An Agent-Based Computational Model of COVID-19 Vaccine Hesitancy

by

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Abstract

Vaccine hesitancy plays a huge role in the trajectory of the COVID-19 pandemic and the time it takes to reach herd immunity. A number of factors, including demographic and geographic characteristics, affect an individual's likelihood to accept a vaccine. An agent-based model can be applied to simulate interactions and behavior change over time. In this study, the Health Belief Model, Transtheoretical Model, Dube Conceptual Model of Vaccine Hesitancy, and the WHO SAGE Vaccine Continuum were used as a foundation to build a conceptual model representing COVID-19 vaccine hesitancy. After collecting relevant data, the FRED agent-based modeling platform was used to simulate outcomes from 12/20/2020 to 3/20/2021 in Jefferson County, Pennsylvania (population of 45,000). Each agent's initial vaccine propensity score, on a continuum between 0.0 and 1.0, assigned them susceptibility and transmissibility values for the competing behavior contagions "acceptance" (closer to 1.0) and "refusal" (closer to 0.0). Based on interactions with other agents, their susceptibility and transmissibility values were modified, to eventually impact the probability they would take the vaccine at the end of each modeled week. In Jefferson County, centering on a propensity score of 0.5, initial population vaccine propensity scores had the largest peaks between 0.30-0.34 and 0.59-0.63. About 15,000 agents took the vaccine after the first week, with \sim 53% of the population taking the vaccine by the end of the simulation. However, with greater incentive to vaccinate and propensity scores centered on 0.6, >20,000 agents took the vaccine after the first week, with approximately 65% taking the vaccine

by simulation end. Contrastingly, with lesser incentive to vaccinate and propensity scores centered on 0.3, <5,000 agents took the vaccine after the first week, with about 14% taking the vaccine by simulation end. This model examined the complex dynamics of linked infectious and behavioral contagions. Results revealed how various factors play a role in vaccine hesitancy, and how agents can influence the behavior of other agents they come into contact with. The public health significance of this study is that the model allows stakeholders and policymakers to understand and evaluate the best methods to combat vaccine hesitancy in the population.

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1.0 Introduction

After reviewing the literature on COVID-19, vaccines and related vaccine hesitancy, and models of behavior change as foundation, a conceptual model and realistic computational simulation of COVID-19 vaccine hesitancy was built using the agent-based modeling approach with FRED. Measurable parameters were identified and relevant data were collected to simulate outcomes over a three-month time period in a population of 45,000 (Jefferson County, PA).

The goal of this model is to help explain two concurrent epidemic processes: the infectious disease contagion of SARS-CoV-2 and the behavioral contagion of vaccine acceptance and refusal. This version 1.0 was created as a basis in understanding the complex dynamics of linked infectious and behavioral contagions. Future directions include engrafting this code onto a larger simulation engine of the epidemic.

1.1 Current State of the COVID-19 Pandemic

Coronavirus disease 19 (COVID-19), caused by the virus SARS-CoV-2, first emerged in Wuhan, China in late 2019 and has since spread around the globe; the World Health Organization declared the outbreak a pandemic on March 11, 2020^{1,2}. Infected individuals present with a variety of symptoms and severity, from fever and cough to chest pain and shortness of breath; further, a significant proportion of infected people are completely asymptomatic, leading to difficulties with diagnosis and containment^{3,4}.

At the time of writing, the United States is the leading country in terms of both cases (>26.6 million) and deaths $(>450,000)^5$, with disproportionate effects on the black population (mortality rate two times higher than non-Hispanic whites), older adults (mortality rate of >80 years of age is five times the average), and people with underlying/comorbid conditions (12 times more likely

to die of COVID-19 than those without)⁶. Keeping this in mind, equitable vaccine distribution is essential to protect the diverse members of the United States population.

1.2 Vaccines Overview and COVID-19

The race to develop safe and effective COVID-19 vaccines became a pressing concern and worldwide mission. The goal of any vaccine is to build immunity against a particular disease by creating a defense system of antibodies and T-lymphocytes; if one were to be exposed, their immune system has the ability to fight the germs and protect the individual from acquiring the disease⁷. Specific to the relentless COVID-19 pandemic, vaccines are essential in protecting the population in terms of reaching herd immunity quickly and restoring pre-pandemic normalcy⁸.

However, the vaccine development process is not simple, with an extensive duration and expensive cost. To shorten development time from the multiple year standard, developers overlap phases during an outbreak, allowing clinical and manufacturing development to occur concurrently⁹. During that time, companies consider the vaccine platform technology (DNA, RNA) and attributes (single dose/multiple doses, speed, scale) through stages of clinical trials and overall validation⁹. This allows for preparation at multiple levels, so that the vaccine can be distributed swiftly after trial completion. This new pandemic paradigm was developed for the COVID-19 pandemic and can be used in future outbreaks⁹.

There are 176 COVID-19 vaccine candidates in pre-clinical development and 66 candidates in clinical development at the time of writing¹⁰. The three candidates in Phase 3 and approved for use in the United States are RNA based vaccines developed by 1) Moderna + National Institute of Allergy and Infectious Diseases (NIAID), breaking the record for reaching trials after only 69 days from virus identification, 2) Pfizer/BioNTech + Fosun Pharma, and 3) Janssen Pharmaceuticals Companies of Johnson and Johnson's (J&J) viral vector vaccine^{10–12}. Vaccine

efficacy, or the difference in infection risk between vaccinated and unvaccinated individuals, is FDA recommended as having a primary or secondary endpoint of laboratory-confirmed COVID-19 or SARS-CoV-2 infection and one or more of these symptoms: fever or chills, cough, shortness of breath/difficulty breathing, fatigue, muscle or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, or diarrhea^{13,14}.

Moderna's vaccine is a two shot, intramuscular injection given 4 weeks apart¹⁰. After a randomized, double-blind trial with 30,420 participants aged 18 and older assigned to either the vaccine or the placebo, Moderna vaccine efficacy was determined as 94.1%¹⁵. Pfizer's vaccine is a two-shot, intramuscular injection given 3 weeks apart¹⁰. After a randomized, double-blind trial with 43,548 participants aged 16 and older assigned to either the vaccine or placebo, Pfizer vaccine efficacy was determined as 95%¹⁶. J&J's vaccine is a one-shot, intramuscular injection; after a trial with 40,000 participants aged 18 and older, J&J's vaccine efficacy was determined as 66.3%¹².

1.3 Factors Related to Vaccine Hesitancy and COVID-19

Even with the high efficacy rates of these three frontrunners, vaccine hesitancy is important when considering uptake; in 2019, the World Health Organization (WHO) declared vaccine hesitancy as a top threat to global health¹⁷. The WHO SAGE Working Group of Vaccine Hesitancy defines vaccine hesitancy as "delay in acceptance or refusal of vaccination despite availability of vaccination services. Vaccine hesitancy is complex and context specific, which means it varies across time, place, and specific vaccines for specific diseases. It is influenced by factors such as complacency, convenience and confidence"¹⁸.

There are many causes of vaccine hesitancy, especially in recent generations because of unfamiliarity with formerly prevalent contagious diseases, that include: fear of adverse reactions and lack of trust in institutions, governments, and pharmaceutical-industrial corporations¹⁹. Taking one example with pertussis, at the individual level, a case control study found that vaccine exemptors had 22.8 times risk of infection compared with vaccinated individuals; at the community level, 42% of pertussis and measles exemptors and 11% of vaccinated individuals were infected due to lack of immunization²⁰. Therefore, it is important to consider not only the individual, but the broader community system when considering interventions to promote acceptance¹⁹. Furthermore, historical events, such as the ethical repercussions of the Tuskegee syphilis study specifically impacting the black population, also affects a group's confidence in new treatments²¹. The Tuskegee study's goal was to chart the natural history of syphilis in black males; however, when penicillin, the standard treatment for syphilis, became available, it was not given to the 600 men in both study arms²². When evaluating real-world policies and rollout strategies in communities, knowing these population differences and historical perspectives is vital.

Specific to COVID-19, a study conducted in May 2020 showed significant demographic and geographic disparities affecting vaccine hesitancy²³. This study highlights that across the U.S., there is a greater risk for COVID-19 infection and death for both low-income and communities of color, so it is vital to tackle any vaccine hesitancy that impacts uptake²³. There were also differences in vaccine acceptance by gender (male—72%, female—63%, other—50%) and age (18-24—59% to 55+—78%). Another study conducted in June 2020 among 804 U.S. adults (English speaking, compensated), with a design meant to reflect the U.S. population, showed similar results, with "multicultural/other race" being least likely to get a vaccine (43.9%), males having a greater likelihood to get a vaccine than females (71.9% to 53.8%), and decreasing likelihood to get a vaccine with decreasing age (18-24—52.5% to 55-64—42.0% to 65+—74.5%) and decreasing household income (<\$40,000—54.3% to \$120,000+—73.3%)²⁴. With the phased distribution of vaccines in the United States and healthcare workers (HCWs) being in the first phase, it is important to note the acceptance rate in physicians, nurses, and other frontline staff and their influence on patients²⁵. One study conducted at a single allopathic medical school in Southeast Michigan found that although >98% of medical students said that it was important to develop a COVID-19 vaccine, 23% were still hesitant to take it immediately after FDA approval²⁶. While limitations of this study included a response rate of 34% at a single school, it is still has value to consider these numbers when looking at the impact of HCWs on general public vaccine acceptance²⁶. Vaccine acceptance among HCWs can also be investigated further by race; in a Web-based survey with 3366 HCWs to look at relationships between race/ethnicity and influenza vaccine uptake, where the study non-Hispanic Black HCW population was proportional to the United States', they found uptake to be 13% lower for non-Hispanic Blacks than White HCWs²⁷. This further highlights the complexity of tackling HCW vaccine acceptance.

Further, the COVID-19 pandemic occurred at a time where a lot of attention was on political figures, including National Institute of Allergy and Infectious Diseases director Dr. Anthony Fauci and President Donald Trump. With politics playing an increased role in vaccine acceptance, one survey's sample trends show the highest vaccine uptake and confidence for those who stand by Fauci stating "the vaccine is safe and effective," and the lowest vaccine uptake and confidence for those who stand by Fauci stating he is "not convinced the vaccine is safe and effective"²⁸. In a different nationwide survey conducted in June 2020, political party identity was a significant predictor of likelihood to get vaccines, with Republican at 62.6%, Democrat at 73.2%, and Independent at 63.0%²⁴. This study also found statistically significant differences by party for acceptance of vaccine conspiracies (p-value 0.006) and COVID-19 threat appraisal (p-value 0.003). This highlights the correlation of political background with vaccine hesitancy.

Aside from HCWs and political leaders influencing those who are considering a vaccine, social media is another huge force in spreading important health information, especially through governmental organizations as the CDC and NIH. However, as social media involves real-time, accessible, reciprocal exchange of ideas, misinformation is also disseminated; this happened during the 2014 Ebola outbreak, the Zika epidemic, as well as the current COVID-19 pandemic²⁹. In a cross-national study looking at the relationship between social media organizations and beliefs about vaccine safety, there was a strong relationship between the percentage of the population that thinks vaccines are unsafe and how often the organization posts on social media (regularly, often, sometimes, rarely, or never)¹⁷. Another study, that had a population of predominantly women from Kansas, found that they used internet news websites and Facebook most often to obtain information during the COVID-19 pandemic³⁰.

1.4 Health Belief, Transtheoretical, and other Vaccine Acceptance Models

Models of behavioral change can be used to incorporate concepts of vaccine hesitancy (acceptance to refusal) to outline an individual's path to taking a certain action.

Health Belief Model

The Health Belief Model (HBM), originating in the 1950s-60s by the work of trained social psychologists, was centered on the idea of daily activities consisting of positive and negative forces³¹. As shown in Figure 1, characteristics of the model include an individual considering their susceptibility to the disease, the severity of the disease, and the tradeoffs of benefits and barriers to taking an action. It also considers modifying factors, such as demographic, sociopsychological, and structural variables, as well as cues to action, such as mass media campaigns and advice from others³¹.

The HBM model has been used to evaluate behavior/action and interventions across a variety of diseases. One specific example includes breast cancer screening, where women consider their susceptibility and severity to disease, the subtraction of the barriers from the benefits, as well as receiving a cue to action to push them to follow mammography recommendations³². This analysis further recognized differences among races, in terms of beliefs of root cause of disease, perceived benefits from early detection, and modesty and fear, leading to varied response to the mammography intervention³².

The HBM is a valuable tool to consider potential action at the individual level. Thinking about COVID-19, individuals lean towards taking appropriate actions when their perceived threat is large, meaning they consider the disease as a serious problem and one they could potentially encounter, they evaluate benefits (such as spending time at home or taking a vaccine) as valuable, and can mitigate barriers (such as housing/food expenses and minor vaccine side effects) to avoid putting themselves in undesirable environments³³.



Figure 1. Adapted Health Belief Model³¹

Transtheoretical Model

The Transtheoretical Model (TTM), first introduced by Prochaska and DiClemente in 1982 and shown in Figure 2, is a behavior change model focused on an ordered set of five to six stages: precontemplation, contemplation, preparation, action, and maintenance, with some including termination^{34,35}.

One intervention that has been used multiple times with the TTM includes smoking cessation. A study published in July 2020 describes quantifying states in the TTM with a population of 436 subjects (46 in the healthcare professional advice experimental group and 390 in the control group) in a quasi-experimental untreated control design study³⁶. They looked at the probabilities of transitioning from stage to stage, and found the advice from healthcare professionals was significant especially in the contemplation (stage 2) to preparation (stage 3) transition³⁶. This study adds value to the TTM, as it sets up the framework of multiple stages for behavior change.

Specific to COVID-19, there have not been many applications of the TTM to evaluate behaviors or interventions as of yet. One study conducted in Kosovo describes using TTM in the context of a questionnaire to evaluate the extent of community pharmacists' potential behavior changes with COVID-19 safeguards and education interventions³⁷. TTM applications for COVID-19 could surround the deliberation of reopening parts of the economy or with vaccine acceptance behavior, and mapping individuals to stages over time.



Figure 2. Adapted Transtheoretical Model³⁵

Dube Conceptual Model of Vaccine Hesitancy

Eve Dube and her group in Canada developed a conceptual model of vaccine hesitancy in 2013, as shown in Figure 3. This model was based off a workshop in Canada where experts in a multitude of fields discussed four large domains that play a role in hesitancy: (1) historic, political and socio-cultural context, (2) public health and vaccination policies, (3) communication and media, and (4) health professionals' recommendations³⁸.

A factor that is unique to this model is the emphasis on trust, with arrows leading from the central hesitancy box to the surrounding domains. There is a clear relationship between risk perception and trust when it comes to vaccination ideas and the influence of health professionals and government/public health institutions³⁸. Therefore, it is important to build trust, or a proxy of trust, into any vaccine hesitancy model.



Figure 3. Adapted Dube Conceptual Model of Vaccine Hesitancy³⁸

WHO SAGE Vaccine Hesitancy Continuum

In October 2014, the WHO released the "Report of the SAGE Working Group on Vaccine Hesitancy," which included Figure 4 to explain the spectrum of vaccine hesitancy, between "accept all" and high demand, and "refuse all" and low demand³⁹. This continuum outlining behavior is a valuable aid to visualize where individuals fall on the scale, without being too narrow (as with the term "vaccine confidence" which offers predominantly binary choices)³⁹.

This report clearly states that while vaccine uptake could be low due to system failures, such as low vaccine stock or transportation issues, those situations are not included for the purpose of this model³⁹. The authors built this model to show vaccine hesitancy and uptake in situations where the vaccine is readily accessible and available, and individuals have the opportunity to choose whether they accept or refuse³⁹. This model could directly apply to COVID-19 vaccine hesitancy and uptake in the United States, where members of the population are hesitant to accept even with adequate supply.



Figure 4. Adapted WHO SAGE Vaccine Hesitancy Continuum³⁹

1.5 Agent-Based Modeling

One way we can use these vaccine acceptance behavioral change models as a conceptual framework in a tractable, quantifiable simulation is with agent-based models (ABMs). ABMs are used to show interactions between microentities, or "agents," in a system over distinct periods of time to model macrosystem responses⁴⁰. Each agent can represent an actual human in a geographic location, with a personal age, sex, race, etc. indicated; their daily behavior can be modified by both other agents they interact with and the surrounding environment⁴⁰. One can even build randomness into the model by setting up probabilities that an agent has certain behavioral characteristics or what combination of factors lead an agent to make a decision^{40,41}. Major strengths of ABMs are their flexibility, ability to show dynamic changes, and incorporation of feedback loops⁴¹.

ABMs have traditionally been used for tracking the spread of infectious diseases. Many models are built upon the "SEIR" framework, where agents transition between states of <u>s</u>usceptible, <u>e</u>xposed, <u>infectious</u>, and <u>r</u>ecovered⁴². One study looked at pertussis infections in a simulated community of 13,876 agents, based on extrapolated Utah data from the 2000 Census⁴². Setting contact rate parameters for households, classrooms, and day cares, they were able to differentiate various symptom states, severity, and duration of disease by the agent's immunity SEIR state⁴². This highlights the importance of applying ABMs to infectious diseases, as the modeler can tweak parameters of contact rates, transmission, and susceptibility to propose various scenarios and points of action to researchers and policy makers.

Additionally, ABMs can be used to study non-infectious diseases, such as behavior. For example, one study that did this successfully considered the relationship between diet quality and location/household incomes to determine if pricing and preference factors could counter effects of segregation⁴¹. After building a conceptual diagram, laying out the agent properties, determining

household vs. store behavior, and creating an equation for utility score, they were able to obtain the main outcome, or average proportion of times each household visited a healthier food store⁴¹.

We can further extend studying behavior with ABMs to an understudied, but incredibly valuable, application of ABMs that includes the *transmission* of behavior among agents in a population. Social contagions are behaviors transmitted by individuals to other individuals they interact with⁴³. One study, looking at crisis management and prevention with fire incidents, tested the hypothesis that when the social contagion of emotions and beliefs are activated, people will evacuate faster⁴⁴. Using an agent-based evacuation model, they found average evacuation time did in fact decrease with recognizing the social contagion⁴⁴. This study is just one example of the variety of projects that can be studied centering on social contagions and ABMs.

1.6 FRED

Epistemix, Inc.'s Framework for Reconstructing Epidemiological Dynamics (FRED) is a powerful agent-based modeling platform that can be used to study infectious and non-infectious disease transmission. FRED includes a prebuilt synthetic population, from RTI International, that uses the US Census Public Use Microdata Sample household and person tables to assign agents to households in that match the census tracts population data⁴⁵. Demographic characteristics as age, sex, and race are associated with each agent⁴⁵. FRED is able to track agents in a simulation over time, with individual privacy protected, because while the overall population reflects the census, each agent does not actually uniquely match up to a real person⁴⁶.

In FRED, one can specify a number of factors, including location (city, county, state) and time-frame of the model⁴⁷. To start modeling, it is important to build **conditions**, that manifest the purpose of the study, and **states** that the agent will traverse through⁴⁷. Within each state, the agent

will (1) complete any actions that are described, (2) wait a defined amount of time, and (3) transition to the next state based on the code outlined⁴⁷.

FRED has been utilized for many published studies. One study modeled measles outbreaks in children living in Texas, looking specifically at the relationship between vaccination rates (reduced by 1% to 10%) and outbreak size⁴⁸. Another study looked at access to primary care services and emergency preparedness, with various scenarios modeled, such as increased provider capacity and swifter mobile health clinic setups⁴⁹. FRED is currently being employed extensively with the COVID-19 pandemic. One case study in Allegheny County, Pennsylvania considered teachers and students infected, and resulting hospitalized cases in each group, when physical attendance was reduced in schools by 50% under high, medium, and low community conditions⁵⁰. This allowed school and district leadership to consider different circumstances in setting up plans that will best benefit their community for the school year. As with this example, Epistemix, Inc. harnesses its modeling capacity to empower leaders in school districts, healthcare, government, and enterprise to make decisions⁴⁶.

1.7 Gaps in the Literature

As the COVID-19 pandemic is currently ongoing, we are still collecting information on vaccine effectiveness and side effects post Phase 3 clinical trials, so we do not know how that will influence vaccine hesitancy. There is a lot of missing/incomplete information on vaccine acceptance by race, which makes it difficult to determine true uptake differences by race. Further, while there is information on number of vaccines administered, data is not available on vaccines distributed, or number of available doses, for all counties in the United States over time.

1.8 Public Health Significance

COVID-19 is a novel, rampant disease in our population, which has infected and killed many individuals. While it is a major accomplishment to have three approved vaccines in the United States, vaccine hesitancy proves to be an issue in uptake and reaching herd immunity. By using the FRED agent-based modeling platform to consider factors that play a role in initial COVID-19 vaccine hesitancy, and assessing agent interactions influencing behavior to accept or refuse a vaccine over time, it will be useful tool in evaluating the current state of the pandemic. These results could further inform policymakers and researchers on groups to target with education and intervention initiatives to increase overall vaccine acceptance.

2.0 Objectives

The objectives of this study were to (1) develop an agent-based conceptual model rooted in the behavioral psychology literature for COVID-19 vaccine hesitancy and (2) to develop a computational representation of COVID-19 vaccine hesitancy. We hypothesize that behavior, specifically vaccine hesitancy, can be modeled as a social contagion, just like an infectious disease. We expect that demographic factors, including age, sex, and race, as well as HBM factors of perceived susceptibility, perceived seriousness, perceived benefits of action, and perceived barriers of action put agents at a starting point on the WHO vaccine hesitancy continuum (between accept all, accept some/delay/refuse some, and refuse all). In addition, we believe there are competing behavior contagions in society: agents who pull others to "acceptance" and agents who pull others toward "refusal". Where an agent falls on the continuum likely influences their transmissibility of "acceptance" or "refusal" behavioral contagions, and therefore their susceptibility to the competing contagion. Building an ABM can represent these features.

3.0 Methods

3.1 Conceptual Model

After reviewing the well-known behavior change models, a vaccine hesitancy conceptual model was generated from aspects of the HBM, TTM, the Dube Conceptual Model of Vaccine Hesitancy, and the WHO Vaccine Hesitancy Continuum. As we wanted the framework to be firmly rooted in existing theory, each of these models were necessary to build the tractable agent-based framework; the TTM accounted for progression from state to state, the HBM model allowed for incorporation of quantitative factors, the Dube Conceptual Model of Vaccine Hesitancy included trust, and the WHO Vaccine Hesitancy Continuum set up a framework for recognizing vaccine hesitancy behavior as transmissible between agents.

3.2 Data Sources

Each component of the vaccine hesitancy conceptual model needed to have a numerical representation in FRED (Table 1). Selection of these four data files was somewhat arbitrary, as it was challenging to find data that matched components of the behavior change models mentioned above. CSV files were built with four columns—the date, the Unix day, the value under study, and that value normalized—and imported into the FRED model. The normalized value, between 0.0 and 1.0, was calculated by (1) obtaining the week with the greatest value under study and (2) dividing *each* week's value by that number, to generate a column of values ranging from 0 and 1.

Table 1. Data S	sources to Inform the Hesitancy Mod	el

Component	Source	Value Under Study	Additional Information
Perceived Susceptibility	USA Facts ⁵¹	• New cases in county by week over time	 Factor of geographic location *Needs new CSV file for each new county under study

Perceived Seriousness Perceived Benefits	CDC COVID Data Tracker ⁵² FiveThirtyEight ^{53,54}	 New deaths in U.S. by week over time Presidential approval rating by week over time (since vaccine introduction), transitioning from 	 "YouGov" pollster chosen, as it had the highest 538 grade (a B on an A-F scale), the mean-reverted bias
		President Trump to President Biden	closest to 0, and the most polls analyzed where there was still weekly adjusted approval data
Perceived Barriers	The New York Times ⁵⁵	• Doses administered in the U.S. by week over time	• Represent the vaccine supply

For trust, which we are representing in the model with demographic modifier data (age, sex, and race), we used the Pew Research Center's November '20 survey results of "% of U.S. adults who say they would definitely/probably get a vaccine for COVID-19 if one were available today" (Table 2)⁵⁶. Risk ratios were calculated by taking the demographic percentage willingness to accept over the population percentage willingness to accept, which was at 60% when the survey was performed.

Demographic Variable	Group Willi- ngness to Take Vaccine (%)	Overall Willi- ngness to Take Vaccine (%)	Risk Ratio (Group/Overall Willingness)
Age, years			
18-29	55	60	55/60 = 0.917
30-49	53	60	53/60 = 0.883
50-64	60	60	60/60 = 1.000
65+	75	60	75/60 = 1.250
Sex			
Male	67	60	67/60 = 1.116
Female	54	60	54/60 = 0.900
Race			
White	61	60	61/60 = 1.017
Black	42	60	42/60 = 0.700
Asian	83	60	83/60 = 1.383

Table 2. Percentage of Adults Definitely/Probably Get a Vaccine for COVID-19, Nov 2020

3.3 Variables

A number of personal variables are associated with each agent as drawn from the data sources mentioned above.

The trust (demographic) personal variable is the result of multiplying the risk ratios of age, sex, and race, and dividing by the largest combination value to normalize between 0 and 1. For example, the intermediate calculation for the trust personal variable for a 20-year-old, white female would be 0.917 * 0.900 * 1.017 = 0.839. However, to normalize between 0 and 1, we have to consider the largest trust variable value (1.929, intermediate calculation for Asian male, 65+). Therefore, the final trust variable value for the 20-year-old, white female would be 0.839/1.929 = 0.435 and for a 65+, Asian male would be 1.929/1.929 = 1.0. The options for the demographic variables in my model are the same as in Table 2, with one additional option for race, which is "other" (calculated by averaging the three races shown). This normalized, personal variable does not change through the simulation.

Susceptibility and seriousness personal variables are pulled from the CSV files at the beginning of each week (Sunday, 12am). The personal variable representing perceived threat is the result of multiplying the three personal variables of susceptibility, seriousness, and trust.

Perceived benefits and perceived barriers personal variables are extracted from the CSV files at the beginning of each week (Sunday, 12am). We similarly set the personal variable representing perceived empowerment as the multiplication of perceived benefits and perceived barriers. Finally, we multiplied perceived threat and perceived empowerment together to create one encompassing personal variable: vaccine propensity. This value is an agent's starting point on the vaccine hesitancy continuum for the week, and ranges from 0.0 to 1.0. Vaccine propensities

closer to 1.0 designate greater acceptance and vaccine propensities closer to 0.0 designate greater refusal.

Vaccine propensities are "centered" on 0.5, meaning that half the agents have a propensity that is above 0.5 and half have a propensity that is below 0.5. However, we can also model scenarios where we center on a different value than 0.5. If there is greater incentive to vaccinate in the population (centering on a value > 0.5), more agents are susceptible and transmitting the "acceptance" contagion, leading to higher probabilities of accepting the vaccine. Contrastingly, if there is overall poor reception to the vaccine in the population (centering on a value < 0.5), more agents are susceptible and transmitting the "agents are susceptible and transmitting the vaccine.

3.4 Vaccine Hesitancy as Transmittable Behavior

Agents are broadly tracked as being in one of four states, as outlined by the TTM precontemplation, contemplation, preparation, or action. The purpose of the precontemplation and contemplation conditions is to set a number of personal variables for agents, as mentioned above, that designates their starting vaccine propensity value (between 0.0 and 1.0) on the hesitancy continuum.

When an agent reaches <u>preparation</u>, behavior is transmittable, and we are actually juggling two competing behavior contagions—that of "acceptance" and of "refusal." For both of these contagion conditions, there is an exposed state, the transmission mode is proximity, and the original transmissibility and susceptibility values (which are equal and between 0.0 and 1.0) are functions of an agent's vaccine propensity.

Personal variables keep track of the number of "acceptance transmissions" and "refusal transmissions." After three transmissions of a condition, an agent's original susceptibility and

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transmissibility can be modified up or down the continuum by calculating the susceptibility modifier value:

Susceptibility Modifier = $\frac{\# \text{Acceptance Exposures}}{\# \text{Acceptance Exposures} + \# \text{Refusal Exposures}} *2$

Note that the modeler can adjust the number of transmissions before calculating susceptibility modification to simulate a slower or quicker behavior change in society (up or down from three).

The susceptibility modifier is multiplied by an agent's previous susceptibility and transmissibility to update the value. Once the "acceptance" susceptibility and transmissibility values are calculated, the reciprocal "refusal" values are calculated by subtracting those values from 1. "Acceptance" susceptibility is always equal to "acceptance" transmissibility; likewise, "refusal" susceptibility is always equal to "refusal" transmissibility. At this point, the personal vaccine probability" variable for "take is set equal to the "acceptance" susceptibility/transmissibility (greater values = greater probability of taking vaccine). Agents repeat this process after every transmission event of "acceptance" or "refusal."

Then, after each week (on Sunday at 12am), the "take vaccine probability" personal variable determines the probability that an agent will move to take the vaccine. Again, greater scores equal leaning towards acceptance, and a greater probability to take the vaccine. If an agent decides to take the vaccine, they are not susceptible to either of the "acceptance" or "refusal" conditions and not transmissible for the "refusal" condition. They can still transmit the "acceptance" condition. They stay in this condition for the rest of the simulation. Table 3 outlines two sample agents, where Agent 1 would take the vaccine at the end of the week and Agent 2 would not. At least three accept or refuse exposures are needed for the susceptibility modifier value to change. "Acceptance" and "refusal" susceptibility/transmissibility is capped at 1.0.

Agent	Day	Starting Vaccine	# of Accept	# of Refuse	Suscepti- bility	Accep- tance	Refusal S/T *	Take Vaccine
		Propen-	E *	E *	Modifier	S/T *		Probability
		sity			Value			
	Sun	0.6	0	0	N/A	0.6	0.4	0.6
	Mon		1	0	N/A	0.6	0.4	0.6
	Tue		1	1	N/A	0.6	0.4	0.6
1	Wed		3	1	1.5	0.9	0.1	0.9
1	Thurs		5	1	1.7	1.5 =	0.0	1.0
						1.0		
	Fri		8	2	1.6	1.0	0.0	1.0
	Sat		12	2	1.7	1.0	0.0	1.0
	Sun	0.2	0	0	N/A	0.2	0.8	0.2
	Mon		0	1	N/A	0.2	0.8	0.2
	Tue		0	1	N/A	0.2	0.8	0.2
2	Wed		0	2	N/A	0.2	0.8	0.2
2	Thurs		0	5	2.0	0.0	1.6 =	0.0
							1.0	
	Fri		0	8	2.0	0.0	1.0	0.0
	Sat		0	12	2.0	0.0	1.0	0.0

Table 3. Example Calculations with Sample Agents

* E = Exposures, S = Susceptibility, T = Transmissibility

If an agent does not take the vaccine, that agent will be sent back to Precontemplation, or the beginning of the model, to update their perceived susceptibility, seriousness, benefits, and barriers, as per the CSV files with varying weekly values over time. This process is repeated through the end of the simulation. However, their "accept transmissions" and "refuse transmissions" counters are not reset, so this allows for building of hesitancy behavior until an agent decides to take the vaccine or the simulation concludes.

While we could just focus on transmission in one direction, human behavior is representative of agents on either end of the spectrum transmitting "acceptance" (pro-vaccine) and "refusal" (anti-vaccine) conditions. Agents on the far ends of the spectrum ("acceptance" at 1.0 and "refusal" at 0.0) have a high transmissibility of their condition and a reciprocal low

susceptibility to the competing condition, compared to agents in the middle that are equally susceptible to both conditions and less likely to transmit.

For example, if Agent 1 is 90% susceptible and transmittable to the "acceptance" condition, they are only 10% susceptible and transmittable to the "refusal" condition. If they come into contact with Agent 2, who has a 30% susceptibility and transmissibility of "acceptance," then the probability of an "acceptance" transmission event is 0.9 * 0.3 * contact rate = 0.27 * contact rate, which is not very probable. The probability of a "refuse" transmission is also low, (1-0.9) * (1-0.3) * contact rate = 0.07 * contact rate. However, if Agent 1 comes into contact with Agent 3, who has an 80% susceptibility and transmissibility of "acceptance," the probability of an "acceptance" transmission event is 0.9 * 0.8 * contact rate = 0.72 * contact rate, which is decently probable.

This notion of continuous bidirectional behavior contagions of "acceptance" and "refusal" is shown in Figure 5. This simple network has nodes as agents and arrows representing transmission links. It is important to note that while this figure only has four nodes/agents, the modeled, county-level populations can have networks of tens of thousands to millions of agents.



Figure 5. Vaccine Propensity and Transmission in a Small Network

4.0 Results

4.1 Conceptual Diagram

Figure 6 shows the final conceptual diagram used in FRED. The overarching states of "Pre-Contemplation," "Contemplation," "Preparation," and "Action" are taken from the TTM, and are meant to track an agent through the model. The yellow boxes "Perceived Threat" and "Perceived Empowerment" are from the HBM, and the factors below (Perceived Susceptibility, Perceived Seriousness, Perceived Benefits of Action, and Perceived Barriers to Action) are quantitatively represented through numerical data.



Figure 6. COVID-19 Vaccine Hesitancy FRED ABM Conceptual Diagram

4.2 Computational Representation with Jefferson County

Using the FRED Platform, a simulation was run from December 20, 2020, right after the Moderna vaccine was first approved, until March 20, 2021 in Jefferson County, Pennsylvania (Figure 7). While this model can be used for any county in the United States, Jefferson County was selected because it includes the borough Punxsutawney, which is well-known for its

Groundhog Day event, which gathers many people and media attention; additionally, it is a smaller county of approximately 45,000 people, which allows for faster model run times for debugging and testing various variables⁵⁷.



Figure 7. Jefferson County on the Map of Pennsylvania⁵⁸

Table 4 outlines the trust (demographic) variables of age, sex, and race in the population. The majority of the population is white, while the age and sex breakdowns are more evenly distributed.

Variables	n (%)			
Age, years				
18-29	15765 (34.8)			
30-49	11709 (25.8)			
50-64	9499 (21.0)			
65+	8345 (18.4)			
Sex				
Male	22122 (48.8)			
Female	23196 (51.2)			
Race				
White	43965 (97.0)			
Black	140 (0.31)			
Asian	62 (0.14)			
Other	1151 (2.54)			

Table 4. Jefferson County Agent Breakdown (N = 45318)

Figure 8 shows an example with starting vaccine propensities, that incorporates these demographic variables into the continuum with the first week of study; the two largest peaks are in vaccine propensity ranges of 0.30-0.34 and 0.59-0.63.



Figure 8. Starting Continuum Vaccine Propensity Centered on 0.5, 12/20/2020-12/26/2020

Figure 9 outlines the new people who would take the vaccine at the end of every week, which shows decreasing values over time, and Figure 10 shows the total percentage of people who take the vaccine in the population over time, which rises to about 0.53.



Figure 9. New Agents That Take Vaccine by Week, Centered on 0.5



Figure 10. Percentage of the Population that Takes Vaccine Over Time, Centered on 0.5

We also modeled scenarios where vaccine propensities were not centered on 0.5. I chose to center on 0.3 and 0.6, because that is where the peaks are with the initial vaccine propensity.

While the number of new agents that take a vaccine centering on 0.6 is over 20,000, it is just under 3,500 when centering on 0.3 (Figure 11).



Figure 11. Vaccine Propensity Centering Variations—New Agent Vaccinations/Week

Centering on 0.6, the percentage of agent vaccinations/total agents is greater and reaches its peak (approximately 65%) at the end of January. Centering on 0.3, the percentage of agent vaccinations/total agents is around 12% at the end of January, and close to 14% at the end of the simulation (Figure 12).





Figure 13 shows the "take vaccine probability" for 20 agents over the first three weeks of the simulation. As shown, agents have different original vaccine propensities between 0.0 and 1.0. Dependent on the agents they interact with through the simulation, each agent's "take vaccine probability" can be modified up, down, or stay the same over time.



Figure 13. Individual Agent Vaccine Acceptance Scores, 12/20/2020-1/10/2020
5.0 Discussion

As hypothesized, vaccine hesitancy behavior can be modeled as a social contagion with the "acceptance" and "refusal" conditions. I built both a conceptual model and computational model using the ABM platform, FRED, on the basis of the HBM, TTM, Dube Conceptual Model of Vaccine Hesitancy, and WHO SAGE Vaccine Hesitancy Continuum. Considering factors of perceived susceptibility, perceived seriousness, perceived benefits of action, perceived barriers, and trust (demographic) factors, an agent's starting propensity on the vaccine hesitancy continuum is set and plays a role in its susceptibility to and transmissibility of reciprocal behavior contagions. Agents move up or down the continuum with each behavioral transmission event, until they accept the vaccine or the simulation ends. This simulation was run on Jefferson County, Pennsylvania, but can be run on any county to help understand the complexity of competing contagions.

It is important to understand the distribution of the population by age, sex, and race, as that sets the starting probability that an agent will take a vaccine. The most important factors that influence the curves and peaks of the graphs include the value that the vaccine propensity scores are normalized on and the count of transmission events an agent needs before their susceptibility and transmissibility are modified. For example, only ~14% of the population end up taking the vaccine if the vaccine propensity is centered on 0.3, compared to ~65% for 0.6. Additionally, if an agent interacts with three other agents of the same behavior contagion in a short period of time, the extreme continuum scores of 0 and 1 for susceptibility and transmissibility are reached very quickly (the agent is strongly accepting or refusing, and has low susceptibility to the reciprocal condition).

Limitations of this work include selection of proxies and racial diversity of the county selected. My goal was to use the behavior change models as a conceptual framework for the agent-

based model. Since the HBM includes perceived benefits and barriers, we selected presidential approval rating per week and number of doses administered per week, as there were data available. However, if we could find a better proxy for benefits, or if data were available for doses *available* to each county by week, instead of doses administered, that would have been included in the model for perceived barriers. Further, we did a majority of tests on Jefferson County, where there is not a lot of racial diversity (97.0% white, 0.309% black, 0.137% Asian, and 2.54% other). It might be interesting to look at transmission in a more diverse county.

Strengths of this work include utilizing well-known behavior change models as the HBM and TTM, as well as the WHO Vaccine Hesitancy model, as a foundation to an ABM model considering the transmission of behavior. Further, we are exploring factors that contribute to vaccine hesitancy with COVID-19, which has caused a global pandemic, with vaccines that are under emergency use authorization; this is a topical subject where there is not a lot of background information and previous studies completed.

One recommendation for future research includes combining this model with that of the vaccine eligibility by phase and availability at point of distribution (POD) models. This would truly elucidate agent eligibility and who wants to take the vaccine over time. Another recommendation includes testing a different equation for the susceptibility modifier. The current equation leads to rapid growth in either the "acceptance" or "refusal" direction when there are 3 or more transmission events of either condition. A different equation that allows for moderate growth, but still considers the effects of accumulating accept and refuse transmission events, might be preferable. Finally, it would be nice to add political party as one of the trust (demographic) modifiers, as it has been shown to be a strong predictor of vaccine hesitancy during the COVID-19 pandemic.

The results of this model are important because they reveal how various factors play a role in vaccine hesitancy, and how agents can influence the behavior of other agents they come into contact with in the simulation. The idea of competing behavior contagions and vaccine hesitancy is novel.

This model has public health significance to aid stakeholders and policymaker efforts to tackle vaccine hesitancy in the population. It is incredibly powerful to represent and visualize entire populations in ABM simulations that are close to reality. By testing and developing policies in silico, the best policies can be evaluated and launched in practice.

Appendix Code

main.fred

```
comment {
   This is the main model to run on Jefferson County, Pennsylvania.
}
simulation {
   start_date = 2020-Dec-20
   #to look at the vaccine propensities after the first week, use end_date = 2020-Dec-26
   #end_date = 2020-Dec-26
   end_date = 2021-Mar-20
   locations = Jefferson_County_PA
}
include VaccineConfidence.fred
include Precontemplation.fred
include Contemplation3.fred
include Preparation3.fred
```

VaccineConfidence.fred

```
comment {
   This model sets the overall COVID-19 Vaccine Confidence trajectories by the structure of the transtheoretical model.
}
condition VACCINECONFIDENCE {
   start_state = Precontemplation
   state Precontemplation {
        wait()
        next()
   }
   state Contemplation {
        set_state(ACCEPTEND,Check)
        set_state(REFUSEEND,Check)
        wait()
        next()
   }
   state Action {
        wait()
        next()
   }
}
```

Precontemplation.fred

This model takes into account perceived susceptibility, perceived seriousness, and turst (demographic modifiers) to quantify perceived threat. Follows the Health Belief Model framework. variables { personal my_race personal my_demographicvar personal my_susceptibilityvar personal my_seriousnessvar personal my_perceivedthreat global_list NewDeaths global_list NewDeathsDates
global_list NewDeathsUnix global list NewDeathsNormalized global_list JeffersonCases
global_list JeffersonCasesDates
global_list JeffersonCasesUnix
global_list JeffersonCasesNormalized global current_new_deaths
current_new_deaths.output = 1 global death_index global current_jefferson_cases
current_jefferson_cases.output = 1 parameters { ameters { NewDeathsDates = read(./CSV_Files/Weekly/WeeklySeriousness.csv, 0) NewDeaths = read(./CSV_Files/Weekly/WeeklySeriousness.csv, 1) NewDeathsUnix = read(./CSV_Files/Weekly/WeeklySeriousness.csv, 2) NewDeathsNormalized = read(./CSV_Files/Weekly/WeeklySeriousness.csv, 3) JeffersonCasesDates = read(./CSV_Files/Weekly/WeeklySusceptibilityJefferson.csv, 0)
JeffersonCases = read(./CSV_Files/Weekly/WeeklySusceptibilityJefferson.csv, 1)
JeffersonCasesUnix = read(./CSV_Files/Weekly/WeeklySusceptibilityJefferson.csv, 2)
JeffersonCasesNormalized = read(./CSV_Files/Weekly/WeeklySusceptibilityJefferson.csv, 3) condition PRECONTEMPLATION { start_state = Start admin_start_state = AdminStart state Start { if (current_state_in_VACCINECONFIDENCE == VACCINECONFIDENCE.Precontemplation) then next(DemographicModifier) default(Start) } state AdminStart { if (today<NewDeathsDates[0]) then current_new_deaths=0 wait(0) f (today==NewDeathsDates[0]) then next(AdminCheck) default(AdminStart) 3 state AdminCheck { wait(24*7) death_index = find_index(today, NewDeathsDates) if(death_index != -1) then current_new_deaths = NewDeathsNormalized[death_index]
if(death_index != -1) then current_jefferson_cases = JeffersonCasesNormalized[death_index] default(AdminCheck)

```
state DemographicModifier {
      wait(0)
      my demographicvar = 0.60
      if(race==african_american) then my_race=2
      if(race==white) then my_race=1
if(race==asian) then my_race=6
      if(race!=african_american & race!=white & race!=asian) then my_race=10
      if (sex==male & my_race==2 & is_in_range(age,18,29)) then my_demographicvar = 0.716
     if (sex==male & my_race==2 & is_in_range(age,30,49)) then my_demographicvar = 0.690
if (sex==male & my_race==2 & is_in_range(age,50,64)) then my_demographicvar = 0.781
if (sex==male & my_race==2 & is_in_range(age,65,120)) then my_demographicvar = 0.977
      if (sex==female & my_race==2 & is_in_range(age,18,29)) then my_demographicvar = 0.578
     if (sex==female & my_race==2 & is_in_range(age,30,49)) then my_demographicvar = 0.556
if (sex==female & my_race==2 & is_in_range(age,50,64)) then my_demographicvar = 0.630
if (sex==female & my_race==2 & is_in_range(age,65,120)) then my_demographicvar = 0.788
      if (sex==male & my_race==1 & is_in_range(age,18,29)) then my_demographicvar = 1.041
if (sex==male & my_race==1 & is_in_range(age,30,49)) then my_demographicvar = 1.002
if (sex==male & my_race==1 & is_in_range(age,50,64)) then my_demographicvar = 1.135
      if (sex==male & my_race==1 & is_in_range(age,65,120)) then my_demographicvar = 1.419
      if (sex==female & my_race==1 & is_in_range(age,18,29)) then my_demographicvar = 0.839
      if (sex==female & my_race==1 & is_in_range(age,30,49)) then my_demographicvar = 0.808
if (sex==female & my_race==1 & is_in_range(age,50,64)) then my_demographicvar = 0.915
      if (sex==female & my_race==1 & is_in_range(age,65,120)) then my_demographicvar = 1.144
      if (sex==male & my_race==6 & is_in_range(age,18,29)) then my_demographicvar = 1.415
      if (sex==male & my_race==6 & is_in_range(age,30,49)) then my_demographicvar = 1.363
if (sex==male & my_race==6 & is_in_range(age,50,64)) then my_demographicvar = 1.543
if (sex==male & my_race==6 & is_in_range(age,65,120)) then my_demographicvar = 1.929
      if (sex==female & my_race==6 & is_in_range(age,18,29)) then my_demographicvar = 1.141
     if (sex==female & my_race==6 & is_in_range(age,30,49)) then my_demographicvar = 1.099
if (sex==female & my_race==6 & is_in_range(age,50,64)) then my_demographicvar = 1.245
if (sex==female & my_race==6 & is_in_range(age,65,120)) then my_demographicvar = 1.556
      if (sex==male & my_race==10 & is_in_range(age,18,29)) then my_demographicvar = 1.057
      if (sex==male & my_race==10 & is_in_range(age, 30, 49)) then my_demographicvar = 1.018
      if (sex==male & my_race==10 & is_in_range(age,50,64)) then my_demographicvar = 1.153
      if (sex==male & my_race==10 & is_in_range(age,65,120)) then my_demographicvar = 1.441
      if (sex==female & my_race==10 & is_in_range(age,18,29)) then my_demographicvar = 0.853
      if (sex==female & my_race==10 & is_in_range(age,30,49)) then my_demographicvar = 0.821
if (sex==female & my_race==10 & is_in_range(age,50,64)) then my_demographicvar = 0.930
if (sex==female & my_race==10 & is_in_range(age,65,120)) then my_demographicvar = 1.162
      my_demographicvar = my_demographicvar/1.929
```

next(SusAndSer)

3



Contemplation.fred

```
comment {
    This model takes into account perceived benefits of action, perceived barriers of action
    to quantify perceived empowerment. Follows the Health Belief Model framework.
}
variables {
    #presidential approval rating/week
    personal my_perceivedbenefits
    personal my_perceivedbarriers
    personal my_perceivedempowerment
    personal my_vaccine_score
    global_list Approvals
    global_list ApprovalDates
    global_list ApprovalUnix
    global_list DosesAdministered
    global_list DosesAdministeredDates
    global_list DosesAdministeredUnix
    global list DosesAdministeredNormalized
    global current_approval
    current_approval.output = 1
    global approval_index
    global current_doses_administered
    current doses administered.output = 1
}
parameters {
    ApprovalDates = read(./CSV_Files/Weekly/WeeklyBenefits.csv, 0)
    Approvals = read(./CSV_Files/Weekly/WeeklyBenefits.csv, 1)
    ApprovalUnix = read(./CSV_Files/Weekly/WeeklyBenefits.csv, 2)
    DosesAdministeredDates = read(./CSV_Files/Weekly/WeeklyBarriers.csv, 0)
    DosesAdministered = read(./CSV_Files/Weekly/WeeklyBarriers.csv, 1)
DosesAdministeredUnix = read(./CSV_Files/Weekly/WeeklyBarriers.csv, 2)
    DosesAdministeredNormalized = read(./CSV_Files/Weekly/WeeklyBarriers.csv, 3)
3
```

```
state Empowerment {
    wait(0)
    my_perceivedempowerment = my_perceivedbenefits*my_perceivedbarriers
    my_vaccine_score = my_perceivedthreat*my_perceivedempowerment
    #centering on 0.5 means that half of agents have score above 0.5 and half below
    #if agents are more inclined to get the vaccine, multiply by value >0.5
    #if agents are less inclined to get the vaccine, multiply by value >0.5
    my_vaccine_score = 0.5 * (my_vaccine_score/0.015859)
    print_csv(Contemplation.csv,id,my_race,sex,age,my_vaccine_score)
    next(ToPreparation)
    default(Excluded)
}
state ToPreparation {
    set_state(VACCINECONFIDENCE,Contemplation,Preparation)
    wait(until(Sun,12am))
    default(Start)
}
```

Preparation.fred



```
#agents can still be exposed during this time
wait(until(Sun,12am))
default(Choose)
```

my_take_vaccine_prob = ACCEPTEND.sus

}



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