Stochastic metapopulation modeling of multi-strain influenza dynamics

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Here we aim at providing a general framework capturing the dynamics of co-circulating influenza subtypes and to characterize replacement and co-existence conditions. We propose a time-continuous metapopulation stochastic model for three co-circulating subtypes incorporating three key processes of influenza dynamics: antigenic drift, seasonal forcing in transmission and temporary full cross-immunity. The model realism is enhanced by considering three age-classes with specific contact rates based on data. The network underlying the metapopulation structure comprises major cities in the world coupled through real passengers flows. The impact of key determinants (basic reproductive ratio – R0, antigenic drift rate, and seasonality) was explored through computer-intensive simulations based on parameters consistent with recent estimations. For realistic mean antigenic drift rates, resident subtypes can be replaced even by a new virus with a smaller R0. When R0=1.5 for all subtypes and assuming a strong seasonality, the probability of replacement tends to 1 for a rapidly evolving new subtype whatever the value of the antigenic drift rate for the resident subtypes. Co-existence of the three subtypes can be obtained for plausible ranges of parameter values. Besides the interpretation of the replacement or coexistence in terms of R0 and antigenic drift rate, our approach highlights the need of additional hypotheses on mechanisms avoiding the extinction of a new strain introduced in a system with two strains at equilibrium.