High turnover drives prolonged persistence of influenza in managed pig herds

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The following is a summary of the stochastic model introduced in"High turnover drives prolonged persistence of influenza in managed pig herds" by Pitzer et al. (2016).[1] Apologies if some sentences are near retypings, sometimes it helps to retype things to better understand them. I wanted to read this paper since I might be working on a similar topic for poultry.

1 Introduction

Current swine influenza surveillance are dependent on opportunistic investigation of clinical incidents. As such, smaller scales are normally investigated, even though it is not clear at what scale may be most efficient for surveillance. This paper sought to understand at what scale influenza persisted in pig herds to better inform surveillance.

Swine populations have empirically and anecdotally noted that swine influenza appears to persist at very small population scales. The authors hypothesize that this may be due to the high, non-seasonal birth rate in pigs (approx. 20 piglets per sow per year) which provides constant replenishment of susceptible pigs, bypassing a lowering of persistence due to immunity.

Critical community size (CCS) refers to the size of a population necessary for likely fade-out, localized elimination, of a pathogen. For measles this has been estimated between 250,000 and 500,000 individuals, whereas for human influenza it may be closer to a billion during the summer months. Critical herd size (CHS) for swine influenza was previously unknown, although it is not expected to be larger during certain parts of the year since it appears to have weak seasonality.

2 Methods

A stochastic $MSIR(S)$ model is created, where M are protected by maternal antibodies and immune to infection, S are susceptible to infection, I are infected and infectious to others and R are recovered and immune to infection. Transitions are modeled as Poisson processes. The transitions are $M \to S$: 1/6 week^{-1}, $S \to I$: variable, $I \to R$: 1 week^{-1}, $R \to S$ (of sows): 1/39 week^{-1}, so maternal immunity wears off faster than natural immunity, and natural immunity lasts for nearly 10 months which is well beyond the infectious period of a week. We note that estimates of the CCS are particularly sensitive to the modeling of the infectious period e.g., it can be overestimated if modeled as an exponential, so the authors model it as a gamma by splitting up the I compartment.

Three farm types were studied:

1. farrow-to-finish farms: 300-3000 growers/finishers (10-24 weeks old), 180-1800 piglets/ weaners (0-9 weeks) and 100-400 sows (up to 3 years)
2. finishing farms (type 1): 250-5000 growers/finishers (10-24 weeks), no piglets, weaners or sows
3. finishing farms (type 2): 250-5000 growers/finishers, 100-2000 weaners, no piglets or sows

Aging was also modeled deterministically except for sows which were replaced by Poisson process (100-400 sows replaced at random intervals every 120 weeks on average). In the simplest case, the authors consider a finishing farm (type 1) where new cohorts of 10-week old pigs were imported either each week or every three weeks. These are continuous flow systems as opposed to all-in-all-out systems. Pigs at 22-24 weeks of age were sent to slaughter every three weeks.

Transmission-mixing matrices for the different age groups are used. In finishing farms, infected pigs are allowed to move, but do not have indirect contact with pigs from other facilities such as piglets or weaners. A similar assumption is made for farrow-to-finish farms where piglets/sows vs. weaners/growers/finishers mixed at rate 10 times higher than mixing between the different groups. The authors explore a range of mixing assumptions from homogeneous-mixing to assortative age-specific mixing.

Two scenarios of endemicity are modeled:

- Endemic, where influenza has circulated consistently in the past creating immunity in the population: the stochatic model is run for 500 years allowing for on average two random reintroductions of infection per year. The authors define the probability of stochastic fade-out as the proportion of years where there were no infectious individuals on the farm for two or more consecutive weeks, and this definition is created such that there is opportunity for reintroduction following fade-out. Even though it is possible for reintroductions to occur during periods of no transmission even when there is truly fade-out, this is true for both groups of a potential comparison, for example population sizes since random reintroduction is not dependent on population size, so the null of having no difference between the two is still satisfied.
- Naive, where there is no prior immunity: the simulation is run 500 times for 1 year and the probability of fade-out is the number of simulations where there were no infectious individuals present at the end of the year.

The CHS for a given $\mathcal{R}_0$ is the minimum population size for which the probability of fade-out is less than 0.05.

The authors ground truth the model by matching the seroprevalence among finishing pigs to the observed seroprevalence found in farms. $\mathcal{R}_0$ was constrained by the observed seroprevalence. Looking at Figure 1, the seroprevalence across farm sizes appear a bit random to me: for a given farm size, it's not clear that the seroprevalence is predictable. Across all simulations they report the mean seroprevalence as well as 95% prediction intervals.

3 Results

The authors generally find across different types of farms and across different birth intervals that relatively small population sizes are necessary for the probability of stochastic fade-out to be below 5%. When $\mathcal{R}_0 \geq 2$ persistence occurs with 1500 pigs and when $\mathcal{R}_0 = 1.5$ persistence occurs with 3000 pigs. Prevalence was generally found to be $\leq 8\%$ in the model. These results are sensitive to certain parameters:

- Persistence was more likely to occur when there was no prior immunity in the population
- When new cohorts of pigs occur every week rather than every three weeks fade-out is less likely to occur
- Farrow-to-finish farms had slightly lower persistence compared to finishing farms. Generally finishing farms were found to have higher persistence, matching intuition since they allow for more direct transmission within age groups, where the $\mathcal{R}_0$ within the compartment can be as high as 9 to 11, although the entire farm $\mathcal{R}_0$ is thought to be around 1.5 – 3
- Peak prevalence occurs 10 weeks of age (Figure 2)

4 Discussion

All-in-all-out strategies may be beneficial to decrease persistence, since there is not a continuous flow of susceptible pigs in this scenario. Generally, anything that can reduce the flow of susceptible pigs, such as having new cohorts of pigs at longer intervals, as well as mixing between pigs of the same age group or indirectly between age groups, can reduce persistence.

Surveillance methods may have a hard time knowing when persistence occurs since this can occur on a very small scale, akin to finding a needle in a hay stack. Each large-scale swine herd can harbor its own strain, making surveillance for a strain with pandemic potential difficult since there are so many herds.

References

[1] Virginia E Pitzer, Ricardo Aguas, Steven Riley, Willie LA Loeffen, James LN Wood, and Bryan T Grenfell. High turnover drives prolonged persistence of influenza in managed pig herds. *Journal of The Royal Society Interface*, 13(119):20160138, 2016.