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The results demonstrated that, for the CC59 MRSA isolates, there were no sublineages for the different onset types. The CC59 isolates generally contained more single-nucleotide polymorphism (SNP) differences than the HA-MRSA CC239 isolates. Compared to the CC239 clone with many transmissions (SNP threshold of ≤20), in the isolates with the HO or HACO onset type, only 6 possible transmissions with 2 or 3 isolates in every cluster were observed for the CC59 clone, and the onset types for these genetically closely related CC59 isolates were generally intermixed (Figure 1). This indicated that the increasingly isolated CC59 MRSA isolates were of a community origin rather than from a nosocomial transmission.

The mixed-onset type of both the USA300 and CC59 phylogenies, even for the genetically related isolates, made the epidemiological definitions of MRSA more confusing. The inconsistency between the genomic and epidemiological correlations may have resulted from insufficient clinical data because, in most situations, we only investigated the clinical data from the hospital from which the isolates were collected, so information bias existed. Similar to the results of the study by Thiede et al, when considering more-comprehensive health care exposures in the hospital discharge dataset, some of the CO-MRSA isolates were actually classified as HACO-MRSA isolates [1].

With the development of genome sequencing technology, we can now understand the molecular epidemiological and transmission dynamics of MRSA much better [5]. In summary, we suggest that it is important to establish regional or national genomic databases with meaningful metadata for pathogens, such as *S. aureus*, which will help us define the concept of CA-MRSA or HA-MRSA and implement infection control interventions [6].

Notes

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Cost-Effectiveness of Adult Universal Hepatitis B Vaccination

To the Editor—In their recent article, Hall et al [1] report on their study of the cost-effectiveness of universal adult immunization against hepatitis B virus (HBV) with either a 2-dose or 3-dose vaccine. While we commend the authors for drawing attention to this important issue, we have some concerns about their analysis.

First, the authors' reported cost-effectiveness ratios (approximately $150 000 per quality-adjusted life-year [QALY] gained) are high in comparison with ratios reported for other vaccines in adults. For example, the cost-effectiveness of influenza vaccination in persons aged 50–65 years is about $28 000 per QALY gained [2], and the cost-effectiveness of the recombinant zoster vaccine in

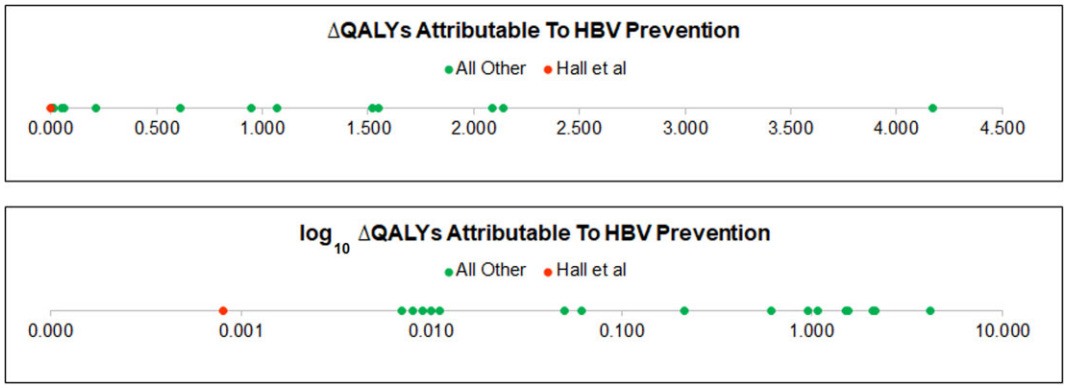

Figure 1. Comparison of reported estimates of quality-adjusted life-years (QALYs) gained with hepatitis B virus (HBV) immunization in Hall et al [1] versus other published studies [4–8].

immunocompetent persons aged >50 years is approximately $30 000 per QALY gained [3]. We believe the authors' high reported cost-effectiveness ratios reflect underestimation of the clinical benefits of HBV prevention.

Comparison of their estimates of QALYs gained with similar estimates reported by authors of other studies of HBV vaccination is instructive. In Figure 1, Hall et al's estimates of QALYs gained are plotted in red, while 16 other estimates of QALYs gained reported in 5 earlier studies are plotted in green [4–8]. A natural number line is used in the top half of the display and a logarithmic scale is used in the bottom half.

While prior studies focused on high-risk populations, differences in the benefits of HBV vaccination as great as a 1000-fold strike us as inconsistent with underlying differences in infection risk. Evidence of potential problems with the authors' methods, however, is not limited to such comparisons.

For example, in Table 2 of Hall et al [1], the authors report that immunization with either a 2-dose or 3-dose HBV vaccine yields estimated lifetime gains of 0.0008 QALYs and 0.0018 life-years (LYs) per person. Although the small estimated gains in QALYs and LYs themselves are concerning, of greater concern is the fact that reported gains in LYs are about 2-fold greater than the gains in QALYs.

This finding is concerning because the authors comment that "within one year, all individuals with an acute HBV infection either spontaneously [clear] their infection and [transition] to the hepatitis B surface antibody (anti-HBs) positivity state in which they [are] no longer at risk for further HBV infection, or [transition to] an active CHB infection state." (Supplementary Material [1]). In their model, the majority of patients move to the anti-HBs state following infection, as only about 8% of patients transition from acute infection to active CHB infection (Supplementary Table 1 [1]). Moreover, once patients transition to the anti-HBs state, most will spend the remainder of their lives in it, because transitions out of the anti-HBs state for reasons other than death are extremely rare (only 0.007 annually; Supplementary Table 1 [1]).

The authors assume that patients in the anti-HBs state experience no excess mortality. Every year of life in this state, however, is assumed to confer a decrement of 0.13 (ie, 0.99–0.86 QALYs; Supplementary Tables 3 and 5 [1]). On an a priori basis, therefore, one might expect that HBV immunization, by preventing people from entering the postinfection anti-HBs state, would produce larger gains in QALYs than LYs, because there are no associated gains in life expectancy. Consistent with our expectations, an earlier economic evaluation reported that gains in QALYs with HBV vaccination were greater than gains in LYs in all population groups examined [5]. Yet, Hall et al report precisely the opposite finding [1].

Reported numbers needed to vaccinate (NNV) also are puzzling, as they seem to be inconsistent with estimated numbers of HBV acute infections avoided. For example, among persons aged 19–29 years, 2-dose and 3-dose vaccines are reported to prevent 12.6% and 26.9%, respectively, of all HBV acute infections (Supplementary Table 6 [1]). NNVs reported for these strategies, however, are 105 and 108, respectively. More effective prevention strategies should be associated with substantially lower—and not almost identical—values for NNV (note, NNV = 1/change in incidence).

Finally, some parameter estimates also appear to be questionable. Seroprotection rates (SPRs) for the 3-dose vaccine, for example, are inconsistent with its assumed cost per dose. Specifically, the TWINRIX package insert is cited as the source for SPRs used for the 3-dose vaccine [9], yet the assumed cost per dose of this vaccine (which was reportedly based on the CDC price list [10]) corresponds to that of ENGERIX-B and not TWINRIX. The cost per dose of TWINRIX, in fact, is almost double that of ENGERIX-B.

Again, while we commend the authors for addressing an important public health issue in their study, we believe their methods require clarification.

Notes

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