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AJIC commentary

Pandemic influenza forecasting: Does past performance indicate future performance?

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Recent fluctuations in the global stock market due to concerns about the subprime lending industry once again prove the old adage that ''past performance does not predict future performance.'' Another example of this thinking can be seen in the many recently published pandemic influenza epidemiologic models that used data from previous influenza pandemics to predict the likely behavior of a future pandemic.[1-4]

Influenza pandemics occur because a new influenza virus arises to which virtually no one has any preexisting immunity. Two separate questions might, therefore, be asked relating to the nature of the next influenza pandemic. The first, of particular interest to vaccine manufacturers, is which influenza subtype will cause the next pandemic? One popular current choice is the avian influenza A(H5N1) virus, which has, so for, killed the majority of the people it has been confrimed to have infected. However, this lethality is atypical of the more recent pandemic influenza viruses seen in the past century, although, admittedly, this may represent the early stages of the virus adapting to humans. Previous pandemic influenza viruses for which we have data—the 1918 ''Spanish'' [influenza A(H1N1)], 1957 ''Asian'' [influenza A(H2N2)], and 1968 ''Hong Kong'' [influenza A(H3N2)]—all had estimated case-fatality rates of 5% or less, which makes good evolutionary sense: you cannot propagate effectively if you kill too many of your hosts too quickly. The emergence of H5N1 as the next pandemic influenza strain is by no means certain and there are other potential avian influenza candidates to be considered for the next pandemic influenza strain, including H9, H6, or even H7 influenza viruses.[5,6]

The second question, of particular interest to infection control teams, is how transmissible the next pandemic influenza virus will be? This will not necessarily depend on the viral subtype, but more likely on the host immune responses—hence the possibility of some individuals becoming ''super-spreaders.'' There is a current debate on whether the next pandemic influenza strain will be transmitted mainly by short-range large droplets or by longer-distance small droplet nuclei (''true airborne'' transmission). The answer to this question is important, because it will determine the recommendations for which forms of personal protective equipment should be worn to reduce transmission and the resulting number of potential secondary cases (eg, surgical masks for large droplet transmission and N95 masks for airborne transmission). Ideally, when dealing with potentially pandemic influenza-infected individuals and until there is a better idea of the transmissibility of the next pandemic strain, all health care workers should wear masks with at least an N95 level of protection, but with the comfort and tolerance of the more conventional surgical masks. This opens up the opportunity for some innovative, new mask designs. This may take just as long and cost just as much as the development of a new H5N1 vaccine; however, it does not result in the same level of redundancy if the next pandemic influenza virus turns out not to be H5N1. Even if the next pandemic influenza virus is an H9, H6, or H7 virus, these masks will still be useful, and may therefore take an even higher priority for stockpiling than any specific vaccine.

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Disclosures: none.

Am J Infect Control 2008;36:466-7.

0196-6553/$34.00

doi:10.1016/j.ajic.2007.12.007

The transmissibility of an infectious agent is characterized by the value of the ''basic reproductive number'' (R_0, the number of secondary cases arising from a single infected index case in an otherwise totally susceptible population). Some of the more recently published epidemiologic models for the next influenza pandemic have implied that the value of R_0 will remain very similar to those seen in previous influenza pandemics by analyzing previous outbreak data, giving a relatively low R_0 of 1 to 4,[2,4] which others have found surprising.[7] Alternative studies have suggested a wider range of possible values for R_0 (2 to 21).[1,3] In fact, accepting a wider range of R_0 values may be a safer, more realistic approach to characterizing the nature of influenza outbreaks for pandemic planning purposes, especially since we know that outbreak reports are somewhat unreliable.[8] Such outbreak reports may have been even more unreliable during the times of the previous influenza pandemics when genomic sequencing and molecular epidemiologic techniques were unavailable, and when the stated cause of death on death certificates may have been in accurate. This would avoid a false sense of security—and certainly, the virus is unlikely to behave as we would like. In addition, R_0 values based on previous influenza pandemics may not be predictive for a future pandemic because the current and future host environment has changed. The world's population (and thus population density, particularly in large conurbations) has increased several times since the previous pandemics of 1918, 1957, and 1968. In addition, rapid, frequent air travel is now the norm in many parts of the world. People generally are far more mobile now than during the previous influenza pandemics—the dramatic consequences of which were clearly seen by the severe acute respiratory syndrome (SARS) outbreaks of 2003,[9] and the recent case of a U.S. citizen who traveled between North America and Europe while infected with extensively drug-resistant tuberculosis.[10]

So is influenza pandemic prediction like stock market forecasting? Yes, in some ways. In the same way, those who are investing in one particular outcome (eg, the H5N1 vaccine) have much to lose (not just in terms of dollars) if it turns out differently, as do those who are basing their plans for a future influenza pandemic on the behavior of previous pandemics. Such predictions may not necessarily come true, with severe consequences for public health policies worldwide. An alternative to new vaccine development that may run in parallel with these programs is the design of new, novel masks, as outlined previously, which may be an essential backup plan if the next pandemic virus does not match any stockpiled vaccines. Therefore, as with stock market investments, although we can follow our instincts and invest in those areas that we feel that will do well, we should have some insurance—just in case things do not turn out as planned.

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