Uninfected or asymptomatic? Diagnostic tests key to forecasting major epidemics

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Credit: Francisco Farias Jr/public domain

Major epidemics such as the recent Ebola outbreak or the emerging Zika

epidemic may be difficult to forecast because of our inability to determine whether individuals are uninfected or infected but not showing symptoms, according to a new study from the University of Cambridge. The finding emphasises the need to develop and deploy reliable diagnostic tests to detect infected individuals whether or not they are showing symptoms, say the researchers.

Emerging epidemics pose a significant threat to human health worldwide. A principal challenge in infectious disease epidemiology is accurately forecasting the threats posed by diseases early in emerging outbreaks. Accurate real-time forecasts of whether or not initial reports of cases of disease will be followed by a major outbreak - an epidemic in which large numbers of people become infected - are necessary to determine which control measures should be deployed.

For all infectious diseases, there is a delay between infection and the appearance of symptoms, known as the 'incubation period', during which infected individuals are classed as 'presymptomatic'. The incubation period, say researchers from the Department of Plant Sciences at Cambridge, can drive significant uncertainty in forecasting during the earliest stages of epidemics.

In research funded by the Biotechnology and Biological Sciences Research Council, the team used mathematical modelling to evaluate the effect of presymptomatic infection on predictions of major epidemics, choosing the Ebola virus as a case study. Their results, published today in the online journal *PLOS Computational Biology*, show for the first time that precise estimates of the current number of infected individuals - and consequently the chance of a major outbreak in the future - cannot be inferred from data based on symptomatic cases alone. This is the case even if factors such as the average infection rate and the death or recovery rates of individuals in the population can be estimated accurately.

"If we are able to use diagnostic tests to determine whether individuals who do not show symptoms are susceptible or are instead infected but not showing symptoms, we'll be in a better position to estimate the chance of a major outbreak," says Dr Nik Cunniffe, who led the study. "Since the reliability of diagnostic tests affects the extent to which forecasting is possible, it's important not just to develop new diagnostic tests, but also to ensure those we have are continually refined and promptly deployed."

Although the researchers chose Ebola as a representative case study of a disease for which reports of initial cases are not always followed by a large epidemic, they say their results are applicable to other outbreaks, including not just those that affect humans.

"These findings - that accurate forecasting relies on informing models with data on presymptomatic infections - hold true for anything from the current Zika outbreak through to animal diseases such as bluetongue and even plant pathogens such as Xylella fastidiosa, that is currently causing such devastation to olive groves in southern Italy," adds first author Robin Thompson, a former PhD student at the Department of Plant Sciences, and now a postdoctoral researcher at the University of Oxford.

The researchers acknowledge that their models are based on an idealised setting, in which symptomatic cases and deaths were recorded perfectly and in which the values of disease transmission parameters were known exactly. However, they say that additional uncertainty will only make forecasting even more challenging. Presymptomatic infection alone makes prediction imprecise, reinforcing the need to better estimate levels of hidden infection in populations using diagnostic testing.

Provided by University of Cambridge

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