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December 2005

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## BIOSECURITY AND THE ROLE OF STATISTICIANS

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Journal of the Royal Statistical Society A, 2005, 168: 263-266

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Bioterrorism is now recognized as a real threat to our society. After the 2001 U.S anthrax attacks, many governments have made it a priority to strengthen public health preparedness to minimize morbidity and mortality in the event of a bioterrorist attack. Significant resources are being committed to that effort. The U.S government alone is planning to invest over 5 billion dollars for vaccines and drugs to enhance biosecurity. These investments to shore-up public health preparedness will pay off in defending against both intentional and naturally occurring outbreaks of infectious diseases.

A coordinated approach is required to effectively address the threats of bioterrorism. A multi-disciplinary team of experts is required including: national security and law enforcement officials to assess the threats; public health planners and policy makers to develop effective response strategies; clinicians and primary care providers to help identify symptoms of the earliest cases; medical care providers and hospitals to plan for mass casualty care; legal experts to address critical questions in the event of an emergency; the mass media to effectively and calmly communicate information to the public; policy makers at an international level to develop

global efforts to improve biosecurity; and biomedical researchers to help develop new drugs, vaccines and diagnostics for the critical pathogens. In this editorial, I offer that statisticians need to be part of this multi-disciplinary team. Statisticians have critical contributions to make to improve biosecurity, although perhaps requiring a different paradigm than traditional statistical work.

There have been few documented breaches of biosecurity. While that is good news, that also poses challenges because that means that there is limited data for developing biosecurity policy. Statisticians who work in public health are most familiar with designing and analyzing large clinical trials and epidemiological studies to answer questions. Yet, few clinical trials or epidemiological studies can be designed and carried out in biosecurity. Certainly we cannot experimentally infect a person with smallpox to see how transmissible smallpox is in today's population. We cannot release anthrax spores into the air to see how it disperses in the atmosphere and over population centers. We cannot perform a randomized clinical trial to estimate vaccine efficacy to prevent a disease which is no longer naturally occurring.

We have very limited *modern* experience with diseases such as anthrax and smallpox which are considered some of the major bioweapons threats. The World Health Organization declared smallpox eradicated over two decades ago. In the last century there were only 17 cases of inhalational anthrax in the United States prior to the 2001 attacks. With this paucity of epidemiological data, how can we develop rational public health policy? How can we assess the roles of vaccines, antibiotics, therapeutics, isolation and quarantine in containing an outbreak? In this regard, mechanistic models of the spread of infectious diseases are essential because without them we cannot begin to answer the "what if" questions (Fraser *et al.* (2004)). However the complexity of these models must be tempered by the limits of available data for estimating

model input parameters. We must use modern statistical tools to estimate model parameters together with sensible mechanistic models for the spread of infectious diseases. Output from these models will depend on a number of critical input parameters. We must be proactive and opportunistic in identifying data sources that might shed light on the critical model parameters. These data sources for example, might be historical smallpox outbreaks, the 1979 Sverdlovsk anthrax outbreak, or animal studies of the bio-threat pathogens which many date back to the 1950s. In biosecurity research, there may not be the luxury of designing and conducting a new study. Instead, we may be forced to glean all we can from whatever worldwide data is available using modern statistical tools. The statistical analyses must be aimed at estimating relevant public health parameters, which I suspect typically won't take the form of a regression coefficient from a linear model. We must develop and routinely apply tools for quantifying and displaying uncertainty that results from estimating parameters using disparate data sources that are then used as inputs into mechanistic models.

Public health policy makers are confronted with an array of critical questions as to how to minimize casualties from a bioterrorist attack. For example, are programs aimed at isolating symptomatic cases of smallpox and quarantining exposed persons adequate to contain an outbreak? Or, must these programs be supplemented with mass pre-attack vaccination programs for the general population? Following the events of 2001, U.S policy officials have struggled with these types of questions. Quantitative models have been developed to help inform these public policy questions and predict the impact of public health strategies to contain an outbreak. Models to address these public policy questions have been developed both for smallpox (Bozzette *et al.* (2003), Halloran *et al.* (2002), Kaplan *et al.* (2002)), and anthrax (Wein *et al.* (2003), Brookmeyer *et al.* (2004)). These models use various approaches including deterministic

and stochastic modeling of population disease dynamics using both analytic and simulation tools. An important challenge of these models is how to effectively communicate uncertainty to policy makers arising from errors in both the input parameters and model assumptions.

It would be unlikely that authorities would immediately recognize that a bioterrorist attack occurred. Rather, in the days following the attack, the pathogen would silently spread and incubate and only be recognized after a critical number of people experienced symptoms. It is during this “silent” period before a public health response is mounted that the pathogen does its most serious damage. We can reduce casualties from a bioterrorist attack by shortening that “silent period.” One way to shorten the silent period is to improve disease surveillance for new outbreaks. Statisticians have been actively engaged in developing and assessing methodological approaches for rapid detection of emerging outbreaks.

One example of an approach to speed outbreak detection is syndromic surveillance which refers to the collection and statistical analysis of vast quantities of public health data to detect early symptoms of a new disease. These data might include the numbers of individuals seeking health care for certain symptoms, emergency department visits, sales of certain medications for flu-like symptoms, and rates of school or job-related absenteeism. Statisticians are currently debating the relative costs and benefits of syndromic surveillance (see for example: Goldenberg *et al.* (2002), Reis *et al.* (2003), Kleinman *et al.* (2004), Stoto *et al.* (2004), Waller (2004)). There are two points of view. On the one hand syndromic surveillance offers the tantalizing possibility of an early warning of an emerging outbreak from data mining rather than waiting until public health officials are notified of confirmed cases of disease from traditional medical care settings. On the other hand, the data sets are inherently very noisy and the high signal to noise ratio sounds a cautionary note about the sensitivity of the approach and the risk of false

alarms. While I think the jury is still out on the relative merits of syndromic surveillance, statistical tools and reasoning can help inform the debate.

Another approach to speed recognition of a bioterrorist attack is air monitoring systems for contaminants and pathogens in the environment. These systems typically involve air quality monitoring stations that routinely test for major pathogens at regular time intervals using polymerase chain reaction or immunoassays of the trapped materials. Proponents of the approach argue that such detection systems could ultimately provide real time alerts of the presence of biological or chemical hazards, even before patients begin developing symptoms. Indeed, the U.S. government has been developing detection systems to be employed in postal facilities motivated by the concern that high speed mail sorting machines could potentially aerosolize anthrax spores sent through the mail (MMWR). There are more ambitious proposals to place these detection systems throughout major metropolitan areas. However, critical questions remain about these detection systems including their false positive and false negative error rates, and if they were to be employed how many would be needed and where should they be located. Again, I think the jury is still out as to whether these detection systems are accurate enough to justify their cost. However, statistical reasoning can help inform the public policy debate.

Which are the best methods to speed recognition of an emerging outbreak? It may be that no single approach is best but rather panoply of complementary approaches is required. Increasing clinical awareness of the signs and symptoms associated with certain pathogens may also be effective in speeding recognition of an emerging outbreak. Indeed in the 2001 anthrax attacks, it was an astute clinician in Florida who identified the very first victim within hours of the patient

showing up at an emergency department. That one physician sounded the alarm to the public health community.

There will be critical questions with regard to remediation and clean-up following an attack with environmental contaminants. For example, after the 2001 U.S anthrax attack, there were questions about whether it was safe to reopen facilities that were contaminated with anthrax spores and whether the clean-up was adequate. The facilities were sampled to detect and quantify the number of spores in various locations. The challenges are which are the optimum sampling designs, and how does one translate those results to produce an estimate of risk of disease. Sampling designs, probabilistic considerations, mechanistic models, and statistical analyses can help quantify the environmental risks following an attack.

Biomedical research is underway to improved diagnostic tests, vaccines and therapeutics for the most worrisome pathogens. New products on the horizon include rapid diagnostic tests for smallpox and an improved anthrax vaccine. We face challenges of how to effectively evaluate these products because we cannot perform the necessary controlled clinical trials with these virulent pathogens. Instead, most likely we will have to rely on animal data, and various immunological markers in humans. These surrogate data will need to be pieced together into a coherent model to help address the question of how these products would perform in the event of a real bioterrorist attack.

Statisticians should be at the forefront in assisting policy makers determine how to apportion limited resources to increase public health preparedness whether the debates involve syndromic surveillance, air monitoring systems, or vaccination programs. Biosecurity policy decisions must be based on the best available science. Statisticians have much to contribute and

should be actively working with multidisciplinary teams of experts. I am convinced statisticians can make a difference.

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