In Search of Useful Methods for Measuring Health and Economic Consequences of Antimicrobial Resistance

To the Editor—In their recent work, Ammerlaan et al analyzed temporal trends in annual incidence densities of nosocomial bloodstream infections (BSIs) to show that nosocomial BSIs caused by antibiotic-resistant bacteria represent an additional burden of disease, as they do not replace BSIs caused by more...
susceptible bacteria [1]. These infections have generated a broad body of literature attempting to quantify the health and economic consequences of antimicrobial resistance from the perspective of a hospital. In detail, useful methods for measuring outcomes of BSIs caused by drug-resistant bacteria with uninfected controls and (2) comparisons of BSIs caused by drug-resistant bacteria with BSIs caused by susceptible bacteria. The question remains which of these 2 methods represents the burden of resistance. The comparison to BSIs caused by susceptible bacteria gives the assumption that BSIs caused by antibiotic-resistant bacteria may be replaced by BSIs caused by more susceptible bacteria if the spread of resistant pathogens was successfully prevented. It may be called the “replacement scenario.” The assumption of “nonreplacement,” however, may lead to the comparison of BSIs caused by drug-resistant bacteria to uninfected controls. Ammerlaan et al presented first evidence for the hypothesis of nonreplacement [1]. Accordingly, the comparison of BSIs caused by antibiotic-resistant bacteria to uninfected controls generates measures for the burden of resistance.

A quick look at the literature draws a different picture: the excess mortality of meticillin-resistant Staphylococcus aureus (MRSA)—related BSIs, for instance, has been determined by many investigators. Three large meta-analyses have been conducted, confirming that MRSA-related BSIs lead to significantly greater mortality than do meticillin-sensitive S. aureus—related BSIs; comparisons with uninfected controls, however, are missing [2–4]. In some recent studies, multicenter data from different European countries were used to determine the excess mortality and length of stay of BSIs caused by antibiotic-resistant bacteria in comparison to both of the described control groups [5–8]. In the first step, the excess burden of BSIs caused by antibiotic-resistant bacteria was determined in comparison to an uninfected control group (scenario of nonreplacement). Second, the excess burden of BSIs caused by susceptible bacteria was determined in comparison to the uninfected controls. Third, the excess burden of BSIs caused by antibiotic-resistant bacteria in comparison to BSIs caused by susceptible bacteria was determined by contrasting the outcomes from the first and second comparisons (replacement scenario) [5–8]. Confounding was addressed by using multivariate regression models. The mortality-related effect measures between the scenarios of replacement and nonreplacement are shown in Figure 1. Obviously, replacement scenario comparisons will potentially underestimate the burden of resistance. Overall, the evidence provided by Ammerlaan et al supports the hypothesis of nonreplacement, which underlines the needs for comparisons with uninfected controls; this, however, may be only the first step and should encourage other researchers to make use of surveillance data to investigate the mechanisms of replacement in hospital settings.

Notes

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References


Figure 1. Excess mortality of Staphylococcus aureus–related bloodstream infections. Results according to fully adjusted analyses only [6–8]. Subdistribution hazard ratio according to de Kraker et al [6] (hospital mortality) and Lambert et al [7] (intensive care unit mortality); hazard ratio according to Wolkewitz et al [8]; odds ratio according to de Kraker et al [6]. *Significant at the 5% level. Abbreviations: HR, hazard ratio; ICU, intensive care unit; MRSA, methicillin-resistant Staphylococcus aureus; MSSA, methicillin-sensitive Staphylococcus aureus; OR, odds ratio; SA, Staphylococcus aureus; SHR, subdistribution hazard ratio.

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