**Transmissibility of Swine Flu**

**Epi Modeling for Infectious Diseases Group Paper**

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**Introduction**

Influenza is a highly variable single stranded RNA virus that is one of the leading causes of death in the United States.[i] The most important aspect of human protection against the virus is the immune system’s ability to recognize virus surface proteins, but these proteins are highly variable so this can be difficult.[ii] Many different subtypes of influenza circulate in the human population, as well as in other animal populations, and some have the ability to cross from one species to another. Hemagglutanin (HA) is a surface protein that mediates virus binding and entry into the host cell, and neuraminidase (NA) is a surface protein that is necessary for mature virus to be released from the host cell after successful viral replication.[iii] These proteins are important in determining the ability of the virus to infect different animal species.

There are only 3 HA subtypes and 2 NA subtypes that are known to have successfully produced epidemics in the human population, so for new subtypes of influenza to be formed that can successfully infect humans, a combination of these HA and NA subtypes must be formed.[iv] There are two ways this can happen. There can be a direct species jump of an avian virus to humans, or there can be a recombination event that occurs in a mixing vessel that produces a virus with avian and human components.[v] Historically, pandemics have been linked to human strains that have recombined with an avian strain to produce a new subtype, using pigs as a mixing vessel.[vi] Understanding transmission dynamics between humans and pigs, a potential mixing vessel for new influenza subtypes, is important because of the epidemic potential of new influenza subtypes in a highly susceptible population.

In their paper, Wong *et al*. (2013) recognize the importance of understanding the transmissibility of an emerging influenza subtype seen in pigs and humans in order to better assess the potential impact the virus had and will have on the population. In this case, they created a model to determine the transmissibility of H3N2v from swine to humans at a fair where there were reports of respiratory illness in humans and swine. Although the results of this model cannot be generalized outside of this particular fair, the investigation and model are still very important for two reasons. The general model can be adapted and used for outbreaks seen at other fairs, and the results of the model can help to determine how transmissible the influenza subtype is, which is important for designing appropriate interventions for controlling the outbreak.

[i] Centers for Disease Control and Prevention. National Center for Health Statistics- Death and Mortality. February 25, 2016. Accessed April 23, 2016.<http://www.cdc.gov/nchs/fastats/deaths.htm>.

[ii] Russell, C.A. (2008). The global circulation of seasonal influenza A (H3N2) viruses. *Science, 320,* pp. 340-346.

[iii] Find review describing protein functions

[iv] Palese, P. (2004). Influenza: old and new threats. *Nature Medicine Supplemental*, *10*(12), pp. S82-S87.

[v] Stevens, J. (2006). Glycan microarray technologies: tools to survey host specificity of influenza viruses. *Nature Reviews Microbiology, 4*, pp. 857-864.

[vi] Stevens, J. (2006). Glycan microarray technologies: tools to survey host specificity of influenza viruses. *Nature Reviews Microbiology, 4*, pp. 857-864.

**Methods**

**Results**

Our model was simulated using the assumptions outlined by Wong et al. (2013). The basic reproductive number for swine-to-swine transmission was assumed to be R0=2. Our model estimated 9.5 swine were infected with H3N2pM over the 9-day duration of the fair. The estimated probability of H3N2v transmission to a susceptible human for each minute of contact with an infectious swine, used in our model, was . The Initial assumption for the model was that 1 swine was initially infectious at the beginning of the fair, or at time 0.

Among the 70,000 attendees of Fair A, 14,910 were estimated to have been exposed to swine and, therefore, were included in the initial population in our model. Among the population in contact with swine at the fair, 10% of the population aged <20 years old (children) and 50% of the population aged 20 years old (adults) were estimated to have preexisting immunity to H3N2v. This was reflected in the initial dynamics of our model as the initial number of susceptible children was 5821.1 and susceptible adults 4221, which represents 90% of the children and 50% of the adults respectively. The model was simulated over a time period of 20 days, in which the first 9 days represented the duration of the fair. The simulated number of H3N2v swine-acquired cases among those aged <20 years old that attended the fair was 81. The simulated number of H3N2v swine-acquired cases among those aged 20 years old was 47 cases. The 81 H3N2v swine-acquired cases among fair attendees aged <20 years old indicates 1.25% of children that had contact with swine became infected. The 47 H3N2v swine-acquired cases among fair attendees aged 20 years old indicates 0.55% of adults that had contact with swine became infected.

Our simulation attempted to reproduce the results from the Wong et al. (2013) simulation of swine-acquired H3N2v among fair attendees. Comparing our results to those of the simulation by Wong et al. (2013), we demonstrated that our simulation produced fairly consistent outcomes, although there are some minor discrepancies. Wong et al. (2013) simulation estimated 80 people aged <20 years old became infected at the fair, in comparison to our simulation, which estimated 81 people became infected; a one-person difference between simulations. The results were less consistent for the cohort aged 20 years old. The Wang et al. (2013) simulation estimated 58 people aged 20 years old became infected with swine-acquired H3N2v. Our model produced a lower estimate, as the number of people aged 20 years old that became infected in our simulation was 47. However, the results for our simulation of 47 people aged 20 years old becoming infected falls within the 95% CI for this value in the Wang et al (2013) study (95% CI: 29-96). Comparing the results of the two simulations in terms of total percentage that became infected with H3N2v from each of the age cohorts, the Wang et al (2013) simulation demonstrated 1.23% people aged <20 years old became infected, which is consistent with the results of our simulation 1.25%. In people aged 20 years old, the Wang et al (2013) simulation demonstrated 0.68% of people aged 20 years old became infected with H3N2v, whereas our simulation resulted in 0.55% of people aged 20 years old becoming infected. Overall, the results from our simulation are consistent with the results from the Wang et al. (2013) simulation and, although there are minor differences, our results fall within the range of potential values calculated in the 95% interval for the Wang et al (2013) simulation.

**Discussion**

The main objective of the paper was to simulate the swine flu outbreak that occurred at an agricultural fair and estimate transmissibility from swine to humans. This model and simulation would provide information on total number of H3N2v infections at the fair and thus predict cumulative incidence of swine flu from Day 0 of the fair up until 10 days after the last day of the fair. According to our results for cumulative incidence, which correlate with the results from the paper, there is an obvious increase in cases from the first day of the fair (Day 1) until around two days after the end of the fair (Day 12). After this point, the cumulative incidence steadies. We observe a peak in incident cases at Day 9 for both humans and swine. The observed and modeled H3N2v infections were similar, meaning the model is an accurate predictor of observed swine flu infections. For example, the model predicted 89 confirmed cases among fair attendees and in a similar real-life scenario, there were 73 confirmed swine flu infections identified.

Based on the results of this study, it is apparent that preventive measures should be put into place to prevent future swine influenza outbreaks from occurring at events with a large number of attendees, especially attendees who comprise younger children, as they may be at greater risk for H3N2v. One preventive measure would be to screen pigs for infectious diseases that could possibly be passed onto fair attendees. If they are found to be infectious, they should be isolated so that contact with humans is non-existent. Further, swine should be vaccinated to reduce the transmission of viral infections to other swine and also to reduce viral shedding. Another preventive measure would be to reduce close physical contact between swine and children, as many children are not yet immune to many forms of bacteria or viruses and thus have low immunity, making them more susceptible to contracting infectious diseases.

Although this study provided significant results, it has several limitations. Unavailability of data from Fair A was one major limitation, as the parameter estimates used for Fair A were largely based on data obtained from Fair B, a fair located in the same county that occurred three weeks after Fair A. Also, the minutes calculated of human-swine contact were an average between individuals in the cohort and other fair attendees. The way in which the study characterized swine contact is not particularly accurate since the researchers only accounted for the minutes an attendee spent at the barn and did not account for factors that could affect the outcome, such as how the pigs were handled and whether there was any direct contact. The reproductive number was based on past studies on swine flu transmission and may not be representative of the R0 in this setting. Lastly, the pigs were not tested for flu at the fair, so the number calculated could have easily been an overestimate or an underestimate. The authors of the paper made an error when describing βss as the force of infection when it is actually the transmission rate.

**Conclusion**

This study is a prime example of how infectious disease modeling can be used to investigate zoonotic outbreaks and determine transmissibility between animals and humans. This would have made for a stronger study if more accurate parameter estimates were utilized in the model, such as swine infection rates and more accurate swine-human contact numerical values based on actual physical contact. Nonetheless, this model can be used to predict incidence of swine flu in similar situations, including large events in which thousands of individuals are likely to come into contact with swine. It is important to be able to predict the outcomes of these types of situations since large populations are involved, children are involved and more likely to become infected, and physical contact between animals and humans is common. Modeling swine flu at fairs can inform ways of handling swine in future events and can play an important role in predicting future swine flu outbreaks at large congregational events.