Notice of the Final Oral Examination
for the Degree of Doctor of Philosophy

of

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MSc (University of Western Ontario, 2011)
MSc (University of Dhaka, 2008)
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“Mathematical Models to Investigate the Relationship between Cross-Immunity and Replacement of Influenza Subtypes”

Department of Mathematics and Statistics

Wednesday, November 22, 2017
9:00 A.M.
Clearihue Building
Room B017

Supervisory Committee:
Dr. Junling Ma, Department of Mathematics and Statistics, University of Victoria (Co-Supervisor)
Dr. Pauline van den Driessche, Department of Mathematics and Statistics, UVic (Co-Supervisor)
Dr. Steve Perlman, Department of Biology, UVic (Outside Member)

External Examiner:
Dr. Viggo Andreasen, Department of Science and Environment, Roskilde University

Chair of Oral Examination:
Dr. Dzifa Dordunoo, School of Nursing, UVic

Dr. David Capson, Dean, Faculty of Graduate Studies
Abstract

A pandemic subtype of influenza A sometimes replaces (e.g., in 1918, 1957, 1968) but sometimes coexists (e.g., in 1977) with the previous seasonal subtype. This research aims to determine a condition for replacement or coexistence of influenza subtypes. We formulate a hybrid model for the dynamics of influenza A epidemics taking into account cross-immunity of influenza strains depending on the most recent seasonal infection. A combination of theoretical and numerical analyses shows that for very strong cross-immunity between seasonal and pandemic subtypes, the pandemic cannot invade, whereas for strong and weak cross-immunity there is coexistence, and for intermediate levels of cross-immunity the pandemic may replace the seasonal subtype.

Cross-immunity between seasonal strains is also a key factor of our model because it has a major influence on the final size of seasonal epidemics, and on the distribution of susceptibility in the population. To determine this cross-immunity, we design a novel statistical method, which uses a theoretical model and clinical data on attack rates and vaccine efficacy among school children for two seasons after the 1968 A/H3N2 pandemic. This model incorporates the distribution of susceptibility and the dependence of cross-immunity on the antigenic distance of drifted strains. We find that the cross-immunity between an influenza strain and the mutant that causes the next epidemic is 88%. Our method also gives an estimated value 2.15 for the basic reproduction number $R_0$ of the 1968 pandemic influenza.

Our hybrid model agrees qualitatively with the observed subtype replacement or coexistence in 1957, 1968 and 1977. However, our model with the homogeneous mixing assumption significantly overestimates the pandemic attack rate. Thus, we modify the model to incorporate heterogeneity in the contact rate of individuals. Using the determined values of cross-immunity and $R_0$, this modification lowers the pandemic attack rate slightly, but it is still higher than the observed attack rates.