A human challenge experiment points towards the importance of viral load dynamics and viral genetics in driving influenza symptoms. Preliminary report.

Multiple within-host models of influenza infection have jointly simulated viral load and symptom score dynamics. Few studies, however, have fit these models to empirical data from humans or considered how these dynamics may depend on viral genetics. Here, we fit the within-host model proposed by Canini and Carrat (2011) to time-course measurements of viral load and symptom scores from a human challenge experiment, and show that this model can successfully capture viral load and symptom score patterns of the study’s volunteers, as well as certain peripheral cytokine dynamics that were not used in model fitting. Allowing inter-individual variation in two parameters (the rate of viral infection and the ratio of viral production to clearance) improves the model fit, as determined by Akaike information criterion. These results indicate that inter-individual variation in viral load dynamics is the primary source of inter-individual variation in symptom score dynamics. We end by utilizing a unique dataset of temporal influenza virus sequencing within these same hosts to present preliminary ‘phylodynamic’ analyses that point towards viral genetics in explaining some of the inter-individual variation in viral load dynamics, with downstream consequences for symptom manifestation. (Received January 20, 2015)