Editor's Summary

[From “Content” -- All research articles are accompanied by an Editors' Summary—a comprehensible summary for physicians in all specialties, as well as patients and their advocates. (http://www.plosmedicine.org/static/information.action)]

Stylistically, less technical than the article itself – job is to pull out the main ideas that all science reports have: context, problem, research question, method, results/data/outcome, discussion

For the article -- Surveillance of Infection Severity: A Registry Study of Laboratory Diagnosed Clostridium difficile (http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1001279)

Background – context of the study – the “big” picture

The ability of bacteria to cause infection and disease (that is, their virulence) is in part determined by bacterial genetic makeup. At any time, there is a great deal of genetic diversity within common kinds of bacteria, which naturally generate new variants all the time. Sometimes organisms arise with a genetic makeup that causes more severe infection in humans and even death. For example, in 2005, spread of a particularly virulent strain (called 027/ST1) of the toxin-producing bacterium Clostridium difficile caused a global epidemic of C. difficile infection.

Why Was This Study Done? – motivating problem and research question/s

In health care settings, general methods of detecting changing virulence to enable the early recognition, control, and optimal management of increasingly severe infections would be highly beneficial. Changing virulence of a bacterial infection is often measured using death rates, but only a small proportion of those with infection die from it, so this may not be the most sensitive method of monitoring. Consequently, in this study the researchers investigated whether the changing virulence of C. difficile infection could be tracked by using common clinical measurements (white blood cell count, neutrophil count, blood urea, and creatinine concentrations, which reflect how unwell patients are) as the basis of an infection-severity surveillance scheme.

What Did the Researchers Do and Find? – method and results

The researchers examined all C. difficile toxin tests obtained from the microbiological lab serving hospitals in Oxford, UK, between February 1, 1998 and August 1, 2009. They also identified all inpatients aged over 18 years with a positive C. difficile test when admitted to hospitals over this time, examined their laboratory blood tests, and noted recorded deaths. The researchers used patients with C. difficile toxin-negative samples as a control group. To further validate their analysis, the researchers also undertook a similar analysis in a hospital in another UK city (Birmingham).
The researchers used statistical models to estimate changes in potential biomarkers (neutrophils, creatinine, and urea) with reference to the *C. difficile* 2005 global epidemic and post-infection death rates. The researchers used another statistical model (an iterative sequential regression technique) to estimate how soon any changes in biomarker/mortality trends would have been detected. Finally, to evaluate these severity-monitoring techniques, the researchers performed two simulation studies in which they assumed a more severe strain of *C. difficile* was introduced into a hospital.

Using these methods, the researchers found that in patients who were positive for *C. difficile* toxin, average neutrophil counts on diagnosis increased from 2003, peaked in 2006–2007, and then declined. They also found that 28-day deaths from *C. difficile* infection increased from early 2006, peaked in late 2006–2007, and then declined. Furthermore, laboratory tests (molecular typing) confirmed these changes were likely due to the severe *C. difficile* strain. The simulation model derived from the observed data suggested the performance of biomarker-based detection was notably higher than that of monitoring deaths post-infection.

**What Do These Findings Mean?** *How do results change/add to the big picture?*

These findings suggest that passively monitoring the severity of infection using routinely measured clinical biomarkers is feasible and can potentially detect important shifts in the virulence of human pathogens, such as *C. difficile*. Furthermore, such a surveillance system is superior to, and has obvious advantages over, monitoring deaths from infection — provided biomarker data is available. It could be used to provide an early trigger for more detailed investigations of patient characteristics, complemented by studies of bacterial genetic makeup, with the aim of tailoring policy and optimizing treatment of infection. Although this study monitored only one bacterial species, as changes in virulence are common to most human pathogens, this surveillance of severity technique could be applied to other organisms.