

## LETTERS TO THE EDITOR

## Methods for Outbreak Detection in Hospitals—Does One Size Fit All?

*To the Editor*—We read with interest a recent communication by Baker et al,<sup>1</sup> who investigated outbreak detection practices using a questionnaire-based survey. Their findings from 33 respondents found nonstandardized methods for outbreak detection, and in general, respondents confined outbreak detection to a limited number of targeted organisms. We were surprised that so few (ie, 31% of academic centers) included invasive aspergillosis and that outbreaks of *Clostridium difficile* infection (CDI) were not a priority. The authors conclude that an “automated, statistically based detection system would greatly improve current outbreak detection practices by facilitating and standardizing outbreak detection and expanding outbreak detection beyond a very small subset of organisms or specific locations.”<sup>1</sup>

The absence of a definition for either “an outbreak” or “a cluster” in the study raises several issues. While such definitions may be considered routine by many infection prevention control staff, the practical implications of these definitions when managing outbreaks are far reaching. For example, should automated systems focus on symptomatic patients alone or include both colonized and infected patients? The transmission of diseases within hospitals is complex, and the route is not always apparent.<sup>2,3</sup> This especially applies to antimicrobial-susceptible microbes when outbreaks are often missed during the initial stages. Our hospital is an 800-bed adult tertiary referral center, with national centers for neurosurgery and renal transplantation. We have policies and criteria for identifying clusters and outbreaks. Laboratory, clinical, patient, and ward-level information are all considered. We acknowledge that an automated system would indeed greatly enhance outbreak detection, but the daily practicality of using such a system is questionable. However, our hospital operates at close to 100% capacity, and we struggle to isolate patients colonized with certain organisms. This situation is compounded by frequent inpatient bed transfers and the need to triage and prioritize patients for isolation, such as those with CDI.<sup>4</sup> While an automated system might provide information that is potentially actionable, implementation may be limited by local infrastructure.

The authors propose that an automated, statistically based method should be used to identify “clusters” across locations and services, taking into account susceptibility patterns. Does identifying a simple increase in the number above a certain threshold or numbers that are “statistically unusual” compared to hospital-specific baseline microbiology identify an outbreak? Assumptions based on antimicrobial patterns are not always correct when tracking the transmission of microbes; similar phenotypes do not necessarily match genetic

phylogeny.<sup>5</sup> Using such an automated system could potentially misdirect valuable time to investigating “outbreaks” that are not substantiated by temporal exposures and could potentially prolong an outbreak when clinical information does not identify a likely risk of cross transmission. The resource implications of using outbreak detection software, regardless of the potential benefits, could be considerable.

We would strongly advise against the sole use of an automated system to identify outbreaks. Seasonal infections largely arising in the community (eg, influenza-like illness and norovirus) have outbreak potential upon importation into the healthcare setting due to rapid dissemination. Based on the premise that social media and Internet search engines are increasingly used internationally to track the onset of community-acquired seasonal infections, we have developed a local database that utilizes clinical information collated by infection prevention and control nurses during daily ward visits.<sup>6</sup> The database was developed to accurately identify such outbreaks in a timely manner, especially when laboratory confirmation may be delayed. Access software (Microsoft, Redmond, WA) is used to extract daily situation summaries and to generate the latest epidemiological curves of symptomatic cases. We have demonstrated that this widely available software can be developed and tailored for timely local surveillance, enhancing outbreak management.<sup>6</sup>

While we acknowledge that an automated system for identifying outbreaks is desirable and may augment current approaches, such systems are only as good as the infection prevention and control personnel that use them. Active daily surveillance and communication, the manual review of available data in combination with automated systems, and the visible presence of infection prevention and control personnel in clinical areas, remain of paramount importance.

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## Necessity of a Competing Risk Approach in Risk Factor Analysis of Central Line-Associated Bloodstream Infection

*To the Editor*—With great interest we read the article by Carter et al<sup>1</sup> investigating risk factors for central line-associated bloodstream infections (CLABSI). For estimating the proportion without CLABSI depending on time, Kaplan-Meier (KM) curves were calculated to account for the at-risk time from insertion until the occurrence of CLABSI or removal of the catheter (which is treated as censoring in the model). If a bloodstream infection occurs during the use of a

central venous catheter it is considered to be catheter associated and it is rather unlikely to develop a CLABSI 48 hours after removal of the catheter.<sup>2</sup> However, KM models assume that the hazard of CLABSI remains unchanged when a censoring event occurs. This censoring assumption is clearly not fulfilled in the case of removal of the catheter since removal leads to a reduction of risk. Hence, removal of the catheter without CLABSI should be considered as a competing event for CLABSI.<sup>3</sup>

Using standard KM models in the presence of competing events leads to overestimation of the cumulative risk.<sup>3</sup> This can be seen in figure 3 of Carter et al.<sup>1</sup> The KM curve lies at approximately 80% without CLABSI, which corresponds to a risk of CLABSI of approximately 20%. But considering the actual number of patients with CLABSI this leads to a risk of CLABSI =  $\frac{385}{5648} = 6.8\%$ .

To illustrate the bias in this setting, we analyzed simulated data of a simplified competing event setting based on values from the article of Carter et al<sup>1</sup> (code is available upon request). We consider 2 constant competing event hazards,  $\lambda_1$  for CLABSI and  $\lambda_2$  for removal without CLABSI. Hence, the cumulative incidence function (CIF) of CLABSI and the CIF of removal without CLABSI are given by this formula<sup>4</sup>:

$$CIF_1(t) = \frac{\lambda_1}{\lambda_1 + \lambda_2} \times (1 - \exp(-(\lambda_1 + \lambda_2) \times t)) \quad (1)$$

$$CIF_2(t) = \frac{\lambda_2}{\lambda_1 + \lambda_2} \times (1 - \exp(-(\lambda_1 + \lambda_2) \times t)) \quad (2)$$

With  $\lambda_i$  being the hazard for event  $i$ ,  $i = 1; 2$ . Formulas 1 and 2 illustrate that the CIFs of the respective events depend on both the hazard for the event of interest and the hazard for the competing event. The right terms of formulas 1 and 2 represent the probabilities that any event occurs at time  $t$ . The left terms  $\frac{\lambda_i}{(\lambda_1 + \lambda_2)}$ , ( $i = 1; 2$ ) display the probabilities that the occurring event at time  $t$  is event  $i$ .

As seen in the formulas above, there is a direct connection between the overall risk of CLABSI and the rates of both events<sup>5</sup>:  $CIF_1(t)$  approximates the overall CLABSI risk  $\frac{\lambda_1}{(\lambda_1 + \lambda_2)}$  for large time points, which is estimated by  $\frac{\#CLABSI}{\#patients} = \frac{385}{5648} = 6.8\%$ . Analogously, the overall probability of removal without CLABSI is  $\frac{5648 - 385}{5648} = 93.2\%$ .

The constant hazard rate  $\lambda_1$  is estimated by  $\frac{\#CLABSI}{\#line-days\ at\ risk}$ . Note that line-days at risk are line-days the patients are actually at risk—that is, line-days from insertion until removal without infection or until CLABSI. If  $D_i$  is the individual line-days contribution of patient  $i$ ,  $\lambda_1$  can also be written as

$$\lambda_1 = \frac{\#CLABSI}{\sum_{\{i=1\}}^N D_i} = \frac{\#CLABSI}{N \times \frac{1}{N} \sum_{\{i=1\}}^N D_i} = \frac{\#CLABSI}{N} \times \frac{1}{\bar{D}} \quad (3)$$

with  $N$  being the number of patients and  $\bar{D}$  being the mean line-days at risk. Similarly, the hazard for removal without