LETTERS TO THE EDITOR

Estimating Infection Incidence in Longitudinal Studies

To the Editor—In a longitudinal study with a maximum follow-up of more than 3 years, Vigil et al[1] found that both intermittent (IC) and persistent (PC) MRSA nares colonization increased subsequent incidence of MRSA infection and that further distinguishing between IC and PC may not improve risk prediction. The authors found increased risks of IC and PC patients in all their statistical analyses, but they also reported and compared conflicting relative frequencies of infection. The aim of this letter is to point out that the proper measure of infection incidence must lie between the numbers reported by Vigil et al., and that the statistical difficulty stems from the longitudinal design, which we believe is an asset of their study.

In their table 1, Vigil et al report so-called incidence proportions[2] (ie, the number of observed infections divided by the number of patients within colonization groups) of 11.2% (IC) and 16.3% (PC). In contrast, the proportions based on a Kaplan-Meier analysis of time-to-infection were 13% (IC) and 21% (PC).

The incidence proportions are too small. The reason is that patients were followed from study entry until infection, death, or closure of the study. Closure of the study leads to censored observations. The incidence proportions, therefore, report proportions of an observed infection. This measure does not address a patient's safety concern. For the individual patient, whether and when an infection occurs is relevant, whether this happens before administrative closure of the observational study is not. The incidence proportions are too small because the probability of the fact that an infection occurs and that it is observed is less than the probability that an infection occurs (irrespective of the observation status).

In contrast, the proportions based on the Kaplan-Meier curves are too large. The reason is that the aim of a Kaplan-Meier analysis is to approximate the incidence proportions in the absence of censoring if the incident event occurs in every patient's life, although possibly after closure of study.[3] Death is such an incident event, and a Kaplan-Meier curve is a technique from the analysis of survival data. Infections, however, may be precluded by death without prior infection, and Kaplan-Meier estimates of infection incidence overestimate the probability of infection because the method implicitly assumes that eventually all patients will be infected.[4]

The proper tool for quantifying absolute infection risks in a longitudinal study as that of Vigil et al is a generalization of the Kaplan-Meier estimator to multiple outcome types. This is the so-called Aalen-Johansen estimator, which decomposes a proper Kaplan-Meier estimator of infection-free survival into approximated proportions of infection and approximated proportions of death without prior infection.[5] Also known as cumulative incidence functions of competing risks, these curves will yield infection proportions that lie between the biased estimates reported by Vigil et al.

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Biased Low Incidence of Central Venous Catheter-Related Bloodstream Infections in Controlled Clinical Trials?

To the Editor—In the 3SITES trial,[1] the incidences of central venous catheter (CVC)-related bloodstream infections (CRBSIs) after 1:1:1 randomized catheterization of the internal