Examining the Implications of a 7th Grade Pertussis Booster Program in the State of Ohio

Thesis

Presented in Partial Fulfillment of the Requirements for the Degree of Master in Mathematical Science in the Graduate School of the Ohio State University

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ABSTRACT

The state of Ohio has been witnessing an increase of pertussis incidence over the past few years. This increase could be attributed to better recognition, reporting, and waning vaccine immunity. As a result, Ohio has implemented a vaccine booster program for 7th graders to try to curb the incidence. We use a model from Hethcote [2] to model the behavior of pertussis in Ohio, based on parameters from Hethcote as well as from literature and data from the Ohio Department of Health. The model is then fit to incidence reports from the Ohio Department of Health and the behaviors are examined. We identified two scenarios that matched the data, one of which has low transmissability but high reporting and the other with high transmissibility and low reporting. The vaccine booster is then implemented in the model with different reporting rates and incidence contributions. We observed that the impact of the booster seemed to be dependent on reporting rate of cases, where the higher reporting rate leads to a greater impact than the lower reporting rate.

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CHAPTER 1

INTRODUCTION

Pertussis is a highly contagious bacterial respiratory disease caused by *Bordetella pertussis*, that is usually transmitted through coughing and sneezing. A main characteristic of pertussis is the uncontrollable coughing attacks that result from infection, which result in an individual being short of breath and thus by taking a deep breath afterwards the individual makes a "whooping" sound [6]. It is from this "whooping" sound that pertussis obtains its other name of "whooping cough." The population who are most susceptible to this infection are young children, with older children as well as adults demonstrating less severe symptoms and at times appearing to be asymptomatic.

There are three stages to the progression of infection with pertussis. The first stage is the Catarrhal stage, which lasts for approximately 1-2 weeks. This stage consists of symptoms that resemble a common cold such as: runny nose, sneezing, low-grade fever, and an occasional cough. Following the Catarrhal stage is the Paroxysmal stage, which lasts about 1-6 weeks. It is at this second stage of infection that diagnosis most often occurs due to the fact that this is where the coughing attacks begin. The final stage is the Convalescence stage which can last weeks to months. After about 2-3 weeks in this stage the cough more or less disappears and recovery is gradual. If the individual acquires another infection during this stage the coughing attacks could return temporarily [1].

The most common method of diagnosis is through a patient reporting the presence of coughing attacks . Lab confirmation is generally done through use of PCR, but cultures may also be used. As a result of lab results taking up to two weeks for results they are not the preferred method of diagnosis. In addition, results are less efficient if taken at a later stage of the infection or if the individual has already received vaccinations or antibiotics. The most common diagnosis method is confirmation of the individual having coughing attacks. Once diagnosis has occurred treatment consists of antibiotics, generally Erythromycin, prescribed to the individual as well as family members to prevent the spread of the infection [1]. Aside from treatment the best line of defense against pertussis comes from completing the vaccination schedule.

The vaccine for pertussis originally was a whole-cell vaccine, but due to the common occurrence of local adverse reactions it was discontinued in the United States in the mid 90s. Currently, vaccinations consist of an acelluar vaccine which contains purified, inactivated components. There are two formulations of the vaccine. The pediatric formulation is DTap meant for individuals 6 weeks of age to 6 years of age, and the other is the adolescent formulation Tdap meant for individuals of ages 10-64 years [1]. In the state of Ohio children should complete a series of four doses of DTap by the age of 5 years. If they have completed the series before their fourth birthday it is recommended that they receive a fifth dose prior to starting school [6].

The state of Ohio has been noticing an increase in pertussis incidence in recent years. Table 1.1 shows the number of confirmed pertussis cases in Ohio from 2001 through 2011. These cases were confirmed by using either method previously mentioned.

We can see from the table that the number of cases increases over a span of a few years and then drops, but that the most recent years have much higher incidence

Table 1.1: Number of Cases in State of Ohio 2001-2011 from ODH Data

Year	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Number of Cases	337	441	325	763	1179	639	836	606	1095	1805	690

than previous ones. This behavior occurs every 3 to 5 years and can be seen in Figure 1.1 showing the total incidence in Ohio from 2001 through 2011.

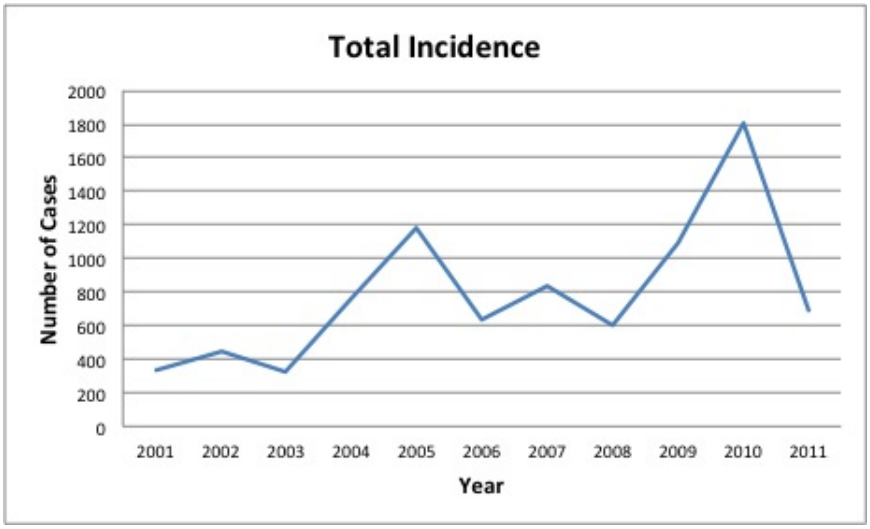

Figure 1.1: Plot of Incidence from ODH data

The question that arises from the data is for what reason would the incidence be increasing. There are several possible reasons. One reason is that as a result of technological advancement it is possible that testing methods have improved so that more cases are confirmed, and on a similar thought due to increased distribution of pamphlets and public service announcements warning of pertussis the disease is

more readily recognized and thus there is better reporting of cases. One of the more serious possible causes of increased incidence is the thought that the acelluar vaccine immunity is waning at a higher rate than the whole-cell vaccine immunity had in the past.

Increased reporting and recognition are likely part of the reason that there has been rising incidence for pertussis. Based on the data obtained from ODH though it would also appear that waning vaccine immunity is also a cause for increased incidence, especially if we look at Figure 1.2 showing the proportion of incidence based on age.

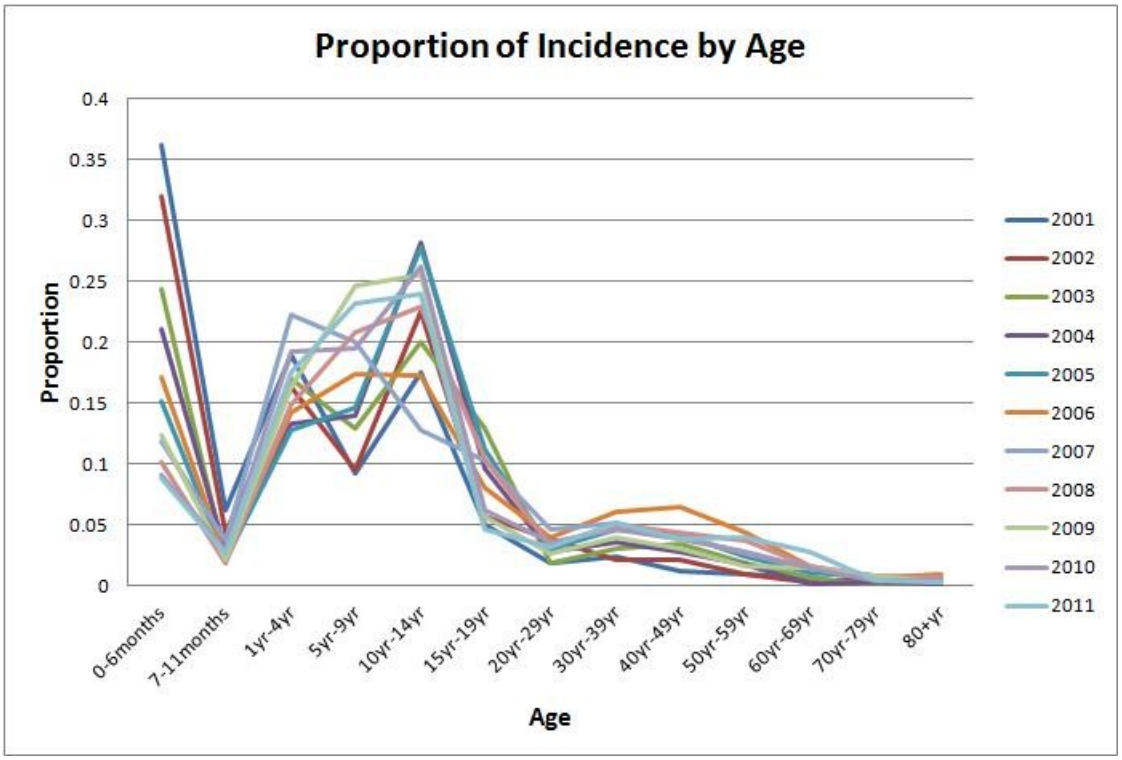

Figure 1.2: Proportion of Incidence from ODH data

Looking at the above figure we can see a disproportionate number of cases in the 10-14 year old age group. Thus as a result of this behavior, in 2010 the state of Ohio came to the conclusion to enact a vaccine booster program for 7th graders, with the hope that this will not only reduce the proportion of incidence in the age group, but also reduce total incidence. Note that 1% of the ages were unknown and thus excluded from the analysis. The purpose of this project is to attempt to mathematically model pertussis in Ohio and the implication of the 7th grade booster program with its effect on incidence.

CHAPTER 2

MODEL

Our model is based on a compartmental SIR-type model including age structure, vaccination, and waning immunity developed by Hethcote [2]. An assumption we have also made for our model is the use of a constant population size. Two reasons for this assumption are that the population size for the state of Ohio from 2001 to 2011 does not change by a large amount based on census data, but also using a constant population size simplifies the model. Figure 2.1 is a schematic for the model, and Table 2.1 lists the parameters and what they stand for. The values for these parameters were in majority taken from Hethcote's paper, but others were obtained through data from ODH as well as through fitting the model to ODH incidence data.

Note that the model includes four different infected compartments represented by $I_{highest}$, I_{high}, I_{med}, and I_{low}. Each of these is meant to represent individuals with varying severity of infection with I_{low} being the least severe and $I_{highest}$ being the most severe. The S compartment is susceptibles and we can see that this compartment has an influx from $Birth$, and then individuals leave either through being infected by the λ term or by receiving a dose of the vaccine. The infected classes recover at a rate of γ, with $\frac{1}{\gamma} = 21$ days corresponding to the expected infectious period. The R classes are where individuals move after being infected in any of the infection compartments. Once an individual recovers from any of the infected classes they move into R_4 where they have the highest level of immunity and cannot be infected.

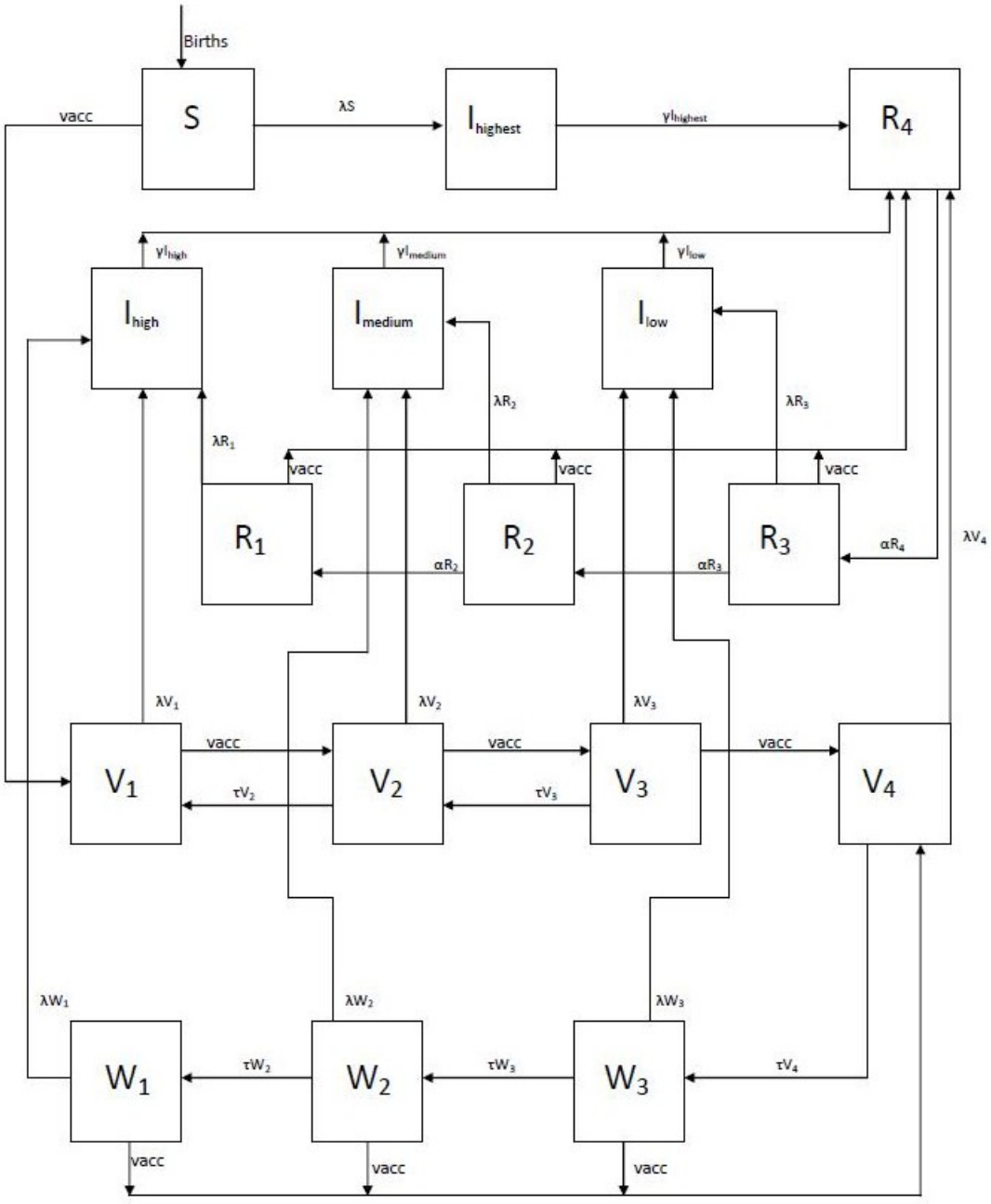

Figure 2.1: Schematic for model, after Hethcote [2]

If enough time goes by individuals move down through the R compartments by a rate of α with $\frac{1}{\alpha} = 5$ years, once they leave R_4 they are then again able to be infected.

Table 2.1: Model Parameters

Parameter	Interpretation	Value/Units	Source
$Birth$	Birth rate per day	$3.5342 \cdot 10^{-5}$ births day^{-1}	ODH Database
α	Waning Natural Immunity Rate	$5.4795 \cdot 10^{-4}$ day^{-1}	Hethcote [2] and ODH Discussions
β	Transmission Rate	Varies Unitless	Fitting Model
γ	Recovery Rate	0.0476 day^{-1}	Hethcote [2] and ODH Discussions
τ	Vaccine Waning Time Rate	0.0014 day^{-1}	Hethcote [2] and ODH Discussions
ϕ	Aging Rate	Depends on Age Class day^{-1}	Fit to Age Groups
$vacc$	Vaccination Rate	0.0085 Vaccinations day^{-1}	ODH Discussions
μ	Natural Death Rate	$1.5 \cdot 10^{-6}$ deaths day^{-1}	ODH Database
ν	Elderly Elevated Death Rate	$3.2 \cdot 10^{-4}$ day^{-1}	Fitting Average Lifespan in Ohio

The V compartments consist of individuals who have received a dose of the vaccine. The V_1 compartment represents individuals who have received the first dose through V_4 , which represents receiving the entire series of 4 doses. Completing the four dose vaccination schedule provides complete immunity in the model, with V_1 through V_3 providing partial immunity. We calculated the value for $vacc$ by observing that ODH estimates an 85% completion rate for the series of vaccinations [5]. We decided to undershoot the completion rate and let it be 0.8 since the values do seem to dip below 85% and then come back up according to their data. In addition we also assumed that each dose had an equal chance of being adminstered and thus we took the fourth root of 0.8, which came out to be 0.95. Using this we determined that the amount

of individuals who would not receive a dose of vaccine was 0.05 and fit our model's parameter to this condition.

The term τ, with $\frac{1}{\tau} = 2$ years, represents waning vaccine immunity whose value was based on discussion with members of ODH as well as from literature. Once an individual's immunity in V_4 begins to wane, they move into the W classes which are waning classes for individuals who have completed the series of vaccinations. Individuals in any of the W classes are susceptible to infection, but can be boosted back to V_4 if they receive another dose of vaccine. It should be noted that although an individual in V_4 has completed the series of vaccinations they can still be infected, and then move directly into R_4 following infection. This infection can be thought of as a booster for V_4 since individuals do not receive any negative effects from the infection and afterwards are in a state where they cannot be infected, thus possessing higher immunity than they previously had.

ODH reports pertussis data according to 12 age groups. We condense these age groups to form 6 age classes in our model. Table 2.2 shows the age groups for ODH as well as the age groups we used for the model.

Table 2.2: ODH Age Groups and Model Age Groups

ODH	<1yr	1-4yr	5-9yr	10-14yr	15-19yr	20-29yr	30-39yr	40-49yr	50-59yr	60-69yr	70-79yr	80+yr
Model	0-5yrs		6-10yrs	11-14yrs	15-19 yrs	20-69yrs					70+yrs	

The reason we have condensed the age groups from ODH is because each age group consists of 16 ordinary differential equations and thus with more age groups we would have more equations. Using only our 6 groups we already have 96 equations.

The differences between the equations of the age groups are mostly that there are no births associated with any age group other than the 0-5 year age group and since that is the age group that recieves the intial series of vaccinations the parameters $Birth$ and $vacc$ only appear in the 0-5 age group. In the 11-14 year age group we have included a parameter $vaccb$ which represents the implementation of the booster program. Each age group possesses a ϕ_i term which corresponds to aging out of its respective age group. The final difference between equations is the inclusion of ν in the elderly. This is an added mortality term for the 70+ age class, calabrated so that the average lifespan in the model matched the averaged lifespan in Ohio.

The following equations are those from the 0-5 age group to give an idea of how they are formulated from the schematic.

$$
\begin{aligned}
\dot{S} &= Birth \cdot N - \lambda_{0-5}S - vaccS - \mu S - \phi_1 S \\
\dot{I_{highest}} &= \lambda_{0-5}S - \gamma I_{highest} - \mu I_{highest} - \phi_1 I_{highest} \\
\dot{I_{high}} &= \lambda_{0-5}(R_1 + V_1 + W_1) - \gamma I_{high} - \mu I_{high} - \phi_1 I_{high} \\
\dot{I_{med}} &= \lambda_{0-5}(R_2 + V_2 + W_2) - \gamma I_{med} - \mu I_{med} - \phi_1 I_{med} \\
\dot{I_{low}} &= \lambda_{0-5}(R_3 + V_3 + W_3) - \gamma I_{low} - \mu I_{low} - \phi_1 I_{low} \\
\dot{R_1} &= \alpha R_2 - \lambda_{0-5}R_1 - vaccR_1 - \mu R_1 - \phi_1 R_1 \\
\dot{R_2} &= \alpha R_3 - \lambda_{0-5}R_2 - vaccR_2 - \alpha R_2 - \mu R_2 - \phi_1 R_2 \\
\dot{R_3} &= \alpha R_4 - \lambda_{0-5}R_3 - vaccR_3 - \alpha R_3 - \mu R_3 - \phi_1 R_3 \\
\dot{R_4} &= \lambda_{0-5}V_4 + vacc(R_1 + R_2 + R_3) + \gamma(I_{highest} + I_{high} + I_{med} + I_{low}) - \alpha R_4 \\
&\quad -\mu R_4 - \phi_1 R_4 \\
\dot{V_1} &= vaccS + \tau V_2 - \lambda_{0-5}V_1 - vaccV_1 - \mu V_1 - \phi_1 V_1 \\
\dot{V_2} &= vaccV_1 + \tau V_3 - \lambda_{0-5}V_2 - vaccV_2 - \tau V_2 - \mu V_2 - \phi_1 V_2 \\
\dot{V_3} &= vaccV_2 - \lambda_{0-5}V_3 - vaccV_3 - \tau V_3 - \mu V_3 - \phi_1 V_3 \\
\dot{V_4} &= vacc(W_1 + W_2 + W_3 + V_3) - \lambda_{0-5}V_1 - \tau V_1 - \mu V_1 - \phi_1 V_1 \\
\dot{W_1} &= \tau W_2 - \lambda_{0-5}W_1 - vaccW_1 - \mu W_1 - \phi_1 W_1 \\
\dot{W_2} &= \tau W_3 - \lambda_{0-5}W_2 - vaccW_2 - \tau W_2 - \mu W_1 - \phi_1 W_1 \\
\dot{W_3} &= \tau V_4 - \lambda_{0-5}W_3 - vaccW_3 - \tau W_3 - \mu W_1 - \phi_1 W_1
\end{aligned}
\tag{2.0.1}
$$

One term from the model that needs to be discussed in greater detail is the force of infection λ_i. The force of infection is a weighted sum which takes into account contact rates between age groups and differential infectivity of the infectious classes. Each age class i has a corresponding force of infection. As can be seen above λ_{0-5} corresponds to the force of infection for the 0 to 5 year old age group.

$$
\lambda_i = \beta \cdot \sum_j (\frac{c_{i,j}}{N_j} \cdot [I_{highest}(j) + 0.75 \cdot I_{high}(j) + 0.5 \cdot I_{med}(j) + 0.25 \cdot I_{low}(j)]) \tag{2.0.2}
$$

The weights associated with each of the infected classes were also taken from Hethcote [2]. The explanation for them is that it would be expected from lower infected classes that those individuals would not be as contagious and their symptoms would be less severe or not appear at all, and thus contribute less to the force of infection than the highest infected classes. The term $c_{i,j}$ represents total contacts per day between individuals in group i with individuals in group j. As stated above in the parameters β represents the transmission rate for the disease. To further explain this we can think of an individual from the 0-5 age group coming into contact with an individual from the 6-10 age group. $c_{i,j}$ in this case would be written as $c_{0-5,6-10}$, meaning that it would be interpreted as the amount of contacts a 0-5 year old would have with a 6-10 year old. Notice that we divide by the population of the 6-10 year old age group. This contact component would then be scaled by the population size for the 6-10 year age class, N_{6-10}. Since $c_{i,j}$ represents the number of contacts an individual in one age group has with a corresponding age group regardless of whether the contact is with an infected or healthy individual, we need to multiply the total contacts by the proportion of infected individuals to make the force of infection represent the contact rate with an infected. It is for this reason that we divide by N_j in the formulation of λ_i. All of the I classes would also be from the individuals in the 6-10 year age class who are infected.

The values for $c_{i,j}$ were obtained from a contact matrix of contacts per day that was condensed from data obtained by Mossong et.al [4]. The data were obtained through cross sectional surveys, where participants would keep contact diaries. These diaries consisted of individuals recording every person they came into contact with as well as details about the contacts, i.e. whether they were physical or non-physical. Their study was conducted over 8 different European countries, but we are only using the data about physical contacts for Great Britain for our model. The contact data from

the study was used by Galvani and Medlock [3] to model influenza dynamics and optimal vaccine distribution in the United States, and thus we decided that it would be appropriate to use the data for our model as well.

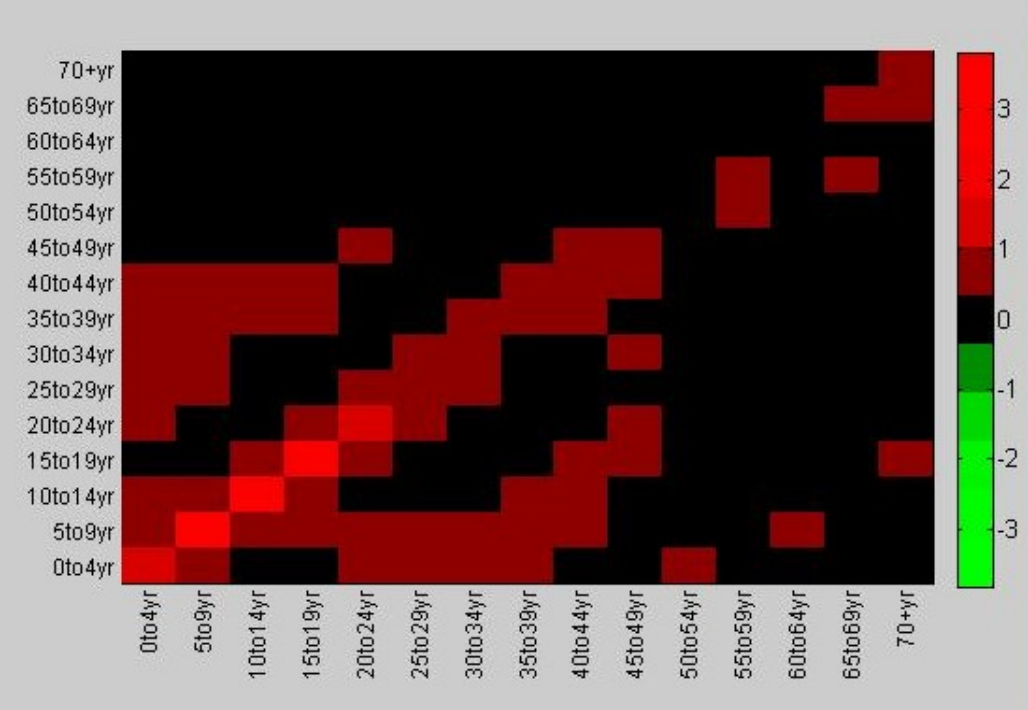

Figure 2.2: Great Britain heat map of physical contacts from Mossong et al. [4]

If we examine the heat map we can note that the densest contact appears across the main diagonal showing that for the majority the highest amount of contact occurs between individuals encountering others in their same age group. Looking at the two off diagonals we can see that these dense contacts occur between pairings of children age groups with middle-aged adults. In addition the highest amount of contact occurs between age groups 20yr to 24yr and below on the main diagonal. The youngest age groups thus encounter the most contacts.

CHAPTER 3

RESULTS

3.1 Model Behavior and Calibration

Table 3.1: Average Incidence Over 2001-2011 by Age Group from ODH Data

Age Group	Average Incidence	Proportion of Incidence
0-5 yrs	372	0.4286
6-10 yrs	156	0.1797
11-14 yrs	150	0.1728
15-19 yrs	63	0.0726
20-69 yrs	120	0.1382
70+ yrs	7	0.0081
Total	868	

Table 3.1 shows the average incidence and proportion of total incidence per age group. We want to fit the model as closely as possible to the values above before running simulations with the vaccine booster present. To do this we are integrating the force of infection term over 1 year once the model has reached equilibrium,

and thus we obtain the total incidence that occurs. Note that $x_i(t)$ stands for the compartments that are susceptible to infection, not specifically the S (Susceptible) compartment.

$$\int_0^{365} \lambda_i(t)x_i(t)dt = \text{Total Incidence for 1 Year} \tag{3.1.1}$$

Since the value obtained is the total incidence it is not accurate to match this to the averages, because in a real-world situation not all cases that occur will be reported. Thus once we obtain the total incidence we will be be multiplying it by a parameter δ which will represent the reporting rate. We can alter total incidence to include all of the compartments susceptible to infection or only some of them. The reason we would not want all of the compartments that are susceptible would be because in older age groups infected individuals would not show symptoms as readily and thus would most likely not be reported as cases. Making this assumption is reasonable due to the fact that adults will be much less likely to report a case for themselves since when they are infected with pertussis it may seem like a "common cold," while young children are much more likely to be taken to a physician when ill even for less severe cases. Table 3.2 shows different calculations for incidence based on the above assumptions and what the reporting rate would need to be to fit the total incidence from the model to the total incidence from the ODH data. The way the values are determined is by fitting the proportion of cases in the 0-5yr age group to the ODH data. Once we find the value of β that gives the correct proportion for the 0-5 age group we can find the proportions for the rest of the age groups, and also the total incidence. We can note that the total incidence from the model is greater than the reported incidence from ODH , and thus we need to incorporate a reporting rate, δ, to fit the total incidence to the reported incidence. The contribution to incidence column in Table 3.2 represents which I classes are considered to contribute to incidence for each age group in each scenario.

$$\delta \cdot \int_0^{365} \lambda_i(t) x_i(t) dt = \text{Reported Incidence} \tag{3.1.2}$$

Table 3.2: Computations of Reported Incidence and Reporting Rates with Proportions (Prop) of Incidence by Age Group

Contribution to Incidence	Total Incidence	Reporting Rate δ	Prop 0-5yr	Prop 6-10yr	Prop 11-14yr	Prop 15-19yr	Prop 20-69yr	Prop 70+yr
0-5 All I classes, other classes only $I_{highest}$	2616.9 cases	$\frac{1}{3}$	0.4335	0.1184	0.1106	0.1405	0.1834	0.0136
0-5 All I classes, others $I_{highest}$ and I_{high}	50,386 cases	$\frac{1}{58}$	0.4299	0.2263	0.1382	0.1065	0.0808	0.0183
0-5 All I classes, 20-69 and 70+ only $I_{highest}$, others $I_{highest}$ and I_{high}	44,346 cases	$\frac{1}{51.0899}$	0.4295	0.2610	0.1716	0.1369	$9.5573 \cdot 10^{-4}$	$1.5773 \cdot 10^{-5}$
0-5 All I classes, 15-19, 20-69, 70+ only $I_{highest}$, others $I_{highest}$ and I_{high}	36,346 cases	$\frac{1}{41.87}$	0.4319	0.3215	0.2345	0.0105	0.0016	$3.0144 \cdot 10^{-5}$

Examining the output from the model we can see that the proportions given are not exactly the same as the data, but that for the majority are quite close. Since there has not been much research into the reporting rate for pertussis we will need to formulate our own assumptions to decide which set-up is best. The highest reporting rate is 1 in every 3 cases reported, and the lowest is 1 in 58 cases. Note that some of the proportions in the last two rows are very small. The elderly class having a small proportion is not a major issue since according to our data they make up less than 1% of the incidence, but in row three we can see that the adult proportion is also very small, which does not match the data. Thus when we run our simulations for varying coverage of the booster we calculate new incidence by allowing all I classes to contribute for the 0-5yr age group and only $I_{highest}$ for the others, with reporting rate

$\delta = \frac{1}{3}$. We will also use the second calculation consisting of all I classes to contribute to 0-5yr age group with $I_{highest}$ and I_{high} for the other age groups, and the reporting rate $\delta = \frac{1}{58}$, since the proportions for this age group are also close to the proportions found from the data.

Table 3.3: Distribution of Incidence in Model with $\beta = 0.2995$

Age Class	Proportion of Total Incidence	Proportion of $I_{highest}$	Proportion of I_{high}	Proportion of I_{med}	Proportion of I_{low}
0-5yr	0.007	0.1107	0.0033	0.0069	0.0085
6-10yr	0.019	0.1101	0.0214	0.0180	0.0151
11-14yr	0.021	0.0930	0.0299	0.0162	0.0115
15-19yr	0.037	0.1352	0.0596	0.0242	0.0175
20-69yr	0.810	0.5168	0.7808	0.8240	0.8448
70+yr	0.105	0.0342	0.1050	0.1107	0.1026

Table 3.4: Distribution of Incidence in Model with $\beta = 2.1765$

Age Class	Proportion of Total Incidence	Proportion of $I_{highest}$	Proportion of I_{high}	Proportion of I_{med}	Proportion of I_{low}
0-5yr	0.0286	0.5956	0.1321	0.0404	0.0136
6-10yr	0.0541	0.2715	0.1708	0.0744	0.0411
11-14yr	0.0448	0.0829	0.1237	0.0654	0.0362
15-19yr	0.0608	0.0356	0.1355	0.0880	0.0521
20-69yr	0.7032	0.0142	0.3598	0.6170	0.7464
70+yr	0.1085	$2.1228 \cdot 10^{-4}$	0.0780	0.1147	0.1105

Tables 3.3 shows how incidence is distributed between the different age groups using $\beta = 0.2995$, corresponding to incidence being calculated where all I classes

contribute to incidence for the 0-5 age group and only $I_{highest}$ for the other classes. Table 3.4 shows how incidence is distributed between the age groups with $\beta = 2.1765$, corresponding to the same condition for the 0-5 age group, but with $I_{highest}$ and I_{high} for all other age groups. A behavior our model demonstrates in both cases is the fact that majority of the incidence occurs in the the 20-69 age group, which implies that in the model infection is driven by the adult population. In the absence of the booster, only the 0-5 age group is vaccinated, and thus this age group would be expected to have the highest proportion of $I_{highest}$ incidence. This holds true for $\beta = 2.1765$, but not for $\beta = 0.2995$.

Table 3.5: Proportion of Population for Ohio by Age Group for ODH Age Groups and Model Age Groups

ODH Age Groups	0-4yr	5-9yr	10-14yr	15-19yr	20-29yr	30-39yr	40-49yr	50-59yr	60-69yr	70-79yr	80+yr
	0.066	0.072	0.073	0.072	0.130	0.147	0.155	0.113	0.076	0.063	0.035
Model Age Groups	0-5yr	6-10yr	11-14yr	15-19yr	20-69yr	70+yr					
	0.080	0.073	0.058	0.072	0.619	0.097					

Table 3.5 provides the distribution of the population throughout the age groups for both the ODH age groups as well as the model age groups. Referencing Table 3.1 where we showed the proportions of incidence for the ODH data based on our age structures it is interesting to see that the 0-5 age group which makes up about 8% of the population contains almost 43% of the incidence while the 20-69 age group which is approximately 62% of the population only contains around 14% of the incidence. Note that with the model proportions the 20-69 age group holds the majority of the population, and thus it makes sense that in both set-ups shown in Table 3.3 and Table

3.4 that the adult population makes up the largest proportion of the total incidence. This difference between the proportions of incidence for the model and ODH data is resolved through the use of δ where we have fit the total incidence of the model to the data as well as the proportions of incidence for each age group.

3.2 Model with Booster

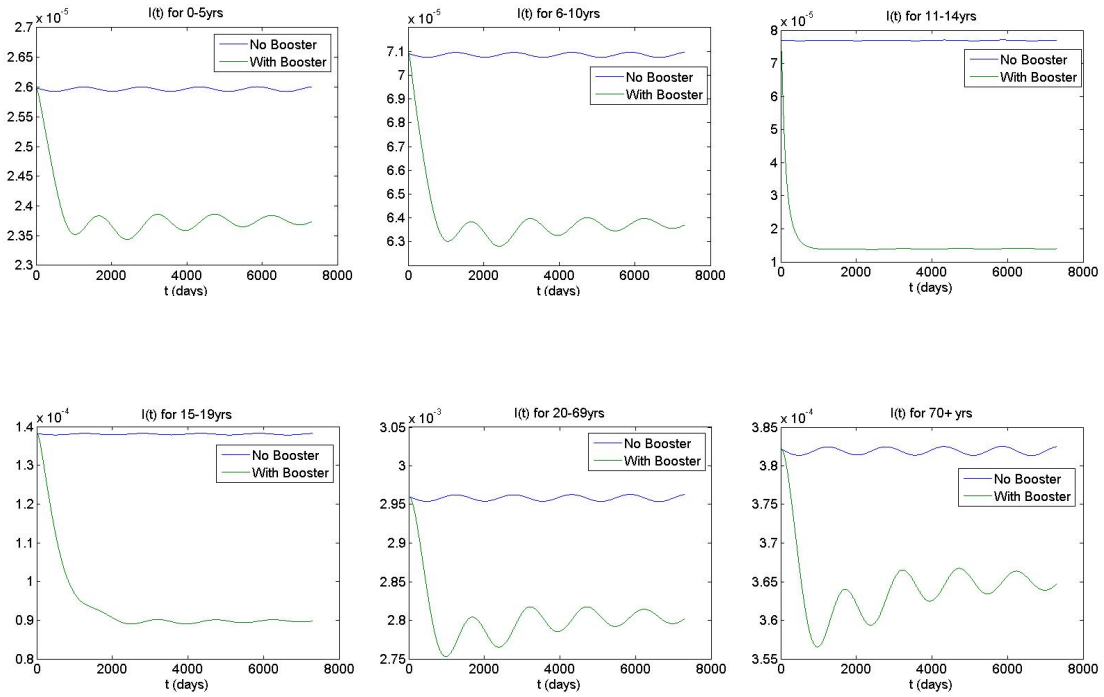

Figure 3.1: Model Output: Infected Compartments Over Time With and Without Booster by Age Group

Figure 3.1 shows how the output of the model changes when the booster is included. We can see that for all classes the amount of infection does decrease with the booster present. We see that with the booster present that incidence decreases throughout the age classes and that majority of the classes demonstrate damped oscillations eventually approaching a new equilibrium. At the current scale it doesn't appear as though the 11-14 age group possesses these damped oscillations and instead reaches its equilibrium much faster. The 15-19 age group also possesses this quicker approach to equilibrium, but also seems to have some damped oscillations.

The following information was found by running the model without the booster until it reach equilibrium and then using those equilibrium as our new initial conditions with the inclusion of *vaccb* in the model, which represents the booster vaccination rate. We assumed that the the booster would be distributed at the same rate as a dose of the vaccine for the 0-5 age group. This assumption seemed reasonable since similar to the series of vaccinations the booster will be required for students to attend school. In addition we ran the model for the equivalent of the booster program being in place for 20 years.

Figure 3.2 represents the reported incidence when incidence is reported for all I classes for the 0-5 age group and only $I_{highest}$ for the other age groups. What we can see from the output is that the total reported cases appears to decrease each year after the booster has been implemented. By year 20 it seems that the model may be approaching a new equilibrium for the booster, which we can note is significantly less than the initial reported incidence prior to booster implementation.

Figure 3.3 represents the reported incidence when incidence is reported for all I classes for the 0-5 age group with $I_{highest}$ and I_{high} for the other age groups. The behavior we notice here is different from the previous calculation. We reach the minimum incidence after booster implementation by year 5. Unlike the previous

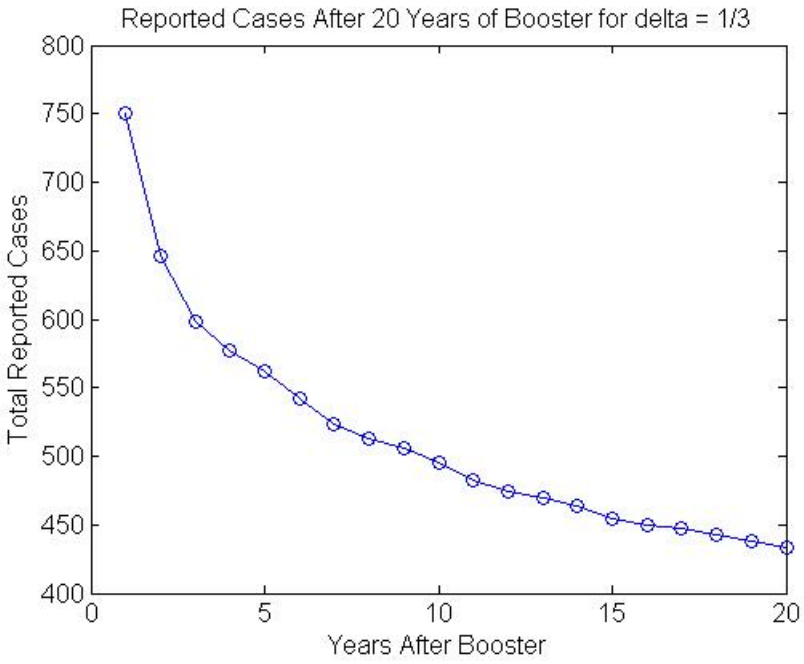

Figure 3.2: Total Reported Incidence for $\beta = 0.2995$

figure it would also appear that the model has already reached its equilibrium in this case.

Table 3.6 allows us to see the behavior we described about the above figures, but in terms of actual numeric values. We can notice that for $\delta = \frac{1}{3}$ the reported incidence drops the most during the first 2-3 years. The values for $\delta = \frac{1}{58}$ in Table 3.6 show us just how quickly we appear to reach equilibrium. In fact, by year 8 we can see that the reported incidence value practically stays the same at 653, but eventually goes up to 654 and stays there from year 14 through year 20.

The information in Table 3.7 allows us to compare our model results for incidence with and without the booster against those from ODH. Notice that the amount of incidence for all of the age groups decreases with the implementation of the booster. We can see the effect the booster has on the 11-14 age group where its new incidence

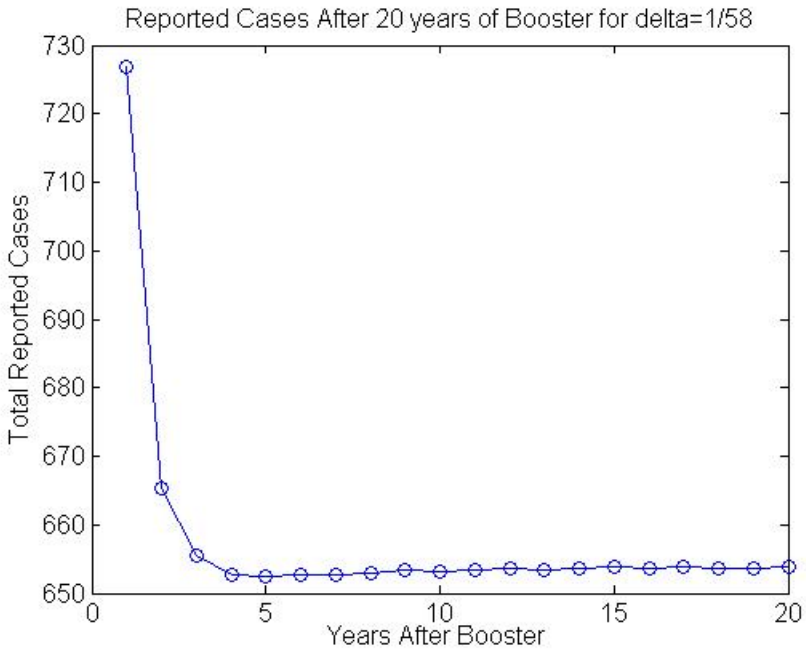

Figure 3.3: Total Reported Incidence for $\beta = 2.1765$

has almost disappeared completely. The 0-5 age group still has a considerable amount of incidence, but it should be noted that within this group are children who are too young to have completed the series of vaccines and also children who are too young to have even received their first dose, making this age group the most susceptible to infection. We can also see that there are 360 less cases for the average total with this reporting rate when compared to the model output without the booster.

As for $\delta = \frac{1}{58}$ we can see that many of the age groups have less incidence than the ODH data, but that overall the change is not as drastic as it was for the other reporting rate. Also, we can see that the incidence for the 70+ age group did not change with the implementation of the booster. Similar to the higher reporting rate the 11-14 age group that is now receiving the booster has drastically decreased in

Table 3.6: Reported Cases Per Year with Reporting Rate from Model with Booster

Reporting Rate	Year 0	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 8	Year 9	Year 10
$\delta = \frac{1}{3}$	750	646	598	577	562	542	523	513	506	495
$\delta = \frac{1}{58}$	726	665	655	653	652	653	653	653	653	653
Reporting Rate	Year 11	Year 12	Year 13	Year 14	Year 15	Year 16	Year 17	Year 18	Year 19	Year 20
$\delta = \frac{1}{3}$	482	474	470	463	455	449	447	443	438	434
$\delta = \frac{1}{58}$	653	654	653	654	654	654	654	654	654	654

incidence. The total incidence with the booster for this δ is about 211 less cases than the model without the booster.

Table 3.8 shows the incidence for an age group caused by a corresponding age group using the calculation for incidence with all I classes for the 0-5 age group and only $I_{highest}$ for the other classes using $\beta = 0.2995$. A major characteristic that can be noticed is that for many of the age groups adults are the cause of a large proportion of their infections. We can see that for the 0-5 age group that almost 50% of the infections arise from the adult population and in the 70+ age group over 70% of their infections come from the adults. Another interesting behavior is that for the 6-10, 15-19, and 20-69 age groups the majority of their infections come from their own age group. Thus these age groups are driving infection within themselves. The 11-14 age group has more interesting behavior from the implementation of the booster, where each of the age groups seem to contribute similar amounts to the 11-14 group's incidence.

Table 3.9 is similar to Table 3.8, but with $\beta = 2.1765$. A major difference with these proportions is that the adult population does not seem to cause as much incidence in other age groups, with the exception being the 70+ age group. Overall with this set-up infection within each age group seems to be driven by the age group

Table 3.7: Average Reported Cases by Age Group from Model with Booster

Age Group	Average Incidence ODH	Average Model Incidence Without Booster $\delta = \frac{1}{3}$	Average Model Incidence With Booster $\delta = \frac{1}{3}$	Average Model Incidence Without Booster $\delta = \frac{1}{58}$	Average Model Incidence With Booster $\delta = \frac{1}{58}$
0-5 yrs	372	379	308	374	335
6-10 yrs	156	103	83	197	188
11-14 yrs	150	97	5	120	11
15-19 yrs	63	123	26	92	45
20-69 yrs	120	160	83	70	64
70+ yrs	7	12	8	16	16
Total	868	873	513	869	658

itself. This behavior is very similar to the behavior we observed from the heat map of contacts between age groups earlier. Unlike the previous set-up we see that for the 11-14 age group the infection due to other age classes is not very similar across the various age groups. In fact, the majority of the infections come from the age groups adjacent to the 11-14 group.

Table 3.8: Distribution of Incidence from Age Groups: $\beta = 0.2995$ where columns correspond to the proportion of cases caused by the age group in the corresponding column

	0-5 yr	6-10yr	11-14yr	15-19yr	20-69yr	70+
0-5yr	0.162	0.189	0.016	0.088	0.468	0.078
6-10yr	0.069	0.533	0.015	0.101	0.245	0.036
11-14yr	0 .027	0.237	0.107	0.205	0.324	0.101
15-19yr	0.010	0.034	0.011	0.507	0.300	0.138
20-69yr	0.011	0.027	0.003	0.028	0.894	0.037
70+yr	0.003	0.010	0.002	0.012	0.741	0.232

Table 3.9: Distribution of Incidence from Age Groups: $\beta = 2.1765$ where columns correspond to the proportion of cases caused by the age group in the corresponding column

	0-5 yr	6-10yr	11-14yr	15-19yr	20-69yr	70+
0-5yr	0.466	0.260	0.019	0.066	0.158	0.032
6-10yr	0.178	0.653	0.016	0.067	0.073	0.013
11-14yr	0.093	0.391	0.153	0.184	0.131	0.049
15-19yr	0.047	0.075	0.021	0.606	0.162	0.090
20-69yr	0.076	0.091	0.010	0.051	0.736	0.036
70+yr	0.025	0.036	0.006	0.023	0.661	0.25

CHAPTER 4

DISCUSSION AND CONCLUSIONS

These results from the model imply that the booster program in Ohio will have some effect on reducing total incidence, but the impact greatly depends on the reporting rate. As a result a next step for the state of Ohio would be to try to gain an idea of what the actual reporting rate for pertussis may be. A study could be conducted in which a sample of the population from various age groups could be swabbed periodically and then tested for infection, then the results of the sampling could be compared to the number of reported cases to determine an estimate of the reporting rate in Ohio.

A general feature of the model is that the adult population acts as a major reservoir for pertussis. Thus, since this population generally has less severe cases it makes sense that they may not report regularly, and that a significant number of cases are being overlooked. We saw according to the results in Table 3.7 that a higher reporting rate corresponds to a large proportion of infections being caused by the adult population. Thus, examining possible ways of implementing a booster program for adults could be beneficial. Currently adults who are expecting a child are encouraged to receive a dose of Tdap to help prevent infection to the newborn, but to have an effect on the total incidence a larger portion of the adult population most likely would need to receive boosters. Based on the lower reporting rate though we notice we do not see any particular age group contributing a majority of the infections and thus

it is difficult to pick any particular age group to boost in addition to the 11-14yr age group. Again, this indicates a reason for Ohio to research the actual reporting rate for pertussis.

A topic that has been discussed since the acelluar vaccine was found to wane faster than the whole cell vaccine for pertussis, is the development of a new vaccine. One of the main aspects of the new vaccine would be to improve the length of protection it would provide for individuals. In addition, the current vaccine only works in preventing infection from *Bordetella pertussis*, but there are other strains that can cause infection. As a result, creating a vaccine that would provide protection for multiple strains of pertussis could aid in reducing the amount of incidence if the length of protection of the vaccine could not be improved.

Hethcote's results indicated that utilizing a booster program for adolescents and adults concurrently will not lead to herd immunity, meaning that the infection cannot be eradicated from the population [2]. Although our model was run with only an adolescent booster we can see that even with the higher reporting rate that infection does not disappear. The level of incidence merely obtains a new equilibrium value, which would agree with Hethcote's findings.

Further improvements to the model could be made including allowing population growth as well as the inclusion of more age groups. Our model could also be used to see what implications a booster program could have if implemented for other age groups, or if there were multiple age group booster programs in place. The issue that would need to be addressed with the case of multiple age group boosting is the coverage of the booster. Since older age groups are generally no longer in school it is difficult to create some kind of requirement for receiving the booster for these age groups, and research would need to be done to estimate these values.

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