Wallinga and Teunis Respond to "Real-Time Tracking of Infection Control Measures"

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We thank Drs. Lipsitch and Bergstrom (1) for their thoughtful commentary on our article (2), which appears in this issue of the *Journal*. They discuss the method we developed in the context of real-time analysis of case notifications. We would like to add a few more thoughts along these lines.

The contribution of the method toward real-time analysis of incoming notifications is, as Lipsitch and Bergstrom aptly summarized, to provide "a means of transforming the time series of cases… into a time series of estimated values for the instantaneous reproductive number on each day" (1, p. 517). The transformation is from calendar time to generation time and from number to relative increase in number. The key variable involved in this transformation is the generation interval, which is the time interval between a primary case and a secondary case. Literature on this key variable has been scant and has been blurred by the use of confusing terminology. We cannot think of a better introduction to the concept of generation intervals than was provided by Professor Paul Fine in a recent article in this journal (3). Fine illustrates the relatedness of the generation interval, epidemic curves, transmission chains, and reproduction numbers. Our contribution is simply to specify these relations further.

In our article (2), we emphasized that under certain technical conditions, only a few simple computational steps are needed to transform the time series of severe acute respiratory syndrome cases into a time series of estimated reproduction numbers. Here we would like to add that such a transformation could be carried out for any infectious disease that is transmitted from person to person. Lipsitch and Bergstrom (1) correctly note that a short generation interval facilitates real-time interpretation of incoming case reports; for infections with a long generation interval (such as human immunodeficiency virus, herpesvirus, or mycobacterial infection), the transformation might be less useful. At the moment, we are studying the possibility of extending the method to account for reporting delay, unobserved cases, and heterogeneous transmission. However, the finding that transformation is in any case feasible, and in many cases computationally trivial, opens up perspectives for estimating reproduction numbers from time series of case notifications.

The reason for emphasizing the relevance of real-time estimation of reproduction numbers of emerging infectious diseases is that after syndromic surveillance systems have signaled the emergence of a new disease, we know little more about the novel infectious agent than that each case has been infected by another case and that successive generations of cases are separated by a typical generation interval. This is not enough information with which to build a mathematical transmission model, but it is sufficient for real-time estimation of reproduction numbers, and hence for real-time estimation of the additional control effort required. Lipsitch and Bergstrom assert that, when the next important outbreak arrives, such almost parameter-free estimation tools for reproduction numbers can be a valuable addition to syndromic surveillance systems and mathematical transmission models. We could not agree more.

REFERENCES

1. Lipsitch M, Bergstrom CT. Invited commentary: real-time tracking of control measures for emerging infections. Am J Epidemiol 2004;160:517–19.
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3. Fine PE. The interval between successive cases of an infectious disease. Am J Epidemiol 2003;158:1039–47.