One-Health Modeling of Pandemic Influenza in Human and Swine Populations

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Background

- Pandemic influenza H1N1 (pH1N1) 2009 has rapidly spread from humans to pigs across many countries with few suspected cases of back transmission from pigs to humans (Howden *et al.*, 2009; OIE, 2010).
- Recently influenza A(H3N2)v virus transmission from pigs to humans with limited spread from human-human was reported in the US (Lindstrom *et al.*, 2012).
- Influenza viruses present a continued pandemic threat; it is therefore important to understand transmission dynamic and control strategies at the swine-human interface.

Objectives

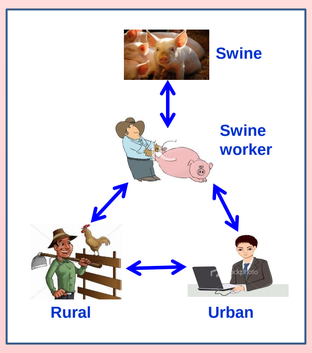
- Study transmission dynamics of pH1N1 2009 at the swine-human interface and investigate alternative intervention strategies.
- Investigate the feasibility of using NAADSM (North American Animal Disease Spread Model) for modeling spread of directly transmitted zoonotic diseases.

Materials and Methods

Study population

- Population data from a selected county in Ontario with high swine farm density and a good mixture of rural and urban settlements were extracted from agricultural census of 2006 (Source: Statistic Canada, 2006).

Populations	Units	Individuals
Swine-herds (SH)	488	733,107
Swine-worker-households (SWH)	733	2,325
Rural non-swine-worker households (RH)	7,879	25,521
Urban-households (UH)	21,095	54,038
Total	**30,195**	**814,991**



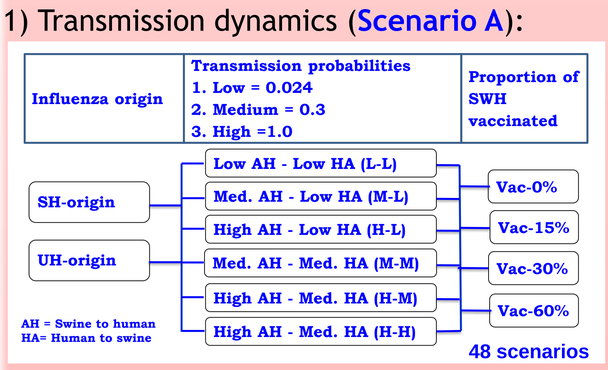
Modeling approaches

- Spatially explicit, stochastic agent-based state transition models were constructed and implemented in NAADSM.
- Unit of simulation was at farm or household level.
- Each scenario was simulated 1,000 times for 365 days.

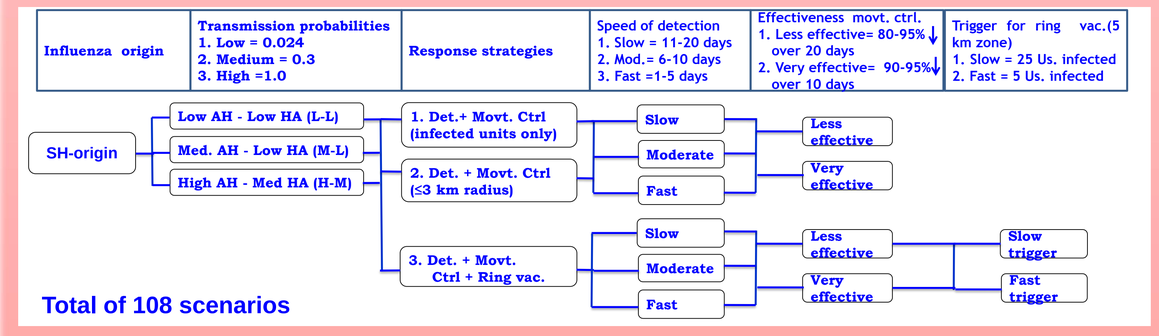
Scenarios

Following scenarios were investigated:

1) Transmission dynamics (**Scenario A**):



2) Response strategies (**Scenario B**) evaluated were:
(a) Transmissibility at swine-human interface (3-levels); (b) 3-response strategies: (i) speed of detection (3-levels) and quarantine and movement control of infected units only; (ii) scenario (i) plus quarantine of all units ≤3 km zone; (iii) scenario (i) and (ii) plus ring vaccination ≤5 km zone. Two levels effectiveness of movement control and speed of implementing ring vaccination were assessed.



Parameters

- Parameters were extracted from the literature and expert opinion.

Contact type	Contact /day	Transm. probability	Distribution of distance of recipient unit
1. Swine – swine	Direct = 0.06	1	BetaPERT (0.8, 20, 100)
	Indirect = 0.196	0.01	BetaPERT (0.8, 20,100)
2. Swine – human	1	0.024; 0.3; 1	Uniform (0.1, 0.5)
3. Human – human			
SWH - SWH	0. 857	0.024	BetaPERT (0.5, 20, 100)
SWH - RH	4.286	0.024	BetaPERT (0.1, 10, 30)
SWH - UH	0.857	0.024	BetaPERT (1, 30, 65)
RH - SWH	0.857	0.024	BetaPERT (0.1, 10, 30)
RH - RH	4.286	0.024	BetaPERT (0.01, 20, 100)
RH - UH	0.857	0.024	BetaPERT (1, 30, 65)
UH - SWH	0.036	0.024	BetaPERT (1, 30, 65)
UH - RH	0.071	0.024	BetaPERT (1, 30, 65)
UH - UH	12.893	0.024	BetaPERT (0.01, 10, 30)

Statistical analyses

- Epidemic duration, and proportion and number of units infected were assessed using multivariable survival, fractional logistic and negative binomial regressions respectively.
- Results were presented as predicted marginal effects.

Results

1. Scenario A

Percentage of units infected (median and range):
(i) SH = 83 (67-100); (ii) SWH = 69 (34-100); RH = 54 (47-61); UH = 36 (34-38).

(a) Duration of outbreak

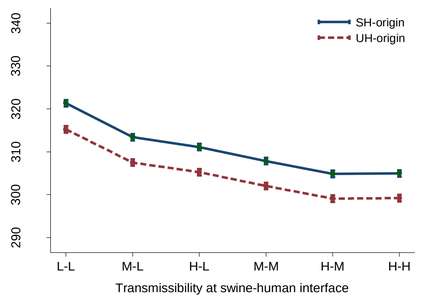


Fig. 1: Shows the effect of virus origin on the duration of outbreak at different levels of transmissibility adjusted for the effect of vaccination. It was relatively shorter for UH origin compared with SH origin. This effect was similar at all levels of transmissibility in the absence of response strategies

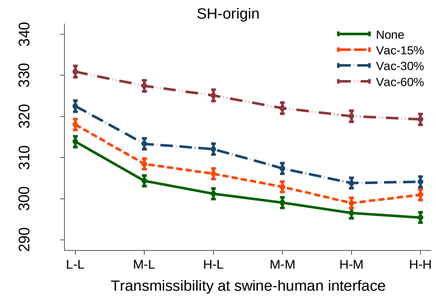


Fig. 2: Shows that the effects of vaccinating SWH and different levels of transmissibility of virus had significant impact on the duration of outbreak. Higher vaccination coverage significantly prolonged the duration of outbreak, whereas higher transmissibility shortened it. These impacts were similar irrespective of the origin of the virus

b) Proportion of units infected

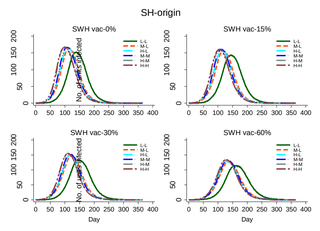


Fig. 3: Epidemic curves showing total units infected over time. Low vs. medium to high transmissibility and vaccinated vs. non-vaccinated delayed day to peak epidemic by 19-40 days and 3-30 days respectively. Corresponding figures for the reduction in no. of peak epidemic day cases were 12-22 and 6-38 units respectively

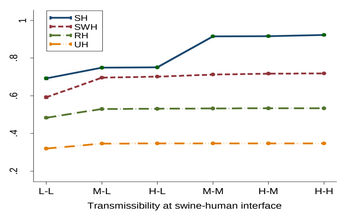


Fig. 4: Shows that the effect of different levels of transmissibility on proportion of units infected was significant only for SH; whereas its effect was negligible on other units (except for some differences observed between L-L vs. other levels for SWH unit). No difference was observed between the two sources of the virus origin

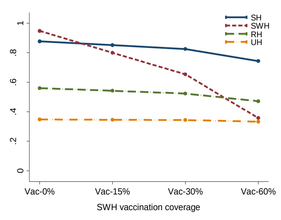


Fig. 6: Shows that the effect of vaccinating SWH at different levels had significant impact on SWH, and some effect on SH and RH. However, it had no impact on UH

2. Scenario B

Number of units infected (median and range):
(i) SH = 2 (1-340); (ii) SWH = 2 (0-490); RH = 0 (0-808); UH = 0 (0-739).

a) Duration of outbreak

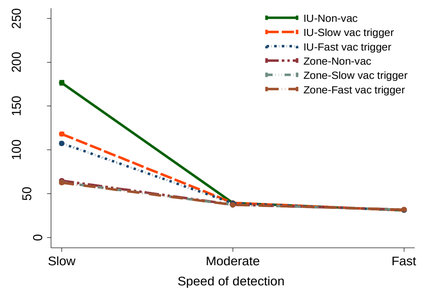


Fig. 7: Shows significant effects of speed of detection, zoning and speed of starting ring vaccination on the disease outbreak duration. Furthermore, effects of these control measures depended on each other. The effects of zoning and ring vaccination had impact only at the low speed of detection

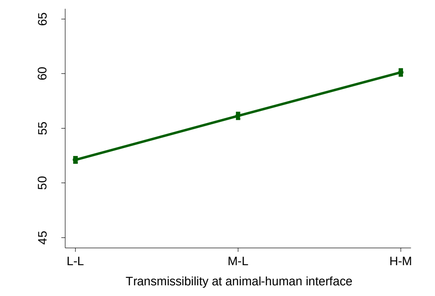


Fig. 8: Shows that the effect of different levels of transmissibility on duration of outbreak was relatively small (approximately <8 days) after adjusting for the effects of other covariates.
No difference between two levels of effectiveness of movement control was observed (result not shown)

b) Number of units infected

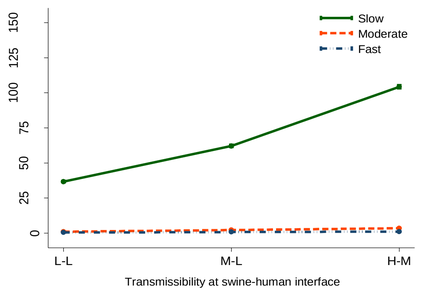


Fig. 9: Shows that the effect of speed of detection on the no. of units infected depended on the levels of transmissibility after adjusting for other covariates. No difference between the moderate and fast levels of detection was observed at all levels of transmissibility, whereas at the low speed of detection more no. of units were infected with increasing transmissibility levels. This association was similar across all units

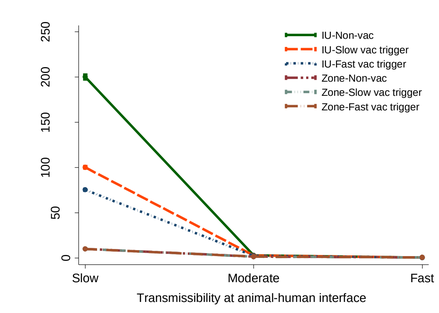


Fig. 10: Shows the significant effects of speed of detection, zoning and ring vaccination on the no. of units infected after adjusting for other covariates in the model. Zoning and ring vaccination had impact only at the low speed of detection.
No difference between two levels of effectiveness of movement control was observed (result not shown)

Discussion and conclusion

- A total of 2.5% (1188/48,000) iterations of scenario A underwent epidemic fade out (all of swine origin), suggesting extent of random extinction which may be happening in real world contexts.
- Targeted vaccination of SWH had beneficial impact by reducing no. of units infected (all except UH) and no. of peak epidemic day cases, and delaying day to peak epidemic. This will provide authority with adequate time to manage any disease outbreak and minimize burden on health care facilities.
- Reducing transmissibility at the swine-human interface to low level had significant impact even in the absence of control measures; therefore swine workers should observe good personal hygiene and avoid direct contact with sick pigs.

Discussion and conclusion

- Effective quarantine measures on infected units alone was adequate to control outbreaks if it was combined with more rapid speed of detection. However this level of compliance may not be achieved in the real world.
- This work allowed us to identify many gaps, in terms of influenza transmission parameters at the swine-human interface, contact frequencies between SWH, RH and UH, and natural infection history at farm and household levels.
- NAADSM provides a feasible platform for modeling such disease under certain simplifying assumptions.
- Our results should be interpreted qualitatively (not quantitative predictions!).

References
Howden, KJ *et al.* (2009) Can Vet J, 50, 1153-61.
Lindstrom, S *et al.* (2012) Emerg Infect Dis, 18, 834–837.
OIE (2010). Weekly Disease Information. Paris (available at: http://www.oie.int/wahis/public.php).

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