Underreporting of Zika is rife; researchers project epidemic's spread

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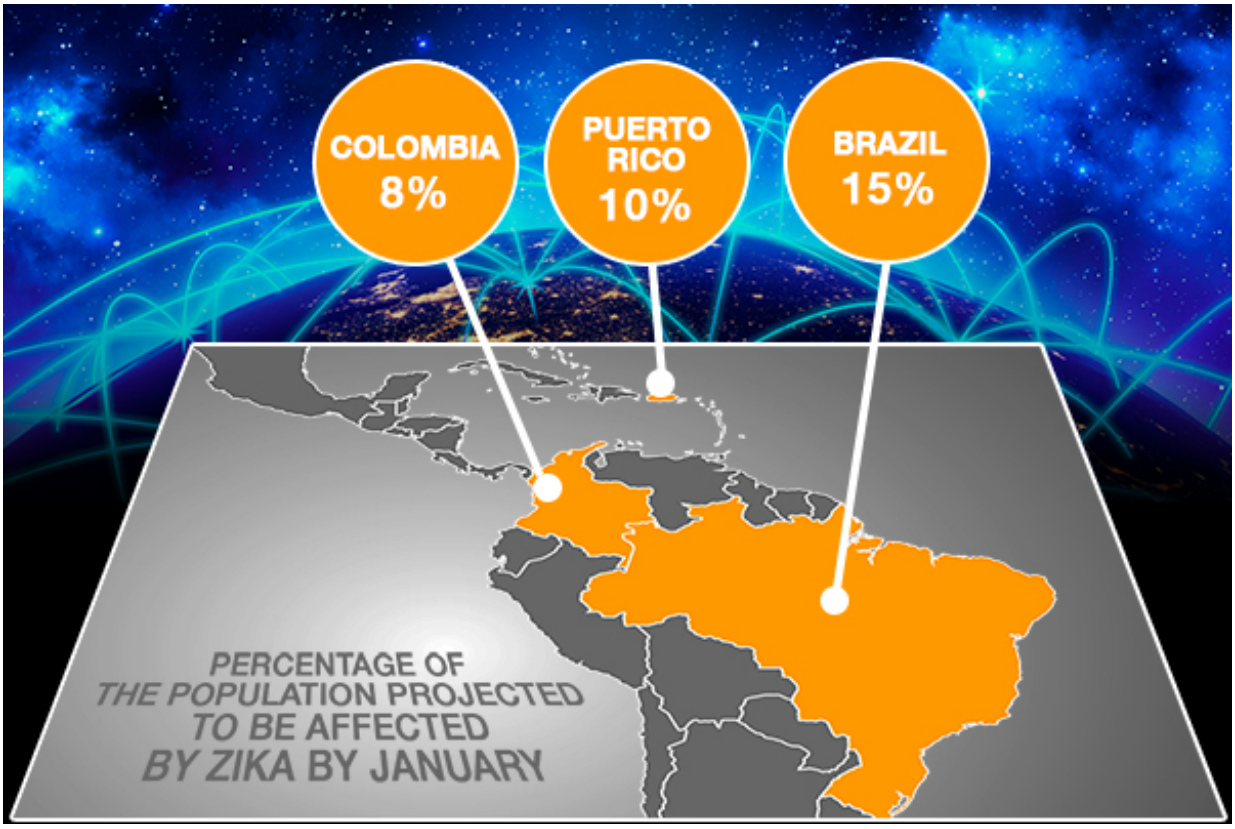

A team led by Northeastern professor Alessandro Vespignani responded to a "call to arms" to model the spread of the Zika virus, revealing the disparity between the number of reported cases and the number of projected cases of this largely asymptomatic disease. The results will help countries in the Americas plan a response. Credit: YoungHee Jang/Northeastern University

With the report from Florida Gov. Rick Scott on Monday that 14 people in the state have been infected with the Zika virus most likely through mosquito transmission, the concern about outbreaks in the U.S. has intensified.

The news comes on the heels of new research by Northeastern professor Alessandro Vespignani that can help countries in the Americas plan a response.

The new study, along with interactive maps, provides current numbers as well projections for the number of Zika cases in the Americas through January 2017. It also provides projections for the number of microcephaly cases associated with the disease through October 2017, a date chosen to allow for the nine months of pregnancy. Microcephaly is a serious neurological birth defect characterized by a smaller than normal head.

The research is a collaboration overseen by the Center for Inference and Dynamics of Infectious Diseases, a Models of Infectious Disease Agent Study Center of Excellence funded by the National Institutes of Health.

Tackling Zika has been "a call to arms," says Vespignani. "We've been working on the modeling around the clock since January," adds Matteo Chinazzi a postdoctoral research associate in Vespignani's laboratory for the Modeling of Biological and SocioTechnical Systems, or MOBS, and a coauthor of the study.

The team of 14 researchers uses large- scale computational epidemic models that integrate socio- demographic and travel data of target populations along with simulations of infection transmission among millions of individuals to reconstruct disease spread in the past and project it into the future.

Under- reporting is rife in affected countries because up to 80 percent of people with the disease are asymptomatic, says Vespignani, Sternberg Distinguished Professor of Physics and director of the Network Science Institute at Northeastern. "Even of those with symptoms, probably only one- third will go to the doctor and get diagnosed," he says.

Indeed, the number of travel- associated cases of Zika in the U.S. reported by the Centers for Disease Control and Prevention may be just the tip of the iceberg, according to the research.

The team, half of which is at Northeastern, projected that as of June 15 there were close to 30,000 cases of travel- related Zika in the U.S., a number 25 times greater than that reported by the CDC on the same date.

The discrepancy results from the difference between reported cases of the mosquito- borne virus—those actually diagnosed and reported to the CDC's surveillance system—and those that fly under the radar but that the researchers' modeling algorithms can project.

"We don't project very large outbreaks in the continental U.S.," says Vespignani, whose lab has been running the simulations of infection transmission—a job that requires using some 30,000 processors at once. "But there is a certain set of countries in the Americas that has the right mosquitoes, the right weather, and the right socioeconomic conditions for major outbreaks." Those conditions include lack of air conditioning, poor sanitation, and little access to education, for example, instruction on preventative measures such as removal of standing water, which attracts mosquitoes.

Among those countries are Brazil, with 15% of the population affected by the virus; Colombia, with 8%, and Puerto Rico with 10%. Puerto Rico is being particularly hard hit right now. "That's because Puerto Rico

is entering mosquito season," says Qian Zhang, a postdoctoral research associate in MOBS and a coauthor of the study. "The weather conditions, including temperature and humidity, are now favorable for the Zika spread."

Still, the risk of contracting Zika as a result of the 2016 Olympics in Rio de Janeiro is extremely small, says Vespignani. That's because the increase in air travel from Zika- affected areas will be minimal—less than 1 percent. The number of cases in Brazil, where the virus surfaced between August 2013 and April 2014, reached its peak in the first half of 2015 and has been declining since, affecting close to 10 to 15 percent of the population.

"The number of people traveling with Zika all over the world has already been huge," says Vespignani. "And Rio is not very much affected at the moment. So the half- million people who will travel there for the Games are just a small perturbation in the entire picture of the virus' spread."

Projecting the spread of Zika has been much more difficult than doing so for Ebola or the flu, says Vespignani, who has mapped both. That's because the disease is primarily transmitted not from person to person but from mosquitoes to people, most often the species *Aedes aegypti* but also *Aedes albopictus*,both of which carry the dengue and yellow fever viruses as well.

Thus data on human mobility, socio- demographics, and temperature changes—the bread and butter of epidemic modeling—must be compounded with data on the mosquitoes, much of which is uncertain, such as their travel patterns, abundance, and lifecycle depending on temperaure. "Unfortunately, mosquitoes do not have a GPS attached to them," says Ana Pastore- Piontti, also a postdoctoral research associate on the MOBS team who has also worked with Vespignani on past disease threats such as the Ebola epidemic.

In addition, reatively little is known about Zika itself, for example, precisely when and where the virus arrived in Brazil, the length of the incubation period in humans and mosquitoes, and whether humans can develop immunity to the virus.

Indeed, with no data available specifically on the relationship between Zika and its host mosquitoes, the researchers had to rely on the historical literature on other mosquito- borne diseases including dengue, malaria, and chikungunya. "But that means that we are making a lot of assumptions that Zika is close to dengue, for example," says Kaiyuan Sun, PhD'19. He and Dina Mistry, PhD'18, are also coauthors of the Zika study.

Given all the uncertainties, the researchers caution that their findings are "projections," rather than "forecasts." "We use 'forecast' when we have a level of confidence in past data—such as the origin of the disease and the progression of outbreaks—that allows us, even with some fluctuations, to project into the future," says Vespignani. "With Zika we are saying, 'These are the scenarios based on a number of assumptions and an attempt to get some plausible path for the future.'"

This study, for the first time, reveals that path. "The modeling results should be interpreted cautiously but the framework emerging from them is crucial for the interpretation of the data that we will continue to collect," says Vespignani. "They provide a baseline for the understanding of the magnitude and timing of the epidemic and can help us plan a response to outbreaks in the Americas."

More information: Projected spread of Zika virus in the Americas, biorxiv.org/content/early/2016/07/28/066456