Epidemiology of The Influenza A Virus Applied to Multi-Pen Pig Farms

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Abstract

Influenza A virus is a major concern in pork production. Influenza does not only affect our swine markets around the world, but it also affects swine care-givers as well as the greater population. In this study, the focus is on the dynamics of swine herds in order to understand the spread of influenza. Understanding the epidemiology of influenza will further support efforts in decreasing infected swine populations and preventing an ongoing pandemic. Matlab and ode45 have helped develop fully continuous mathematical models that represent a multi-pen pig farm. These models allow us to examine the differences in model dynamics between the populations of pigs separated by age, resulting in the use of one, two and four class models. Three basic SEIR models were constructed to understand the spread of influenza in swine herds and discovered that population size is inversely related to infection activity. To summarize the observations, greater swine populations resulted in less rapid influenza spread between the swine pens. With the three assortments of pig populations, additional experimentation dove deeper into sensitivity, vaccination and r0. For sensitivity, manipulation of parameters indicated each parameter's influence on population numbers and transmission rates of swine herds. Vaccination studies allowed the examination of how maternal immunity transferred to piglets affects model dynamics as well as the differences between homologous and heterologous vaccinations. Models from previous research [10] predict that piglets can obtain immunity from their mothers vaccination but is not lifelong and may lead to the piglets becoming susceptible again. The analysis of r0 guides research towards differentiating the severity of influenza in comparison to other viruses. Additionally, the results demonstrate the significant impact influenza A has in swine herds all over the country. Controlling the spread is vital in regards to public health and in understanding epidemiology.

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1 Introduction

Among the zoonotic diseases known to modern science, influenza has been one of the most costly, deadly, and infectious diseases to date. Swine demand and consumption has led it to be one of the highest produced meats, maintaining a stable consumption rate of about 67 pounds per capita from 1999 to 2001 [7]. Even though there is a growing amount of knowledge on the influenza pandemic, there is not any necessary data regarding the decrease of transmission within certain population of swine. By the nature of zoonoses, careful understanding of the organism capable of transmitting such a devastating infection to our population is the bare minimum.

The pigs that are consumed and exist today stem from the Eurasian Wild Boar [4] of the past. Pig domestication has been traced back to the Near East at around 9000 BC [4]. After a short period of time, agriculturists began integrating these animals into their farms and then breeding them for public consumption. These creatures exhibit behaviors depicting them as highly sociable beings that spend large amounts of time rooting for food. Until recent history, farming consisted of a mix of harvesting plots and livestock with small populations of pigs. In modern farming, more than billions of pigs are bred and slaughtered each year for the meat industry. Within the pig farming industry there are various housing methods applied. These housing methods range from immense control over environmental and individual pig territory to less regulated enclosures. In general, three categories exist on the "spectrum" of pig housing. The first being intensive, this housing method has the most regulations and restrictions. Breeding animals are kept indoors in close confinement systems were temperature and ventilation are tightly controlled for the entire enclosure. The second method, semi-intensive, maintains the same indoor enclosure system with separation of farrowing sows into crates and less committed control onto temperature and ventilation. Extensive housing is the third method which utilizes the most relaxed conditions to mimic a pigs natural outdoor habitat.

Because pork is one of the highest meat consumption rates in the US [7], safety and bio-security is crucial in pig farms. A pigs life cycle in a pig farm occurs in four different stages; gestation, farrowing, nursery, and growing/finishing [3]. The cycle as a whole takes about six months on average, however females can move through the cycle multiple of times. Gestation is also known as the pregnancy of a gilt. A normal gestation period is 116 days on average and the goal during this stage is to conserve exemplary weight [2],[3]. The pregnant swine are in a controlled and comfortable environment so the risk of losing the pregnancy is not an outcome. When the pregnant swine are ready to give birth, they go into the farrowing phase which takes

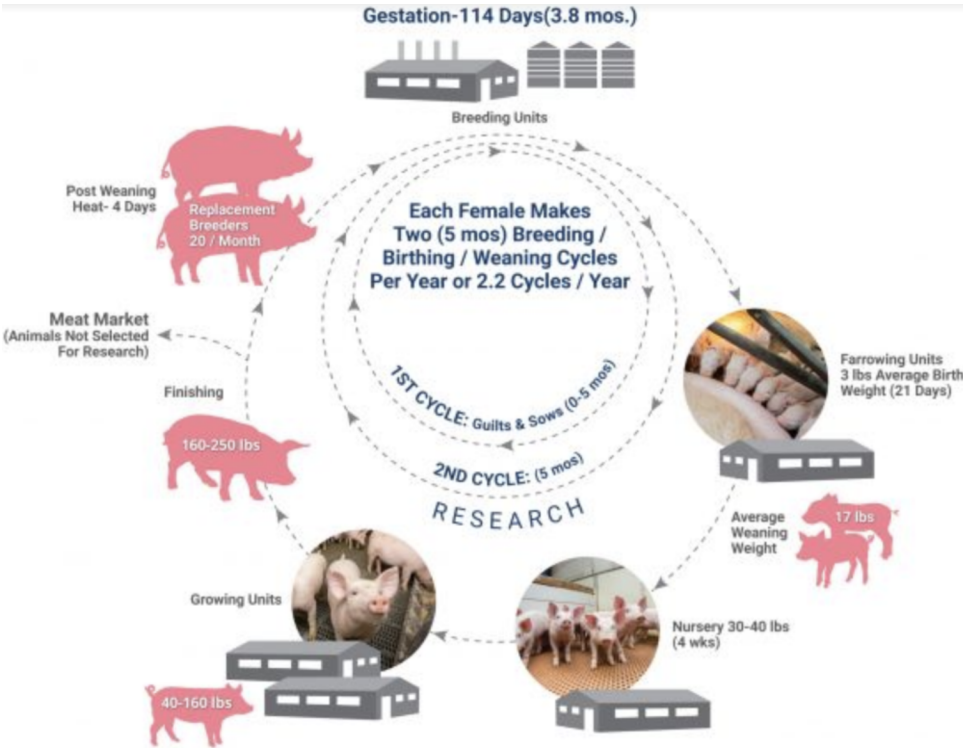

Figure 1: This Figure depicts the stages of a pigs breeding life cycle on a farm, [2].

on average 21 days [2]. In this phase they are moved to a new pen with enough room for their litter of piglets which can range anywhere from 4-20 [3]. The sows nurse their piglets for the 21 day period and after the stage, the piglets should weigh about 14 pounds [2]. For the next six to eight weeks, piglets are moved to the nursery phase. In this phase they are with other piglets and they tend to grow up to 50-60 pounds [3]. The goal of this stage is to slowly change the piglets diet from dairy to a more plant based protein [2]. An intensive housing method is crucial here due to the biosecurity needed to keep the piglets healthy and at ideal body weight. Once the piglets are their ideal body weight, they are moved to growing pens to finish their cycle. Once the six month mark hits, the swine should be a desirable weight of about 280 pounds [3],[8]. Before the swine reach the market, females who have superior structure will be chosen to go through the breeding process [2].

Earlier forms of Influenza A were found in swine and over time, the virus has adapted to impact not only pigs but humans as well. It is a very contagious respiratory disease and can be transmitted to humans through direct and/or direct contact. Humans and pigs can acquire the disease by contact with other pigs who are infected or environments that may be contaminated with the virus. [10]. The rate at which pigs are infected with the influenza virus is subject to the swine's age, vaccination status, and whether or not they have antibodies in their system [10]. Vaccinations are frequently used in many farms to control the spread

of influenza. It has been proven that the infection rate as influenza spreads decreases when vaccinations are used, however specific tendencies on which type of vaccination works best. [11]. Maternal immunity can be derived from mother to offspring once the mother has been vaccinated. However, the piglets' derived immunity only lasts for about 3 weeks [10], which adds to the difficulty in understanding and controlling influenza within multi-pen pig farms. Because little is known about how vaccination affects the transmission of influenza within different pig populations [11], in this study, the dynamics between homologous or heterologous vaccinations are examined.

Mathematical modeling is used to create real life scenarios and help in providing insight with different diseases, business sales, weather patterns, etc [8]. In this experiment, it is used to portray variations in the population of pigs; whether that be one class of pigs, two classes of pigs, or four classes of pigs, and how that may or may not contribute to the transmission rates of the Influenza A. Although there is some research on disease transmission in pig farms, such as Salmonella [6] and influenza [10], there is no distinct research on separating the pig farms into different classes and reviewing the comparison. In this study, the focus is on influenza transmission rates. The models created are based on recent experimental data on influenza within swine farms, specifically transmission rates [10].

Acknowledging multi-pen pig farm cycles is crucial in this experiment because each 'class' is separated by a stage in the pig farm cycle. Swine farm cycles occur in 4 stages; gestation, farrowing, nursery, and growing/finishing [2]. Completing the cycle takes about six and a half months. Gestation occurs when a gilt (female pig) becomes pregnant and gives birth to a piglet. Sows (mother pigs) typically give birth to about 13 piglets per litter. Piglets continue through the cycle and in the growing/finishing stage are ready to either be transferred out of the farm or chosen to give birth and go through the cycle once again [2]. These four stages of pig farms are important in understanding how fast an infection spreads between the different classes of population.

In this study, models that mimic a swine farm are created to represent the characteristics of a swines' life cycle and the epidemiological barriers that are created from influenza. The goal of this experiment is to portray the evolution of infection within each population. Based on a previous study, it was estimated that piglets have the highest infection levels of influenza on swine farms [10]. It is hypothesized that piglets, being in their own class will derive maternal immunity from their mothers vaccination but depending on how long the piglets have the immunity, the influenza rates could increase at a later time. It is also hypothesized that once all swine are separated into different classes, the classes with the most population will have a lower transmission rate. The goal is to portray (a) the dynamics of infection within one class of

swine (2500 swine), (b) the dynamics of infection within two classes of swine (one pin having 1000 and the other pin having 1500 swine), and (c) the dynamics of infection within four classes of swine (gestation, gilt, farrows, and piglets). Within all of these models, two things will be experimented on, (a) the sensitivity of the transmission rates, and (b) the vaccination status within each class of swine.

2 Methods

2.1 One Class Model

The model mirrors a multi-pen swine breeding farm. Gilts, sows, and piglets are incorporated in the meta-population model simulating the different housing and time periods of each stage and the movement from one stage to another. The movement of swine throughout the farm is a fully continuous model created using ODE45 in MATLAB. Figure 2 shows one class of 2500 swine. Once a swine enters the farm, it is placed in either a S, E, I, or R category. Every pig is susceptible and once it becomes exposed, it has the potential to move through the different stages in order to be recovered, as seen in Figure 2. The exposed period for swine lasts two days and after those two days they are infected for another five [10]. During this time frame, the swine are infected for the full seven days. If the swine happen to not get infected by the influenza virus at all, there is a black arrow in Figure 2 that represents the birth cull rate. This birth cull rate indicated the number of swine leaving the group of pigs at one time, in this case that number is assumed and it is kept constant at 12.

2.1.1 Transmission Flow Chart

2.1.2 Equation and Parameters For One Class of Pigs

Our breeding model represents a continuous meta-population epidemiological model that revolves around all 2500 pigs being in one pen. We define separate SEIR differential equations for the one class of swine.

$$\frac{dS_1}{dt} = BC - \beta * S_1 * I_1 * -\mu * S_1 \tag{1}$$

$$\frac{dE_1}{dt} = \beta * S_1 * I_1 * -\mu + \sigma * E_1 \tag{2}$$

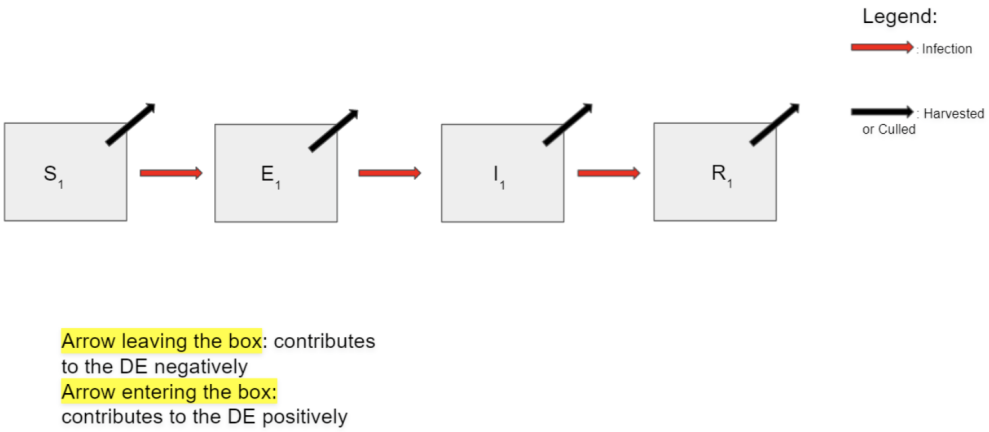

Figure 2: This Figure depicts the changes in susceptible, exposed, infected, and recovered pig population during 46 days with 2500 pigs initially.

Initial Conditions		
t0	0	Time (days)
tf	46	Time (days)
N	2500	Total population of pigs
y0=[S(0), E(0), I(0), R(0)]	[2499,0,1,0]	Initial Values

Table 1: Initial Conditions within the differential equations of the swine breeding farm model with one class of pigs.

$$\frac{dI_1}{dt} = \sigma * E_1 * -(\mu + \gamma) * I_1 \tag{3}$$

$$\frac{dR_1}{dt} = \gamma * I_1 - (\mu) * R_1 \tag{4}$$

In equations 1-4 above, S_1 represents the number of susceptible swine in class 1, E_1 represents the number of swine who have been exposed (but not yet infected), I_1 represents the number of swine who are infectious, and R_1 represents the number of swine who have been recovered from the infection. Every swine in the farm is categorized in one of these states. We use a parameter of N which equals 2500. This is an assumption as to how many swine are in the farm at all times.

Model Parameter	Value	Meaning
BC	12	Birth cull rate
β	0.285	Direct transmission rates for sows and gilts
σ	0.5	Reciprocal of average duration of latent/exposed period
μ	$\frac{12}{2500}$	natural death rate for sows and gilts
γ	0.2	reciprocal of average duration of infectious period (or recovery rate)

Table 2: Parameters involved within the differential equations of the swine breeding farm model with one class.

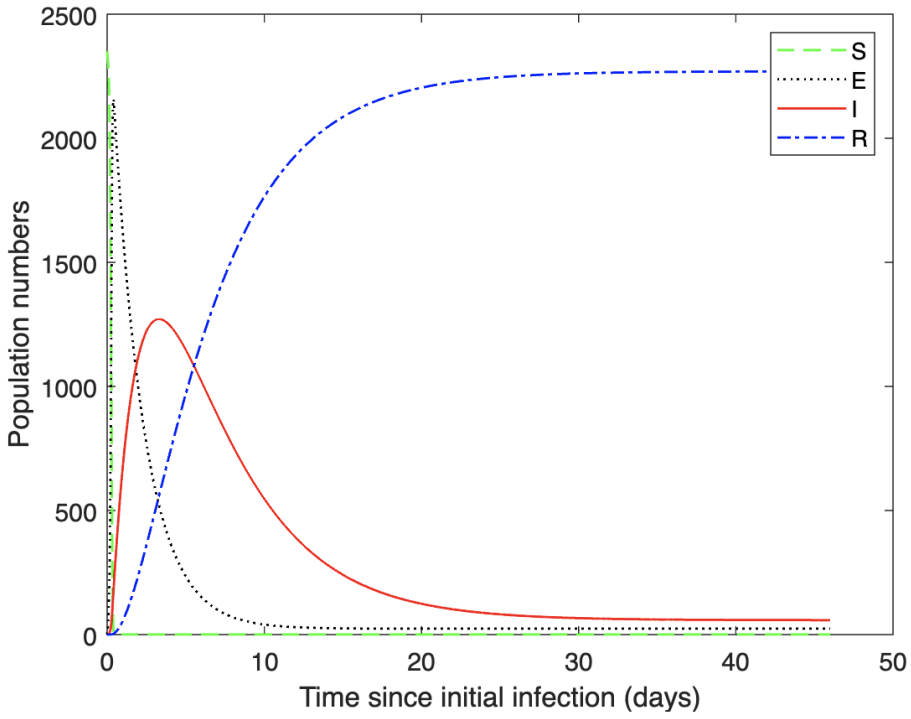

Figure 3: This Figure depicts the changes in susceptible, exposed, infected, and recovered pig populations during 46 days with 2500 pigs. ODE45 was used in Matlab.

2.1.3 SEIR Model

2.2 Two Class Model

The two class model illustrates a multi-pen swine breeding farm as well, however there are differences in parameters. Unlike the first model, in the second model all 2500 pigs have been separated into two groups. This has been done to determine and compare transmission rates of influenza. It is assumed that the population in the first pen, also known as N1 consists of 1500 pigs and the population in the second pen, also known as N2 consists of 1000 pigs. Because the population numbers vary in the two class model, so does the transmission rate of Influenza. The more populated we have an area, the less time it will take for the disease to spread. The infection rate in the first pen is .285 and the infection rate in the second pen is .0016. We define separate SEIR differential equations for the two classes of swine:

2.2.1 Equations and Parameters For Two Classes of Pigs

$$\frac{dS_1}{dt} = BC - \beta 1 * S_1 * I_1 - \beta_2 * S_1 * I_2 - BC * S_1/N_1 \tag{5}$$

$$\frac{dE_1}{dt} = \beta_1 * S_1 * I_1 + \beta_2 * S_1 * I_2 - (BC/N_1 + \sigma) * E_1 \tag{6}$$

$$\frac{dI_1}{dt} = \sigma * E_1 - (BC/N_1 + \gamma) * I_1 \tag{7}$$

$$\frac{dR_1}{dt} = \gamma * I_1 - BC * R_1/N_1 \tag{8}$$

$$\frac{dS_2}{dt} = -\beta_1 * S_2 * I_2 - \beta_2 * S_2 * I_1 + BC * S_1/N_1 - BC * S_2/N_2 \tag{9}$$

$$\frac{dE_2}{dt} = \beta_1 * S_2 * I_2 + \beta_2 * S_2 * I_1 + BC * E_1/N_1 - BC * E_2/N_2 - \sigma * E_2 \tag{10}$$

$$\frac{dI_2}{dt} = \sigma * E_2 + BC * I_1/N_1 - BC * I_2/N_2 - \gamma * I_2 \tag{11}$$

$$\frac{dR_2}{dt} = \gamma * I_2 + BC * R_1/N_1 - BC * R_2/N_2 \tag{12}$$

In equations 5-12 above, the population is separated into two different classes, one with 1500 pigs (class 1) and one with 1000 (class 2). The equations for class 1 are denoted with a subscript of 1 whereas the equations for class 2 are denoted with a subscript of 2. The BC value of 12 stays the same; here it is defined as the birth cull rate at which 12 pigs are removed from the second pin only and moved to a different farm, etc. The σ and γ values remain the

Initial Conditions		
t0	0	Time (days)
tf	46	Time (days)
N_1	1500	Total Population of Pigs in Pen 1
N_2	1000	Total Population of Pigs in Pen 2
y0= [$S_1(0)$, $E_1(0)$, $I_1(0)$, $R_1(0)$] $S_2(0)$, $E_2(0)$,$I_2(0)$,$R_2(0)$]	[1499,0,1,0,1000,0,0,0]	Initial Values

Table 3: Initial Conditions within the differential equations of the swine breeding farm model with two classes of pigs.

Model Parameter	Value	Meaning
BC	12	Birth cull rate
β_1	0.285	Infection rate pen 1
β_2	0.0016	Infection rate pen 2
σ	0.5	Reciprocal of average duration of latent/exposed period
γ	0.2	reciprocal of average duration of infectious period (or recovery rate)

Table 4: Parameters involved within the differential equations of the swine breeding farm model with two classes.

same as the first class. Comparing differential equations to the transmission model Figure 5 the subtraction in the equations refers to the arrows leaving the boxes, hence the arrows entering the boxes refers to an area in the differential equation where addition is used. This is a practical and common method in differential equations when SEIR models are involved.

2.2.2 SEIR Models

2.2.3 Transmission Flow Chart

2.3 Four Class Model

The four class model exhibits a multi-pen swine breeding farm that encompasses each stage in the pig cycle process. The four classes that the swine were separated in are gestation, gilts, farrowing, and piglets. These differential equations exhibit a fully continuous model with differences in parameters when compared to the first class and second class models. In the four class model, all 2500 pigs are split up into 4 groups which means the population across the different groups varies. In this case we are specifically looking at what stage makes the swine more susceptible to contracting influenza. We define separate SEIR differential equations for four classes of swine:

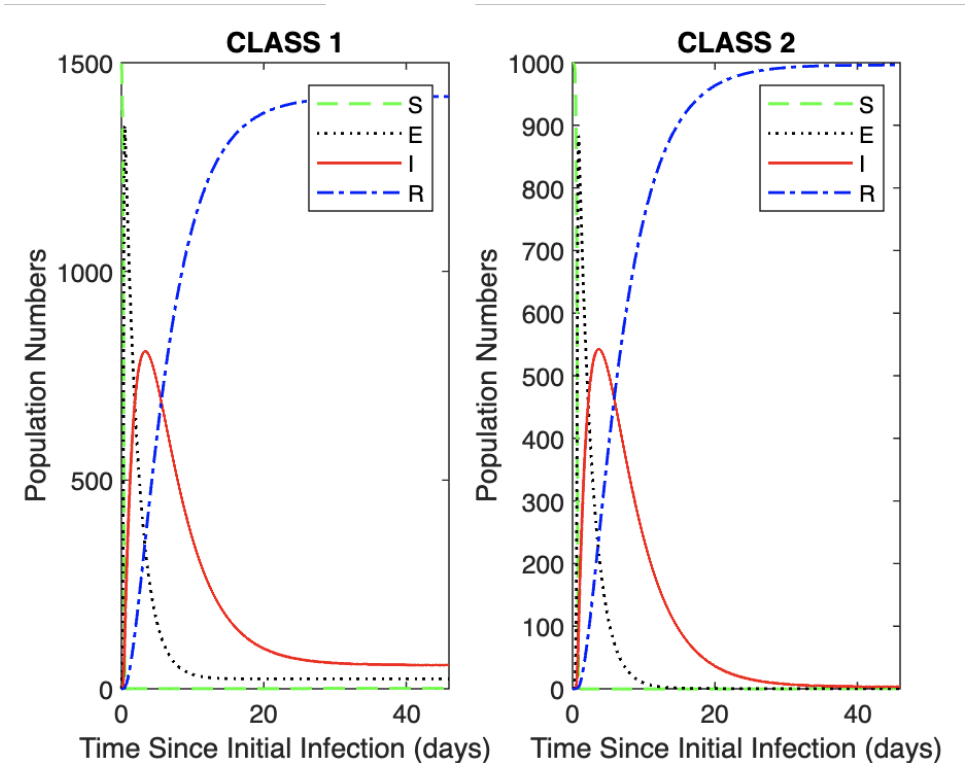

Figure 4: This Figure depicts the changes in susceptible, exposed, infected and recovered pig populations of two interacting pens over the duration of 46 days

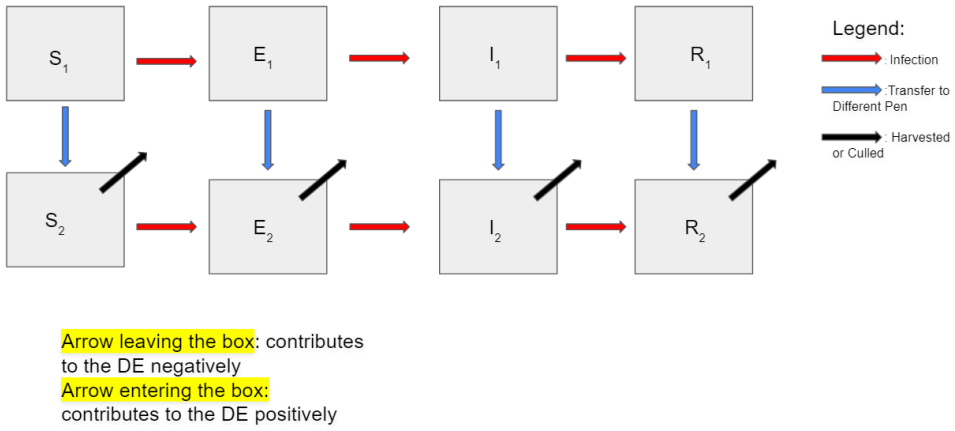

Figure 5: This Figure depicts the changes in susceptible, exposed, infected, and recovered pig populations during 46 days with 2500 pigs initially.

2.3.1 Equation and Parameters for 4 Classes of Pigs

$$\frac{dS_1}{dt} = BC - \beta_1 S_1 I_1 - \beta_2 S_1 (I_2 + I_3 + I_4) - BC\frac{S_1}{N_1} \tag{13}$$

$$\frac{dE_1}{dt} = \beta 1 S_1 I_1 + \beta 2 * S_1 (I_2 + I_3 + I_4) - BC\frac{E_1}{N_1} - \sigma_1 E_1 \tag{14}$$

$$\frac{dI_1}{dt} = \sigma_1 E_1 - \frac{BC}{N_1} I_1 - \gamma_1 I_1 \tag{15}$$

$$\frac{dR_1}{dt} = \gamma_1 * I_1 - \frac{BC}{N_1} * R_1 \tag{16}$$

$$\frac{dS_2}{dt} = -\beta_1 * S_2 * I_2 - \beta_2 * S_2 * (I_1 + I_3 + I_4) + BC * \frac{S_1}{N_1} - BC * \frac{S_2}{N_2} \tag{17}$$

$$\frac{dE_2}{dt} = \beta_1 * S_2 * I_2 + \beta_2 * S_2 * (I_1 + I_3 + I_4) - BC * \frac{E_2}{N_2} + BC * \frac{E_1}{N_1} - \sigma_1 * E_2 \tag{18}$$

$$\frac{dI_2}{dt} = \sigma_1 * E_2 + \frac{BC}{N_1} * I_1 - \frac{BC}{N_2} * I_2 - \gamma_1 * I_2 \tag{19}$$

$$\frac{dR_2}{dt} = \gamma_1 * I_2 + \frac{BC}{N_1} * R_1 - \frac{BC}{N_2} * R_2 \tag{20}$$

$$\frac{dS_3}{dt} = -\beta_1 * S_3 * (I_3 + I_4) - \beta_2 * S_3 * (I_1 + I_2) + BC * \frac{S_2}{N_2} - BC * \frac{S_3}{N_3} \tag{21}$$

$$\frac{dE_3}{dt} = \beta_1 * S_3 * (I_3 + I_4) + \beta_2 * S_3 * (I_1 + I_2) + BC\frac{E_2}{N_2} - BC * \frac{E_3}{N_3} - \sigma_1 * E_3 \tag{22}$$

Model Parameter	Value	Meaning
BC	12	Birth cull rate
β_1	0.285	Infection rate pen 1
β_2	0.0016	Infection rate pen 2
σ_1	0.5	Reciprocal of average duration of latent/exposed period
γ_1	0.2	reciprocal of average duration of infectious period (or recovery rate)
PP	$N_3 * 12$	Population of Piglets
BRP	$12 * \frac{N_3}{28}$	Birth rate of Piglets

Table 5: Parameters involed within the differential equations of the swine breeding farm with four classes.

$$\frac{dI_3}{dt} = \sigma_1 * E_3 - \gamma_1 * I_3 + BC * \frac{I_2}{N_2} - BC * \frac{I_3}{N_3} \tag{23}$$

$$\frac{dR_3}{dt} = \gamma_1 * I_3 + BC * \frac{R_2}{N_2} - BC * \frac{R_3}{N_3} \tag{24}$$

$$\frac{dS_4}{dt} = BRP - \beta_1 * S_4 * (I_3 + I_4) - \beta_2 * S_4 * (I_1 + I_2) - BRP * \frac{S_4}{PP} \tag{25}$$

$$\frac{dE_4}{dt} = \beta_1 * S_4 * (I_3 + I_4) + \beta_2 * S_4 * (I_1 + I_2) - BRP * \frac{E_4}{PP} - \sigma_1 * E_4 \tag{26}$$

$$\frac{dI_4}{dt} = \sigma_1 * E_4 - \gamma_1 * I4 - BRP * \frac{I_4}{PP} \tag{27}$$

$$\frac{dR_4}{dt} = \gamma_1 * I_4 - BRP * \frac{R_4}{PP} \tag{28}$$

In equations 13-28 above, there are 16 distinct differential equations. The subscript 1 is denoted for the first class of swine, the subscript 2 is denoted for the second class, the subscript 3 is denoted for the third class, and the subscript 4 is denoted for the fourth class. There are changes in parameters in these equations; population numbers and beta values. The group with piglets have a higher population because there is so much more of them; 13 per mother sow [10]. The equations follow the same model; we subtract the exposed from the susceptible category and add it in to the exposed category while also subtracting a birth cull rate, and so on within every class of swine. In class 3 however, there is an instance where piglets can develop an infection of influenza from their mother, this is denoted in I_3.

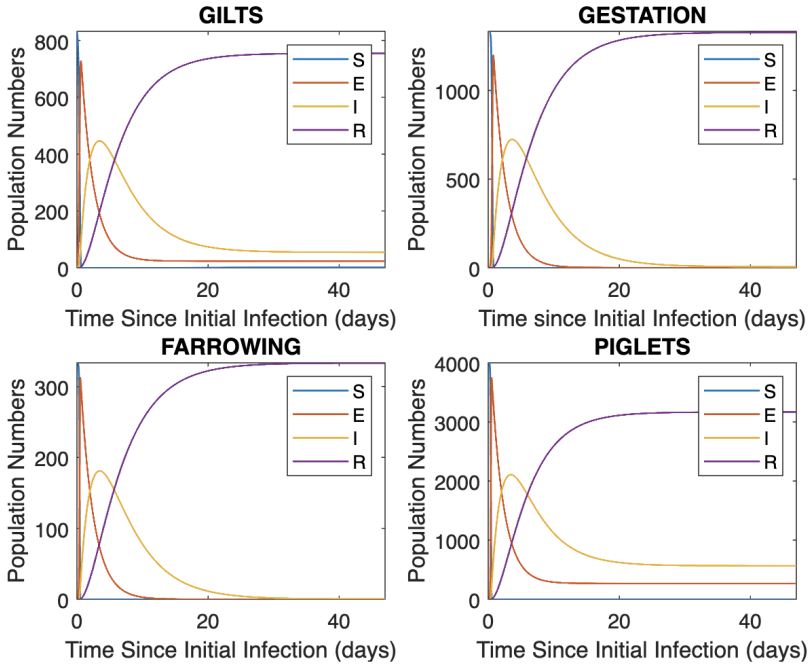

Figure 6: This Figure depicts the dynamics of four interactive pens each with lines representing the susceptible, exposed, infected, and recovered pig population over the time span of 46 days.

Initial Conditions		
t0	0	Time (days)
tf	46	Time (days)
N_1	833	Number of pigs in pin 1
N_2	1333	Number of pigs in pin 2
N_3	333	Number of pigs in pin 3
y0=[$S_1(0)$, $E_1(0)$, $I_1(0)$, $R_1(0)$] $S_2(0)$, $E_2(0)$,$I_2(0)$,$R_2(0)$ $S_3(0)$, $E_3(0)$,$I_3(0)$,$R_3(0)$ $S_4(0)$, $E_4(0)$,$I_4(0)$,$R_4(0)$]	[832,0,1,0,1333,0,0,0,333,0,0,0,PP,0,0,0]	Initial Values

Table 6: Initial Conditions within the differential equations of the swine breeding farm model with four classes of pigs.

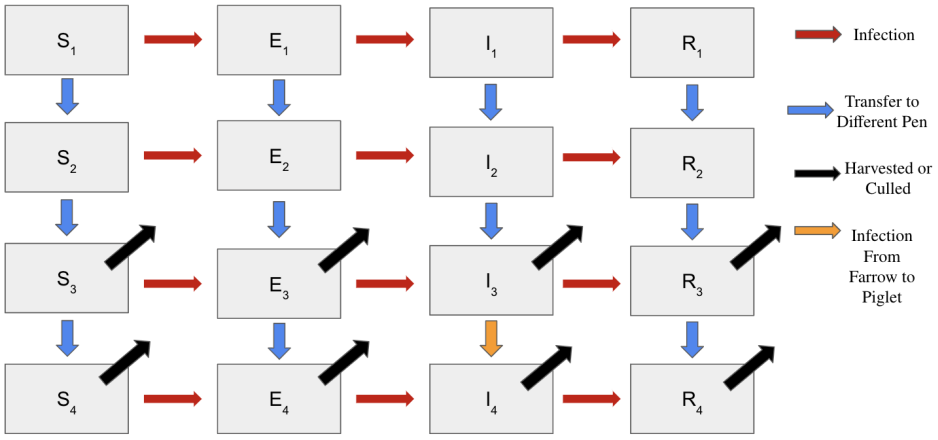

Figure 7: This Figure depicts the changes in susceptible, exposed, infected, and recovered pig populations during 46 days with 2500 pigs initially.

2.3.2 SEIR Models

2.3.3 Transmission Flow Chart

In the Figure 7 there are four classes, class 1 refers to the gilts, class 2 refers to gestation, class 3 refers to the farrowing stage, and class 4 refers to piglets. All of these stages are interactive within one another. In this instance we have two areas where the sows can be 'culled' out of the farm. In the third class; farrows can be chosen to go through the cycle again and give birth to more piglets and in the fourth stage, piglets can be 'culled' to a different farm. This is shown with the black arrows in Figure 7. Besides that, the SEIR model is used as usual where each pig is placed in one category S,E,I, or R, and they move throughout the process, either becoming infected - to recovered or moving from class 1 to class 2, etc.

3 Model Modification: Sensitivity

As discussed, the specific parameters that drive the models take into account real life statistics to create a more realistic curve. Manipulating these parameters, specifically the infection rate among pigs, allows researchers to observe how each change impacts the dynamics of the model. Epidemiological mathematical models depend on precise and accurate parameters that represent various phenomena such as transmission rates, reproduction rates, death rates, and other occurrences that impact model dynamics. Because no one can ever realistically know how fast the transmission rates of any disease is, doing a sensitivity analysis helps portray a

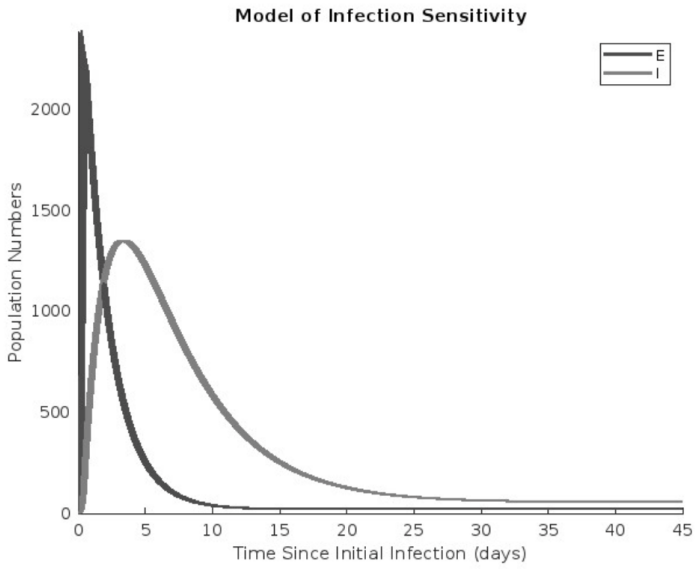

Figure 8: This Figure depicts the impact on the exposed and infected pig populations when varying the beta parameter within a 95 percent confidence interval on the one class model.

realistic model which in return can help reduce outbreaks and future infections.

In this experiment, we incorporated all of the previous SEIR models and differential equations to indicate how sensitive our transmission value of influenza is. We examined the one class of pigs, the two classes of pigs, and the four classes of pigs. All parameters remained the same besides our β value which is the direct transmission rate. With the help of MATLAB and ode45, β was declared to be a global variable and we incorporated lower bounds and upper bounds as to what our β value could potentially be. Below are graphs that depict the change and sensitivity of β. While we are manipulating how direct and indirect transmission rates of influenza inside the swine pens, the model maintained an incredibly similar dynamic. Though we adjust our β for a wide array of values, the infection population does not vary profoundly from the initial β determination. Our experimentation utilizes 'one at a time' sensitivity measures in order to inspect dynamics differences between parameter values. This method solely applies constant values for point estimates chosen for the parameters [5].

3.1 Sensitivity for One Class

In figure 8 there is a sensitivity analysis done on the first class of pigs. We are specifically comparing the global 'infected' plot to our original to determine how accurate our β value of .285 is. So, this model depicts multiple β values on top of each other to give us a thick line indicating the average values. The values of β that were used are values increasing by a

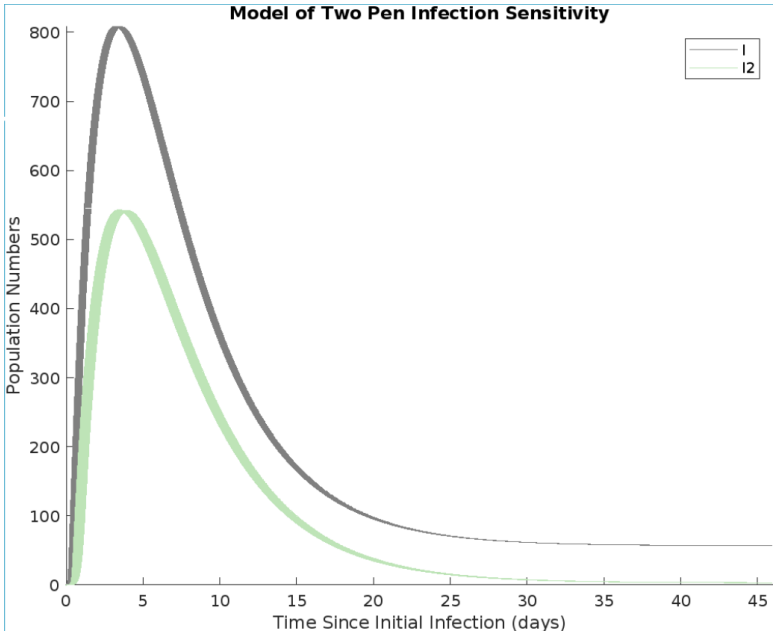

Figure 9: This Figure depicts the impact on the infected pig populations when varying the beta parameter from 0.91 to 1.091 on the two class model.

hundredth from 0.091 to 0.9. Naturally, since β represent our constant of infection 'chance', a higher β value will relate to a higher infection curve and vice versa for a smaller β value. In our single class model, the infection rate is the same for every pen, given by the single β representation in the equation. Figure 8 reflects the impact of infection rate variation on both the exposed and infectious population. Comparing 8 to figure 3, there is very little deviation from the basic rise and fall dynamic of the infectious population curve

3.2 Sensitivity for Two Classes

In figure 9 there is a sensitivity analysis done on the second class of pig. We are examining both infected populations from the first class and the second class. I1 represents the infected population from class 1 and I2 represents the infected population from class 2. Because there are two different variations of β for each class, β is used as a global variable twice in this instance. Once again, the values of β that were used to determine sensitivity rates are values increasing by a hundredth from 0.091 to 0.9.

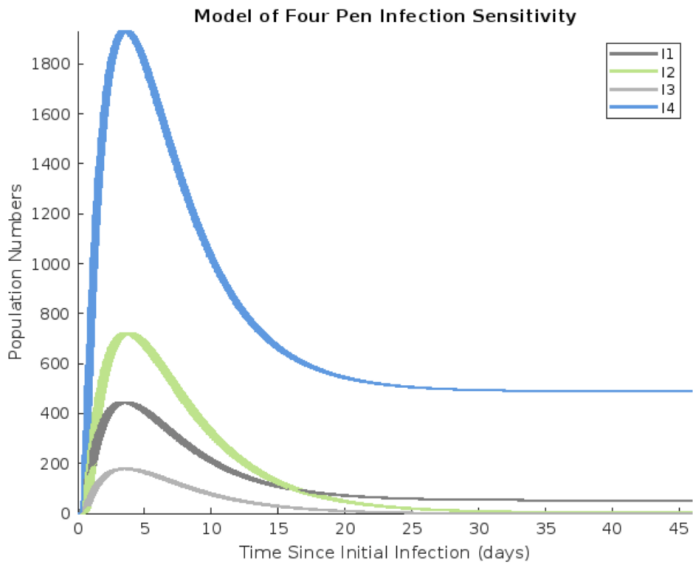

Figure 10: This Figure depicts the impact on the exposed and infected populations when varying the beta parameter from 0.91 to 1.091 on the four class model.

3.3 Sensitivity for Four Classes

In Figure 10 there is a sensitivity analysis done on the four classes of pigs. Similar to Figure 9, we are examining the difference in the infectious populations within the four classes. I1 to I4 where I1 represents the first class and so on. In this instance we are still using β as a global variable but now we are utilizing four β values instead of two. The β bounds stay the same at 0.091 to 0.9.

4 Model Modification: Vaccination

Vaccination is commonly used within swine farms to control influenza [10]. There are two main types of vaccinations that are used in a swine farm; mass vaccination and pre-farrow vaccination. Mass vaccination refers to all sows and gilts being vaccinated at once whereas pre-farrow vaccination is when sows are vaccinated 5-3 weeks prior to giving birth. Pre-farrow vaccination is important when regarding maternal immunity [10]. Pigs can be born with antibodies to fight off the influenza virus if their sow has been vaccinated. However, this maternal immunity has been seen to decline after 3 weeks, leaving the pigs at risk once again. Therefore, the pre-farrow vaccination is an ongoing process unlike the mass vaccination [10]. Within the pre-farrow procedure, vaccinations can either be homologous or heterologous. Homologous refers to a vaccine with samples of influenza from the specific population of the

Initial Conditions		
$\beta 1$	0.285	Original Transmission Rate
$\beta 2$	0.014	Pre-farrow Homologous Vaccination
β_3	0.174	Pre-farrow Heterologous Vaccination
β_4	0.0275	Mass Heterologous Vaccination

Table 7: Initial Conditions within the vaccination study.

farm itself [1]. Heterologous indicates a vaccine with samples of influenza from not only the original farm population but from samples of a wide variety of farms [1]. This can better help the pigs in gaining antibodies they need if they ever come into contact with different strains of influenza.

The difference between heterologous and homologous vaccinations are strategically important when discussing the influenza outbreak. Because vaccine development can take almost several months, the disease has the ability to create different and more lethal strains [9]. Strains of influenza that are more fatal can result in another swine flu pandemic which in return will impact farm markets and eventually production rates around the country. It is hypothesized that swine who receive the heterologous vaccinations will be less susceptible to become infected from all variations of the swine flu across farms. When discussing immunology, it is known that ones immune memory can be educated and can remember certain lymphocytes that can portray innate responses [12], this means that ones immune system has the ability to store data, or in this case cells and antibodies. This is important because if a vaccination has more than one strain of the same virus (heterologous), then ones immune system has a better chance to fight the disease off. Therefore, the heterologous vaccination seems to be the most beneficial in this case because it has the potential to give the swine long lasting protective responses due to the different strains that the cells of the swine will be exposed to [12].

4.1 Vaccination for One Class

Figure 11 illustrates the vaccination protocols used on one class of swine; all 2500 swine in one pin. The four options used for vaccination are no vaccination, mass heterologous, pre-farrow heterologous, and pre-farrow homologous. We are again plotting only the infectious populations regarding their vaccination status. To do this, β is used as a global variable and we change the transmission rates because once vaccination is in the picture, transmission rates will maneuver according to whether or not the vaccination strategies are beneficial. There are four different β values used in the vaccination experiment. First, our no vaccination status gives us a β_1 value of the original transmission rate, which was β_2 =0.285. The direct transmission rates

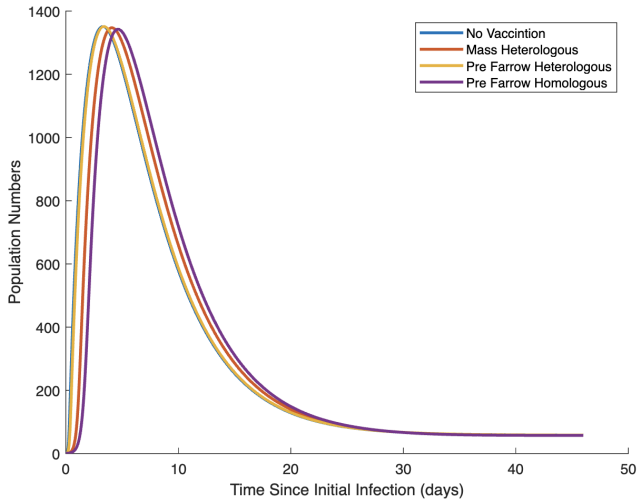

Figure 11: This Figure depicts the different types of vaccinations used for one class of pigs.

for swine that are vaccinated with the pre-farrow homologous vaccination is $\beta_3 = 0.014$. The rates for swine that are vaccinated with the pre-farrow heterologous vaccination is $\beta = 0.174$. Lastly, the mass heterologous vaccination rate is $\beta = 0.0275$. These transmission rates for β are incorporated from previous research done on vaccination strategies; [10].

4.2 Vaccination for Two Classes

In Figure 12 there has been a vaccination study done on the two class model. The same types of vaccinations are used as well as the same β values. Only the infectious populations are being plotted in respect to their vaccination status. Looking at the two figures, there is not any significance in denoting the pros and cons of vaccination. The first class of swine looks very similar to the second class of swine and we see that the no vaccination parameter is very similar to the pre-farrow heterologous; both lines are on top of one another. This makes sense because our β values for these two vaccinations are the most similar. Looking at the model for the first class of pigs, it seems like there is a slight change in the time since the initial infection days. The first class of pigs seem to recover quicker than the second class of pigs. This could be because of the variation in populations, as mentioned before, class one has 500 more swine then class two does.

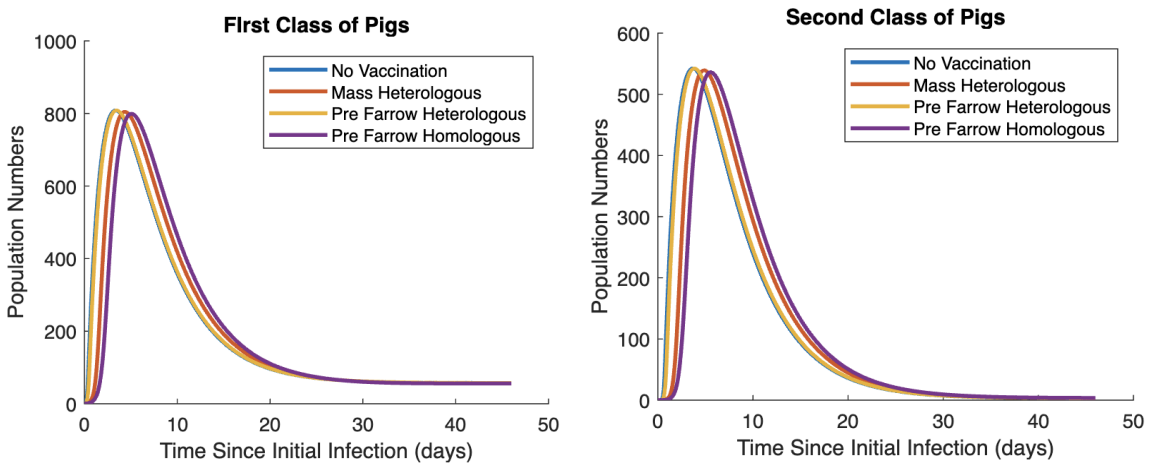

Figure 12: LEFT: This Figure depicts the different types of vaccinations used for the first class of pigs. RIGHT: This Figure depicts the different types of vaccinations used for the second class of pigs.

4.3 Vaccination for Four Classes

In Figures 13 and 14 we have the four class model vaccination strategies. The vaccination strategies are similar to that of the one class and two class model; no vacciantion, mass heterologous, pre-farrow heterologous, and pre-farrow homologous. The β values remain the same once again as we use β as a global variable. Each different infected class is being viewed separately. Overall, there does not seem to be any significant changes within transmission rates, population, and vaccination strategies. The models once again show that no vaccination and pre-farrow heterologous vaccinations are very similar in keeping the constant β value whereas the peak of infection starts a little later with the mass heterologous pre-farrow homologous vaccination. The piglets vaccination model, Figure 14 shows an interesting curve. Although the β infection rates aren't deterred enough, there is a later start at which infection occurs. However, looking forward into the figure, that eventually fades and the peak of infection starts once again. This is hypothesized to have to do with maternal immunity and the three week period where piglets are immune to the influenza disease [11].

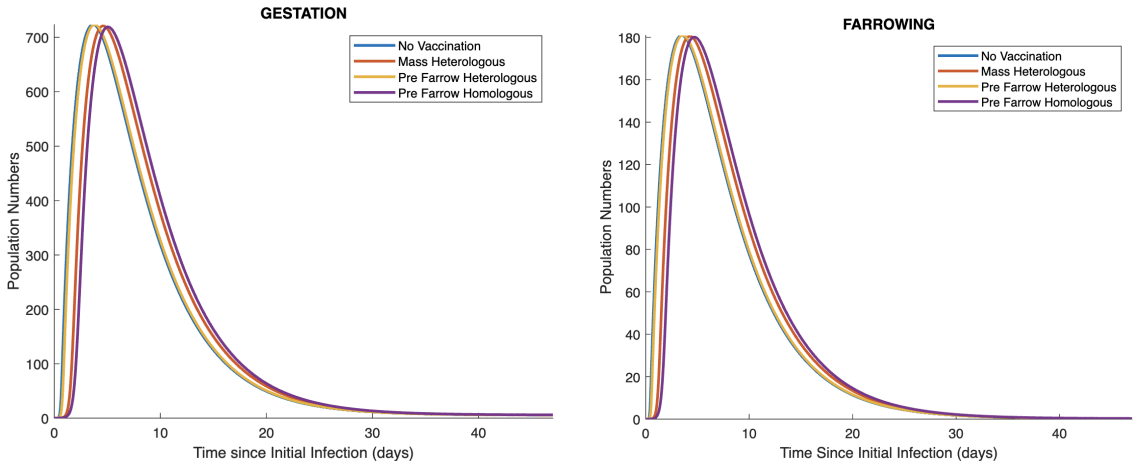

Figure 13: LEFT: This Figure represents the 'Gestation' group of the four class model and how each type of vaccination impacts the transmission of the influenza A virus. RIGHT: This Figure represents the 'Farrowing' group of the four class model and how each type of vaccination impacts the transmission of the influenza A virus.

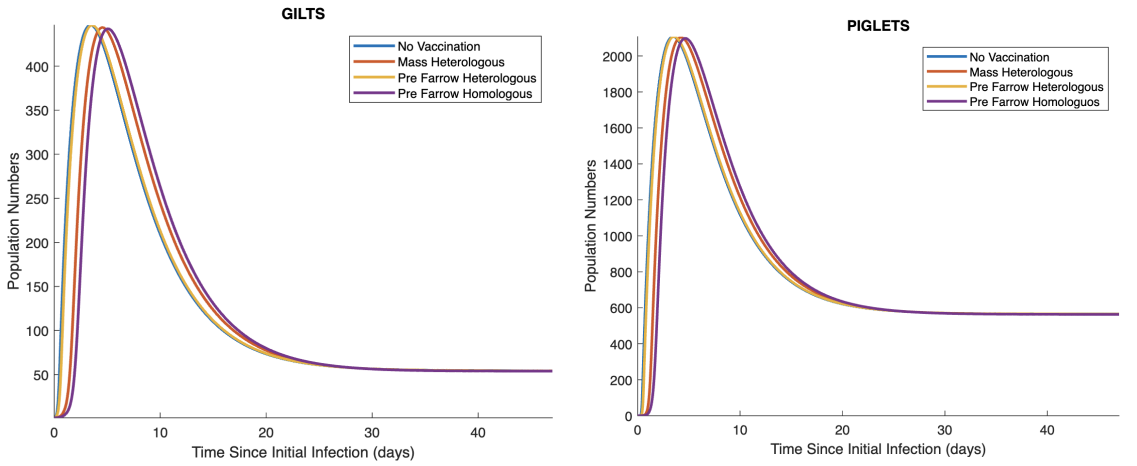

Figure 14: LEFT: This Figure represents the 'Gilts' group of the four class model and how each type of vaccination impacts the transmission of the influenza A virus. RIGHT This Figure represents the 'Piglets' group of the four class model and how each type of vaccination impacts the transmission of the influenza A virus.

5 R0

Using the next generation method, we calculate R_0 by assuming that $S = 1$ i.e. there is one susceptible individual and look at the operators surrounding the equations for the exposed and infected pigs. The operations surrounding the E and I terms are written as $\mathcal{T}$=$\mathcal{F}$-$\mathcal{V}$. Next, the uppercase Roman letters F and V are denoted as the Jacobean matrix, or matrix of first order partial derivatives associated with each the operators $\mathcal{F}$ and $\mathcal{V}$. Finally, R_0 is the largest eigenvalue FV^{-1}.

In the case of a single pen model with one class each of E and I, we have that

$$F = \begin{bmatrix} 0 & \beta_1 \\ 0 & 0 \end{bmatrix},$$

and

$$V = -\begin{bmatrix} -\frac{BC}{N} - \sigma_1 & 0 \\ \sigma 1 & -\gamma_1 - \frac{BC}{N} \end{bmatrix}.$$

Using Matlab, we substitute the parameter values and compute the eigenvalues of FV^{-1} which in this case is 1.3784.

In the case of a two-pen model with two classes each of E and I we order the variables the same as in the ODEs. We then can write

$$F = \begin{bmatrix} 0 & \beta_1 & 0 & \beta_2 \\ 0 & 0 & 0 & 0 \\ 0 & \beta_2 & 0 & \beta_1 \\ 0 & 0 & 0 & 0 \end{bmatrix},$$

and

$$V = -\begin{bmatrix} -\frac{BC}{N_1} - \sigma_1 & 0 & 0 & 0 \\ \sigma_1 & -\gamma_1 - \frac{BC}{N_1} & 0 & 0 \\ \frac{BC}{N_1} & 0 & -\frac{BC}{N_2} - \sigma 1 & 0 \\ 0 & \frac{BC}{N_1} & \sigma_1 & -\gamma_1 - \frac{BC}{N_2} \end{bmatrix}.$$

Using Matlab, we substitue the parameter values and compute the eigenvalues of FV^{-1} which in this case is 1.3611, which is lower than for the single pen model.

Next, we consider the full case of three classes of pigs and a class of piglets. In this case we

have four classes each of E and I.

So we have

$$F = \begin{bmatrix} 0 & \beta_1 & 0 & \beta_2 & 0 & \beta_2 & 0 & \beta_2 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \beta_2 & 0 & \beta_1 & 0 & \beta_2 & 0 & \beta_2 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \beta_2 & 0 & \beta_2 & 0 & \beta_1 & 0 & \beta_2 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \beta_4 & 0 & \beta_4 & 0 & \beta_4 & 0 & \beta_3 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix},$$

and V is equal to

$$-\begin{bmatrix} -\frac{BC}{N_1} - \sigma_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \sigma_1 & -\gamma_1 - \frac{BC}{N_1} & 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{BC}{N_1} & 0 & -\frac{BC}{N_2} - \sigma_1 & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{BC}{N_1} & \sigma_1 & -\gamma_1 - \frac{BC}{N_2} & 0 & 0 & 0 & 0 \\ 0 & 0 & \frac{BC}{N_2} & 0 & -\frac{BC}{N_3} - \sigma_1 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{BC}{N_2} & \sigma_1 & -\gamma_1 - \frac{BC}{N_3} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \frac{BRP}{PP} - \sigma_1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \sigma_1 & -\gamma_1 - \frac{BRP}{PP} \end{bmatrix},$$

.

Using Matlab, we substitute the parameter values and compute the eigenvalues of FV^{-1} which in this case is 1.3619, which is lower than for the single pen model, but slightly higher than the two pen model due to the piglet infections.

6 Discussion

Our multi-month simulation of influenza infection dynamics within swine farms displayed the multilayered relationships between pen separation, β variation, and differing vaccination strategies. Firstly, the direct relationship between population size and time until complete population recovery supports previous research. Displayed by the pen separation, larger population sizes or less population separation results in delayed recovery time. The four pen model displays rapid recovery rates in comparison to the remaining two models. Sensitivity studies involving

a varying β within a controlled range presented predictable results. Increasing β values, the infection constant, directly increased the infection population numbers over time. Additionally, vaccination strategies involving immunity from maternal swine being passed onto their offspring revealed interesting results. Though this immunity being transferred from parent to child was effective, the immunity was not everlasting. After a short period of three weeks, the piglets were no longer protected by the parental immunity and were vulnerable to infection.

Our predictions happen to be interchangeable when compared to this field of research on influenza A in swine farms. Encouraged by the results of a previous experimental study [10] we modified populations and experimented on the different sub populations of swine in respect to influenza rates. The models examined consisted of one class, with 2500 swine grouped in the same pen, two classes, with a separation of the 2500 swine in each pen, and four classes with the stages of a pig farm cycle incorporated as a class/pen. With the pen separation, we tested vaccination strategies as well as a sensitivity analysis. Our model results depict that the vaccination strategies chosen are not abundant enough to eradicate influenza in swine farms all together. Looking forward, solutions may consist of different vaccinations, intensive biosecurity measures such as temperature and ventilation, and separating the population of pigs into even smaller sub populations to strictly deter influenza. One other future research question might be quarantine. If a susceptible pig becomes exposed, maybe placing that pig in quarantine for a certain amount of days will cause the spread of influenza in swine farms to decrease rapidly. However, that would require more focused watch on all of the pigs which can be costly and time consuming.

In this study, we had multiple limitations. We had an assumption of one farm with 2500 swine. The results to this study could change depending on the number of farms we experimented on. We also only focused on one strain of influenza with a short time period. If we looked at a different strain of influenza we may or may not see some different results depending on the intensity of the virus. Another option would have been to also look at different viruses in comparison to influenza, such as salmonella. Taking into considerations the limitations and assumptions, the dynamics of influenza in a swine farm can change with future research.

7 Acknowledgements

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