will depend on the rate of partner change. At very high rates of partner change, long-term survival of the host is less important; at low rates of partner change, the host must survive long enough to infect others. In a survey of viral loads of HIV-infected individuals performed by one of us (B.A.) in Orange Farm, South Africa, the viral loads had an interquartile range of 11,000–882,000 copies/mL. Significant changes in treatment availability and initiation practices may select particular strains from this very diverse virus population. Starting treatment soon after infection, as part of a policy to reduce transmission [2], might select against viral strains associated with long-term survival, low viral load, and high CD4+ cell counts. Reductions in the rate of partner change, on the other hand, might select against strains associated with short-term survival, high viral load, and low CD4+ cell counts.

The suggestion by Crum-Cianflone et al [1] that the observed changes in CD4+ cell counts reflects viral evolution raises questions concerning the future impact of new drugs and more aggressive treatment. These questions require more detailed data and rigorous modeling of viral evolution.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

Brian G. Williams,1,a Alex Welte,1 Bertran Auvert,2 and John Hargrove3

1South African Centre for Epidemiological Modelling and Analysis, Stellenbosch, and 2University of the Witwatersrand, Johannesburg, South Africa; and 3University of Paris, Paris, France

References


Underestimation of Invasive Meningococcal Disease Case Fatality Rates

To the Editor—In preparing a related health-economic model, we found a discrepancy with computations presented in an article by Ortega-Sanchez et al [1] in Clinical Infectious Diseases.

The authors stated that “Case-fatality ratios (CFRs) were calculated using the number of meningococcal disease–related deaths caused by vaccine serogroups recorded by Active Bacterial Core Surveillance for the period 1993–2002” [1, p. 3]. We understand this to mean that the authors intended to perform the following calculation [2]:

\[
\text{CFR C, Y, W135} = \frac{\text{Deaths C, Y, W135}}{\text{Cases C, Y, W135}}.
\]

However, doing so does not produce the results shown in their table. The authors results can be obtained by performing the following calculation:

\[
\text{CFR C, Y, W135} = \frac{\text{Deaths C, Y, W135}}{\text{All Cases}}.
\]

The results of each calculation are shown in Table 1. Because the model considers only cases of invasive meningococcal disease involving serogroups C, Y, and W-135 and attempts to calculate deaths resulting from these cases, we believe that the correct calculation is represented by the first equation provided above. If so, this may have substantial consequences, because CFRs are an important determinant of the cost-effectiveness outcomes estimated in Ortega-Sanchez et al’s [1] modeling study. Moreover, other researchers may rely on the Ortega-Sanchez et al study for inputs into their own models, as did we before we noted this anomaly.

Acknowledgments

Potential conflicts of interest. P.C. is an employee of sanofi pasteur, the manufacturer of Menactra, a vaccine against meningococcal diseases used in the United States; D.G. is an employee of United BioSource Corporation, a company working with sanofi pasteur on several projects that has received funding from sanofi pasteur and other vaccine companies.

Table 1. Comparison of Invasive Meningococcal Diseases Case Fatality Rates (CFRs) Calculated for the Period 1997–2002

<table>
<thead>
<tr>
<th>Age group, years</th>
<th>All serogroups</th>
<th>Serogroups C, Y, and W135</th>
<th>Recalculated CFR serogroups C, Y, and W135, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>9.6</td>
<td>4.5</td>
<td>12.4</td>
</tr>
<tr>
<td>1</td>
<td>2.9</td>
<td>1.9</td>
<td>4.5</td>
</tr>
<tr>
<td>2–4</td>
<td>6.5</td>
<td>5.9</td>
<td>14.4</td>
</tr>
<tr>
<td>5–10</td>
<td>6.5</td>
<td>4.5</td>
<td>8.0</td>
</tr>
<tr>
<td>11–17</td>
<td>12.7</td>
<td>10.8</td>
<td>18.8</td>
</tr>
<tr>
<td>18–22</td>
<td>13.7</td>
<td>9.3</td>
<td>17.4</td>
</tr>
<tr>
<td>23–32</td>
<td>12.0</td>
<td>9.6</td>
<td>17.9</td>
</tr>
<tr>
<td>33–64</td>
<td>16.4</td>
<td>12.3</td>
<td>20.4</td>
</tr>
<tr>
<td>≥65</td>
<td>18.5</td>
<td>11.9</td>
<td>16.1</td>
</tr>
<tr>
<td>Overall</td>
<td>10.0</td>
<td>8.0</td>
<td>13.2</td>
</tr>
</tbody>
</table>

* From Table 1 of Ortega-Sanchez et al [1].
Reply to Crépey and Getsios

To the Editor—We are very pleased that our analysis published in Clinical Infectious Diseases [1] received a close examination by Crépey and Getsios [2]. However, in their letter, Crépey and Getsios stated that they found a discrepancy between the case fatality rates (CFRs) used in our study and their own computations. Specifically, they believe that in our study there exists a significant underestimation of invasive meningococcal disease CFRs attributable to—in their argument—an incorrect calculation.

We disagree with their argument. As we stated in our study [1], we did use meningococcal serogroup-specific CFRs that are concurrent with surveillance data. Figure 1 presents case fatality data from the Active Bacterial Core surveillance system for serogroups C, Y, and W135 by age group averaged over the period 1993–2002 (dark gray bars). These CFRs were estimated using precisely the method represented by the first equation in the letter from Crépey and Getsios [2].

To consider year-to-year variations, these CFRs were imputed into our simulation model. Specifically, with use of standard risk analysis techniques, we fitted probability distributions to the CFR of each age group with feasible and evidence-supported upper and lower values. Figure 1 presents the probability values of the CFRs from each age group (light gray bars) as well as the ranges over which fitted probability functions were distributed. As usually observed when fitting probability distributions and performing simulations, minor differences (mean difference, 5%) were observed between some modeled values reported in our study [1] and the actual data. However, in all cases, the range of probability functions includes the surveillance rate value.

To facilitate comparison, Figure 1 (triangles) also presents the “recalculated” estimates as reported in table 1 of the letter from Crépey and Getsios [2]. It is unclear what source of data they used in their attempt to recalculate the CFRs but, taken at face value, it can be seen that, with the exception of 3 age groups whose rates values are relatively close to the higher end of the intervals used in our model, most of the values presented by Crépey and Getsios show a marked inflation. Even with year-to-year variations, the rates presented by Crépey and Getsios are beyond that of the values presented by Crépey and Getsios, which are on average 75% higher than the Active Bacterial Core surveillance system rates, will overestimate the number of deaths attributable to the C, Y, and W135 serogroups and would have substantial and questionable consequences for any cost-effective analysis. On further evaluation, we still support our modeling approach, data, and results.

Acknowledgments

We would like to recognize the personnel of Centers for Disease Control and Prevention’s Active Bacterial Core surveillance program and all 50 state health departments in the United States. Potential conflicts of interest. All authors: no conflicts.

Ismael R. Ortega-Sanchez, Elizabeth Zell, Amanda Cohn and Nancy Messonnier
Centers for Disease Control and Prevention, Atlanta, Georgia

References