag.org/lookup/doi/ ... scitranslmed.aan5325](http://stm.sciencemag.org/lookup/doi/...scitranslmed.aan5325)

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