Title: Multiscale modeling of influenza infection for related intervention strategies

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Background: Influenza recurs each year in flu season and there are lots of studies about the aspect of prediction, surveillance, and intervention of the disease. Most of them focus on the transmission in a whole city or whole country. However, the transmission rate should be different for different age group and the community to community transmission is dominant in the spread of influenza. Besides, in previous SEIR (suspicious, incubative, infectious, and recovered) model, some critical parameters such as the state transition coefficients are set experientially, which may lead to a bias in the prediction.

Methods: We presented a multiscale SEIR model to model the transmission of people between two communities using the population based data collected in Wake Forest Baptist Hospital. The patients were divided into three groups, day care group (0-3 ys), school groups (4-18 ys), and company group (19+ ys). Each group was regarded as a community. Four states, suspicious, incubative, infectious, and recovered were considered. Specially, we calculated the state transition coefficients using animal model and correlate them with individual model. In order to understand the immune mechanism against influenza virus infection, animal data (including virus titer, immune cell number, cytokine/chemokine concentration, and so on) were first used to train and obtain the qualitative immune system. Clinical data, then, were used to train the qualitative model and obtain the quantitative model specific for human. The output from the within-host module is the profile of the viral dynamics, from which the state transmission rates for different age groups described above could be predicted based on the specific definition. Then, the transmissions within and between two communities were modeled. By adjusting the transmission parameters in the model, we could predict the outbreak of the diseases and evaluate the efficiency of interventions, such as school closure. We also investigated the effectiveness of influenza vaccination and presented the relationship between the coverage of vaccination and transmission rate.

Results: We estimated that children in day care have 2.37 times probability to be infected than kids in school and have 4.34 times probability to be infected than adults in company. We also estimated that during flu season, closing day care for 2 weeks may reduce the infectious rate 26%, and closing school for 2 weeks may reduce the reflection rate 18%, closing both can reduce the infection rate almost 40%. 50% coverage of vaccines helps reduce the reflection rate 30%.Conclusion: To decrease the transmission of influenza, effective intervention may be considered. School and day care closure may be a choice. But vaccine is the most effective intervention. Combination of strategies can increase the effectiveness of individual strategies.