Modeling the spread of vaccination beliefs and behaviors through the lens of cultural evolution

by
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CHAPTER 1. INTRODUCTION

The interplay between culture and disease

Health-related human behaviors, including disease-transmitting and preventative health behaviors, are influenced by the wider cultural landscape, and thus are subject to cultural evolution—the transmission and change of cultural traits over time (Luigi Luca Cavalli-Sforza and Feldman 1981). For example, the Bubonic Plague that ravaged Europe during the early 14th century was introduced to various regions as a result of increased trade across Eurasia (Raoult et al. 2013; Davis 1986). The spread was further facilitated by the housing and hygienic practices of the time—it was commonplace in Europe for people to share living spaces with livestock, and houses were built with thatched roofs (Shrewsbury 2005). These behaviors provided a breeding ground for the rats that carried the fleas that acted as plague vectors, and provided these fleas with easy access to human and animal hosts (Raoult et al. 2013). A well-known example of cultural practices affecting both the prevalence of infectious disease and the selection pressure on a genetic trait is the link between farming practices in central Africa, the prevalence of malaria, and the incidence of sickle-cell disease. Water-intensive farming practices expanded a breeding ground for *Anopheles gambiae*, the vector for the malaria parasite (Wiesenfeld 1967). Increased prevalence of malaria drove selection for the protective phenotype found in humans with one copy of the sickle-cell allele. (Durham 1982; K. N. Laland, Odling-Smee, and Feldman 2000; Wiesenfeld 1967). Another example of a disease linked to a cultural practice is Kuru, a fatal neurodegenerative disease found only in the Foré people and their immediate neighbors in the Okapa District of the Eastern Highlands Province of Papua New Guinea (Alpers 2008). This disease is transmitted via their mortuary practice of consumption of the body of a dead person, including the infected brain tissue, particularly by female relatives and their children, resulting in the high prevalence of the disease in women and children.

Alongside diseases, preventative health practices can also spread between people and affect health outcomes. For example, culturally integrated practices such as hand washing and regular bathing have led to a reduction in disease burden (Vermeil et al. 2019; Langford, Lunn, and Panter-Brick 2011; Haverstick et al. 2017), and vaccines are estimated to currently prevent about five million deaths per year (Carter et al. 2021). As I will discuss, anti-vaccine sentiments are based in aspects of culture, such as religion, and values, such as personal liberty (Jackson 1969). Also, the recent unexpected and seemingly illogical shift in vaccination beliefs and

behaviors towards hesitancy in the United States suggest that there are other factors in play besides an understanding of vaccine benefits. Vaccination practices, therefore, could be considered culturally motivated behaviors. In fact, several authors (Streefland, Chowdhury, and Ramos-Jimenez 1999; de Figueiredo et al. 2020) use the term "local vaccination cultures" to describe the shared beliefs among individuals within a community about vaccine-preventable disease etiology, prevention, and treatment. Vaccination culture, which can be shaped by the larger cultural landscape, can affect an individual's vaccine attitudes and decisions. Therefore, it is fitting to use cultural evolutionary modeling frameworks to model vaccination behavior. However, as I describe below, most health-related models and vaccination behaviors do not account for cultural evolutionary dynamics and are thus likely to miss important influences affecting disease transmission.

Interventions to prevent disease spread before vaccines

Human populations have coevolved with various pathogens that infect them. As a result, human populations have evolved physiological defenses—i.e., innate and adaptive immune responses—as well as preventive health practices, both of which enable individuals to fight these infections. Occasionally, however, as pathogens evolve and vectors adapt, populations are exposed to novel infections that evade these preventative measures and immune responses; this could result in disease outbreaks with the potential to spread widely—possibly resulting in a pandemic—or to remain persistently (i.e. become endemic) in certain regions (Racaniello 2004). Infectious disease outbreaks and endemic disease are naturally recurring phenomena that have been shaping populations and cultures throughout human history (Lederberg 2000; Morens 1998; Morens, Folkers, and Fauci 2004). Alongside endemic disease, there have been about 20 recorded pandemics to date, from the Justinian Plague in 541 AD to the current COVID-19 pandemic (Piret and Boivin 2020). Endemic disease and emerging infections continue to be a concern across the world as hundreds of thousands to millions die each year as a result of infectious disease (CDC-Centers for Disease Control and Prevention 2009; Excler et al. 2021).

Vaccines are a relatively recent development on the timescale of human-disease interactions. Prior to vaccines, common practices to prevent illness and disease-spread included quarantine—the detention and segregation of subjects suspected to carry a contagious disease (Gensini, Yacoub, and Conti 2004), restrictions on gatherings, and isolation mandates or lockdowns (Morens, Taubenberger, and Fauci 2021). Quarantines for sailors, for example, were

implemented at ports beginning in 1377 to combat the plague in Europe, and in 1423 a dedicated plague hospital (*lazaretto*) was opened in Venice on an island separated from the city (Tognotti 2013). These practices, termed "non-pharmaceutical interventions", are still employed today, especially in cases of emerging infections before there are effective vaccines or treatments, such as during an Ebola outbreak, COVID-19, and pandemic influenza (Markel et al. 2007; Morens, Taubenberger, and Fauci 2021). Variolation, also referred to as *inoculation,* was the precursor to vaccination. The practice was implemented after the observation that previous exposure to smallpox (variola) or similar diseases (such as cowpox) conferred some level of protection against severe disease (Riedel 2005). Variolation was developed as a method of immunizing patients against severe smallpox (variola major) by infecting them with small amounts of material from the sores of patients with a mild form of the disease (variola minor) (Plotkin 2011; Dumbell, Bedson, and Rossier 1961). The earliest record of variolation dates back to 15th century China, which included "nasal insufflation" with powdered smallpox material, such as scabs (Weniger and Papania 2013). Various forms of variolation were commonly practiced in other parts of Asia and Africa, as well (Langer 1976a). The practice was formally introduced to Western Europe in 1721 by Lady Mary Wortley Montague, an English aristocrat who lost several family members to smallpox and insisted that her children be inoculated by physicians after learning about the practice during her stay in the Ottoman empire (Riedel 2005). Bolstered by the smallpox outbreak in Boston, the introduction of variolation in the American colonies occurred around the same time and was driven by the efforts of Reverend Cotton Mather, who learned about it from Onesimus, his former slave (Riedel 2005; T. H. Brown 1988). However, since knowledge of variolation came from an African source, there was initially widespread fear and distrust of the practice, with Cotton Mather receiving threats and many in the Boston medical community expressing skepticism "that Africans were capable of medical innovation" (Minardi 2004; T. H. Brown 1988).

The invention of the smallpox vaccine in 1796 by Edward Jenner, which involved inoculating patients with the cowpox virus (*vaccinia*), marked the beginning of the end of variolation (Riedel 2005). Despite natural skepticism—manifesting in rumors of the vaccine turning people into cows (Lau 2020), and the concern of a loss of potency (Brimnes 2004)—Jenner's thesis was widely accepted by the great majority of physicians, and vaccination practice spread quickly. Vaccination was viewed as preferable to variolation, as the resulting

infection was safer and vaccinated individuals were less likely to be the source of smallpox infection (Gronim 2006; Brimnes 2004; Langer 1976a), and by the 1800s the practice had reached most European countries and the United States (Riedel 2005). Gradually, vaccination replaced variolation worldwide, and variolation was prohibited in England by the Vaccination Act of 1840 (Didgeon 1963).

Human perception and response to emerging diseases can change with respect to familiarity with the disease and the availability of resources to combat the disease (Medley and Vassall 2017). Prior to the development of the Polio vaccine in the 1950s, Poliomyelitis was one of the most feared infections in the United States, especially during the summer months when the virus seemed to peak (CDC 2022). However, the elimination of polio has shifted the public perception of polio to one of a rare disease that is largely confined to the developing world (Elsevier 2014; Centers for Disease Control and Prevention 2015; Martinez-Bakker, King, and Rohani 2015). As another example, the 1918 influenza pandemic was responsible for at least 50 million deaths worldwide; populations implemented various interventions to limit the spread of this disease, including quarantines, mask mandates, and limitations on mass gatherings (Short, Kedzierska, and van de Sandt 2018). In contrast, seasonal influenza is viewed very differently. Even though approximately 400,000 people die each year from seasonal outbreaks (Paget et al. 2019), influenza vaccine uptake is relatively low (for example, ~10% of the population in China and ~45% in the United States ("Flu Vaccination Coverage, United States, 2016-17 Influenza Season" 2023; Q. Wang et al. 2018)). Finally, in the 1950s, measles was so common as to be considered a "rite of passage" but still caused widespread complications and death in children; since the vaccine, the severity of measles has been downplayed as a "rash" by those who are skeptical of the vaccine (Berche 2022; Mastroianni 2019).

The overall concept that pre-exposure to infectious agents can confer immunity still drives other traditional practices such as "pox parties", in which children are intentionally exposed to diseases like chickenpox, measles, and rubella, and most recently "COVID Parties" (Orenstein and Garon 2016; Bok et al. 2022; "'Pox Parties' Still Pose Risk for Severe Chickenpox Complications" 2016). These intentional exposure events are strongly discouraged by public health officials for a number of reasons that are analogous to the risks of variolation, such as the possibility of severe disease or complications and the potential to spread the disease to at-risk individuals, but the practice persists (Young 2009).

Types and sources of vaccine hesitancy

Following in the steps of its predecessor, variolation, vaccination is one of the most important and successful public health achievements of the last century (Fenner 1982; Kim-Farley et al. 1984; D. Salk 1980). However, in developed countries, there has been a recent resurgence of vaccine-preventable diseases (VPDs) despite the demonstrated safety and efficacy of vaccines and the generally high childhood vaccination rates (Atwell and Salmon 2014; Kubin 2019; Falagas and Zarkadoulia 2008; Dubé et al. 2013). Because of the risks of these vaccine-preventable disease outbreaks worldwide (Glanz et al. 2009), in 2019, the World Health Organization named vaccine hesitancy as one of its ten threats to global health (Scheres and Kuszewski 2019).

Developing an operational definition for vaccine hesitancy has been challenging for researchers due to the difficulty in categorizing vaccination attitudes and the complex interaction of different social, cultural, political and personal factors in vaccine decision-making (Dubé et al. 2013). Since vaccine hesitant attitudes are not always coupled with reduced vaccine uptake (as vaccine-hesitant individuals may accept all recommended vaccines in a timely manner, but still have significant doubts in doing so), it has been difficult to fully understand vaccine hesitancy at the population level (Dubé et al. 2013). This difficulty in painting a clear picture has manifested in the development of several vaccine acceptance and resistance models, with most focusing on parental decision-making (Dubé et al. 2013). In 2015, after an extensive review of these models, the SAGE Working Group on Vaccine hesitancy concluded that vaccine hesitancy "refers to delay in acceptance or refusal of vaccination despite availability of vaccination services. Vaccine hesitancy is complex and context specific, varying across time, place and vaccines. It is influenced by factors such as complacency, convenience and confidence," (MacDonald and SAGE Working Group on Vaccine Hesitancy 2015) which are the components of the "3 Cs" model, first proposed to the WHO EURO Vaccine Communications Working Group in 2011. The "3 Cs model" has been viewed as being the most readily understandable conceptual framework for disentangling the complexity of vaccine hesitancy (MacDonald and SAGE Working Group on Vaccine Hesitancy 2015). Each of the three categories—complacency (the belief that vaccination is unnecessary when the perceived risk of VPDs is low), convenience (the accessibility and affordability of vaccines), and confidence (the level of trust in the efficacy and safety of the vaccine, and in the healthcare system)—are influenced by a number of other factors

such as the motivation of policy makers, self-efficacy, and cultural context (MacDonald and SAGE Working Group on Vaccine Hesitancy 2015; Dubé et al. 2013). Unlike the social determinants of health, which tend to influence health behaviors in a single direction, vaccine hesitancy determinants, such as education and socio-economic status, have been associated with both higher and lower levels of vaccine acceptance (MacDonald and SAGE Working Group on Vaccine Hesitancy 2015).

Vaccine hesitancy and vaccination opposition are, however, not recent phenomena: public opposition to vaccinations has been based in theology, politics, law, and general skepticism since their creation in 1796 (Schwartz 2012; Koslap-Petraco 2019; Siddiqui, Salmon, and Omer 2013; Callender 2016). Similar pushback against preventative health measures existed in the preceding century with the practice of variolation, particularly since there was a small chance of death and of spreading smallpox after inoculation (Chorba and Esparza 2022; Riedel 2005; Bernoulli 1760; Blower and Bernoulli 2004). Variolation was argued to be against the will of God by English and French clergy (Langer 1976a). Writers and religious leaders against inoculation discredited the practice by emphasizing its origins in Turkey, "a land of harems," and its associations with "a few Ignorant Women, amongst an illiterate and unthinking People" (Wagstaffe 1722), in reference to the introduction of variolation to Europe by Lady Mary Wortley Montague (Riedel 2005). As the practice of variolation ran counter to 18th century medical theories, physicians were also hesitant to adopt the practice; these medical theories were grounded in an understanding of treating disease as expelling "excessive or corrupted" materials from the body, therefore the idea of healing by intentionally inserting infection into the body was unfamiliar and illogical (Gronim 2006).

Two persistent themes of vaccine hesitancy include, first, the idea that vaccinations are more harmful than the diseases they intend to prevent—this theme, reminiscent of the "artificial smallpox" arguments of 18th century (Blower and Bernoulli 2004; Bernoulli 1760), usually occurs at the introduction of new vaccines (Schwartz 2012). The second theme, usually occurring after compulsory vaccination mandates, is the idea that vaccines may not be necessary during a decline in disease (Schwartz 2012). With the introduction of compulsory vaccination in the 19th century came the precursors of contemporary vaccination exemptions (Durbach 2005; Swales 1992a) which include non-medical exemptions on the basis of religious, philosophical, and personal beliefs (E. Wang et al. 2014; Phadke et al. 2016). The Anti-Vaccination League,

founded in mid-19th-century London, argued that compulsory vaccination invaded the people's liberties (Wolfe and Sharp 2002). A 1969 review of mandatory vaccination in the United States revealed a similar objection—"infringement on personal liberty"—along with an aversion to government intrusion on religious beliefs and a general distrust of medical science (Jackson 1969). Thus, since the advent of vaccinations, cultural context has interacted with vaccine-related beliefs and in turn influenced vaccination behaviors, ultimately affecting population-level immunity and public health.

Mathematical models of disease dynamics

In addition to driving the invention of the vaccine, smallpox also prompted the first mathematical models of disease; these models led to the first mathematical predictions of how severe a disease outbreak would be and how many lives could be improved by an intervention. In 1766, Daniel Bernoulli aimed to convince the public about the benefits of whole population "inoculation" in the first application of a mathematical model to infectious disease (Dietz and Heesterbeek 2002; Bernoulli 1760). This model became a precursor to the compartmental model most commonly used in infectious disease modeling today. Bernoulli's model, which calculated the gain in life expectancy at birth if smallpox were to be eliminated as a cause of death, estimated a gain in 1/9 the average lifespan with smallpox inoculation (Bernoulli 1760). His work in the prolongation of life expectancy and competing risks had immediate financial impact as annuities were being sold at the time; as a result, Bernoulli's work received considerable attention in actuarial literature (Dietz and Heesterbeek 2002). In 1927 the Kermack–McKendrick model—the SIR (Susceptible-Infected-Recovered) model we know today—was published (Kermack and McKendrick 1927), but it was not until 1960 (Brambilla, n.d.) that the infectious disease epidemiological applications of Bernoulli's compartmental model were fully recognized (Dietz and Heesterbeek 2002). In more recent applications, researchers have added additional compartments to represent more complex scenarios, such as Exposed, Vaccinated, Died, Reported, Unreported, Latent (Liu et al. 2020; Calafiore, Novara, and Possieri 2020; Schlickeiser and Kröger 2021). With the 20th century came a number of additional developments in infectious disease epidemiology, such as mathematical models incorporating age structure of the population (G. F. Webb 1985; Thomas and Clark 2011). In addition, "catalytic" models, which have their roots in chemistry, apply the law of mass action to explain epidemic behavior (Muench 1959; Griffiths 1974). For example, in a catalytic model, the force of infection, which

in a traditional SIR model could be a constant rate at which susceptible individuals become infected, can instead be represented as a function of the age of the individual or the year of infection (Cauchemez et al. 2019). In epidemiological applications, it could also be assumed that the rate of new infections is proportional to the relative numbers of infected and susceptible individuals in a population (Muench 1959). Catalytic and compartmental models have accurately predicted the dynamics of malaria (Ross 1910), measles (Griffiths 1974), the plague (Kermack and McKendrick 1927), and AIDS (Huang and Villasana 2005), and continue to be applied to understand COVID-19 dynamics and vaccine efficacy (G. Webb 2021; Demongeot et al. 2022).

Mathematical models of population behaviors

Mathematical models have not only been a staple in the field of epidemiology due to their capability in reproducing real world disease phenomena, but have also proved useful in understanding the behavior of populations. In 1798, Thomas Malthus published *An Essay on the Principle of Population*, in which he speculated that populations experience exponential growth while food production experiences arithmetic growth (Malthus 1872). The Malthusian theory, as this came to be known, suggested that populations have a tendency to increase beyond the means of subsistence and are necessarily limited by the food supply and other resources. Therefore, populations would quickly outpace their food supply, resulting in reduced living standards, famine, war, and population decline (Malthus 1872). Taking note of the unrealistic nature of Malthus' population growth model, Alphonse Quetelet and Pierre François Verhulst added a term to Malthus' equation to represent a population's increasing resistance to further growth (Cramer 2002). This addition of a carrying capacity would result in an exponentially growing population arriving at an upper limit or saturation level over time (Cramer 2002). Verhulst published his suggestions, deriving the "*courbe logistique*" or logistic function, in three papers between 1838–1847 (Cramer 2002; Verhulst 1845, 1838, 1847). However, it was not until the rediscovery of his work by Raymond Pearl and Lowell J. Reed in the early 20th century that its use became widely accepted in statistics (Pearl and Reed 1920, 1922; Cramer 2002).

Populations are naturally composed of various potentially evolving subgroups, with individuals and groups simultaneously connected and interacting in a variety of ways. Social network models were developed to capture these types of population dynamics. Broadly, social network models are statistical models that are used for the analysis of relational data (Amati 2020) and social network analysis uses network and graph theory to investigate social structures

(Otte and Rousseau 2002). Though the application of mathematics to social structures has roots in the late 19th century (Freeman 2004; Macfarlane 1882), major development to the field of social network analysis occurred in the 1930s in several disciplines (J. Scott and Carrington 2011; Lewin 1936; Moreno 1934). In 1934, psychologist Jacob L. Moreno invented the 'sociogram' as a way of visually representing social networks with points and lines; he referred to this approach as 'sociometry' (Moreno 1934). Moreno's work and that of his colleague Kurt Lewin (Lewin 1936) most explicitly focused on examining ways in which the structures of small groups influenced the perceptions and action choices of their individual members. By the 1950s, sociometry took the form of an emphasis on group dynamics, becoming an important application in education and community studies (Cartwright and Zander 1958; Harary and Norman 1953). These more modern social networks often represent individuals as nodes in a network, with edges between nodes indicating connections between pairs of people, enabling researchers to model the likelihood of information or disease to spread in the population.

While social network analysis is essentially graph theory at its core, other types of mathematical models have been employed to highlight specific features of network structure. With the "blockmodeling" technique, researchers can simplify a complex social network to a more readily analyzable one by grouping units (i.e. nodes or individuals) of the network based on their social positions or statuses (J. Scott and Carrington 2011; Lorrain and White 1971; White, Boorman, and Breiger 1976; Boorman and White 1976). Most recently, agent-based models have been used to explore processes of change in networks. An agent-based model is a computational model for simulating the actions and interactions of autonomous agents, which can be individual or collective entities (Laubenbacher, Hinkelmann, and Oremland 2013). In this type of model, each agent individually assesses its situation and makes decisions on the basis of a set of rules (Bonabeau 2002; Laubenbacher, Hinkelmann, and Oremland 2013).

Behavior-change models are a class of mathematical models that simulate changes in behaviors in response to internal or external motivators (Verelst, Willem, and Beutels 2016). These types of models typically complement disease models to more accurately represent the disease transmission landscape by incorporating behavioral changes, such as preventative health behaviors, in response to information about the disease. A widely used theoretical framework of behavior-change models is that of game theory. Though some game-theoretic ideas can be traced to the 18th century, major developments of the theory began in the 1920s with the work of the

mathematicians Emile Borel and John von Neumann (John Von Neumann and Morgenstern 1944; Borel 1921; J. Von Neumann 1928). A limitation for game theoretic models in particular is the assumption that humans are rational decision-makers capable of accurately assessing their environment (Verelst, Willem, and Beutels 2016; Voinson, Billiard, and Alvergne 2016). Game theory presupposes that a decision-maker ("player") chooses the best action among all the actions available to them according to their preferences and interactions with other players (Osborne 2004; Colman 2016). Predictions are made using various behavioral assumptions about how deeply people reason and how they react to observed behavior (Camerer 2009). Perhaps the most famous example of game theory's application to the study of cooperative behavior is the prisoner's dilemma, in which a pair of agents can either cooperate or defect, and each individual has an incentive to choose to defect, whereas cooperating would be better for the group (Yasukawa 2010; Poundstone 1993).

Agent-based modeling has a number of advantages over other widely used models, as they are able to incorporate the increasing complexity of social systems. It is also difficult to model population heterogeneity and identify emergent behavior using ordinary or partial differential equations (ODEs and PDEs) or game theoretic frameworks (Bonabeau 2002; Laubenbacher, Hinkelmann, and Oremland 2013). Agent-based social network models are able to capture emergent phenomena, and can more easily be used to represent spatial heterogeneity (Bonabeau 2002; Laubenbacher, Hinkelmann, and Oremland 2013). They can also simulate stochasticity in human decision making, for example, by accounting for imitation behavior (Ndeffo Mbah et al. 2012).

Behavior–change models and models of cultural evolution in the context of disease

Given their broad usage in modeling behaviors and epidemiological processes, mathematical models make useful tools for understanding human behavior in the context of disease. The spread of infectious disease is intrinsically linked to human behavior, and it has become increasingly common for epidemiological models to incorporate aspects of human behavior and behavioral response to disease (e.g (Perra et al. 2011; Mao and Yang 2012b; Bauch 2005; Chauhan, Misra, and Dhar 2014; Funk, Salathé, and Jansen 2010; Tanaka, Kumm, and Feldman 2002)). Vaccination and social distancing are the most common forms of disease interventions modeled by these behavior-change models (Verelst, Willem, and Beutels 2016; Fenichel et al. 2011; Azizi et al. 2022). A series of compartmental models have represented the

spread of disease alongside the spread of either beliefs or behaviors, terming these "coupled contagions" in which simulated individuals can be "infected" by cultural factors such as vaccine hesitancy, fears, information, or health-related behaviors, which can in turn alter the likelihood of being infected by the disease (Epstein, Hatna, and Crodelle 2021; Smaldino and Jones 2021; Epstein et al. 2008a; Mehta and Rosenberg 2020). For example, a coupled contagion model showed that the spread of anti-vaccine sentiment, modeled alongside the vaccine-preventable disease, could cause epidemics that would otherwise not have occurred (Mehta and Rosenberg 2020). Homophily, the tendency for individuals to associate with others more like themselves, and outgroup aversion, the desire to not engage in activities associated with the outgroup, are examples of other properties that change the interactions between individuals that these models can also incorporate (Smaldino and Jones 2021; Smaldino et al. 2017).

Cultural evolutionary models, models that delineate change in cultural traits over time, have not yet become prominent among researchers who implement behavior-change models. Cultural evolutionary models were first proposed as an analogue to theoretical population genetics, to illustrate how cultural traits could be transmitted—and be subject to evolutionary forces—in a way that often parallels biological evolution (Cavalli-Sforza and Feldman 1973; Cavalli-Sforza and Feldman 1973; Creanza and Feldman 2016). Typically, behavior change models do not account for factors such as intergenerational effects, nonrandom assortment in interactions or mating preferences, and biased transmission of behavioral traits. Cultural evolution models are able to readily account for these factors and thus allow us to track the evolution of health beliefs and behaviors (Creanza, Kolodny, and Feldman 2017). These types of models are also able to capture the effects of vertical and intergenerational transmission as well as oblique (community) influences (L. L. Cavalli-Sforza and Feldman 1981; Boyd and Richerson 1988; Creanza, Kolodny, and Feldman 2017). This is important when modeling vaccination cultures, as parents' vaccine decisions have been shown to be influenced by grandparents (Karthigesu, Chisholm, and Coall 2018) and non-family influences (Dubé et al. 2013). Insights from cultural evolution have been used to quantify the viral spread of information (Barkow, O'Gorman, and Rendell 2012) which is of particular concern in understanding vaccine adoption and the spread of vaccine hesitancy. Cultural evolutionary models hold the potential to provide unique insights into the complexity of human health-specific behavior.

Research Aims and Dissertation Structure

As human behavior adds complexity to disease dynamics, it is imperative that we not only continue to include behavioral effects in models of disease, but also consider the forces behind these evolving behaviors. Disease spread and human behavior are studied across a variety of disciplines, each adding unique insights to understanding and securing human health. My dissertation work provides a unique addition to the collection of behavior-change models and vaccination/vaccine hesitancy models, by intertwining mathematical and cultural evolution methods and theory with social and behavioral science. My work also aims to uncover potential cultural drivers of unexpected vaccination environments, such as decreasing vaccine confidence in highly vaccinated populations or vice versa.

In **Chapter 2**, I aim to show that a cultural evolutionary framework is a robust way to model scenarios in which parental behaviors regarding their children are influenced, but not fully dictated, by their beliefs. Examples of this belief-behavior interaction include beliefs surrounding various aspects of childrearing such as formula feeding, sleep training, circumcision, attachment parenting, and homeschooling, as well as childhood vaccination adoption and the spread of vaccine hesitancy, which is the focal example of my work. With these studies, I explore how the interplay of intergenerational dynamics, vaccine perception and assortative mating affect vaccination adoption and vaccine hesitancy.

Vaccination behaviors have shifted throughout history in response to changing vaccination policies. These shifts, in the long term, result in the formation of varying and sometimes unexpected vaccine belief-behavior dynamics cultures. Therefore, in **Chapter 3,** I examine how external forces, such as vaccination mandates and vaccine inaccessibility, interact with social factors to affect the vaccination belief-behavior equilibrium.

Finally, in **Chapter 4,** I use agent-based modeling to explore the dynamics of novel vaccine uptake with the consideration of various decision biases present in a population as well as the effects of individuals outside of the focal population with outsized cultural influence (“influencers”). COVID-19 management has involved the development and deployment of new vaccines. The novelty of the COVID-19 vaccine has made its acceptance more uncertain compared to the acceptance of established vaccines. The interplay of cognitive biases could partially explain fluctuations in vaccination rates and the failure to achieve herd immunity.

Given, as I described above, that vaccines that have now been accepted as part of the health culture in developed countries were themselves once novel and met with outspoken criticism, I sought to build a model that could speculate on the time it takes for herd immunity to be achieved in an environment of increased behavioral stochasticity.

To conclude, in **Chapter 5,** I draw links between Chapters 2-4, discuss the implications of the models presented therein, and suggest avenues for future study.

CHAPTER 2.
A CULTURAL EVOLUTIONARY MODEL OF THE INTERACTION BETWEEN PARENTAL BELIEFS AND BEHAVIORS, WITH APPLICATIONS TO VACCINE HESITANCY

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Introduction

Niche construction is a process in which organisms modify their local environment, thus altering selection pressures on themselves and the other organisms in that environment (K. Laland, Matthews, and Feldman 2016; John Odling-Smee, Laland, and Feldman 2013). Mathematical models of niche construction have traditionally been used in a biological and ecological context, with organisms altering their physical environment. In *cultural* niche construction, humans modify their cultural environments—such as their beliefs, behaviors, preferences, and social contacts—in ways that subsequently alter evolutionary pressures on themselves and/or their culture (John Odling-Smee, Laland, and Feldman 2013). Since human evolution is also directed by human culture, models incorporating these types of cultural evolutionary dynamics have been expanded to encompass a broad range of scenarios in which evolutionary pressures are altered by non-genetic traits, with applications to religion, fertility, and the evolution of large-scale human conflict (Fogarty and Creanza 2017; John Odling-Smee, Laland, and Feldman 2013; O'Brien et al. 2012; Fuentes 2013; Creanza, Fogarty, and Feldman 2012; Creanza and Feldman 2014). Using a niche construction framework allows for the exploration of a broad range of complex feedback scenarios in cultural evolution. Here, we propose a cultural niche construction model of the interactions between beliefs and behaviors, where a belief can be defined as an individual's stance in either supporting or opposing a particular behavior. In this type of model, an individual's beliefs can influence their behaviors, and these belief-behavior interactions can be affected by and shape the broader cultural and biological landscape. We apply this model to the interactions between vaccine-related beliefs, such as vaccine opposition by individual parents, and vaccination behaviors, such as a pair of parents vaccinating their offspring. Modeling the belief-behavior interactions underlying vaccination coverage using a cultural evolution framework allows us to better understand how vaccination "cultures" are formed and how they can be transformed to promote public health.

Understanding vaccination behaviors is a crucial aspect of preventing infectious disease outbreaks. The implementation of childhood vaccination policies has led to the eradication of smallpox and the elimination of poliomyelitis (polio) in the United States (Fenner 1982; Kim-Farley et al. 1984; D. Salk 1980). The high efficacy of the measles vaccine, combined with wide vaccine acceptance in developed countries, had resulted in measles previously being targeted for elimination by 2020 (Thompson et al. 2013). However, over the past decade, there

has been a resurgence of vaccine-preventable diseases (VPDs) in developed countries despite the safety and efficacy of vaccines and high overall childhood vaccination rates (Atwell and Salmon 2014; Kubin 2019; Falagas and Zarkadoulia 2008; Dubé et al. 2013). Vaccine hesitancy, named one of the World Health Organization's ten threats to global health in 2019 (Scheres and Kuszewski 2019), is believed to be responsible for decreasing vaccination coverage and thus increasing the risk of vaccine-preventable disease outbreaks worldwide (Glanz et al. 2009). Vaccine hesitancy is a complex and context-specific individual attitude influenced by multiple factors, such as complacency (the belief that vaccination is unnecessary when the perceived risk of VPDs is low), convenience (the accessibility and affordability of vaccines), and confidence (the level of trust in the efficacy and safety of the vaccine, and in the healthcare system) (MacDonald and SAGE Working Group on Vaccine Hesitancy 2015; Dubé et al. 2013). Additionally, anti-vaccine sentiments are still on the rise despite well-documented vaccine efficacy and safety, including numerous studies debunking the spurious connection between vaccines and autism (Eggertson 2010) and other anti-vaccination arguments (Rao and Andrade 2011). The spread of these sentiments and disease outbreak risk are further exacerbated by homophily—the tendency of individuals to choose social contacts and mates who are similar to themselves (Burley 1983; Creanza and Feldman 2014; Creanza, Fogarty, and Feldman 2012; Gimelfarb 1988). Network-based simulations suggest that individuals with similar vaccine-hesitant opinions form groups that are more susceptible to vaccine-preventable diseases, impeding the attainment of herd immunity and substantially increasing the likelihood of disease outbreak in these clusters (Salathé and Bonhoeffer 2008).

It has become increasingly common for epidemiological models to incorporate aspects of human behavior and behavioral response to disease (e.g (Perra et al. 2011; Mao and Yang 2012b; Bauch 2005; Chauhan, Misra, and Dhar 2014; Funk, Salathé, and Jansen 2010; Tanaka, Kumm, and Feldman 2002)), with vaccination and social distancing being the most common forms of disease interventions modeled (Verelst, Willem, and Beutels 2016; Fenichel et al. 2011; Azizi et al. 2022). A series of compartmental models have represented the spread of disease and the spread of either beliefs or behaviors as "coupled contagions", where individuals in the model can be "infected" by cultural factors such as vaccine hesitancy, fears, information, or health-related behaviors, which can alter the likelihood of being infected by the disease (Epstein, Hatna, and Crodelle 2021; Smaldino and Jones 2021; Epstein et al. 2008a; Mehta and Rosenberg 2020).

These coupled contagion models have illustrated that the spread of anti-vaccine sentiment could cause epidemics that would otherwise not have occurred (Mehta and Rosenberg 2020). These models can also incorporate other properties that change the interactions between individuals, such as homophily and outgroup aversion (Smaldino and Jones 2021).

Traditionally, most "behavior change models" aim to describe the adoption of new behavior in response to a disease or to non-disease influences, using a game-theoretic framework (Marshall et al. 2012; Morin et al. 2010; Gray et al. 2011). However, game theoretic models can make unrealistic assumptions such as population homogeneity, as well as rational and cost minimizing decision making (Verelst, Willem, and Beutels 2016). Network models have aimed to improve upon these assumptions, for example, by accounting for heterogeneity and imitation behavior (Ndeffo Mbah et al. 2012). These behavior change models, however, typically focus on a single generation of a population, whereas cultural evolution models can account for intergenerational effects, allowing us to track the evolution of vaccination beliefs and future vaccination behaviors. Thus, we aim to diversify the pool of disease-related behavior change models by employing a cultural evolution framework which allows parental behaviors to affect offspring and accounts for parental transmission of cultural beliefs. It is important to understand how parents' beliefs, which may differ from one another, interact with their perceptions of the relative risks of disease and vaccines to shape the decision to vaccinate their children, which in turn affects the future risk of vaccine-preventable disease outbreaks. Indeed, belief systems can act as the main barrier to vaccination, as opposed to lack of vaccine access, particularly in wealthier countries (Salathé and Bonhoeffer 2008; May and Silverman 2003). For example, increasing rates of non-medical exemption from vaccines (exemption on the basis of religious, philosophical, and personal beliefs), have been observed in the United States (E. Wang et al. 2014; Phadke et al. 2016). Without these considerations, models commonly used in public health may be misleading; thus, understanding and incorporating the underlying health cultures and their evolution, including the interplay between beliefs and behaviors, will allow us to build more comprehensive and representative models of vaccination dynamics and better support public health efforts.

In this study, we propose a cultural evolution framework to represent the interactions between parental beliefs and behaviors, and we use this framework to model the spread of vaccine hesitancy and childhood vaccination, incorporating the transmission of vaccine attitudes

both from parents and from the community. We aim to assess the dynamic interactions between beliefs (shaped by social interactions) and behaviors (influenced by these beliefs). Using vaccine beliefs and vaccination behaviors as a focal example of belief-behavior interactions, we explore the situations in which vaccine hesitancy is most likely to spread, potentially reducing childhood vaccination rates and leading to an increase in vaccine-preventable disease outbreaks. In addition, we consider that the perception of the relative risks of a disease and its preventive vaccine can fluctuate based on the prevalence of vaccination (Bauch 2005), such that the population's vaccination coverage can influence the decision to vaccinate one's children. Finally, we take into account that the decision to vaccinate a child is often the joint consideration of two individuals who might have different vaccine attitudes, and we further incorporate homophily (assortative mating) to understand how social subcultures might influence parental behaviors. Overall, we propose that a generalizable modeling framework for belief-behavior interactions can help inform public health strategies by improving our understanding of the cultural dynamics of vaccine hesitancy.

Methods

A generalized framework for modeling the interactions between beliefs and behaviors

To model the cultural evolution of beliefs and behaviors, we build on the cultural niche construction framework of (Creanza, Fogarty, and Feldman 2012) to assess the effects of parental attitudes on vaccination behaviors and on the resulting vaccination landscape. We use this adapted model to explore how vaccination patterns evolve in a population when a cultural trait, such as vaccine hesitancy, can influence but not perfectly predict a behavior, such as vaccinating one's children. As we will describe, the parental beliefs influence their likelihood of enacting a behavior that affects their children. In addition to the links between vaccine hesitancy and childhood vaccination behaviors, which we explore in detail below, examples of this type of belief-behavior interaction include beliefs surrounding diverse aspects of childrearing such as formula feeding, sleep training, circumcision, attachment parenting, and homeschooling, which influence but do not perfectly predict a parent's likelihood of enacting the associated behaviors. Thus, we first describe the model as a general framework for belief-behavior interactions, and then we outline modifications to the model that enable us to apply it to vaccine hesitancy and parental vaccination behaviors.

We consider two cultural traits: **V**, a trait that accounts for the effect of a parental behavior on offspring, and **A**, a belief trait that can be transmitted to offspring. Each trait has two possible states, V^+ (affected by the parental behavior) or V^- (unaffected) and A^+ (a belief supporting the behavior) or A^- (opposing), respectively. In other words, when parents who either support or oppose the focal behavior decide to enact the focal behavior, the children are affected by the behavior and acquire the V^+ state. Parents can also transmit a supporting belief or an opposing belief to their children. Thus, there are four possible phenotypes: V^+A^+ (type 1: affected and supporting), V^+A^- (type 2: affected and opposing), V^-A^+ (type 3: unaffected and supporting), and V^-A^- (type 4: unaffected and opposing), whose population frequencies are denoted by x_1, x_2, x_3, and x_4, respectively, with $\sum_{i=1}^{4} x_i = 1$.

The belief trait (**A**) can influence the dynamics of the behavior trait (**V**) in two ways: by influencing the likelihood that couples enact the behavior, and by determining with whom each adult will preferentially pair in assortative interactions. The state of the belief trait (**A**) informs the value of an assortative mating parameter (α_k), which measures the departure from random mating. We define a 'choosing parent', arbitrarily, as the first member of each mating pair. The choosing parent's **A** state dictates the level of assortative mating, that is, the degree to which an individual of a given **A** state will preferentially mate with another individual of the same state, expressed by parameters α_k where $k = \{1, 2\}$ and $0 \leq \alpha_k \leq 1$ (**Table S2.1**). If the choosing parent is A^+, this individual mates preferentially with other A^+ individuals with probability α_1, and mates randomly with probability $1-\alpha_1$, whereas if the choosing parent is A^-, this individual mates preferentially with other A^- individuals with probability α_2, and mates randomly with probability $1-\alpha_2$. There are sixteen possible mating pairs from the four phenotypes described, and we use the notation $m_{i,j}$ to indicate the frequency of a mating between a choosing parent of type i and the second parent of type j where $i, j = \{1, 2, 3, 4\}$ (**Table S2.1**); for example, $m_{1,3}$ represents the mating frequency of V^+A^+ (x_1) and V^-A^+ (x_3).

Table 2.1: List of parameters, their definitions, and default or initial values

Parameter	Meaning	Parameter	Meaning
V	Effect of parental behavior (V^+ affected, V^- unaffected) In our focal example: V^+ vaccinated, V^- unvaccinated	**A**	Belief trait (A^+ supporting, A^- opposing) In our focal example: A^+ vaccine confident, A^- vaccine hesitant
$\boldsymbol{m_{ij}}$	Mating frequencies (given in **Table S2.1**)	α_k	Assortative mating parameter (homophily) **Default: $\alpha_1 = 0$, $\alpha_2 = 0$**
$\boldsymbol{B_{m,n}}$	Probability that parental pairs enact the behavior, which depends on whether they were affected by the behavior themselves in childhood ($\boldsymbol{b_m}$) and their beliefs ($\boldsymbol{c_n}$) (given in **Table S2.2**)	$\boldsymbol{C_n}$	Probability that parental pairs transmit 'supporting' belief to their children **Default: $C_0 = 0.01$, $C_1 = C_2 = 0.5$, $C_3 = 0.99$**
$\boldsymbol{b_m}$	Probability that parental pairs enact the behavior given whether they were affected by the behavior **Default: $b_0 = 0.01$, $b_1 = b_2 = 0.5$, $b_3 = 0.99$**	$\boldsymbol{c_n}$	Probability that parental pairs enact the behavior given their beliefs **Default: $c_0 = 0.01$, $c_1 = c_2 = 0.5$, $c_3 = 0.99$**
σ	Comprehensive selection coefficient for V^+, dependent on the fraction of individuals affected by the behavior (see **Figure 2.1**)	$\boldsymbol{\sigma_{max}}$	The highest additional benefit that can be conferred by the behavior **Default: $\sigma_{max} = 0.1$**
Initial Phenotype Frequencies		$\boldsymbol{x_1}(V^+A^+) = 0.81$, $\boldsymbol{x_2}(V^+A^-) = 0.1$, $\boldsymbol{x_3}(V^-A^+) = 0.07$, $\boldsymbol{x_4}(V^-A^-) = 0.02$	

Since the two traits (**A** and **V**) are transmitted vertically, for each phenotype we must specify the probability that the mating produces an offspring of that phenotype. The supporting belief trait (A^+) is transmitted with probability C_n, and the opposing belief trait (A^-) is transmitted with probability $1-C_n$ (for $n=\{0, 1, 2, 3\}$ as shown in **Tables 2.2** and **Table S2.2**). If $C_0 = 0$, two A^- parents will always produce A^- offspring, and if $C_3 = 1$, two A^+ parents will always produce A^+ offspring. However, if $C_0 > 0$, two A^- parents can produce A^+ offspring at some probability, and similarly if $C_3 < 1$, two A^+ parents can produce A^- offspring with some probability.

In contrast, parents' beliefs (**A**), in addition to their own affected states (**V**), can influence their behavior towards their offspring via a set of "influence parameters" that inform their probability of enacting the behavior (V^+ with probability $B_{m,n}$ for $m, n = \{0, 1, 2, 3\}$; **Table 2.1**). The probability that each mating pair produces an offspring with the V^+ trait (i.e. affects their offspring) is a scaled product of the influence of parental beliefs (c_n for $n = \{0, 1, 2, 3\}$) and the influence of parental effect states (b_m for $m = \{0, 1, 2, 3\}$) (**Tables 2.2 and Table S2.2**). For example, for mating pair $V^+A^+ \times V^+A^-$, the combined effect states ($V^+ \times V^+$) will influence the affecting behavior by b_3, and the combined belief states, ($A^+ \times A^-$), will influence the affecting behavior by c_2. Therefore, a $V^+A^+ \times V^+A^-$ mating will produce a V^+ offspring with probability $B_{3,2} = c_2\left(\frac{1+b_3}{2}\right)$; this pair will also produce an A^+ offspring with probability C_2 based on their combined belief states. Thus, according to the model, this pairing will produce a V^+A^+ offspring with probability $B_{3,2}C_2$ and a V^+A^- offspring with probability $B_{3,2}(1-C_2)$. We note that assortative mating ($\alpha_k > 0$) will increase the frequency of matings between individuals that share a belief trait, with these non-random interactions in turn skewing behavioral outcomes toward those of same-state couples (via c_0 and c_3).

Transmission and influence probabilities are constant throughout a single simulation, with values ranging from 0 to 1. At default settings, the influence parameters b_m and c_n, and the transmission parameter C_n would take the following values: C_0, b_0, $c_0 = 0.01$; C_1, C_2, b_1, b_2, c_1, $c_2 = 0.5$; and C_3, b_3, $c_3 = 0.99$. In our model, the influence of parental beliefs (c_n) is greater than the influence of whether they were affected by the behavior in childhood (b_n) on their likelihood of affecting their offspring with the behavior. Therefore, offspring being affected by the behavior is guaranteed at some probability only if $c_n > 0$.

Table 2.2: Presence (+) and absence (–) subscript assignments. Demonstrating the trait presence (+) and absence (–) combinations associated with m, n subscripts. For example, the + × – combinations is associated with m and n subscript value 2: an $A^+ \times A^-$ pairing transmits A^+ at probability C_2. This rule applies to parameters C_n, b_m, $B_{m,n}$, c_n, as shown in **Table S2.2**.

Subscript Value (m, n; e.g. b_m, C_n)	Associated Pairing (e.g. V × V, A × A)
0	– × –
1	– × +
2	+ × –
3	+ × +

The cultural selection pressure on the behavior is given by the parameter σ, such that the frequency of the V^+A^+ and V^+A^- phenotypes are multiplied by 1+σ after vertical cultural transmission has occurred. At the end of each timestep, the frequency of each phenotype is divided by the sum of all four frequencies, ensuring that the frequencies sum to 1. This cultural selection coefficient is implemented in the same way as a selection coefficient in a population-genetic model, but unlike the latter, it accounts for both biological fitness and cultural selection pressures, including perceived risks or benefits of the effect of the behavior itself, personal cost-benefit analyses of enacting the behavior, and the structural or societal-level factors influencing the behavior (Pruitt, Kline, and Kovaz 1995; L. L. Cavalli-Sforza and Feldman 1981). The cultural selection (σ) parameter modulates whether there are more or fewer affected individuals than expected: in other words, when σ>0, individuals affected by parental behavior are more common in a set of offspring than would be expected strictly based on the parental beliefs and whether the parents were affected by the behavior themselves.

Thus far, we have described vertical cultural transmission from parent to offspring. The model also incorporates a second phase with community influences (i.e. influence from non-parental adults), in which individuals can change their inherited beliefs (**A**) due to influence from other adults in the population. There are two probabilities associated with belief modulation: the probability that an opposing (A^-) individual adopts the supporting (A^+) belief (A^- to A^+ transition probability, given by $A_{\rightarrow Supporting}$), and the probability that an A^+ individual

adopts the A^- state (A^+ to A^- transition probability, given by $A_{\rightarrow Opposing}$). These transitions can occur at constant rates or be represented as functions of the frequency of either trait in the population, as we outline below.

To compute the frequency of a given phenotype in the next iteration, we sum the probability that each mating pair produces offspring of that phenotype over each of the sixteen possible mating pairs. Cultural selection (σ), described above, then operates on offspring with the V^+ trait. The full recursions, giving x_i' phenotype frequencies in the next iteration in terms of x_i in the current iteration, are given in **Supplementary Text S2.1**. If x_i' is equal to x_i, the system is at equilibrium. As we do not incorporate a birth-death process or population asynchrony in this model, iterations in the discrete-time format of our model should not be strictly interpreted as years or generations. We instead interpret each iteration broadly as a timeframe in which the specified cultural interactions could occur, which varies among individuals, populations, and cultures.

Modeling the interactions between vaccine-related beliefs and vaccination behaviors

To model the evolution of vaccine beliefs and behaviors, we build on the cultural niche construction framework described above to assess the effects of vaccine attitudes on vaccination behaviors and on the resulting vaccination culture. We use this adapted model to explore how vaccination patterns evolve in a population when a cultural trait, such as vaccine hesitancy, can influence but not perfectly predict a behavior, such as vaccinating one's children. For simplicity, we define beliefs as one of two vaccination stances: supporting vaccines (i.e. vaccine-confident attitude) and opposing vaccines (i.e. vaccine-hesitant attitude). We also assume no gender-biased differences in trait transmission, such that offspring are equally likely to be vaccinated with a vaccine-hesitant mother as with a vaccine-hesitant father.

To apply this model to vaccine beliefs and vaccination behaviors, we assign parameters as listed in **Table 2.1**, with V^+ being vaccinated, V^- being unvaccinated, A^+ being vaccine-confident and A^- being vaccine-hesitant. Because of the parent-to-offspring transmission of vaccinations in our model (i.e. parents make a decision to vaccinate their offspring and that offspring remains immunized for a substantial amount of time), our model is most readily applicable to established childhood vaccines, as opposed to a novel vaccine such as the COVID-19 or an annual vaccine such as the influenza vaccine. Thus, the initial phenotype

frequencies were estimated using reports of Measles-Mumps-Rubella (MMR) vaccination rates (~91% coverage in the United States) and estimates of vaccine attitude frequencies obtained from various sources in the literature (Kennedy, Brown, and Gust 2005; Leask 2011) and the Centers of Disease Control ChildVax database (Hill et al. 2019, 2017). Unless otherwise stated, the model is initialized with phenotypic frequencies based on United States data: x_1 (frequency of V^+A^+) = 0.81, x_2 (V^+A^-) = 0.1, x_3 (V^-A^+) = 0.07, x_4 (V^-A^-) = 0.02.

To capture the effects of herd immunity on reducing vaccination behaviors—for example, the belief that vaccines are unnecessary when most others are vaccinated (Omer et al. 2009)—we make the cultural selection coefficient a vaccine-frequency-dependent function. Because the cultural selection coefficient for vaccination depends on the fraction of the population that is already vaccinated, we calculate σ in each timestep as a function of the current vaccination coverage (frequency of V^+, i.e. $x_1 + x_2$), and in each simulation we specify σ_{max} as the maximum cultural selection pressure for getting vaccinated ($-1 \leq \sigma_{max} \leq 1$) (see the cultural selection coefficient function in **Figure 2.1**). To incorporate this relationship into the model, we constructed a function by defining our assumptions (incorporating evolutionary game theory, e.g. that herd immunity decreases the incentive to vaccinate) and then choosing a curve with a trajectory that met these pre-specified conditions: with unvaccinated individuals holding baseline fitness at 1, we assume that when vaccination coverage is low, the real and perceived benefits of vaccination are highest, and thus, the cultural selection pressure is near σ_{max}, however, as vaccination coverage increases toward the level of herd immunity (for simplicity, ≥ 70% vaccination coverage), the perceived benefits of vaccination decrease and the cultural selection pressure is reduced, i.e. offspring can be "free riders," reaping the benefits of high vaccination coverage without a perceived vaccination cost to themselves or their parents (**Figure 2.1**) (Bauch and Bhattacharyya 2012).

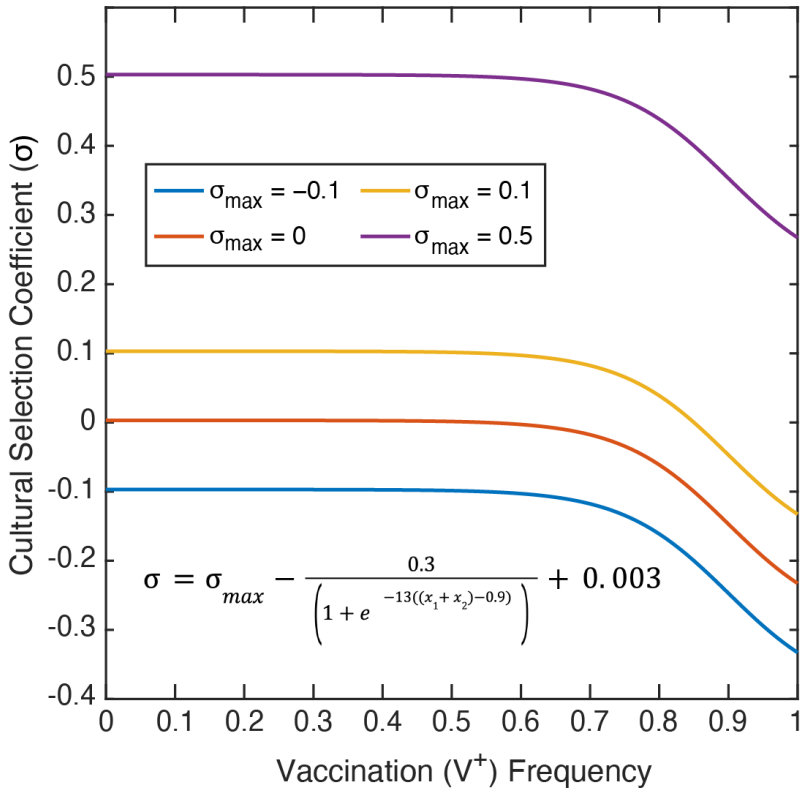

Figure 2.1: Cultural selection coefficient function. The cultural selection coefficient function was constructed by fitting a curve to specified conditions, considering both health- and non-health-related effects (see **Methods**). The selection coefficient (σ; vertical axis) is dependent on the frequency of vaccinated individuals (V^+) in the population (horizontal axis). σ_{max} is the maximum cultural selection coefficient associated with being vaccinated. Perceived vaccine benefit is reduced as vaccination coverage increases, since the negative effects of the disease will be less apparent. Note: Of the σ_{max} values shown, only $\sigma_{max} = 0.1$ allows the cultural selection pressure to be either positive or negative at a given timepoint depending on the frequency of vaccination.

We also allow individuals to change their beliefs after vertical transmission, transitioning from vaccine confidence to hesitancy and vice versa. For this manuscript, we have modeled the dynamics of these transition probabilities in three ways, drawing on existing literature (e.g. (Epstein, Hatna, and Crodelle 2021; Perra et al. 2011; Ndeffo Mbah et al. 2012; Jacobson, St Sauver, and Finney Rutten 2015)): (1) with belief transition being dependent on the frequency of vaccinated (V^+) individuals in the population such that vaccine confidence wanes at high

vaccination frequencies ("herd-immunity-driven hesitancy" (**Figure 2.2**), (2) with belief transition being dependent on the frequency of vaccinated (V^+) individuals in the population such that vaccine hesitancy wanes at high vaccination frequencies ("vaccine-fear-driven hesitancy" (**Figure S2.1**) and (3) with belief transition being dependent on the frequency of vaccine-confident (A^+) individuals in the population such that vaccine hesitancy wanes at high vaccine confidence frequencies ("obliquely transmitted hesitancy" (**Figure S2.2**). Note that for our application to vaccine beliefs and childhood vaccination behaviors, we primarily employ the "herd-immunity-driven hesitancy" behavior-dependent framework to account for the influence of disease prevalence outlined in **Figure 2.2,** where $A_{\rightarrow Supporting}$ is analogous to $A_{\rightarrow Confident}$, and $A_{\rightarrow Opposing}$ to $A_{\rightarrow Hesitant}$. As the frequency of vaccinated individuals (V^+) increases in the population, confident individuals (A^+) are more likely to become hesitant ($A_{\rightarrow Hesitant}$ probability increases) and vaccine-hesitant individuals (A^-) are less likely to become confident ($A_{\rightarrow Confident}$ probability decreases). When vaccination coverage is low, we assume in this scenario that the negative effects of the disease and the benefit of the vaccine are more apparent and the transition to vaccine confidence is more likely; on the other hand, when vaccination coverage is high, the perceived risks of the vaccine can be more salient than the risks of the disease, and the transition to hesitancy is more likely (Coelho and Codeço 2009). Similar to the cultural selection function, we generated the belief transition functions by first choosing a baseline function with a shape that aligned with our general assumptions and then modifying the function to fit specific criteria: 1) probabilities could approach zero, but not equal zero, 2) transition to supporting belief and transition to opposing belief are equally likely at 50% population frequency, and, specifically for the focal example of vaccination, and for herd-immunity-driven hesitancy 3) that high vaccination frequencies (above herd-immunity levels of vaccination coverage) promote the transition to vaccine hesitancy (Jacobson, St Sauver, and Finney Rutten 2015; Kennedy, Brown, and Gust 2005). To set an upper bound for the belief transition functions, we use the percent difference between vaccine refusal rates in 1991 and 2004 in the United States to estimate transition probabilities between 1–2% (Omer et al. 2009). The assumptions for the oblique-transmitted hesitancy framework and vaccine-fear-driven hesitancy framework are outlined in the supplement (**Figure S2.1-S2.2**).

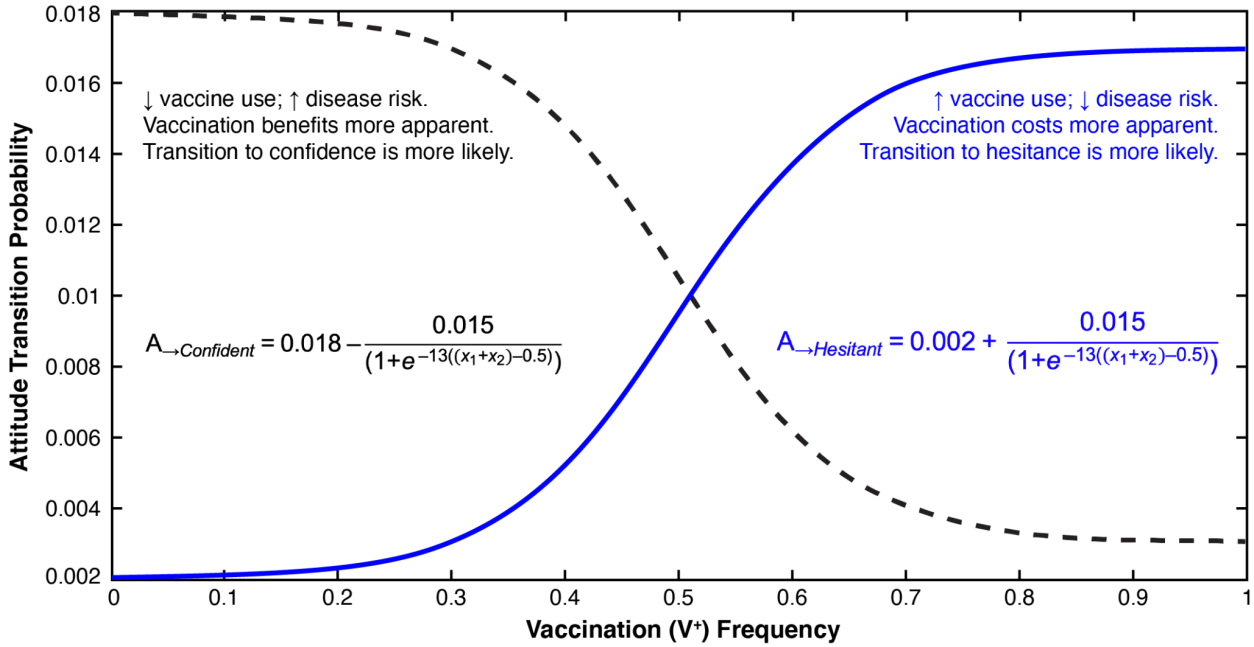

Figure 2.2: Attitude transition probability function ("Herd-immunity-driven hesitancy"). Attitude transition probability functions were constructed by fitting a curve to specified values based on the assumptions pictured and outlined in **Methods**. Attitude transition probability (vertical axis) is a function of the vaccination frequency in the population (V^+; horizontal axis). The probability that a vaccine-hesitant individual adopts vaccine confidence (A^- to A^+ transition probability, shown in dashed black) is determined by the function $A_{\rightarrow Confident}$, and the probability that a vaccine-confident individual adopts vaccine hesitancy (A^+ to A^- transition probability, shown with a solid blue line) is determined by the function $A_{\rightarrow Hesitant}$.

Results

To test our model, we first initialized a population with a set of phenotype frequencies and examined the changes in these frequencies over time with a given set of parameters . Then, we evaluated the effects of each parameter by running simulations at multiple parameter combinations and recording the population frequencies of each phenotype once the system approached an equilibrium. In our first set of simulations, we include only vertical transmission dynamics, i.e. only parent-to-offspring transmission, varying parameter values in turn to test their effects on population vaccination behavior and attitudes. In the vertical transmission phase of the model, parents choose whether to vaccinate their offspring (i.e., transmit V^+) or to not vaccinate (V^-), and parents also transmit a vaccine attitude (confidence, A^+, or hesitancy, A^-), each with a

specified probability given the phenotypes of the parents. In the community-influence phase of the model, we incorporate the influence of non-parental adults on offspring attitudes. The parental attitude state, vaccination status, assortative mating levels, and cultural selection parameters interact to affect vaccination coverage (frequency of V^+ in the population) and vaccine confidence (frequency of A^+).

Temporal dynamics of vaccine-related beliefs and behaviors

To test whether the equilibrium phenotype frequencies were sensitive to starting frequencies, we plotted the dynamics of each phenotype over time at default parameters (given in **Table 2.1**). For each set of initial phenotype proportions tested, the phenotype frequencies in the population quickly adjusted to approach equilibrium values and then gradually plateaued to a stable equilibrium (vertical transmission: **Figure 2.3 and Figure S2.3**; vertical + herd-immunity-driven vaccine hesitancy: **Figure S2.4**. This demonstrates that equilibrium frequencies of vaccination coverage and vaccine confidence are determined by the parameter conditions rather than by the initial frequencies.

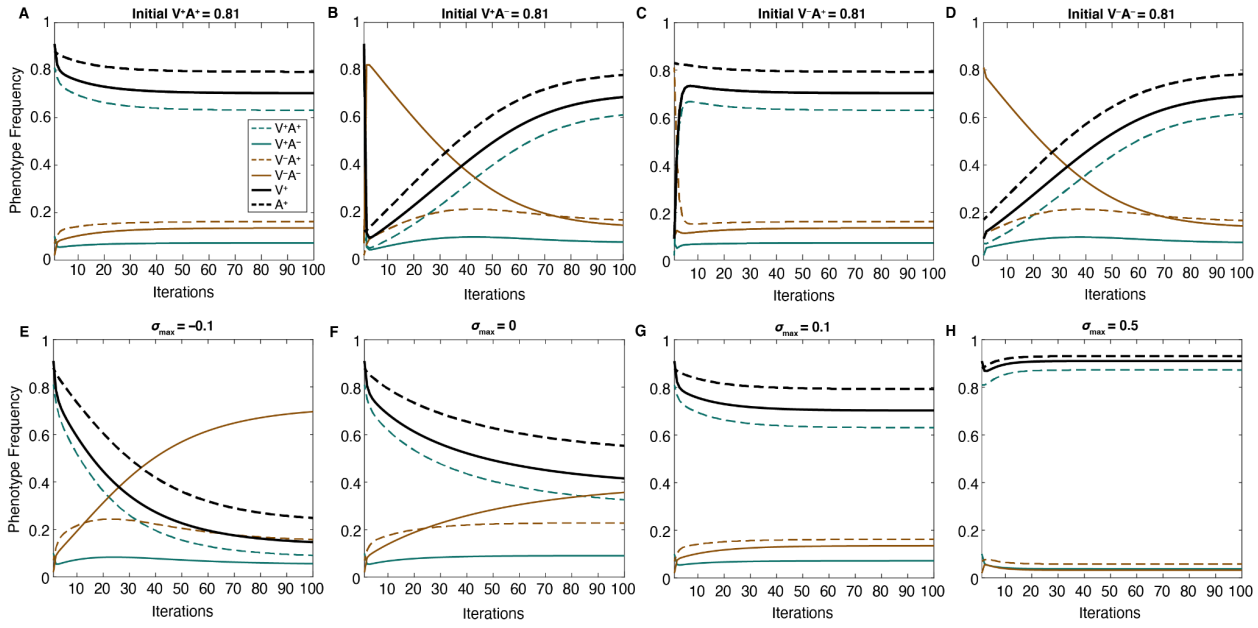

Figure 2.3: Equilibrium frequencies are determined by the parameter space, not by initial frequencies. The change in each of the four phenotype frequencies and the total V^+ and A^+ frequencies (vertical axis) over 100 iterations of the model **with vertical transmission only** (horizontal axis). **Top row:** Initial frequencies are varied, such that we begin each simulation with a different phenotype at an initial high frequency (0.81): V^+A^+ in panel **A**, V^+A^- in panel **B**, V^-A^+ in panel **C**, V^-A^- in panel **D**; the remaining phenotypes are set to lower frequencies (0.1, 0.07, 0.02). See **Figure S2.3** for a full listing of these initial frequencies. **Bottom row:** The maximum cultural selection coefficient (σ_{max}) is varied: **E**. $\sigma_{max} = -0.1$; **F**. $\sigma_{max} = 0$; **G**. $\sigma_{max} = 0.1$; **H**. $\sigma_{max} = 0.5$. Cultural selection against vaccinated individuals increases the frequency of V^-A^-, decreasing the other frequencies (**E**), whereas increased cultural selection favoring vaccinated individuals increases V^+A^+ frequencies while decreasing the other frequencies (**F, G, H**). In all panels, the remaining parameters are held at default values (**Table 2.1**).

Low confidence transmission ($C_1 = C_2 = 0.1$, **Figure 2.4A**) increases the frequency of vaccine hesitancy (A^-) in the population over time, increasing the probability that more couples choose not to vaccinate their offspring. However, the increase in vaccine hesitancy does not occur equally in vaccinated and unvaccinated individuals: A^- frequency may increase overall in this environment, but V^+A^- frequencies are lower and V^-A^- frequencies are higher (compared to **Figure 2.4B-C** and **Figure S2.6**). At neutral confidence transmission probabilities (i.e. when

couples with one confident and one hesitant parent are equally likely to transmit either attitude), there is a higher chance that the vaccinated but vaccine-hesitant (V^+A^-) phenotype is replenished. However, if vaccine confidence is highly transmitted ($C_1 = C_2 = 0.8$), the V^+A^- frequency will be reduced, as this phenotype is more likely to produce A^+ offspring than A^-, thus increasing V^+A^+ phenotype frequencies in the population (**Figure 2.4** and **Figure S2.6**). If we turn to the other conflicting phenotype, unvaccinated but vaccine-confident (V^-A^+) individuals become more common when A^+ increases in frequency in the population as $C_1 = C_2$ increases from 0.1 to 0.5 (**Figure 2.4** and **Figure S2.6**). In contrast, higher vaccine confidence transmission ($C_1 = C_2 = 0.8$) can lead to a vaccination-promoting environment in which V^- frequencies are reduced over time; thus the V^-A^+ phenotype becomes rare and V^+A^+ predominates (**Figure 2.4** and **Figure S2.6**).

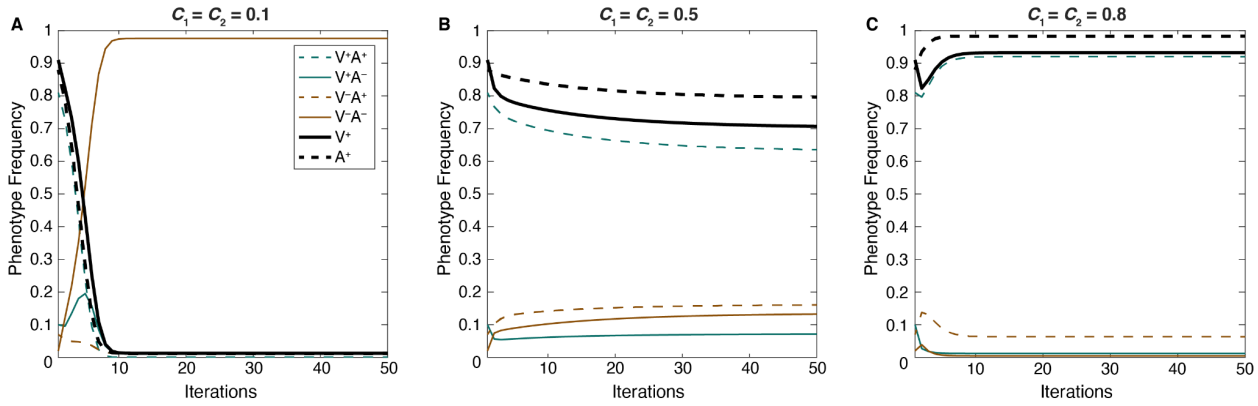

Figure 2.4: **Temporal effects of confidence transmission**. The change in phenotype frequencies over 50 iterations as vaccine confidence transmission in mixed-attitude couples ($C_1 = C_2$) is varied (**A**. $C_1 = C_2 = 0.1$; **B**. $C_1 = C_2 = 0.5$; **C**. $C_1 = C_2 = 0.8$) **with vertical transmission only,** while other parameters are held at default values (**Table 2.1**). The population equilibrates at over 90% A^-V^- at low confidence transmission (A). Increasing the probability of confidence transmission results in less vaccine hesitancy and, in turn, higher vaccination frequencies (V^+A^+).

Parent-to-Offspring Interactions (Simulations with vertical transmission only)

Vaccination coverage increases as vaccine confidence transmission is more likely

Since our assessment of the temporal dynamics demonstrated that our simulations approach stable equilibria, we then modulated different sets of parameters and recorded the phenotype frequencies at equilibrium, generating heat maps showing the results across a range of

parameters. In the first of these, we tested the relationship between vaccination probability and vaccine confidence transmission. To directly alter vaccination probabilities while still accounting for the couple's vaccine attitudes, we set ranges of values for $B_{m,n}$ that vary along the horizontal axis of **Figure 2.5**, with the vaccination probability for two hesitant parents ($B_{0,0}$) on the lower end of the range and the vaccination probability for two confident parents ($B_{3,3}$) on the higher end of the range (**Table S2.3**). Confidence transmission probabilities are also structured in this "range shift" manner (**Figure 2.5A-B, Table S2.3**). If we vary both confidence transmission parameters and vaccination probability parameters by implementing range shifts in both C_n and $B_{m,n}$, we observe a positive interaction between confidence transmission and vaccination probability: vaccination coverage increases as either of these parameters are increased (**Figure 2.5A**).

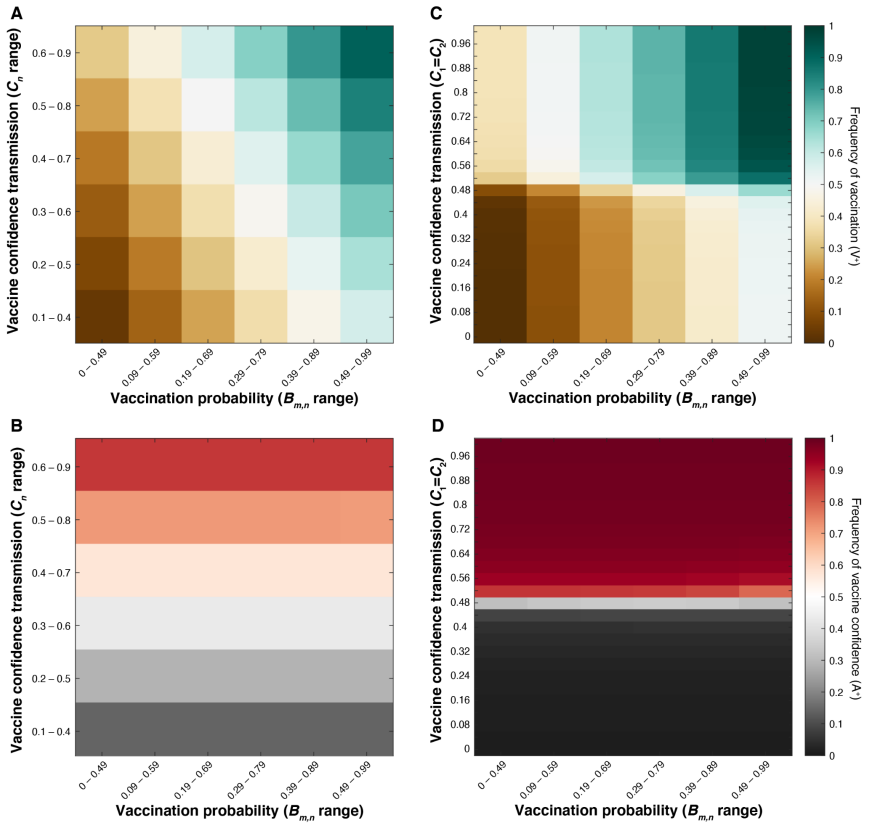

Figure 2.5: Vaccination coverage levels are determined by an interaction between confidence transmission and vaccination probability. Heatmaps showing final vaccination coverage (**A, C**) and corresponding vaccine confidence (**B, D**) after 100 time-steps **with vertical transmission only**. In **A** and **B**, confidence transmission probabilities (C_n) are set within the range indicated on the vertical axis, and vaccination probabilities ($B_{m,n}$) are set within the range indicated on the horizontal axis with $B_{0,0}$, $B_{1,0}$, $B_{2,0}$ and $B_{3,0}$ taking the lowest value and $B_{3,3}$ taking the highest value (**Table S2.3**). In **C** and **D**, confidence transmission in mixed-attitude couples ($C_1 = C_2$) is varied along the vertical axis, while the vaccination probabilities ($B_{m,n}$) are set within the range indicated on the horizontal axis as in **A** and **B**. (**Table S2.3**). We show increased equilibrium vaccination coverage with increasing vaccination probability and confidence transmission probability ranges, while confidence levels are primarily dictated by proportion of the population transmitting confidence or hesitancy.

Confidence transmission dominates the vaccination coverage and confidence patterns at equilibrium

However, couples with mixed vaccination and/or attitude states ($V^+ \times V^-$, $A^+ \times A^-$) are assumed to be more variable in their decision to vaccinate their offspring than parents who share the same state. Thus, in the simulations that follow, we primarily modulated the specific probabilities associated with these mixed-state pairings. In **Figure 2.5C-D**, we varied vaccination probabilities ($B_{m,n}$) across the full range of individuals but modulated confidence transmission probabilities only for mixed-attitude couples ($C_1 = C_2$), i.e. those with one vaccine-hesitant parent and one vaccine-confident parent. In these tests, we observe increasing equilibrium vaccination coverage as $B_{m,n}$ probabilities increase, with higher coverage in high-confidence transmission environments (**Figure 2.5C-D**).

In both aforementioned simulations (**Figure 2.5**), we confirm vaccination coverage levels are determined by an interaction between confidence transmission and vaccination probability, whereas confidence levels are dictated primarily by levels of confidence transmission. In sum, the degree to which parents with mixed vaccine-hesitant and vaccine-confident attitudes transmit vaccine confidence instead of vaccine hesitancy to their offspring is a key factor in determining population trait majorities which can drastically shift population dynamics.

We compared the effects of varying the confidence transmission probabilities for mixed-attitude couples (C_1 and C_2) in combination with multiple factors: 1) the maximum cultural selection coefficient (σ_{max}) (**Figure 2.6A-B**), 2) the vaccination influence parameters b_1 and b_2 (**Figure 2.6C-D**), 3) the attitude influence parameters c_1 and c_2 (**Figure 2.6E-F**), and 4) the vaccination probabilities of couples with mixed states, $B_{1,1}$, $B_{1,2}$, $B_{2,1}$, $B_{2,2}$ (**Figure 2.6G-H**). In each examination, we observed a C_n threshold: there is a mid-range value of C_n at which vaccination coverage and vaccine confidence traits are polymorphic, i.e. both forms of each trait coexist in the population). This C_n threshold value is more sensitive to σ_{max} than to b_m, c_n, or $B_{m,n}$: the threshold value is lowered as σ_{max} increases (diagonal line in **Figure 2.6A-B**). Although vaccination probability ($B_{m,n}$) is dependent on both c_n, the influence of parental vaccine attitude, and b_m, the influence of parental vaccination state (**Table S2.2**), modulating either type of influence of mixed-state parents has little effect on the level of vaccination coverage and negligible effects on confidence levels at each non-threshold C_n (**Figure 2.6C-F**).

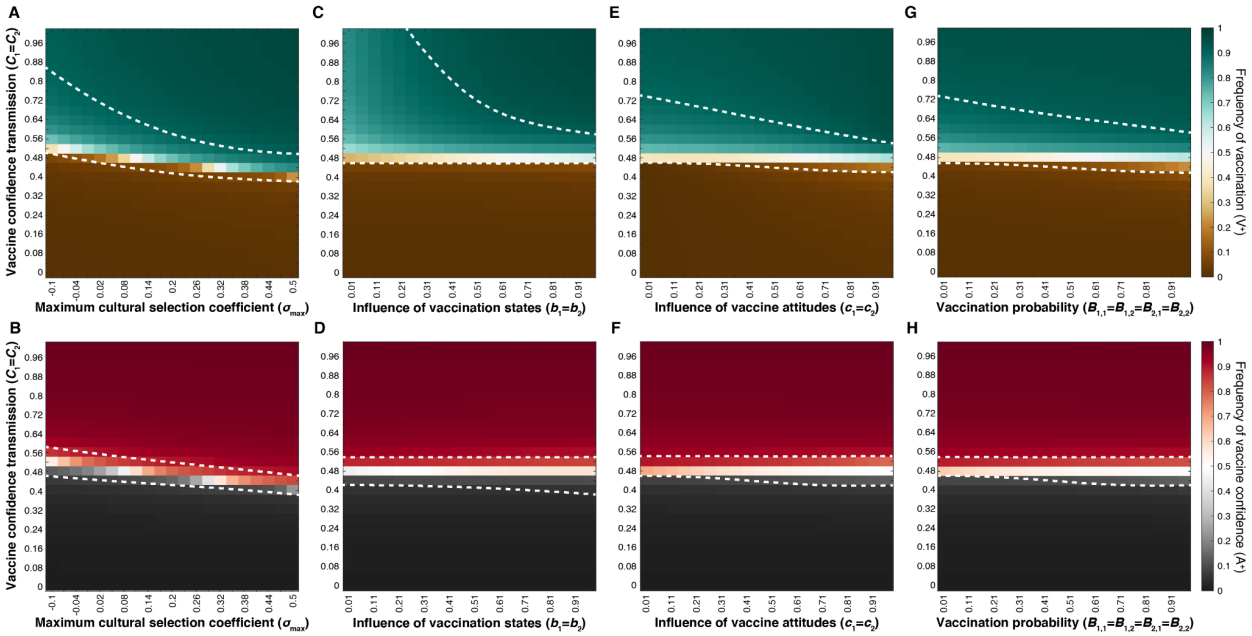

Figure 2.6: **Vaccine confidence transmission dictates vaccination coverage and confidence levels**

Heatmaps showing final vaccination coverage and vaccine confidence after 100 time-steps **with vertical transmission only**. The top row (**A, C, E, G**) shows vaccination coverage (i.e. frequency of V^+ in the population) with low coverage in brown and high coverage in green; the bottom row (**B, D, F, H**) shows the corresponding final vaccine confidence (i.e. frequency of A^+), with low confidence in black and high confidence in red. Unless varied on the horizontal or vertical axis, other parameters are set to the default values given in **Table 2.1**. In our model, parents' likelihood of vaccinating their children depends on both their vaccination state and their attitude state. This figure shows that the strength of parental transmission of vaccine confidence (C_n) has a much stronger effect on the equilibrium levels of both vaccine coverage (V^+) and confidence (A^+) than other parameters: the maximum cultural selection coefficient, σ_{max} (**A, B**), the influence of parental vaccination state, b_m (**C, D**), the level of influence of parental vaccine attitudes on their vaccination behaviors, c_n (**E, F**), and the probability that mixed-state parents vaccinate their offspring $B_{m,n}$ (**G, H**). Dashed white lines demarcate the region in which equilibrium frequencies are between 0.1 and 0.9.

Interestingly, direct modulation of the mixed-state couple vaccination probability ($B_{1,1}$ = $B_{1,2}$ = $B_{2,1}$ = $B_{2,2}$) also has little power in affecting coverage and confidence levels at equilibrium

(**Figure 2.6G-H**). We hypothesize that predominantly high or predominantly low confidence transmission within a population reduces the occurrence of "mixed-state" pairings, i.e. if the majority of the population becomes confident or hesitant, there are fewer confident-hesitant and vaccinated-unvaccinated pairings. Thus, the effect of modulating mixed-state vaccination probabilities ($B_{1,1}$, $B_{1,2}$, $B_{2,1}$, $B_{2,2}$) is significantly minimized as these couples approach low frequencies in the population, and confidence transmission dominates the vaccination patterns.

Cultural selection determines trait equilibrium levels at fixed confidence transmission probabilities

Next, we hold vaccine confidence transmission (C_n) at default probabilities, reminiscent of Mendelian transmission, such that two vaccine-confident or two vaccine-hesitant parents predictably transmit their vaccine attitude, and parents with differing vaccine attitudes each have a ~50% chance of transmitting their own state, e.g. C_0 near 0, C_1 and C_2 at 0.5, C_3 near 1 **(Table 2.1)**.

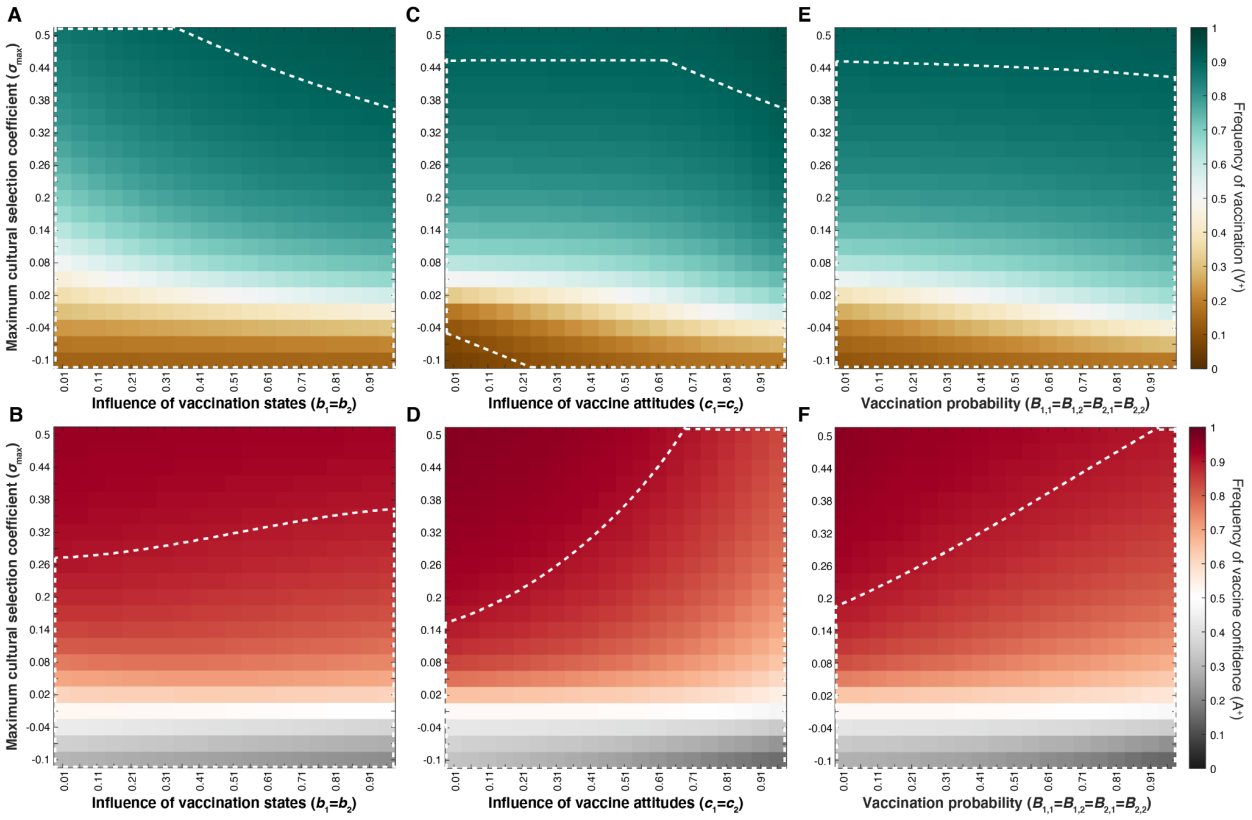

Figure 2.7: **Cultural selection influences vaccination coverage and vaccine confidence.** Heatmaps showing final vaccination coverage (**A, C, E**) and final vaccination confidence (**B, D, F**) after 100 time-steps **with vertical transmission only**, only parent-to-offspring transmission. As in previous figures, parameters not varied here are given in **Table 2.1**. Parents' likelihood of vaccinating their children depends on both their vaccination state and their attitude state. At default probabilities of vaccine confidence transmission (C_n values in **Table 2.1**), these figures show that modulating the maximum cultural selection coefficient affects the equilibrium levels of vaccination coverage and vaccine confidence across the range of specified parameters: parental vaccination state influence, b_m (**A, B**), parental attitude state influence, c_n (**C,D**), and offspring vaccination probability, $B_{m,n}$ (**E,F**). Unless directly modulated (as in panels **E-F**), $B_{m,n}$ varies with b_m and c_n: $B_{m,n} = c_n\left(\frac{1+b_m}{2}\right)$. Dashed white lines demarcate the region in which equilibrium frequencies are between 0.1 and 0.9.

We then varied cultural selection in combination with vaccination-associated probabilities (b_m, c_n, $B_{m,n}$). With C_n held constant, cultural selection (σ_{max}) is the primary factor determining

vaccination coverage and confidence levels (**Figure 2.7**). Raising the maximum cultural selection coefficient increases the equilibrium level of vaccination coverage and vaccine confidence across various levels of vaccination state influence (b_m) (**Figure 2.7A-B**), vaccination attitude influence (c_n) (**Figure 2.7C-D**), and vaccination probability ($B_{m,n}$) (**Figure 2.7E-F**). Unlike in **Figure 2.6**, vaccine confidence does not always mirror vaccination coverage across all levels of attitude influence (c_n) or vaccination probabilities. Instead, vaccine confidence levels decline with increased c_n and increased $B_{m,n}$ for $\sigma_{max} \lessapprox 0.3$ (**Figure 2.7D, F**), as well as for both increased c_n and increased b_m (**Figure S2.7**). This dynamic is interesting as these parameters inform vaccination behavior, hinting that high vaccination rates could reduce a populations' expected vaccine confidence. Vaccination coverage and vaccine confidence remain low when cultural selection does not favor vaccination ($\sigma_{max} \lessapprox 0$), i.e. parents vaccinate their children at or below the levels expected based on cultural transmission rates.

Offspring can change their inherited hesitancy state (vertical dynamics and community influences)

Increased exposure to the attitudes of the broader community (non-parental adults in the population) and personal experiences with the disease could influence and change vaccination beliefs inherited in childhood. Therefore, we next included these community influences in our model to understand how they might modulate vaccine confidence and vaccination coverage levels. In the belief transition phase of the model, offspring can change their vaccine attitude with some probability based on the frequency of vaccination in the population (**Figure 2.2**). Thus, in addition to the vertical transmission of attitudes and behaviors, phenotype frequencies are further affected by the probability that adult offspring change their attitude (i.e. transition from vaccine confident (A^+) to hesitant (A^-) and vice versa). By modulating the attitude transition probabilities according to the vaccination coverage ("herd-immunity-driven hesitancy"), we assume that when vaccine coverage (V^+ frequency, $x_1 + x_2$) is low, disease occurrence is high and the negative effects of the disease are experienced widely, thus the benefits of being vaccinated (and the costs of not being vaccinated) are more evident (Gangarosa et al. 1998; Ozawa et al. 2012). As vaccination coverage (V^+) increases in the population, and thus disease occurrence is low, the benefits to being vaccinated are less obvious, while

low-probability costs such as adverse reactions become more apparent and could be perceived as being riskier than the disease itself.

Community influences expand the polymorphic space at moderate confidence transmission

The addition of herd-immunity-driven hesitancy produces a pattern of vaccination coverage and vaccine confidence similar to that of simulations run with solely vertical transmission (**Figure 2.6** and **Figure 2.7** compared to **Figure 2.8** and **Figure 2.9, and Figure 2.3-2.4** compared to **Figures S2.4-S2.6**)—the level of (vertical) vaccine confidence transmission still largely determines the level of vaccination coverage and vaccine confidence (**Figure 2.8**). However, these community influences expanded the polymorphic space, resulting in a wider range of confidence transmission probabilities for mixed-state couples (C_1=C_2) in which the different states of each trait (vaccinated, unvaccinated, confident, and hesitant) are well represented in the population. In other words, there is a wider band of moderate values outlined by the dashed white lines in **Figure 2.8** than in **Figure 2.6**). Herd-immunity-driven hesitancy appears to shift the equilibrium levels of vaccination coverage and vaccine confidence away from extreme values. We also tested a more traditional understanding of oblique transmission, i.e. confidence-dependent belief transition ("obliquely transmitted hesitancy") in which individuals are more likely to transition to vaccine confidence when they interact with more vaccine-confident people (**Figure S2.2**). The results of these simulations are similar to those without belief transition, i.e., the equilibrium levels of vaccination coverage and vaccine confidence approach either high or low values near the threshold (compare **Figure 2.6**, **Figure 2.8** and **Figure S2.8**). Similarly, if we structure belief transition in a manner that reflects an influence of vaccine fear reduction after widespread adoption, i.e, individuals are more likely to adopt vaccine confidence if vaccination frequency is high, the pattern of outcomes show a lower occurrence of moderate values at equilibrium (**Figure S2.9**).

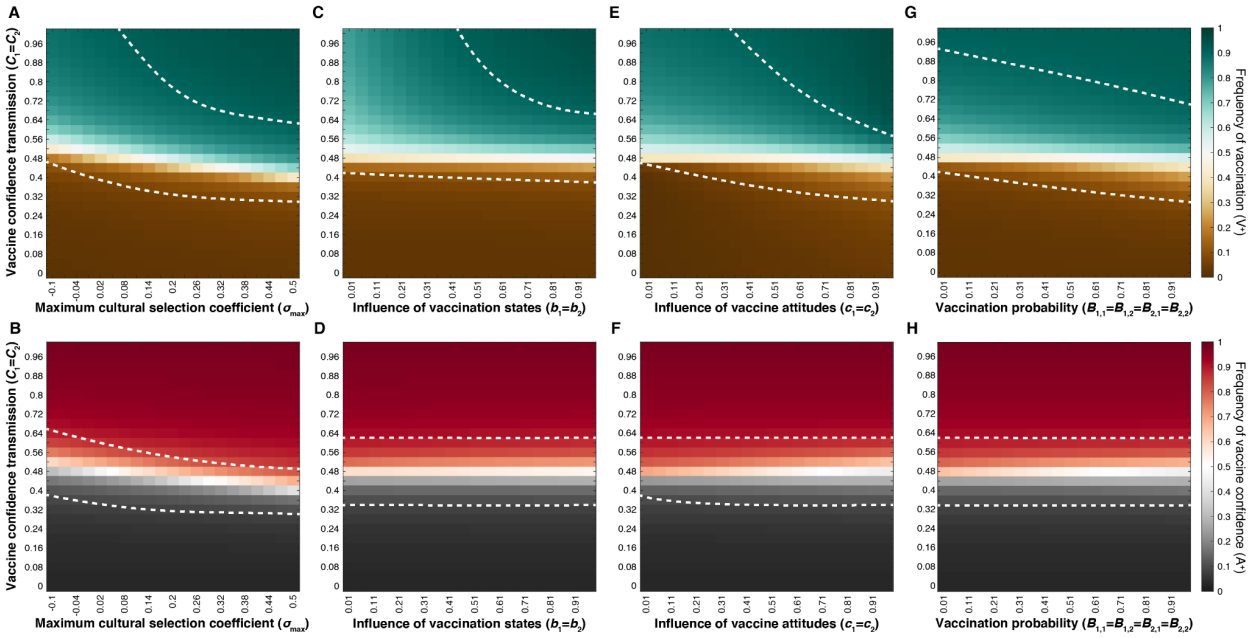

Figure 2.8: Vaccine confidence transmission dictates vaccination coverage and confidence levels (with herd-immunity-driven hesitancy). Heatmaps showing final vaccination coverage (i.e. frequency of V^+ in the population, with low coverage in brown and high coverage in green (**A, C, E, G**)) and final vaccine confidence (i.e. frequency of A^+, with low confidence in black and high confidence in red (**B, D, F, H**)) after 100 time-steps in which attitude transition can occur after parent-to-offspring transmission of beliefs. The likelihood that individuals change their vaccine beliefs depends on the current vaccination coverage of the population (**Figure 2.2**). Unless varied on the horizontal or vertical axes, other parameters are set to the default values given in **Table 2.1**. Parents' likelihood of vaccinating their children depends on both their vaccination state and their attitude state; these figures show that the strength of parental transmission of vaccine confidence (C_n) has a much stronger effect on the equilibrium levels of both vaccine coverage (V^+) and confidence (A^+) than other tested parameters do: the maximum cultural selection coefficient, σ_{max}, (**A,B**), the influence of parental vaccination state, b_m, (**C, D**), the level of influence of parental attitudes on their vaccination behaviors, c_n, (**E,F**), and offspring vaccination probability, $B_{m,n}$ (**G,H**). Dashed white lines demarcate the region in which equilibrium frequencies are between 0.1 and 0.9.

Community influences reduce equilibrium values at constant confidence transmission

With neutral confidence transmission ($C_1 = C_2 = 0.5$), we also observe an expansion of the polymorphic space when we modulate cultural selection (σ_{max}) alongside the influence and transmission parameters, with an overall reduction of vaccination coverage and vaccine confidence levels at equilibrium (**Figure 2.9** compared to **Figure 2.7**). Similarly to simulations without belief transition, as the influence of vaccine attitudes (c_n) and vaccination probabilities ($B_{m,n}$) increase (**Figure 2.9C-F**), the population's equilibrium vaccination coverage increases while its vaccine confidence decreases. This pattern persisted across all tested levels of maximum cultural selection (σ_{max}) (**Figure 2.9C-F**). In other words, we observe higher levels of confidence when the influence of vaccine attitude is low for mixed-attitude parental pairs (**Figure 2.9D**) and vaccination probabilities are low for mixed-trait parental pairs (**Figure 2.9F**) than we do at higher values.

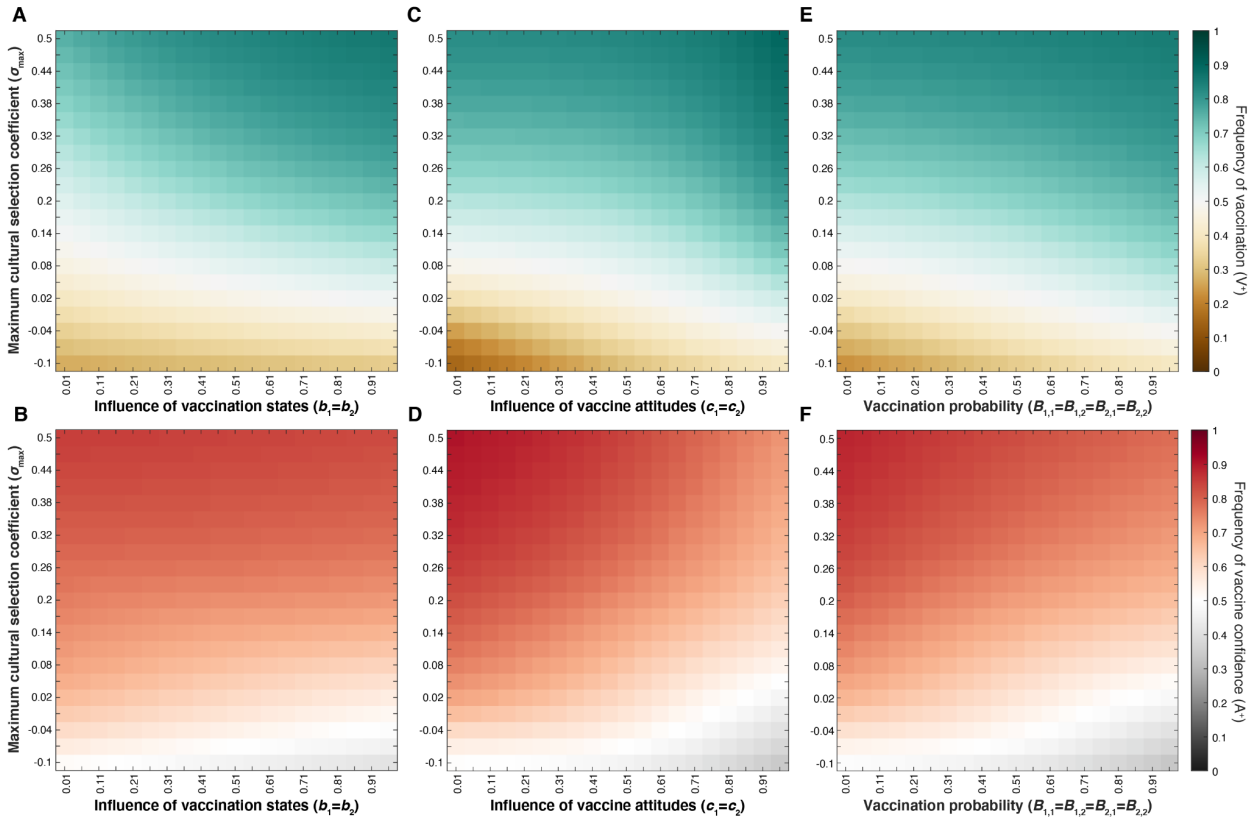

Figure 2.9: Cultural selection influences vaccination coverage and vaccine confidence (with herd-immunity driven hesitancy). Heatmaps showing final vaccination coverage (**A, C, E**) and final vaccination confidence (**B, D, F**) after 100 time-steps **with herd-immunity-driven hesitancy**. As in previous figures, parameters not varied are given in **Table 2.1**. Parents' likelihood of vaccinating their children depends on both their vaccination state and their attitude state. At default probabilities of vaccine confidence transmission (C_n), these figures show that modulating the maximum cultural selection coefficient affects the equilibrium levels of vaccination coverage and vaccine confidence across the range of specified parameters: parental vaccination state influence, b_m (**A, B**), parental attitude state influence, c_n (**C,D**), and offspring vaccination probability, $B_{m,n}$ (**E,F**) for mixed-trait pairs. Unless directly varied (as in panels **E-F**), $B_{m,n}$ varies as b_m and c_n are varied, as shown in **Table 2.1**. [Note: All vaccination and confidence equilibrium frequencies are between 0.1 and 0.9.]

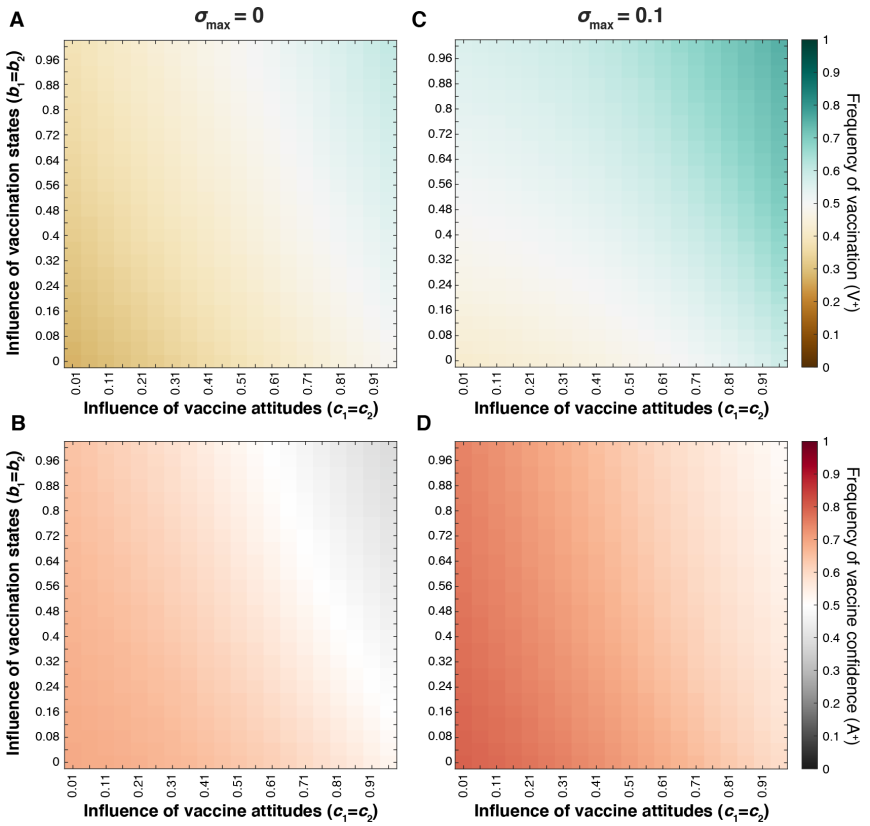

Figure 2.10: **The influence of parental traits on vaccination coverage and vaccine confidence at different levels of cultural selection.** Heatmaps showing final vaccination coverage (**A, C**) and final vaccination confidence **(B, D)** after 100 timesteps **with herd-immunity-driven hesitancy**. We modulate the interaction between vaccination state influence (b_m; vertical axis) and attitude influence (c_n; horizontal axis) at various maximum cultural selection coefficients: $\sigma_{max} = 0$ (**A, B**) and $\sigma_{max} = 0.1$ (**C, D**). As in previous figures, unvaried parameters are given in **Table 2.1**. Vaccination frequency increases as both influence probabilities increase and vaccination confidence decreases as both influence probabilities increase.

Modulating the influence of parental traits reveals uncoupling of trait equilibrium frequencies

We explored the interaction between the influence parameters, b_m and c_n, at various maximum cultural selection coefficients (σ_{max}) (**Figure 2.10**). Vaccination coverage and vaccine confidence equilibrate at frequencies between 0.1 and 0.6 across the range of b_m and c_n, indicating that these trait frequencies are not particularly sensitive to either parameter. Cultural selection favoring vaccination increases the equilibrium level of vaccination coverage and

vaccine confidence (**Figure 2.10 and Figure S2.10**). The most notable deviation between equilibrium confidence and vaccination frequencies occurs at the intersection of the highest influence parameter values (b_m and c_n), circumstances in which the parents' vaccination states and vaccine attitudes overwhelmingly support offspring vaccination. In this top right section of the heat maps, vaccination coverage is high while vaccine confidence is lower, indicating a behavioral pattern in which mixed-trait couples are more inclined to vaccinate their offspring than transmit vaccine confidence. Overall, the addition of vaccination-frequency-dependent belief transition to a population that would otherwise equilibrate at high vaccination coverage (**Figure S2.7**) leads to increased attitude transition to vaccine hesitancy and subsequently lower vaccine coverage.

Cultural selection modulates the effect of homophily on equilibrium outcomes

We hypothesized that mating preference (assortative mating) could modulate belief and behavior dynamics and thus the vaccination coverage and confidence levels in the population. If individuals are more likely to pair with individuals of the same vaccine attitude, such that same-attitude couples become more common and mixed-attitude couples are less common, the parameter values for mixed-attitude couples may have less impact on vaccination coverage and confidence dynamics. Therefore, we analyzed the interaction between A^+ homophily (with α_1 indicating the preference of A^+ individuals for other A^+ individuals) and A^- homophily (with α_2 indicating the preference of A^- individuals for other A^- individuals) at various σ_{max} levels. When vaccine attitudes are affected by community influences and there is neither cultural selection for nor against being vaccinated ($\sigma_{max} = 0$), we observe a threshold region at roughly equal mating preferences ($\alpha_1 \approx \alpha_2$; diagonal lines in **Figure 2.11C-D**); above this boundary (when $\alpha_1 > \alpha_2$) vaccination coverage and confidence are much higher than below this boundary (when $\alpha_1 < \alpha_2$). When cultural selection explicitly does not favor vaccination (e.g. $\sigma_{max} = -0.1$, **Figure 2.11A-B**), low vaccination coverage and confidence can occur even when there are more vaccine-confident couples in the population than hesitant couples ($\alpha_1 > \alpha_2$). Likewise, if cultural selection favors being vaccinated ($\sigma_{max} > 0$, **Figure 2.11E-H**), the threshold between high and low equilibrium values is shifted, such that high coverage and high confidence levels can potentially be attained even when vaccine-hesitant individuals preferentially pair with each other more than vaccine-confident individuals do ($\alpha_1 < \alpha_2$). We observe qualitatively similar patterns when vaccine attitudes are only transmitted from parent to offspring (**Figure S2.11**); as we have

previously observed in **Figures 2.8-2.10**, the addition of vaccination-frequency-dependent belief transition leads to a broader polymorphic region than vertical transmission alone. However, if belief transition is obliquely influenced or influenced by fear of the vaccine, the range of the polymorphic region is similar to that observed in simulations without community influences (compare **Figure 2.11**, **Figure S2.12**, and **Figure S2.13**). These patterns illustrate two overarching themes: 1) preferential interactions between individuals with similar vaccine beliefs can dramatically shift the equilibrium levels of vaccination coverage and confidence with all other parameters remaining equal, and 2) the actual and perceived quality and efficacy of the vaccine are important to determining vaccine acceptance.

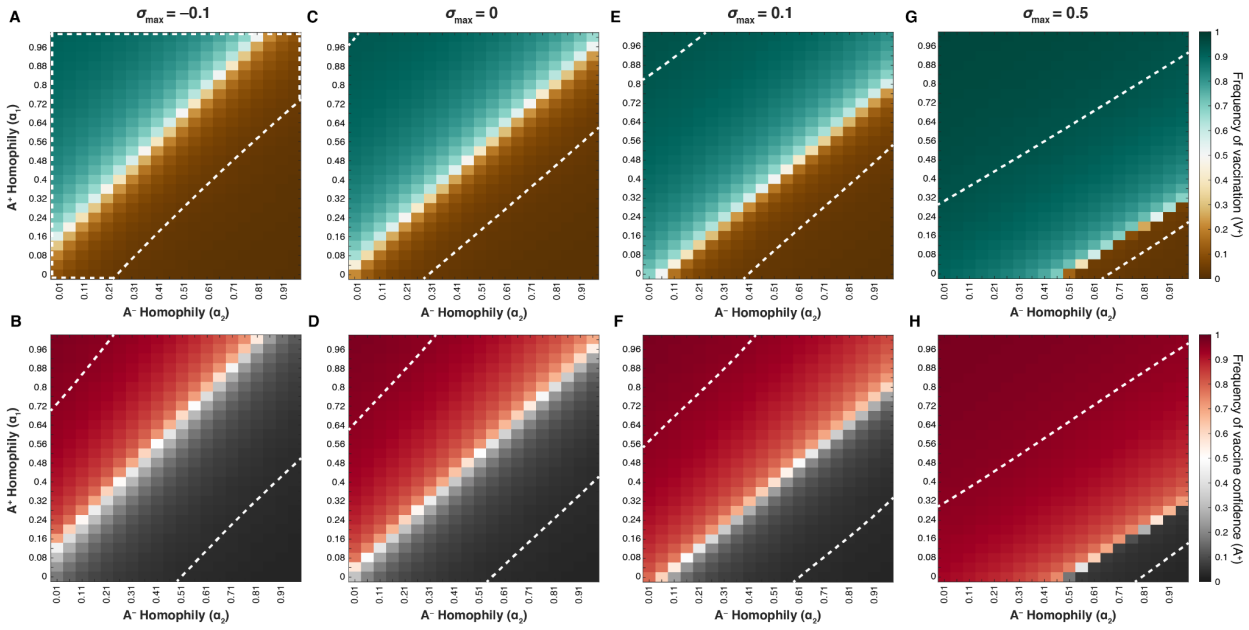

Figure 2.11: Homophily between individuals with similar vaccine beliefs can shift equilibrium frequencies of both vaccination coverage and confidence. Heatmaps showing final vaccination coverage (**A, C, E, G**) and final vaccine confidence (**B, D, F, H**) after 100 timesteps **with herd-immunity-driven hesitancy.** As in previous figures, unspecified parameters are given in **Table 2.1**. As vaccine-hesitant individuals (A^-) increasingly prefer to pair with one another (α_2; horizontal axis), vaccine-confident individuals (A^+) must also preferentially interact to maintain high vaccine coverage (α_1; vertical axis); this tradeoff is modulated by the cultural selection pressures on vaccination (σ_{max} = -0.1 (**A, B**), σ_{max} = 0 (**C, D**) and σ_{max} = 0.1 (**E, F**), σ_{max} = 0.5 (**G, H**)). Dashed white lines demarcate the region in which equilibrium frequencies are between 0.1 and 0.9.

Discussion

In this manuscript, we present an application of a generalized cultural evolution framework by modeling the spread of vaccine attitudes and their effects on childhood vaccination frequency in a population. Increasing and maintaining sufficient vaccination coverage to combat disease is more complex than simply increasing vaccine availability or providing accurate information. A number of factors affect a person's vaccine-related beliefs and parents' decision to vaccinate their children, including their history with vaccinations and perception of the disease and vaccine effects. As such, it is important to understand how these personal factors can shape vaccination cultures and thus affect public health. Using a cultural

niche construction framework, we modeled the transmission of vaccine attitudes and vaccination behavior in a variety of circumstances and measured the resulting levels of vaccination coverage and vaccine confidence in the population. Using this novel approach of modeling dynamically interacting beliefs and behaviors, we are able to explore the interplay of cultural factors that drive vaccine attitudes and vaccination behavior, providing insight into how vaccination cultures are formed, maintained, and evolve.

Cultural parameters predict future vaccination coverage and vaccine confidence

Our model demonstrates that the cultural landscape—here, the parameters in the model that aim to reflect transmission patterns of beliefs and behaviors, the level of preferential assortment based on beliefs, etc.—can be more predictive of future levels of vaccine coverage and confidence than current coverage and confidence levels in the population (i.e. the initial conditions). Our simulations each approached a stable equilibrium, and in general we could infer that a population with high vaccination coverage will have low rates of vaccine hesitancy and vice versa. Further, our model shows vaccine confidence transmission (C_n) to be the parameter that most strongly determines vaccination coverage and confidence levels. That is, even though parents' decision to vaccinate their children is based on both their level of confidence in vaccines and a consideration of their own vaccination status, the probability of transmitting vaccine-positive attitudes is a stronger predictor of future vaccination coverage than the probability of vaccination itself (**Figures 2.6 and 2.8**). Finally, our simulations also suggest that a pro-vaccination health culture can be undermined by a vaccine hesitancy "echo chamber", possibly formed by a higher degree of preferential assortment (homophily) among vaccine-hesitant individuals, who then form pairs more likely to transmit vaccine-hesitancy to their children.

Positive perception of the vaccine is sufficient to maintain vaccination coverage

This model also shows that the perceived value and efficacy of a vaccine are important to maintaining sufficient levels of vaccination coverage, especially if vaccine confidence is not being robustly transmitted (or maintained in adulthood). Individuals essentially perform an internal cost-benefit analysis based on their circumstances and interpretation of accessible information when deciding to vaccinate. We aimed to be inclusive of their various considerations via our comprehensive cultural selection coefficient. Increasing positive public perception

through honest and effective communication and reducing public concern about vaccines and increasing vaccine safety could together drive increased vaccination trust and acceptance. Achieving the optimal vaccination coverage lies not only in the hands of the public by vaccinating themselves and their children, but also in the efforts of health officials and leaders in creating an environment that fosters confidence by assuring the public of vaccine efficacy, safety, and value, while providing convenient avenues to attain vaccines.

Interestingly, there is a large region of the parameter space (such as $C_1=C_2>0.6$ in **Figures 2.6 and 2.8, panels A, C, E, G**) in which the vaccination coverage equilibrates at a level that is comparable to the rates of established childhood vaccines in the United States (e.g. ~91% coverage for the MMR vaccine (Hill et al. 2019, 2017)). One difference from the expected rates in the US, however, is that in these simulations the level of vaccination coverage tends to equilibrate at a lower level than the vaccine confidence, whereas in the US the fraction of vaccine-hesitant individuals is thought to be higher than the fraction of vaccinated individuals (Gowda and Dempsey 2013). The discrepancy between expected and observed hesitancy rates could be the result of policies that promote public health by encouraging childhood vaccination, such as school requirements for immunization records.

Limitations of the model

As with any model, we cannot fully capture the complex reality of the relationship between vaccine hesitancy and vaccination behavior. First, though vaccination frequency data is available for numerous vaccines, frequency data for vaccine attitudes are much less common, with the two traditionally not surveyed together. Thus, there is no dataset that exactly estimates the phenotypes presented here, for example, the number of vaccinated but hesitant (V^+A^-) individuals in a population. The goals of vaccination attitude surveys have been primarily to identify themes of vaccine hesitancy, and to a lesser degree, the themes of vaccination. However, they generally do not report parent vaccination states or whether the child was actually vaccinated (on schedule). With data presenting parent vaccination states alongside their vaccine attitudes and vaccination decisions, we would be able to more accurately inform phenotype frequencies, possibly extending the model to incorporate various types of hesitancy. We note, however, that our results did not depend on the initial proportions of vaccination status or vaccine hesitancy, so these data would primarily be for comparison to our equilibrium outcomes.

We were also constrained by limited data to inform our cultural transmission and transition probabilities. In our model, baseline confidence transmission and influence probabilities are structured according to a simple pattern of inheritance, such that each parent is equally likely to influence an offspring's phenotype. However, cultural traits and vaccination attitudes may not strictly follow this pattern: one parent might have more influence, or one variant of a trait might be more likely to be transmitted. In addition, transmission probabilities are constant in our model, remaining unaffected by changing cultural conditions throughout each simulation, but in reality, these probabilities may fluctuate in response to a variety of factors including vaccine type or family structure. Future developments of the model could include modulating the probability of vaccine confidence transmission according to other aspects of the cultural environment, such as the attitude frequencies in the population. We could also use the current frequency of these cultural traits across different populations to generate more specific hypotheses about their underlying cultural transmission processes (Kandler and Powell 2018; Kandler, Wilder, and Fortunato 2017). Our cultural selection coefficient did vary with the frequency of vaccination coverage, and we tested multiple attitude transition probability functions that varied with either vaccination frequency or confidence levels. However, the exact relationships between trait distribution and vaccine perception or attitude transition probabilities could not be informed by existing data. Modulating both the attitude transition probabilities and the cultural selection coefficient according to the level of vaccination coverage in a population, however, reflects that perceptions about the vaccine and its associated effects on health could be meaningfully different in a population with high vaccination coverage than in one with low coverage. In testing three forms of belief transition, we are able to explore how different community influences could shape vaccination coverage and hesitancy levels.

Though vaccination coverage and vaccine confidence stabilized in our simulations, in reality vaccination rates fluctuate over time in response to changing population dynamics, perhaps never arriving at a stable equilibrium. For example, the increasingly rapid spread of information (Hornik et al. 2015) may cause attitudes and behaviors to change frequently over short periods of time. In our model, most of the phenotype frequency fluctuations occur in the first few iterations before quickly adjusting to an equilibrium. Unlike some models of population dynamics, this model has a discrete-time format and does not consider asynchrony in population turnover. Thus, the timescale of our model might not translate directly to years or generations,

and we avoid interpreting the number of iterations in literal terms. It is possible that if more realistic birth and death processes were incorporated, the cultural dynamics would occur at different timescales and would continue to fluctuate instead of approaching a stable equilibrium. In addition, the grandparents of the children to be vaccinated also influence the parents' vaccination decisions (Karthigesu, Chisholm, and Coall 2018). A restructuring of the timescale or the incorporation of population asynchrony in our model could allow for consideration of these influences.

In this model, we constructed the offspring vaccination probability to be informed primarily by parents' vaccine attitudes and secondarily by their own vaccination status. Though it is understood that there is an interaction between parents' beliefs and their own experiences with vaccines regarding their decision to vaccinate their children, accurately modeling the relative contribution of these two factors could benefit from empirical studies on parental willingness to vaccinate based on their beliefs and vaccination status. With our current formula ($B_{m,n}$, **Table S2.2**), vaccine-confident parents who did not themselves receive childhood vaccines have a reduced likelihood of vaccinating their offspring than vaccinated parents. In reality, parental vaccine attitudes might even further outweigh their own vaccination status in their decision-making process than we model here.

Future Explorations

Finally, future developments of this model could include homophily of oblique interactions, that is, if vaccine-related beliefs influenced not only one's mate choice but also one's choice of social groups or information sources. On one hand, individuals who disproportionately interact with vaccine-hesitant contacts would have a biased perspective that vaccine hesitancy is more prevalent in the population than it actually is, which can reduce their likelihood of vaccinating their children (Brunson 2018); on the other hand, a high degree of homophily in oblique interactions has been hypothesized to hinder the transmission of vaccine hesitancy to vaccine-confident individuals, reducing the spread of the belief overall (Mehta and Rosenberg 2020). Another potential further exploration of the model includes modeling preferential assortment based on vaccination status rather than vaccine attitude, which has been shown to occur in an empirical contact-network study of high school students (Barclay et al. 2014).

Our model can be readily applied to other scenarios in which the effects of a parental behavior are long-lasting and potentially influenced by beliefs. For example, other aspects of childrearing such as formula feeding, sleep training, circumcision, attachment parenting, and homeschooling could provide additional avenues of exploration with this type of model. Like vaccines, these decisions employ an assessment of social, cultural, and economic costs and benefits, to parents and offspring.

Recommendations

Our findings suggest that broad efforts to encourage and inform the public about vaccine safety and efficacy will foster higher vaccine coverage, and thus points toward several recommendations for public health policy and outreach. We recommend that accurate information about vaccines be readily accessible through a variety of means, be easily understood, and be supported by personal anecdotes since individuals who are skeptical about vaccines might invest more time in seeking out information about them (Gowda and Dempsey 2013; Ellithorpe, Adams, and Aladé 2022; Benin et al. 2006), and that dialogue between people with different beliefs and attitudes be encouraged as it can help to break the "echo chambers" of homophily, encouraging individuals to communicate and empathize with one another. Therefore, to address vaccine hesitancy, our results underscore the importance of considering the cultural beliefs and community influences that underpin health behaviors.

CHAPTER 3.
INTERNAL AND EXTERNAL FORCES AFFECTING VACCINATION COVERAGE: MODELING THE INTERACTIONS BETWEEN VACCINE HESITANCY, ACCESSIBILITY, AND MANDATES

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Introduction

A comprehensive understanding of health behaviors and their potential for exacerbating or mitigating disease risk requires insight into how cultural beliefs influence these behaviors. Local vaccination cultures—the shared beliefs among individuals within a community about vaccine-preventable disease etiology, prevention, and treatment—can affect an individual's vaccine attitudes and decisions (Streefland, Chowdhury, and Ramos-Jimenez 1999; de Figueiredo et al. 2020). The definition of "vaccine hesitancy" varies between sources, spanning from an attitude of uncertainty about vaccines to the behavior of vaccine refusal. Here we use the definition from (Larson, Gakidou, and Murray 2022): "a state of indecision and uncertainty that precedes a decision to become (or not become) vaccinated." In 2019, vaccine hesitancy was named one of the World Health Organization's ten threats to global health (Scheres and Kuszewski 2019) because of its link to reduced vaccination coverage and more frequent outbreaks of vaccine-preventable diseases (VPDs) worldwide. Vaccine hesitancy is a key indicator of the vaccination culture of a population, and both modeling (e.g. (Funk, Salathé, and Jansen 2010)) and public health studies (e.g. (MacDonald and SAGE Working Group on Vaccine Hesitancy 2015; Dubé et al. 2013)) have considered vaccine hesitancy to be influenced by multiple societal- and individual-level factors, such as the vaccination coverage of the population, the perceived risk of vaccine-preventable diseases, the level of trust in specific vaccines, and the confidence in the healthcare system.

Theoretical studies have modeled how the spread of disease can be affected by aspects of human behavior, particularly vaccination and social distancing behaviors (Bauch 2005; Chauhan, Misra, and Dhar 2014; Funk, Salathé, and Jansen 2010; Mao and Yang 2012a; Perra et al. 2011; Tanaka, Kumm, and Feldman 2002; Verelst, Willem, and Beutels 2016). Other models have examined a phenomenon known as "coupled contagion," in which individuals can transmit not only a disease itself but also cultural factors such as vaccine adoption, disease-related fears, and (mis)information, which can in turn modulate their disease susceptibility in the simulation (Epstein et al. 2008b; Epstein, Hatna, and Crodelle 2021; Smaldino and Jones 2021; Mehta and Rosenberg 2020). In real populations, health policies and other external factors can play a role in shaping vaccination cultures; two such factors are vaccine mandates, which drive vaccination uptake (even among vaccine-hesitant people), and vaccine inaccessibility, which hinders vaccine uptake (even among vaccine-confident people). Compulsory vaccination policies have been met

with opposition since their implementation in the 1800's (Durbach 2005; Swales 1992b). This opposition, intertwined with religious and political ideas, led to the allowance of vaccination exemptions based on medical and non-medical (e.g. religious or philosophical) reasons (Blume 2006). Though the implementation of compulsory vaccinations generally results in a drastic reduction in disease incidence and mortality (Lawler 2017; Abrevaya and Mulligan 2011), the high vaccination coverage that follows can facilitate the public perception of reduced disease severity and thus reduced vaccine necessity; this phenomenon has been observed in real populations (P. E. Fine and Clarkson 1986; P. Fine, Eames, and Heymann 2011) and incorporated into modeling studies (de Figueiredo et al. 2020; Funk, Salathé, and Jansen 2010; Reluga, Bauch, and Galvani 2006). In this vein, non-medical exemptions to compulsory vaccinations have been increasing, particularly in wealthier countries where theoretical predictions suggest that belief systems can act as the main barrier to vaccination, as opposed to lack of vaccine access (Salathé and Bonhoeffer 2008; May and Silverman 2003). This rise in non-medical exemptions appears to have a non-trivial effect on public health, since these exemptions are correlated with the recent increase in VPD outbreaks in the United States (Aloe, Kulldorff, and Bloom 2017; Phadke et al. 2016). However, the circumstances under which vaccine mandates might lead to increased vaccine hesitancy remain uncertain.

Even less understood is the potential association between vaccine (in)accessibility and vaccine attitudes. Vaccine accessibility issues are external pressures that negatively impact vaccination rates and coverage. Challenges to vaccine accessibility are particularly prevalent in low and middle-income countries as well as rural areas in developed countries (Zaffran et al. 2013; Zerhouni 2019). For example, storage capabilities, distribution logistics, and affordability can limit the number of vaccine doses available in a specific area, and thus reduce the number of individuals who can receive a vaccine, leaving vulnerable communities at risk for a VPD outbreaks (Zaffran et al. 2013; Mahoney et al. 2007). This limited access may also interact with psychological and cultural factors, such as distrust in the healthcare system, potentially exacerbating the effects of low vaccine accessibility. Further, vaccination cultures can be shaped by experience with vaccines and the disease: for example, living in a rural area could limit exposure to the disease and alter the perception of disease risk, and a lack of vaccine access for an extended period could entrench certain attitudes about vaccines in a culture. Thus, to explain the differences in vaccination outcomes and resulting disease risk across human populations, it is

crucial to better understand how cultural beliefs and behaviors interact with external pressures that increase or reduce vaccination coverage.

Cultural niche construction theory describes a process in which humans modify their cultural environments—for example, their beliefs, behaviors, preferences, and social contacts—in ways that subsequently alter evolutionary pressures on the population and its culture (John Odling-Smee, Laland, and Feldman 2013). Mathematical models of cultural niche construction have been used to explain the evolution of behaviors related to religion, fertility, and large-scale human conflict (Fogarty and Creanza 2017; John Odling-Smee, Laland, and Feldman 2013; O'Brien et al. 2012; Fuentes 2013; Creanza, Fogarty, and Feldman 2012; Creanza and Feldman 2014). Since health cultures can be shaped by or influence the larger cultural landscape, the cultural niche construction framing can give insight into the cultural dynamics shaping disease risk. By using this type of model to simulate the interactions between beliefs and behaviors, we seek to understand how vaccination cultures affect vaccination coverage, as well as how vaccine-related beliefs and behaviors are affected by external forces, such as the availability of vaccines and the degree to which they are compulsory.

We adapted a cultural niche construction framework to model vaccination beliefs and behaviors, incorporating the transmission of vaccination culture both from parents and from the community (Anderson and Creanza 2023). Using this model, we previously demonstrated that the overarching cultural landscape, including the likelihood of adopting vaccine hesitancy and the probability of transmitting it to one's children, determines the equilibrium levels of vaccination coverage and vaccine hesitancy in a population. In addition, we demonstrated that the transmission of vaccine confidence and positive vaccine perception are imperative to maintaining high levels of vaccination coverage, especially when individuals preferentially choose a partner with shared vaccine beliefs. In this manuscript, we expand the scope of this model to explore how the vaccination coverage and vaccine hesitancy in a population could be affected by external forces. In particular, we focus on vaccine mandates and vaccine inaccessibility, which both lead to a decoupling of parental vaccine beliefs and their vaccination behaviors such that vaccine mandates can increase the chances that vaccine-hesitant parents will vaccinate their children, and vaccine inaccessibility can decrease the chances that vaccine-confident parents will vaccinate their children. We explore the effects of these external forces on the dynamics of both vaccine beliefs and vaccination coverage, providing insight into

the differences between cultural development in the opposing contexts of mandates and inaccessibility.

Methods

We build on a more general cultural niche construction framework of (Creanza, Fogarty, and Feldman 2012; Anderson and Creanza 2023) to assess the effects of vaccine mandates and vaccine accessibility on the resulting landscape of vaccination coverage and vaccine confidence. For a population of individuals, we track the status of vaccination coverage and vaccine confidence over time; within this population, individuals mate, decide whether to vaccinate their offspring, and transmit a vaccine attitude trait. Their decision to vaccinate is influenced by their own beliefs and their vaccination states, and population trait frequencies are further modulated by vaccination frequency dependent cultural selection pressures.

General Framework of the Model

Each individual in our model (depicted in **Figure 3.1**) has a vaccination (**V**) trait, either V^+ (vaccinated) or V^- (unvaccinated), and an attitude (A) trait, either A^+ (vaccine confident) or A^- (vaccine hesitant), resulting in four possible phenotypes (V^+A^+, V^+A^-, V^-A^+, and V^-A^-) that we initialize with frequencies structured to represent those of the United States: V^+A^+ (i.e. frequency of vaccinated, vaccine confident individuals) = 0.81, V^+A^- = 0.1, V^-A^+ = 0.07, V^-A^- = 0.02. These frequencies were estimated using reports of Measles-Mumps-Rubella vaccination rates and estimates of vaccine attitude frequencies obtained from various sources in the literature (Kennedy, Brown, and Gust 2005; Leask 2011). In each iteration, individuals mate randomly within the population. Each parental pair vaccinates their offspring with probability $B_{m,n}$ (i.e., vertical transmission of vaccination, with the subscript m denoting the vaccination trait pair and n denoting the attitude trait pair of the parents; see **Table 3.1** and **Table 2.2**); in general, this probability increases with each vaccinated and vaccine-confident parent. This vaccination probability is influenced by two factors: whether each of the parents are themselves vaccinated (b_m), and whether each of the parents are vaccine confident or hesitant (c_n). The probability that a couple vaccinates their offspring is calculated as $B_{m,n} = c_n\left(\frac{1+b_m}{2}\right)$, to account for the influence of both vaccination states and vaccine attitudes . We model varying levels of vaccine mandates and inaccessibility by modulating the influence that parental vaccine attitudes have on the likelihood that they vaccinate their offspring (by increasing or decreasing c_n): for example, a

vaccine mandate will make a vaccine-hesitant parent more likely to vaccinate their child, and vaccine inaccessibility will make a vaccine-confident parent less likely to vaccinate their child.

Each parental pair also transmits a vaccine attitude trait to their offspring (i.e., vertical transmission of beliefs) with vaccine confidence transmitted at probability C_n and vaccine hesitancy at probability 1-C_n. We set the probability of transmitting vaccine confidence to be highest for two vaccine-confident parents and lowest for two vaccine-hesitant parents (**Table 3.1**). For simplicity, we set the baseline confidence transmission probabilities (C_n) to values reminiscent of Mendelian transmission, such that two vaccine-confident or two vaccine-hesitant parents predictably (~100% likely) transmit their vaccine attitude, and parents with differing vaccine attitudes each have a ~50% chance of transmitting each state: C_0 near 0, C_1 and C_2 at 0.5, C_3 near 1 **(Table 3.1)**. Influence parameters, b_m and c_n, are valued similarly and predict the probability that the couple vaccinates their children according to the equation $B_{m,n} = c_n\left(\frac{1+b_m}{2}\right)$, such that parents who are both vaccine confident and vaccinated are most likely to vaccinate, vaccine hesitant and unvaccinated parents are least likely to vaccinate, and parental pairs with mixed states of one or both traits will have intermediate likelihoods of vaccinating.

Next, cultural selection (σ) operates on the resulting phenotype frequencies such that the frequency of vaccination in the population is greater or less than expected given the predicted probabilities that vaccine-confident and -hesitant parents vaccinate their offspring. The proportion of vaccinated individuals in the population is multiplied by 1+σ, such that a positive σ increases the proportion of vaccinated individuals and a negative σ decreases it. This process encompasses the various factors that might make parents more or less likely to vaccinate, including the severity of the disease and the general trust in the healthcare system. Since the perceived benefit of the vaccine might vary based on the vaccination coverage in the population, we allow σ to depend on the frequency of the V^+ trait: when the frequency of vaccination is low, the effects of the disease are more evident and individuals are more likely to vaccinate (high σ), but when the frequency of vaccination is high, the risks of the disease are masked and individuals are less likely to vaccinate (lower σ) (see **Supplementary Text S3.1** for a more detailed explanation of how σ is calculated as a function of vaccination coverage (V^+)). The equation relating the frequency of V^+ and σ is given in **Figure 2.1**. In genetics, the selection coefficient is traditionally small (in the range of -0.1 to 0.1 (Eyre-Walker and Keightley 2007));

at baseline in our model, we kept the maximum cultural selection coefficient at 0.1 which allowed for both positive and negative selection depending on the frequency of vaccinated individuals in the previous iteration.

Finally, oblique interactions (cultural influences from non-parental individuals) then act to further modify trait frequencies in the population. Individuals in the simulation can change their vaccine attitudes based on interactions with others and their perceptions of their surroundings. If the vaccination coverage in the population is low, we consider the negative effects of the disease to be more apparent and thus people will be less likely to adopt a vaccine-hesitant attitude, and if the vaccination coverage is high, the negative effects of the disease are prevented (amplifying the perception of the vaccine's risks and costs, however small) and people might be more likely to become vaccine hesitant (**Figure 2.2**). Each subsequent iteration of the model begins with the phenotype frequencies produced at the end of the current iteration. The simulation is run until phenotype frequencies reach equilibrium (**Figure 3.1, Table 3.1**). For more detail see **Supplementary Text S3.1** and (Anderson and Creanza 2023). All code to run the simulations is provided at www.github.com/CreanzaLab/VaccineModel and http://doi.org/10.6084/m9.figshare.22493317.

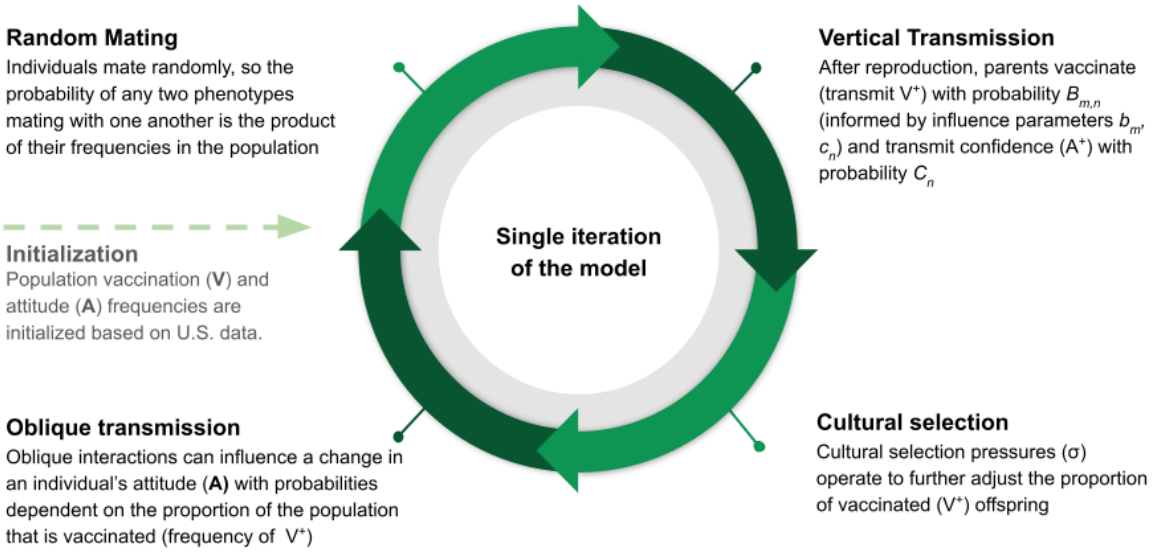

Figure 3.1: Workflow of a single iteration of the model. The schematic shows the processes within a single model iteration. The model is initialized with the phenotypic frequencies (V^+A^+, V^+A^-, V^-A^+, V^-A^-) in the population. After individuals mate and reproduce, they vertically transmit vaccination and attitude traits to their offspring. Vaccination trait frequencies are further modulated by cultural selection. Oblique transmission (cultural transmission from non-parental adults in the population) follows, which may lead offspring to alter their attitude state. (Parameters, their definitions, and baseline values are listed in **Table 3.1**)

Table 3.1: List of parameters, their definitions, and baseline values.

Parameter	Meaning
V	Vaccination state (V^+ vaccinated, V^- unvaccinated)
A	Vaccine attitude (A^+ confident, A^- hesitant)
$B_{m,n}$	Probability that parental pairs vaccinate their children, which depends upon the parents' vaccination states (b_m) and vaccine attitudes (c_n) (given in **Table S2.2**)
C_n	Probability that parental pairs transmit vaccine confidence to their children **Baseline: C_0= 0.01, C_1= C_2 = 0.5, C_3 = 0.99**
b_m	Probability that parental pairs support offspring vaccination given their vaccination states **Baseline: b_0= 0.01, b_1= b_2 = 0.5, b_3 = 0.99**
c_n	Probability that parental pairs support offspring vaccination given their vaccine attitude **Baseline: c_0= 0.01, c_1= c_2 = 0.5, c_3 = 0.99**
σ	Comprehensive selection coefficient for V^+, dependent on the population-wide vaccination rate (see **Figure 2.2**)
σ_{max}	The highest additional benefit that can be conferred by vaccination **Baseline: σ_{max}= 0.1**
Parameter subscripts indicating traits of the mating pair (m and n in b_m, c_n, C_n, and $B_{m,n}$)	**$V^-\times V^-$:** m=0**; $V^-\times V^+$:** m=1; **$V^+\times V^-$:** m=2; **$V^+\times V^+$:** m=3 **$A^-\times A^-$:** n=0; **$A^-\times A^+$:** n=1; **$A^+\times A^-$:** n=2; **$A^+\times A^+$:** n=3

Parameterization for Compulsory Vaccination and Vaccine Inaccessibility Simulations

We hypothesize that parental vaccine attitudes influence their use of exemptions and thus levels of non-vaccination will differ based on parental attitudes under a mandated vaccination system. Therefore, we simulate the effects of compulsory vaccination by modulating the influence of a couple's vaccine attitudes on their likelihood of vaccinating their offspring (c_n); in other words, a vaccine mandate alters the influence of a couple's vaccine attitude on their decision to vaccinate. We assume the implementation of mandates would increase vaccination in couples with at least one vaccine-hesitant individual. If vaccination exemptions are permitted, we expect that $A^- \times A^-$ couples (those with two vaccine-hesitant individuals) would be most likely to obtain exemptions, followed by mixed attitude ($A^- \times A^+$ or $A^+ \times A^-$) couples, with vaccine confident couples ($A^+ \times A^+$) being least likely. Hence, to model the effects of implementing a vaccine mandate, we increase attitude influence parameters from baseline values (**Table 3.1**) to represent two levels of mandate strictness, a strict mandate in which $c_0 = 0.5$, $c_1 = c_2 = 0.9$, $c_3 = 0.99$ and a more lenient mandate in which $c_0 = 0.3$, $c_1 = c_2 = 0.7$, $c_3 = 0.99$ (**Figure 3.2**).

Similarly, to represent a vaccine inaccessibility scenario, we reduced the influence of parental vaccine attitudes on vaccination behaviors for couples with at least one confident individual (i.e. reducing c_1, c_2, c_3 from baseline values). In this simple representation of a vaccine-scarce environment, we assume that parents' confidence in vaccines would have reduced influence on their ability to vaccinate their offspring, that is, their vaccine confidence does not ensure their ability to overcome vaccine inaccessibility. Hesitant couples are least likely to vaccinate their offspring regardless of vaccine availability, but couples who would likely vaccinate their offspring given the chance would have difficulty doing so due to the lack of access. We modeled two levels of vaccine inaccessibility– a somewhat inaccessible vaccine in which $c_0 = 0.01$, $c_1 = c_2 = 0.3$, and $c_3 = 0.7$ and an inaccessible vaccine in which $c_0 = 0.01$, $c_1 = c_2 = 0.1$, $c_3 = 0.5$. Assuming mixed attitude ($A^- \times A^+$ or $A^+ \times A^-$) couples exhibit the most variability in their likelihood of transmitting vaccine confidence, we then examined the effect of the interaction between the maximum cultural selection coefficient (σ_{max}) and mixed-attitude confidence transmission probability (C_1=C_2) for a scenario with baseline parameters (no active mandate and an accessible vaccine), with a lenient mandate, and with a somewhat inaccessible vaccine (**Figure 3.2**).

We next examined the effects of varying the transmission probability of vaccine confidence parameters for all couple types (C_0, C_1, C_2 and C_3), instead of focusing on the vaccine confidence transmission of mixed-attitude couples. We varied all C_n parameters simultaneously within a specified range of values (**Table S2.3**) across different levels of mandate strictness (**Figure 3.4**) and vaccine inaccessibility (**Figure 3.5**). As before, we varied these parameters in conjunction with the maximum cultural selection coefficient σ_{max}.

Results

Compulsory Vaccination and Vaccine Inaccessibility

We examined the effect of the interaction between the maximum cultural selection coefficient (σ_{max}) and confidence transmission probability of mixed-attitude couples ($A^- \times A^+$ and $A^+ \times A^-$; C_1=C_2) (**Figure 3.2**). Modeling the effects of a vaccine mandate reveals a decoupling of vaccination coverage and vaccine confidence trajectories when parents are more likely to transmit vaccine hesitancy (**Figure 3.2C-D**). Even when vaccine confidence is very low (specifically at mixed-trait couple confidence transmission probabilities below 0.5; red region in **Figure 3.2D**), vaccination coverage is higher with a lenient mandate than without the mandate

(compare **Figure 3.2C-D** to **Figure 3.2A-B; Supplementary Table S3.1**). However, the leniency of the mandate in **Figure 3.2C-D** means that many vaccine-hesitant couples can obtain an exemption, and vaccination coverage remains lower when vaccine hesitancy is common. This suggests that an external pressure to vaccinate helps overcome the opposing cultural pressure imposed by hesitancy in the population, but a mandate would have to be stricter to achieve herd immunity in a predominantly vaccine-hesitant population.

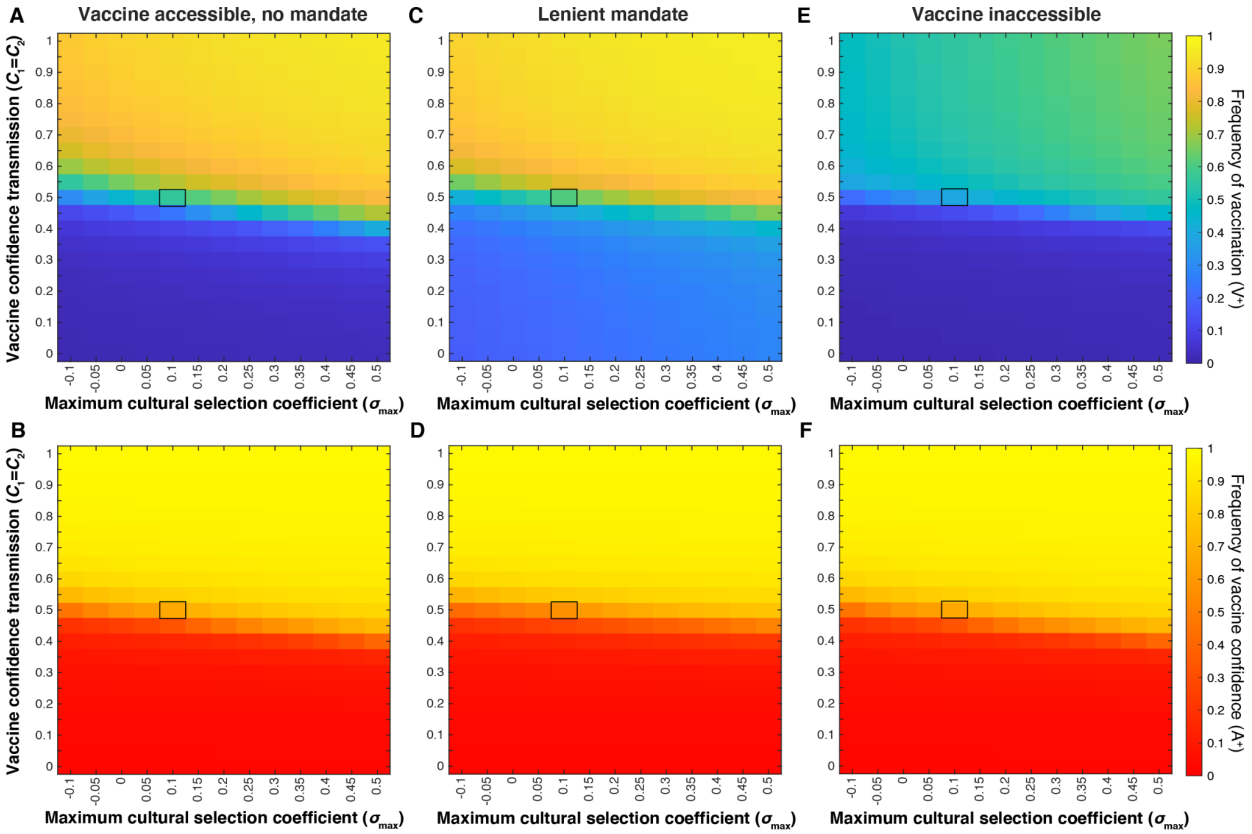

Figure 3.2: External factors (vaccine mandates and vaccine scarcity) decouple equilibrium levels of vaccine confidence from vaccination coverage. Heatmaps showing equilibrium vaccine coverage and vaccine confidence levels with an accessible vaccine and no active mandate (**A, B**), with an accessible vaccine and a lenient mandate (**C, D**) and an environment with vaccines somewhat inaccessible (**E, F**). Assuming mixed-attitude couples might have the most variability in their likelihood of transmitting vaccine confidence to their offspring, we vary $C_1 = C_2$ (confidence transmission probability of mixed-attitude couples) on the vertical axis, and maximum selection coefficient σ_{max} (indicative of the perceived value of vaccinating offspring) on the horizontal axis. A lenient mandate (**C, D**) is modeled by $c_0 = 0.3$, $c_1 = c_2 = 0.7$, $c_3 = 0.99$; vaccine inaccessibility (**E, F**) is modeled by $c_0 = 0.01$, $c_1 = c_2 = 0.3$, $c_3 = 0.7$. Unspecified parameters are given in **Table 3.1**. These simulations show an inverse correlation between vaccination coverage and vaccine confidence at $C_n < 0.5$ under a lenient mandate, and $C_n > 0.5$ when vaccine access is limited. Baseline conditions (**Table 3.1**) are highlighted by black boxes in each heatmap. To facilitate comparisons between panels, the mean and median for the section of the heatmaps with $C_1 = C_2 < 0.5$ are presented in **Supplementary Table S3.1**.

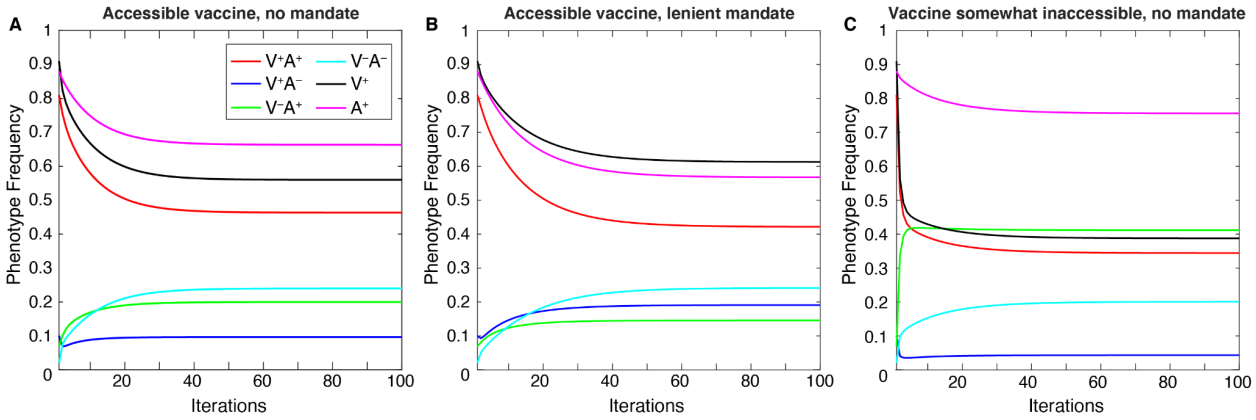

Figure 3.3: Vaccine mandates and inaccessibility drive different distributions of both vaccination coverage and vaccine confidence. Phenotype and trait frequencies are plotted over 100 model iterations. Compared to baseline transmission levels (panel **A**, parameter values given in **Table 3.1**), a lenient vaccine mandate ($c_0 = 0.3$, $c_1 = c_2 = 0.7$, $c_3 = 0.99$; panel **B**) leads to increased vaccination coverage at equilibrium (black line) but decreased vaccine confidence levels (magenta line). In contrast, when a vaccine is somewhat difficult to access ($c_0 = 0.01$; $c_1 = c_2 = 0.3$, and $c_3 = 0.7$; panel **C**), vaccination coverage is lower than in panel **A** but vaccine confidence is higher. The specific simulations shown here are highlighted with black rectangles on the heatmaps in **Figure 3.2**.

Table 3.2: Change from Baseline Equilibrium Frequencies. Final equilibrium frequencies for baseline, a lenient vaccine mandate, and a somewhat inaccessible vaccine are shown along with the percent difference from baseline frequencies. Colored lines in the first row correspond to the line colors in **Figure 3.3**. Negative changes are indicated by a red downward pointing triangle; positive changes are indicated by green upward pointing triangle. A vaccine mandate leads to increased vaccination among vaccine-hesitant individuals, and vaccine inaccessibility leads to decreased vaccination and increased vaccine confidence among unvaccinated individuals.

Phenotype		V^+A^+ —	V^+A^- —	V^-A^+ —	V^-A^- —	V^+ —	A^+ —
Baseline Equilibrium Frequencies		**46.3%**	9.7%	20%	**24%**	**56%**	66.3%
Percent Diff. from Baseline	**Mandate**	**42.1%** (-9%)▼	19.1% (97%)▲	14.6% (-27%)▼	**24.2%** (0.8%)▲	**61.3%** (9%)▲	56.8% (-14%)▼
	Inaccessibility	**34.4%** (-26%)▼	4.3% (-56%)▼	**41.2%** (106%)▲	20.1% (-16%)▼	38.8% (-31%)▼	**75.6%** (14%)▲

When vaccines were somewhat inaccessible, vaccination coverage was noticeably reduced overall, while vaccine confidence increased slightly across the parameter space. Juxtaposed with the mandate scenario **(Figure 3.2C-D)**, our vaccine scarcity models produce an opposite deviation of vaccination coverage from vaccine confidence levels: when vaccines are mandated, we observe increased vaccination coverage in low-confidence environments, and when vaccines are inaccessible, we observe lower than expected vaccination coverage (<50%) in a predominantly vaccine-confident environment (>90%) (**Figure 3.2**).

Compulsory vaccination may increase vaccination coverage at the expense of confidence, while vaccine inaccessibility promotes confidence

In the three scenarios examined thus far—baseline (no mandate and accessible vaccines), a lenient mandate, and somewhat inaccessible vaccines—most of the variability in equilibrium frequencies across the parameter space occurs at confidence transmission levels between $C_1 = C_2 = 0.4$ to 0.6 (**Figure 3.2**). This threshold region separates definitively higher and definitively lower vaccination coverage and vaccine confidence outcomes. The effect of actual and perceived vaccine fitness (σ) is also most noticeable in this region of the heatmap: as cultural selection for vaccination increases at any fixed probability of confidence transmission, vaccination coverage and vaccine confidence levels at equilibrium are increased. Changes in vaccination and confidence frequencies are not independent of each other, as these effects are the consequence of

changes in phenotypic frequencies. Therefore, for each scenario, we plotted the temporal dynamics of each phenotype (**VA**) and the vaccination (V^+) and confidence (A^+) traits at baseline parameter values (**Figure 3.3**), then calculated the difference in frequency from baseline equilibrium (**Table 3.2**). With an accessible vaccine that is not mandated (**Figure 3.3A, Table 3.2**), the phenotype frequencies of the system equilibrate generally with either vaccinated and vaccine confident (V^+A^+) or unvaccinated and vaccine hesitant (V^-A^-) individuals most abundant (**Figure 3.3A, Table 3.2**). Though these two phenotypes remain the most abundant when a lenient vaccine mandate is implemented, the equilibrium frequency of vaccinated but vaccine-hesitant individuals (V^+A^-) is greatly increased compared to baseline (**Figure 3.3B**, **Table 3.2**). Interestingly, a mandate also results in a higher frequency of unvaccinated and vaccine-hesitant individuals (V^-A^-), while reducing vaccinated and vaccine-confident individuals (V^+A^+) in the population. Vaccine inaccessibility, on the other hand, resulted in approximately double the frequency of unvaccinated but vaccine-confident (V^-A^+) individuals. In summary, compared to baseline outcomes, implementation of a mandate increases vaccination coverage at the expense of confidence by driving vaccination in hesitant individuals, and vaccine inaccessibility promotes confidence despite low vaccination coverage by driving confidence in unvaccinated individuals.

Vaccination and confidence frequencies are more variable when offspring beliefs are more likely to differ from their parents' beliefs

The clear disjunction between higher and lower vaccination (V^+) and vaccine confidence (A^+) frequencies observed in **Figure 3.2** is not observed when the probability of confidence transmission is modulated for all couples (**Figure 3.4**). When mixed-attitude couples transmit confidence to their offspring at high ($C_1 = C_2 > 0.5$) or low ($C_1 = C_2 < 0.4$) probabilities, which skews population attitude frequencies to either highly confident or highly hesitant, the subsequent offspring are more likely to vaccinate (in a confident population) or not vaccinate (in a hesitant population) (**Figure 3.2**). Similarly, if all couple types are transmitting confidence at lower probabilities or higher probabilities (i.e. C_0, C_1, C_2, and C_3 are all lower or higher, respectively), vaccination frequencies will equilibrate at either lower levels or higher levels (**Figure 3.4A**). However, if all couples are transmitting confidence at mid-range probabilities (or C_1 and C_2 are closer to 0.5), the population equilibrates at more polymorphic frequencies, that is, both forms of each trait coexist in the population at moderate frequencies.

Equilibrium vaccination coverage increases as cultural selection for vaccination increases in both mandated vaccines (**Figure 3.4C, E**) and vaccine inaccessibility scenarios (**Figure 3.5C, E**); confidence frequencies remain more consistent across the range of cultural selection pressures (**Figure 3.4D, F, Figure 3.5D, F**). When we model an increase in vaccine mandate strictness (increased difficulty in obtaining exemptions), vaccination frequencies are increased (**Figure 3.4C, E**). On the other hand, greater degrees of inaccessibility lead to larger reductions in vaccination coverage (**Figure 3.5C, E**), and lower coverage occurs despite higher levels of vaccine confidence

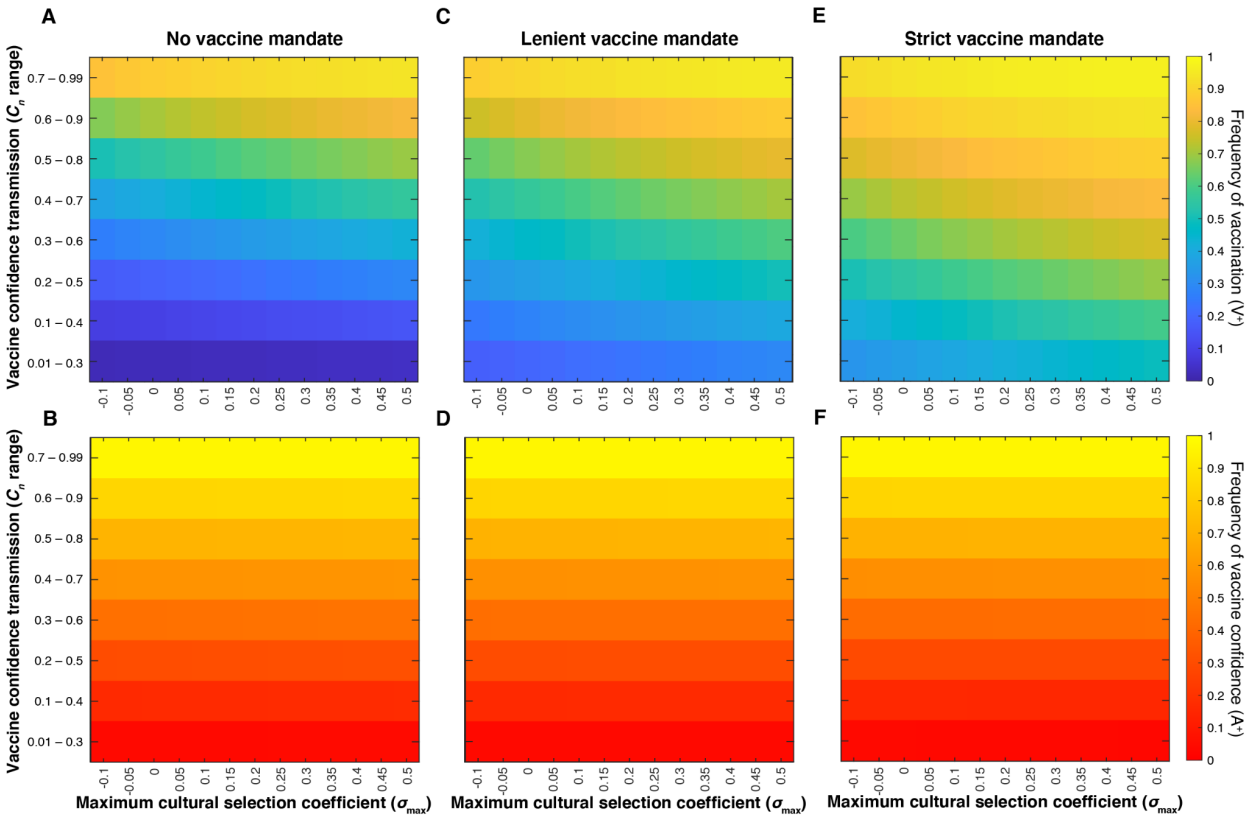

Figure 3.4: Increasing mandate strictness and increased cultural selection drive vaccination coverage . Heatmaps showing final vaccination coverage (**A, C, E**) and corresponding vaccine confidence (**B, D, F**) after 100 time-steps while simultaneously varying all confidence transmission probabilities (C_n; vertical axis) and maximum selection coefficient (σ_{max}; horizontal axis). We show an accessible vaccine with no mandate (c_0= 0.01, c_1= c_2 = 0.5, c_3 = 0.99) (**A, B**), a lenient mandate (c_0 = 0.3, c_1 = c_2 = 0.7, c_3 = 0.99) (**C, D**), and a strict mandate (c_0 = 0.5, c_1 = c_2 = 0.9, c_3 = 0.99) (**E, F**). C_n values are set within the range indicated on the vertical axis with C_0 taking the lowest value, C_1 and C_2 taking intermediate values, and C_3 taking the highest value (**Table S2.3**).

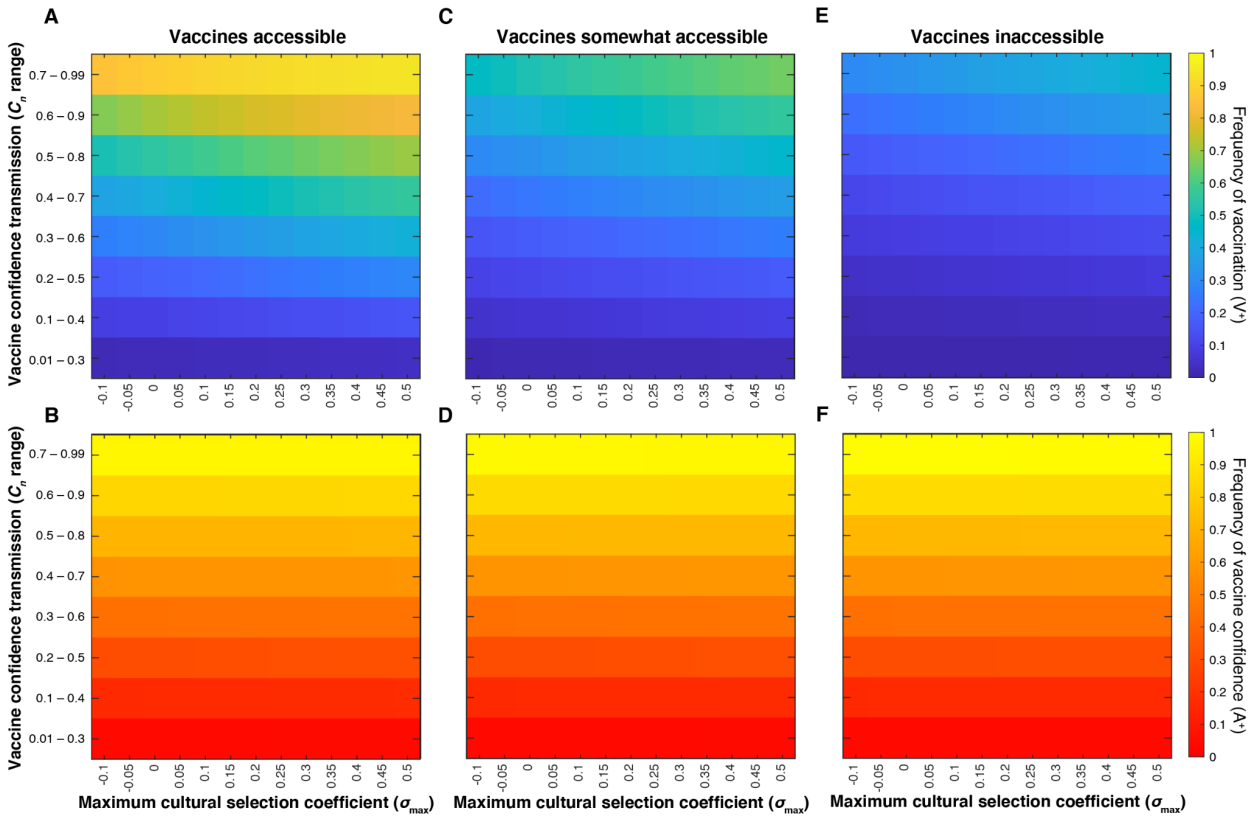

Figure 3.5: Vaccine inaccessibility reduces vaccination coverage despite high levels of vaccine confidence. Heatmaps showing final vaccination coverage (**A, C, E**) and corresponding vaccine confidence (**B, D, F**) after 100 time-steps while simultaneously varying all confidence transmission probabilities (C_n; vertical axis) and maximum selection coefficient (σ_{max}; horizontal axis). C_n values are set within the range indicated on the vertical axis with C_0 taking the lowest value, C_1 and C_2 taking intermediate values, and C_3 taking the highest value (**Table S2.3**). We simulate an accessible vaccine and no mandate (c_0= 0.01, c_1= c_2 = 0.5, c_3 = 0.99) (**A, B**), a somewhat inaccessible vaccine (c_0 = 0.01 ; c_1 = c_2 = 0.3 , and c_3 = 0.7) (**C, D**) and an inaccessible vaccine (c_0 = 0.01, c_1 = c_2 = 0.1, c_3 = 0.5) (**E,F**).

Changing the relationship between vaccination coverage and cultural selection can alter vaccination behavior when the vaccine is accessible

In the previous analyses, we assumed that the cultural selection for vaccination would begin to decrease from its maximum value as members of a population with widespread vaccination coverage (exceeding 70% vaccination coverage, see **Figure 2.1**) might perceive a reduced cost of the disease and thus a reduced pressure to vaccinate their children. To assess the robustness of our model to different relationships between vaccination coverage and cultural

selection pressures, for example representing variations in herd immunity criteria or in parent priorities, we tested the same simulations with multiple cultural selection functions. We examined the interaction between mixed-attitude pair confidence transmission probability ($C_1 = C_2$) and a range of maximum cultural selection coefficients (σ_{max}) for these different cultural selection functions (shown in **Figure S3.1A** for $\sigma_{max} = 0.1$). In line with cultural selection acting primarily on the vaccination trait, most of the differences among the cultural selection functions are observed in the vaccination equilibrium frequencies and not the confidence equilibrium frequencies, particularly when no mandates or lenient mandates are imposed (**Figure S3.1B-C**). Compared to the baseline function used in **Figures 3.2-3.5** (also shown in **Figure S3.1, column 3**), when we reduce the vaccination coverage level at which "herd immunity" is achieved and σ decreases, vaccination coverage is reduced most noticeably at the intersection of low values of σ_{max} and high values of mixed-attitude pair confidence transmission (**Figure S3.1B-C, column 4**). When the level required for herd immunity is increased, vaccination coverage is increased in this low σ_{max} high confidence transmission area of the heatmap (**Figure S3.1B-C, column 2**). The overall patterns we observed with the original cultural selection function are robust to the particular function we used. At higher values of C_1=C_2 and σ_{max} (top right corner of the heat maps), vaccination coverage was reduced when the σ function was more negatively correlated with vaccination coverage (columns 3 through 6 in **Figure S3.1**). In addition, we observed that the largest differences in vaccine coverage between cultural selection (σ) functions occurred when vaccines were accessible and there were no mandates (**Figure S3.1B**); differences in the cultural selection function had less of an effect on vaccination coverage when a lenient mandate was imposed (**Figure S3.1C**), and had little effect on vaccination coverage when vaccines were inaccessible (**Figure S3.1D**). The least variation is observed when vaccines are inaccessible: across confidence frequencies, the cultural selection function did not meaningfully alter the equilibrium vaccination coverage or vaccine confidence (**Figure S3.1D**). This result is intuitive, since most differences between cultural selection functions occur in regions of high vaccination coverage, and the simulations with inaccessible vaccines do not not lead to high vaccination coverage for any parameter combination.

Discussion

Here, we build on the cultural niche construction framework proposed by (Anderson and Creanza 2023) to model the cultural spread of vaccine attitudes and vaccination behavior in the

presence of external forces imposed by two scenarios: vaccine mandates and vaccine inaccessibility. Multiple factors influence an individual's vaccine-related beliefs and a couple's decision to vaccinate their offspring, including their own vaccination status and their perception of the relative risks of the disease and the vaccine. As such, it is important that we understand how public health policies, such as vaccine mandates and barriers to vaccination, such as geography or affordability, can shape vaccination cultures and thus affect public health. Using a cultural niche construction approach allows us to explore the effects of the interplay between external forces and cultural factors providing further insight into how vaccination cultures are formed, maintained, and evolve.

With our initial model (Anderson and Creanza 2023), we showed that when population traits are at or near an equilibrium, we can infer that a population with high vaccination coverage will have low rates of vaccine hesitancy and vice versa. However, when there are external pressures as modeled here, such as increased pressure to vaccinate or difficulty in acquiring vaccination exemptions, an undercurrent of vaccine hesitancy can persist in a relatively well-vaccinated population, potentially limiting the adoption of newly introduced vaccines. This possibly contributes to the unexpected lag in uptake of newer vaccines, such as the COVID or HPV vaccines, in communities with otherwise high vaccination rates (Gilkey et al. 2017; Hanson et al. 2018; Wong et al. 2021). The perceived increase in hesitancy surrounding new vaccines may actually be existing vaccine hesitancy becoming apparent. In addition, "fence sitters", those who have not made a firm stance regarding vaccines and thus could be more influenced by targeted campaigns (Leask 2011), may develop higher levels of uncertainty about new vaccines than their parents had about existing ones.

In contrast to the effect of vaccine mandates, by modeling vaccine inaccessibility we illustrate another important pattern: reduced vaccination coverage in a vaccine-confident culture. In a vaccine-scarce environment, an individual's attitude regarding vaccines has less influence on vaccination behavior due to the barrier imposed by resource availability. As a result, a population may be undervaccinated despite holding vaccine-affirming beliefs. In addition, a health culture previously shaped by vaccine inaccessibility could potentially ingrain specific behavioral practices (for example, visiting the doctor only when a child is sick and not for a regular vaccine schedule) that are not easily modified even if vaccines become more readily available. These vaccine scarcity scenarios are most likely to exist in low- and middle-income countries in which

vaccine acquisition, storage and/or distribution resources are insufficient (Smith, Lipsitch, and Almond 2011; Mathieu et al. 2021; Burki 2021) whereas the opposite scenario (low vaccine confidence–high vaccination coverage) after vaccine mandates is most common in developed nations (Solís Arce et al. 2021). In summary, we find that vaccine mandates can result in high vaccination coverage even in a culture of hesitancy, and that lack of access to vaccines can produce the inverse: low vaccination coverage in a culture of confidence.

It is difficult, as with any system, to fully capture the complex reality of vaccine hesitancy and vaccination behavior with a mathematical model. Caveats of this model include the lack of empirical data to inform how we model the influence of vaccine confidence on vaccination behaviors in the face of mandates or vaccine inaccessibility. In addition, our model simplifies the process of human population turnover with discrete generations; in reality, of course, population turnover is asynchronous and multiple generations can have cultural interactions with one another (Anderson and Creanza 2023). However, this simple model is able to demonstrate interesting scenarios that confirm the importance of understanding the culture of the communities in which public health policies act, and how the cultural landscape might affect specific outcomes. A community is most protected from VPD outbreaks if two conditions are met: vaccination coverage achieves or exceeds herd immunity levels, and future vaccinations are not threatened by underlying vaccine hesitancy. The effects that we observe as a result of varying the cultural selection function suggest that an "unwavering" (positive) perception of vaccination is better for maintaining higher levels of vaccination coverage, than one that varies with vaccination coverage. This highlights a significant issue in increasing vaccination in the absence of (severe) disease as perceptions are shaped by experience of both the disease and measures used to address the disease. Since increasing vaccination coverage might require different strategies than increasing confidence, we encourage public health policymakers to consider both beliefs and behaviors patterns in their outreach efforts and information campaigns.

The results of our simulations are congruent to those observed in other behavior change model studies (Verelst, Willem, and Beutels 2016). For example, Epstein *et al*. (Epstein, Hatna, and Crodelle 2021) demonstrated using a "triple contagion" model, in which a disease, fear of a disease, and fear of a vaccine can each be transmitted between individuals, that high vaccination coverage may be achieved when fear of a vaccine is low and fear of the disease is high. Though our model uses different methods of transmission, we arrive at similar conclusions; for example,

our model predicts higher vaccination coverage when the cultural selection coefficient is high, suggesting a higher perceived value of vaccination (and thus lower fear of the vaccine). Similarly, faster spread of vaccine fear in the Epstein *et al.* study could be interpreted similarly to higher probabilities of transmitting vaccine hesitancy (lower $C_1 = C_2$ values) in our model, and we also observe reduced vaccination coverage in these scenarios.

In addition, an experimental study of the effects of COVID-19 vaccine scarcity (Pereira et al. 2022) found that vaccine scarcity could decrease the willingness to vaccinate, but it did not, however, affect the perception of risk or protection associated with the vaccine. Though the perceived risk in our model is modulated according to vaccination frequency (that is, in our model, perceptions are modulated by vaccination coverage), our simulations reveal an intuitively similar pattern: vaccination is reduced overall when vaccines are scarce. However, while perception may be modulated in our model, we do observe an increase in vaccine confidence under conditions that result in low vaccination coverage. This is in line with the findings of (Pereira et al. 2022) as vaccine-confident individuals may choose to forgo vaccinations for the benefit of others if resources are limited, while still maintaining (and transmitting) their vaccine beliefs. The Pereira *et al*. study, however, focused on adult vaccination with the COVID-19 vaccine, a novel vaccine that is not part of the traditional child vaccination schedule on which our model was based. The differences between the vaccine target populations (e.g. child vs. adult) and the interacting individual values (e.g. compassion for higher-risk individuals in foregoing one's own vaccinations when vaccines are scarce) may produce differing dynamics requiring different public health approaches.

In sum, our model shows, in both mandate and inaccessibility scenarios, that the probability of transmitting vaccine-positive attitudes is a strong predictor of whether future vaccination coverage is high or low (**Figures 3.2, 3.4-3.5**). We also demonstrate that vaccine efficacy and perceived value are important to maintaining sufficient levels of vaccination coverage, especially if vaccine confidence is not being robustly transmitted (or maintained in adulthood), regardless of vaccination scenario (**Figures 3.2, 3.4-3.5**). Thus, our model demonstrates the importance of clear and accurate communication about vaccines even when vaccination is compulsory and resulting coverage is high, to reduce the spread of inaccurate information that can foster vaccine hesitancy and hinder the uptake of future vaccines. Taken together, our model suggests that combatting low or declining vaccine uptake would take a

sophisticated approach that targets the physical vaccination behavior (availability and mandates) while simultaneously addressing a population's constantly evolving vaccine perceptions.

CHAPTER 4.
EXPLORING THE EFFECTS OF CULTURAL TRANSMISSION AND DECISION-MAKING BIASES ON THE ACCEPTANCE OF NOVEL VACCINES

Introduction

Vaccine hesitancy and anti-vaccine sentiments have existed since Edward Jenner created the smallpox vaccine in 1796 (Schwartz 2012), despite vaccination being safer than its predecessor, variolation (Langer 1976b; Riedel 2005). However, today, vaccination remains an established part of the routine standard of care in childhood health practices, with childhood vaccination frequencies exceeding 90% in most of the developed world (Luman et al. 2005; Ventola 2016). As vaccines continue to be developed and improved, the adoption of vaccines for new diseases, new vaccines for existing diseases, or even new methods of delivery could be faced with public reluctance. For example, in contrast to other vaccine-preventable diseases in the developed world, the COVID-19 pandemic recently affected the daily lives of people around the globe. Yet, despite the novelty of the disease, widespread fear and concern of contracting the disease, and public health efforts to promote the vaccine, COVID-19 vaccination coverage has fallen short of expected goals (Sallam 2021; Cénat et al. 2023; Curtis et al. 2022). Since the choice to vaccinate is influenced by both external and internal pressures, these factors also affect the rate of uptake, and thus the time it takes for a novel vaccination practice to be established as part of a health routine.

Understanding and working within a cultural context and understanding how people make decisions is important to improving and maintaining public health. Health decisions are shaped by a number of personal and social factors, such as past experiences, current priorities, media influences, and beliefs about the disease (Bury 1997; Clark and Weale 2012). These factors may lead individuals to under- or overestimate their epidemiological risk (Voinson, Billiard, and Alvergne 2015). Decision-making can be an “iterative” process – in which priorities are revised in light of new information, to correct errors or to adapt to a changing environment (Sharot et al. 2023; Clark and Weale 2012). In the same vein, individuals might reassess, for example, their health beliefs and personal values during health crises or, less urgently, the introduction of a new form of a routine health practice. Thus, priorities and decision-making

dynamics could vary over the course of a lifetime, or from day to day. For instance, during the initial vaccine introduction stage of the COVID-19 pandemic, people were more likely to express an intention to vaccinate if they surmised that more of their social circle supported the vaccine (Roy et al. 2022). This trend is consistent with studies of HPV and influenza vaccines: knowing one's social contacts had been vaccinated influenced an individual's decision to vaccinate themselves (Allen et al. 2009; Bruine de Bruin et al. 2019). In contrast, "established" vaccines are often accepted as routine, and parents who decline childhood vaccines such as MMR most commonly cite concerns about the side effects of the vaccine and a lower perceived vaccine effectiveness and importance (K. F. Brown et al. 2010). Thus, the process of making decisions about a novel vaccine differs from that of an established vaccine—there is limited information, a lack of experience, and perhaps new considerations on which individuals base their vaccination decision.

It has become increasingly common to incorporate aspects of human behavior and the social environment, such as fear, information spread, and social networks, into quantitative models of infectious disease dynamics (e.g (Perra et al. 2011; Mao and Yang 2012b; Bauch 2005; Chauhan, Misra, and Dhar 2014; Funk, Salathé, and Jansen 2010; Tanaka, Kumm, and Feldman 2002; Epstein et al. 2008b; Epstein, Hatna, and Crodelle 2021)). Since culturally specific behaviors have been linked to the spread and endemism of disease (Alpers 2008; Raoult et al. 2013; Yoder and Dworkin 2006; Gastañaduy et al. 2016; Wolff and Madlon-Kay 2014; Bahta and Ashkir 2015), models of cultural evolution have also been employed to understand how cultural forces such as homophily and social learning interact with the disease epidemiological landscape to shape health cultures (Anderson and Creanza 2023, 2022; Verelst, Willem, and Beutels 2016).

An inaccurate yet prevalent assumption of behavior adoption and social learning models is that the rate of susceptibility to the adoption of a behavior is proportional to the prevalence of the behavior in the population (Walters and Kendal 2013). Models incorporating decision making typically assume agents are rational and thus make decisions that maximize their payoffs (Ndeffo Mbah et al. 2012; Bauch 2005; Voinson, Billiard, and Alvergne 2015). Disease transmission models tend to also incorporate the assumption that individuals make an objective evaluation of epidemiology and statistical probability (Voinson, Billiard, and Alvergne 2015). However, people also make vaccination decisions based on non-epidemiological factors, such as advice

from others and their own research (Brunson 2013b, [a] 2013). In addition, humans' decision-making skills are often inefficient at dealing with uncertainty and computing probability when considering epidemiological factors (Voinson, Billiard, and Alvergne 2015; Gigerenzer and Selten 2002). To address this issue, researchers have explored the effects of heuristics—shortcuts humans use to make decisions (Todd and Gigerenzer 2012). Decision-making biases, sometimes known as cognitive biases, are one type of heuristic that humans often use; in the context of health behaviors, researchers have investigated conformity bias, when individuals are disproportionately likely to adopt the most common belief or behavior, and content bias, when individuals are more likely to adopt traits with particular characteristics (Walters and Kendal 2013; Thoma et al. 2021). This research has shown that the strength of conformist tendencies is linked to how likely a behavior is to become established in a population. However, anti-conformism, the tendency to adopt the minority trait in a population, has also been theorized to explain within-group similarity among human cultural groups and guard against population collapse in periods of high environmental variation (Boyd and Richerson 1988; Eriksson and Coultas 2009; Denton et al. 2020; Grove 2019; Latané and Wolf 1981).

Decision-making biases do not operate independently, as they interact with surrounding social factors such as the behaviors and beliefs of one's direct contacts and other relationships which influence decisions. Decision-making biases are also diverse and employed differentially among individuals (Blumenthal-Barby and Krieger 2015; Efferson et al. 2008; Morgan et al. 2012). As such, homophily plays a key role in driving or hindering the effects of cognitive biases. Homophily, the propensity for individuals to choose social contacts and mates who are similar to themselves (Burley 1983; Creanza and Feldman 2014; Creanza, Fogarty, and Feldman 2012; Gimelfarb 1988), can shape one's social circle and may also influence the ways in which an individual interacts with these contacts. An association between decision-making biases and homophily may present itself simply as such: consider someone who surrounds themself with similar people, or preferentially seeks out information from specific sources. If this person holds conformity bias, they might be inclined to adopt the beliefs of those in the circle they manufactured. However, if this person is anti-conformist, they might be less inclined to adopt the same beliefs as those in their immediate surroundings.

As discussed, a number of factors, including the iterative process of priority setting and differences in decision-making biases, could partially explain fluctuating rates of established

vaccine uptake and stochastic rates of novel vaccination (Azarpanah et al. 2021; Luz, Nadanovsky, and Leask 2020; Walters and Kendal 2013; Voinson, Billiard, and Alvergne 2015). Taking note of and expanding on the considerations presented in previous research (Walters and Kendal 2013; Voinson, Billiard, and Alvergne 2015)(Voinson, Billiard, and Alvergne 2015), we propose a model that captures the rapid dynamics of vaccine beliefs and behaviors when a novel vaccine is deployed, incorporating stochasticity and variations in decision-making patterns. We consider the effects of the distribution of three forms of decision-making biases in the population (such that cultural traits can be transmitted in conformity biased, anti-conformity biased, and unbiased ways). We also incorporate the effects of distal opinion leaders (thought influencers who can transmit cultural information without direct contact with an individual) and homophilic interactions with social contacts. We show that the spread of vaccine confidence and the adoption of a novel vaccine is differentially impacted by the distribution of biases in a population.

Methods

In this agent-based model, we simulate a population of $i \times j$ individuals, arranged on a two-dimensional matrix such that the element $M_{i,j}$ of a matrix is associated with individual (i, j) We construct four $i \times j$ matrices, with each matrix holding one of four qualities attributed to each individual (i, j): a vaccination state (vaccinated (V^+) or unvaccinated (V^-)), an attitude state (vaccine confident (A^+) or vaccine hesitant (A^-)), a disease state (uninfected/susceptible (D^0), infected (D^+), or recovered (D^-)), and "bias" state (anti-conformity biased (B^-), unbiased (B^0), conformity biased (B^+)). At the start of each simulation, all individuals (i, j) in the population are unvaccinated (V^-), and other parameters are assigned according to pre-specified probabilities (**Table 4.1**). At initialization, we specify the attitude threshold, i.e. the percent of the initial population to be vaccine confident (A^+), and the disease threshold, the percent of the initial population that is infected (D^+), then the attitude state and disease state of each individual in the matrix is assigned randomly according to these specified probabilities. Each individual (i, j) is also assigned one of the three decision-making biases according to pre-specified probabilities **(Table 4.1**).

There are two influencers in this model: a vaccine-confident influencer and a vaccine-hesitant influencer. Influencer conditions (the attitude of the influencer, and their "reach," the percent of population in each timestep that has the chance to adopt the influencer's beliefs) and homophily presence (whether individuals change location in the matrix at random or

based on their vaccine attitude) are also initialized at the start of the simulation to the values in **Table 4.1**. The results presented herein are those of a population of 400, run for 100 timesteps.

Table 4.1: Parameters and initial conditions, with citations when values were informed by the literature

Parameter	**Initial value**
Vaccination state ($\mathbf{V}^+$ vaccinated, $\mathbf{V}^-$ unvaccinated)	States change within simulation
Attitude state ($\mathbf{A}^+$ vaccine confident, $\mathbf{A}^-$ vaccine hesitant)	States change within simulation
Starting confident population (confidence threshold)	0.8
Disease state (Susceptible ($\mathbf{D}^0$), Infected ($\mathbf{D}^+$), Recovered ($\mathbf{D}^-$))	States change within simulation
Initially infected (disease threshold)	0.2
Bias: (Novelty ($\mathbf{B}^-$), Unbiased ($\mathbf{B}^0$), Conformist ($\mathbf{B}^+$)	Initialized with various combinations
Probability of infection (not previously infected or vaccinated; ***P(I)***) (Alimohamadi, Taghdir, and Sepandi 2020; World Health Organization 2021)	0.3
Probability of infection if vaccinated ($\boldsymbol{P(I\|V^+)}$) (Lipsitch et al. 2022)	0.1
Probability of infection if previously infected (not vaccinated) ($\boldsymbol{P(I\|D^-)}$) (N. N. Nguyen et al. 2022)	0.16
Reach of confident influencer (Shearer, Forman-Katz, and Khuzam 2021)	0.3
Reach of hesitant influencer (Shearer, Forman-Katz, and Khuzam 2021)	0.4

Disease Transmission

At the start of each simulation we set a disease threshold value that indicates the initial frequency of infected individuals in the population. We also specify three probabilities of infection: the probability of infection if an agent has never been infected or vaccinated ($P(I)$); the probability of infection if an agent has never been infected but is vaccinated ($P(I|V^+)$); vaccine efficacy parameter); and the probability of infection if an agent has been previously infected but is not vaccinated ($P(I|D^-)$; infection-induced immunity parameter)). If an agent has been infected and is vaccinated (both D^- and V^+), the probability of infection is the product of $P(I|V^+)$ and $P(I|D^-)$.

Our goal with this model is not to study the disease dynamics in particular, but to provide insights with regards to how cultural and decision-making tendencies interact with disease epidemiology to affect vaccination and vaccine belief outcomes. As such, we employ a simplified pattern of disease transmission, focusing primarily on disease as a factor influencing vaccine beliefs and vaccination behavior. After initialization, the probability that an individual becomes infected in subsequent timesteps depends on 1) whether they were exposed to the disease, that is, whether they were in immediate contact with an infected individual in the previous timestep, 2) whether they are vaccinated and 3) whether they had been previously infected. After recovery, individuals are assigned the state D^- (recovered with infection-induced immunity status). We also included the introduction of a random infection to the population every five timesteps, since the population is not meant to be a completely closed system.

Vaccination

In this model, individuals vaccinate themselves based on their vaccine attitude (A^+ or A^-), their decision-making bias (B^-, B^0, B^+) and the number of vaccinated and infected individuals in their immediate contacts (**Figure 4.1**). There are four primary assumptions on which we construct vaccination probability: 1) Vaccine-confident individuals are more likely to vaccinate themselves than vaccine-hesitant individuals regardless of social network composition (vaccinated and infected proportions); 2) Individuals who hold a conformity bias are more likely than unbiased and anti-conformity biased individuals to vaccinate as the number of vaccinated individuals in their contacts increases, and those who hold an anti-conformity bias are more likely to vaccinate as the number of unvaccinated contacts increase; 3) Both vaccine-confident and vaccine-hesitant individuals are more likely to vaccinate themselves as the number of infected individuals in their direct contacts increases (increased risk of infection); 4) Confident individuals with an unbiased decision-making strategy are more likely to vaccinate than hesitant individuals with unbiased strategy. Based on these assumptions, we constructed a set of functions that we use to calculate partial vaccination probabilities: $P_D(V)$: vaccination probability based on the number of infected contacts **(Figure 4.1A)** and $P_V(V)$: vaccination probability based on the number of vaccinated contacts (**Figure 4.1B).** Taken together, final vaccination probability ($P_F(V)$) is the product of the infection frequency-based probability (**Figure 4.1A**), the disease infectivity ($P(I)$), vaccination frequency-based probability (**Figure 4.1**) and vaccine efficacy (1 –

$P(I|V^+)$) (Equation in **Figure 4.1** caption). Once vaccinated, individuals remain vaccinated for the remainder of the simulation.

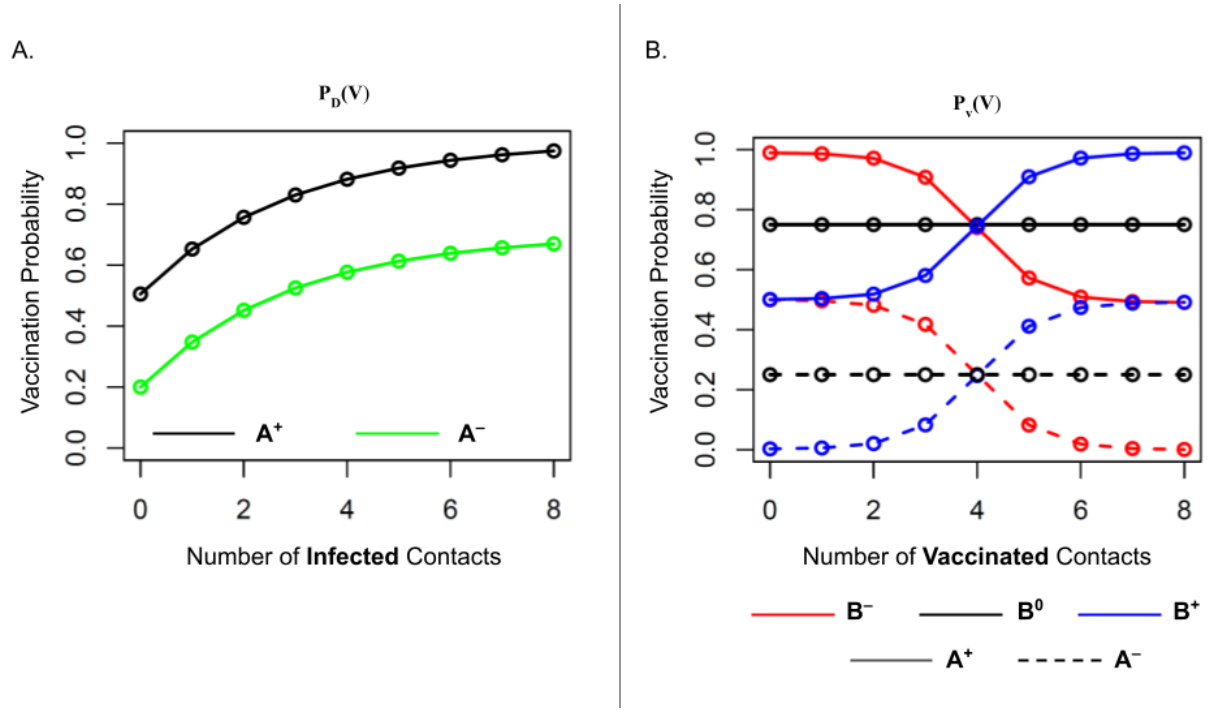

Figure 4.1: Vaccination Probability Functions. Vaccination probability functions were constructed according to specific assumptions outlined above. The final vaccination probability $P_F(V)$ is the function of two other probabilities: **A)** the probability ($P_D(V)$) that an agent decides to vaccinate (vertical axis) based solely on their vaccine attitudes (confident (A^+) in black, hesitant (A^-) in green) and the number of infected individuals in their direct contacts , and **B)** the probability ($P_V(V)$) that an agent decides to vaccinate based solely on their bias (red – anti-conformist (B^-), black – unbiased (B^0), blue – conformist (B^+)), their attitude (solid – confident (A^+), dashed – hesitant (A^-)), and the number of vaccinated individuals in their direct contacts . These calculations are then used to determine $P_F(V)$ via the equation $P_F(V) = P_D(V) \times P(I) \times P_V(V) \times (1 - P(I|V^+))$**.** Functions in panel **B** were modified from (Anderson and Creanza 2023).

Attitude Transition

During each timestep, an individual is able to change their vaccine attitude (i.e. transition from vaccine hesitant to vaccine confident or vice versa). The probability that an individual changes their attitude is influenced by their bias, the attitudes of their direct contacts, and whether they follow an influencer. The "influencer" in our model is an individual outside of the population (external force) who influences the attitude transition of a predetermined proportion

of the population at each timestep. There are two potential external influencers in our model, a vaccine-confident (A^+) influencer and a vaccine-hesitant (A^-) influencer. At initialization, we set the reach of each influencer, i.e. the proportion of the population following the influencer (**Table 4.1**). During each timestep, individuals are chosen at random, within the constraints of the influencer's reach, to be "followers". As described in more detail below, if the individual is a follower, their attitude can also change in response to the influencer, depending on whether their attitude matches the attitude(s) of their influencer(s) (**Figure 4.3**).

The initial probability that an individual changes their attitude state is determined by a function informed by the individual's bias (anti-conformity, unbiased or conformity) and the number of surrounding vaccine-confident individuals **(Figure 4.2)**; we use one set of functions for confident to hesitant transitions and a complementary set of functions for hesitant to confident transitions. These functions were constructed according to the following assumptions: a confident individual with a novelty bias is more likely to become vaccine hesitant as more of their direct contacts become vaccine-confident, whereas conformity-biased confident individuals are less likely to change their attitude state under the same conditions (**Figure 4.2A**). The opposite is assumed for vaccine-hesitant individuals: those who hold a conformity bias are more likely to become vaccine–confident as more of their direct contacts become vaccine confident, whereas vaccine hesitant individuals with anti-conformist bias individuals are more inclined to remain vaccine hesitant (**Figure 4.2B**). Unbiased individuals, regardless of attitude, remain 50% likely to change their belief independent of the frequency of confident individuals in their direct contacts. **(Figure 4.2)**.

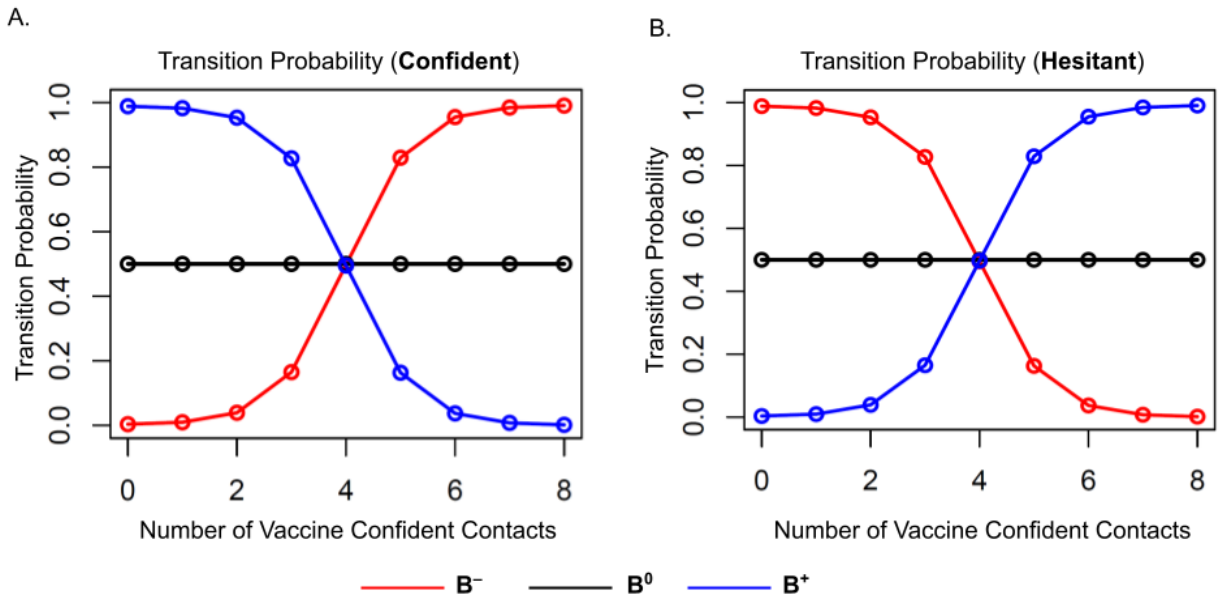

Figure 4.2: Attitude Transition Probability Functions. Vaccination probability functions were constructed according to specific assumptions outlined above (equations modified from (Anderson and Creanza 2023) **A)** The probability of a vaccine-confident agent transitioning to vaccine hesitant based on their decision-making bias (red – anticonformist (B^-), black – unbiased (B^0), blue - conformist (B^+)), and the number of confident individuals in their direct contacts. **B)** The probability of a vaccine–hesitant agent transitioning to vaccine-confident.

If an individual is a follower, their transition probability may be further adjusted based on the individual's attitude, and the attitude(s) of their influencer(s) (**Figure 4.3**). If an agent is following a single influencer with whom they share the same attitude, the probability of attitude transition is unchanged. However, if the agent is following both the confident and hesitant influencers then the probability of attitude transition transition is reduced by some factor. If the agent is following a single influencer of the opposite attitude, then the probability of transition to the influencer's attitude is increased.

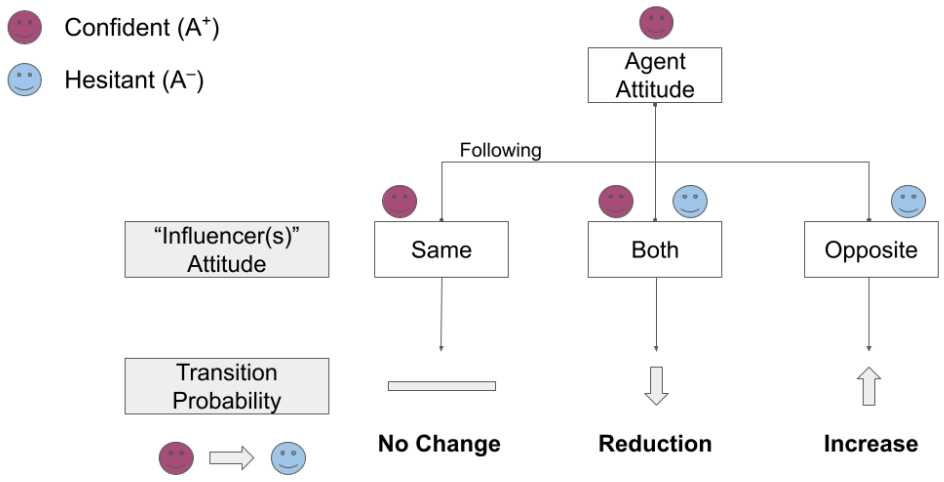

Figure 4.3: Description of the effect of the influencer on follower attitude transition. Attitude transition probability is reduced if an agent is following both influencers, but increased if an agent is following an influencer with the opposing attitude. An example with a confident agent is shown.

Homophily

A simulation can be run with or without the effects of homophily, i.e. with attitude-based relocation to another position in the matrix or with random relocation. If the simulation is run with homophily enabled, a prespecified number of individuals, selected at random, may switch positions in the matrix based on their attitude state. Selected individuals may relocate to positions where they will be surrounded by more individuals of the same vaccine attitude (homophily). During each timestep, two individuals are chosen at random (Agent 1 and Agent 2), and we then sum the number of vaccine-confident individuals in each agent's direct contacts. If Agent 1 is vaccine-confident and Agent 2 is vaccine-hesitant, and there are more vaccine-confident agents currently surrounding Agent 2 than surrounding Agent 1, then there is a probability that Agent 1 will switch places with Agent 2. Similarly, if Agent 1 is vaccine-hesitant and Agent 2 is vaccine-confident, and there are less vaccine-confident people surrounding Agent 2, than surrounding Agent 1, then Agent 1 may switch places with Agent 2. If Agent 1 and Agent 2 share the same attitude, or a possible switch is unfavorable to any party, no switch occurs. This process continues for a prespecified number of individuals.

If the simulation is run without homophily, selected individuals may change locations within the matrix at random, that is, without attitude dependence. We expect homophily to subsequently decrease attitude transitions, since an individual is more likely to be near clusters of other individuals who share beliefs with one another and attitude transitions depend on the fraction of neighbors with each belief.

Results

Temporal Analysis and Homophily Effects

To determine whether dynamics differed between populations with different distributions of decision-making biases, we held all other parameters at default values **(Table 4.1)** and tracked the population frequencies of confident, vaccinated, infected, and recovered individuals over time for six distributions of decision-making bias in the population **(Figure 4.4–4.5)**. Concurrently, we tested whether the presence of homophily had an effect on outcomes (compare **Figures 4.4–4.5** top row vs. bottom row). The effect of homophily was negligible except when the total population (**Figure 4.4C, F**) or majority of the population (**Figure 4.5A, D**) is conformity biased. In these higher conformity-biased environments, the presence of homophily-motivated movement reduces maximum average vaccination frequency achieved by the end of both simulations (**Figure 4.4C, F** and **Figure 4.5A, D),** but reduces confidence frequency in only the all-conformist environment (**Figure 4.4C-F**).

A homogeneously conformist population and a homogeneously anti-conformist population display other notable patterns. Only when the population is homogeneously conformist is the confidence increased from the starting frequency (**Figure 4.4C, F**), and though initially reduced, confidence is highly stochastic in a population that consists solely of novelty biased individuals **(Figure 4.4A, D)**.

Using a threshold of 70% vaccination coverage as a proxy for herd immunity (demarcated by the horizontal dashed line on our line plots (**Figures 4.4-4.5**)), these tests show no significant effect of bias distribution or influencer effect (not shown, see discussion) on time to herd immunity. Even though individual simulations may have resulted in herd immunity frequencies at later timesteps, on average 70% vaccination was achieved for all tests before 10 timesteps.

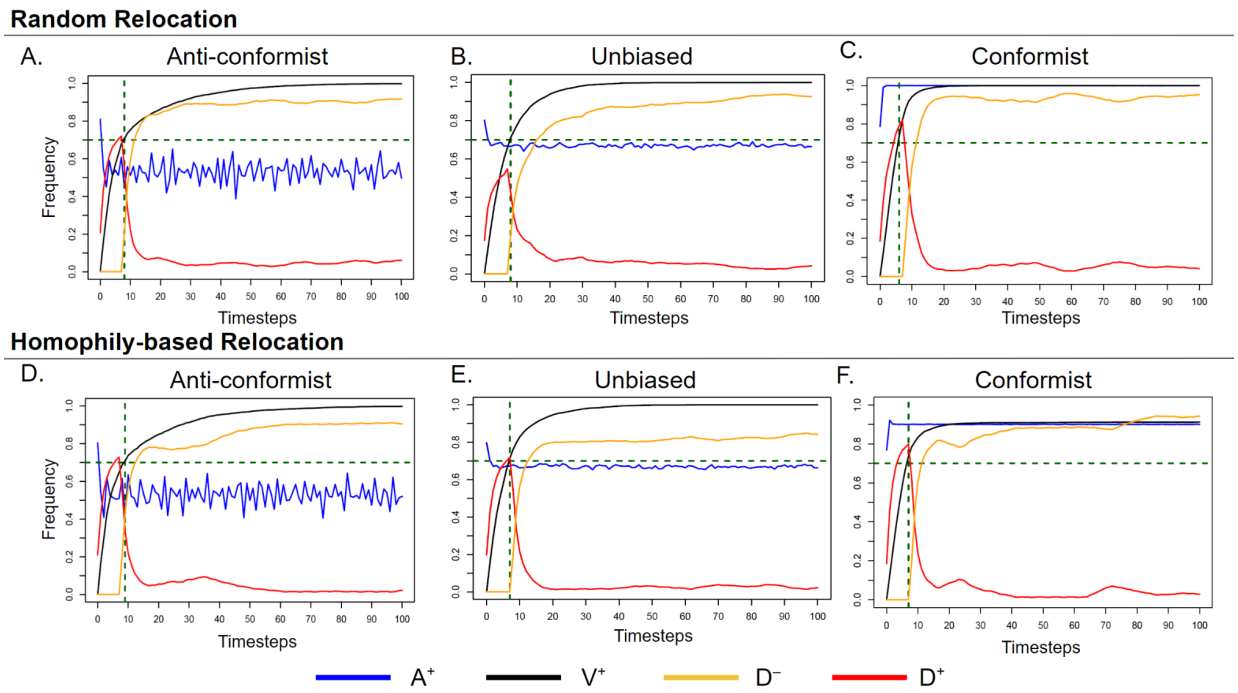

Figure 4.4: Temporal analysis of trait dynamics with homogeneously biased population. Each plot was created by running 10 simulations and plotting the average frequency of A^+ (blue), V^+ (black), D^- (yellow) and D^+ (red) at each timestep. Initial parameters for each simulation were set to those shown in **Table 4.1** while varying population bias distribution– homogeneously anti-conformity-biased population **(A, D)**; homogeneously unbiased population **(B, E)** and homogeneously conformist-biased population **(C, F).** Each simulation was run with homophily-based movement **(D–E)** and without homophily, i.e. random relocation **(A–C)**.

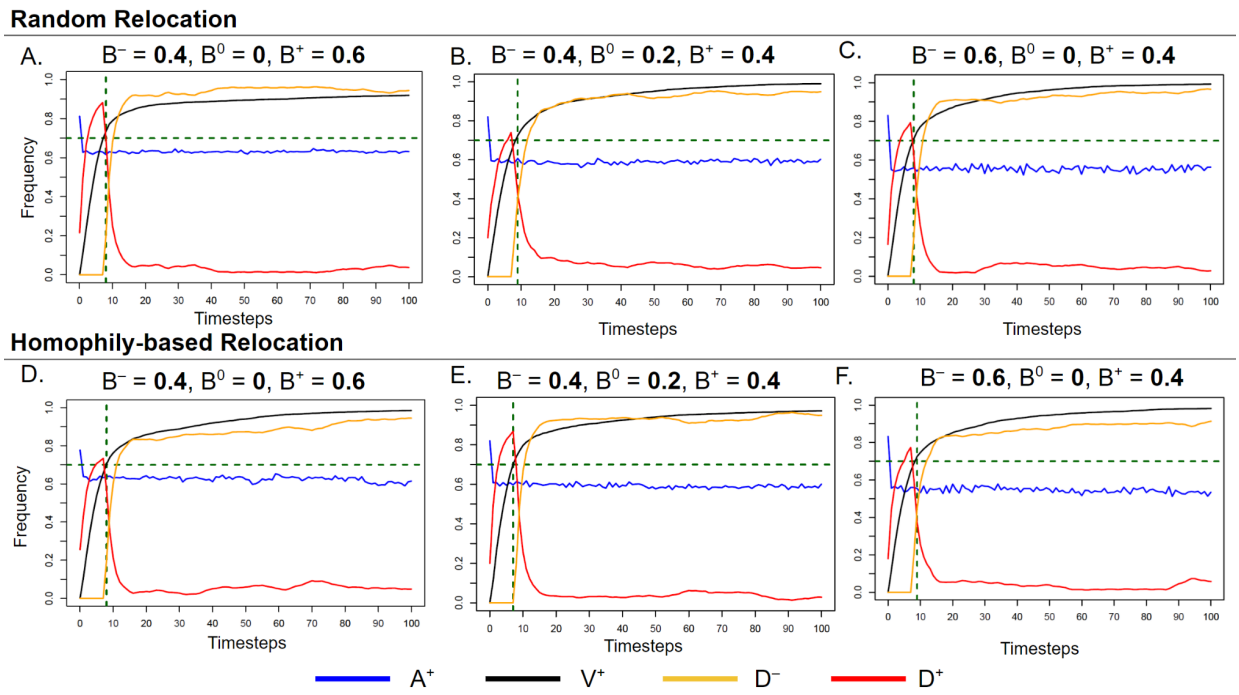

Figure 4.5: Temporal analysis of trait dynamics with heterogeneously biased population. Each plot was created by running 10 simulations and plotting the average frequency of A^+ (blue), V^+ (black), D^- (yellow) and D^+ (red) at each timestep. Initial parameters for each simulation were set to those shown in **Table 4.1** while varying population bias distribution:individuals are either anti-conformist or and conformist-biased, with higher conformist frequencies **(A, D)**; individuals can be anti-conformist, conformist, or unbiased **(B, E)** and all individuals are either anti-conformist or conformist biased, with higher novelty frequencies **(C, F)**. Each simulation was run with homophily based movement **(D–E)** and without homophily, i.e. random relocation **(A–C)**.

Sensitivity Analysis

Next, we conducted a sensitivity analysis, varying the probability of infection if an agent has never infected or vaccinated ($P(I)$) and the probability of infection if an agent has never been infected but is vaccinated ($P(I|V^+)$), under two decision-making bias scenarios: 1) all biases present in the population at proportions $B^- = 0.4$, $B^0 = 0.2$, $B^+ = 0.4$ (**Figure 4.6A-B**, and 2) a homogeneously conformist population **(Figure 4.7A-B)**. For each pair of conditions, we plot the average vaccination and confidence frequencies of 10 simulations at each of 100 timesteps. These simulations are run with homophily-based relocation, and all other parameters are as listed in **Table 4.1**.

If individuals are completely susceptible to infection (never infected and unvaccinated; $P(I)>0$), the model produces a tradeoff between vaccine efficacy ($1-P(I|V^+)$) and the probability of infection (**Figure 4.6B** and **4.7B**). Vaccine uptake is reduced when the probability of vaccine breakthrough infections is higher (**Figure 4.6B** and **4.7B**), while vaccine uptake is increased when the risk of infection to completely susceptible individuals is higher (**Figure 4.6B** and **4.7B**). This behavior is more readily observed in the heterogeneous population (**Figure 6B**), as the homogeneously conformist population exhibits more irregularities in the pattern of vaccination uptake (**Figure 4.7B**).

Interestingly, we note that population confidence and vaccination frequency patterns do not mirror one another in the simulations with a heterogeneously biased population (**Figure 4.6**). That is, confidence frequencies under particular conditions do not predict vaccination frequencies (**Figure 4.6**). Also, in contrast to vaccination, varying the parameters tested did not lead to a distinctive pattern of confidence adoption in the heterogeneous population (**Figure 4.6**); all simulations represented in the heatmap have roughly similar confidence levels. The average final confidence frequency for each condition approached midrange values (~0.6), both when varying the probability of infection ($P(I)$ of completely susceptible individuals) and varying the starting vaccine confidence (A^+) frequency in conjunction with the probability of infection (vaccinated) (**Figure 4.6A, C**). Vaccination frequencies, however, responded differentially to each case: low vaccination uptake was linked to both low risk of infection and low vaccine efficacy (**Figure 4.6B**), but vaccination frequencies were mostly consistent at each level of vaccinated probability of infection despite the variations in starting confidence (**Figure 4.6D**).

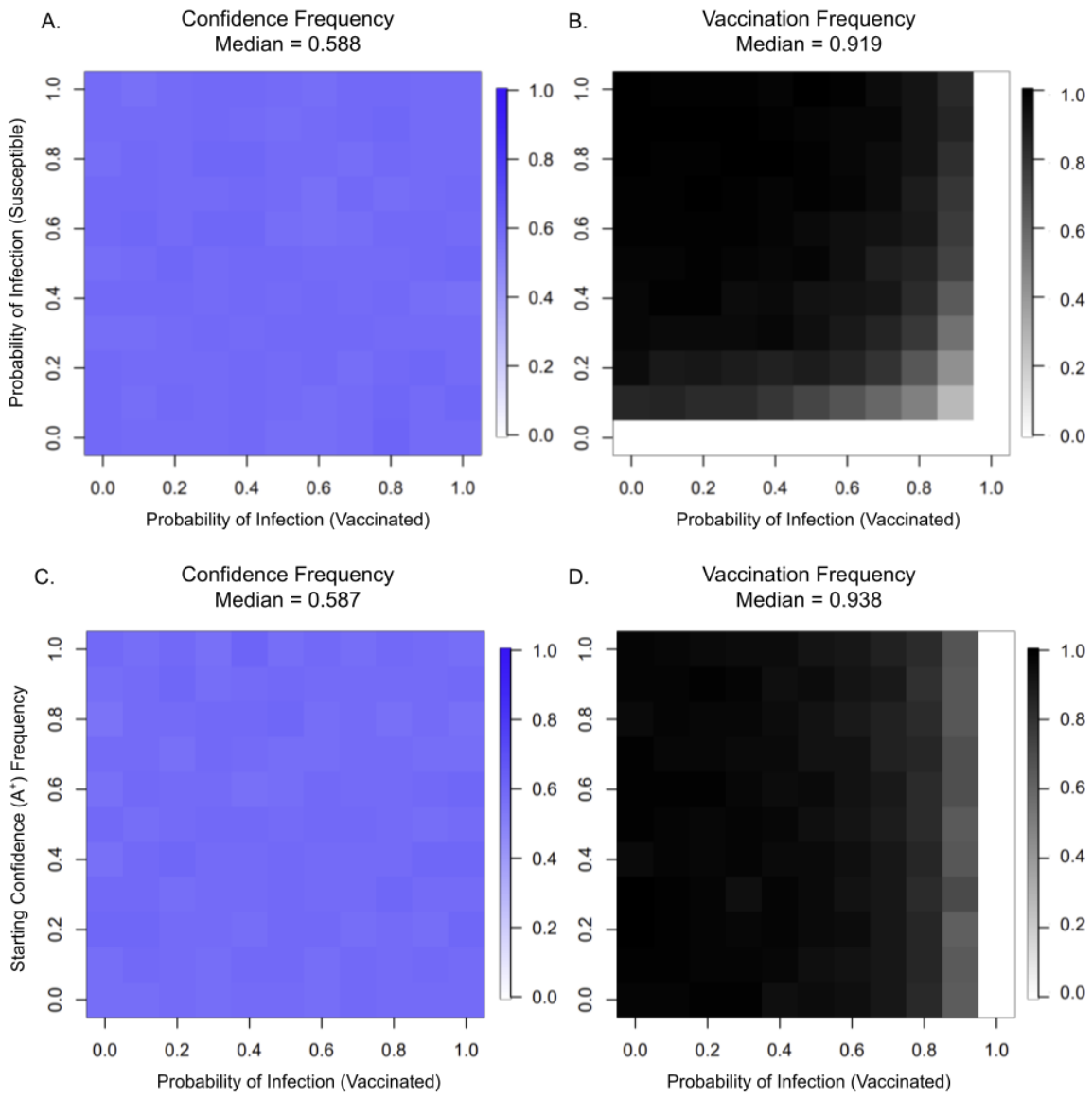

Figure 4.6: Confidence frequencies remain stable as vaccination uptake is affected by infection probabilities in a population with heterogeneous decision-making biases. Each heat map shows the average confidence frequency (in blue; **A, C**) and vaccination frequency (in black; **B, D**) at the final timestep (100) of 10 simulations at each of the conditions specified on the axes in a population with heterogeneous decision-making biases ($B^- = 0.40$, $B^0 = 0.20$, $B^+ = 0.40$). Panels **A** and **B** show the outputs at various susceptible infection probabilities (vertical axis) and vaccinated probability of infection (horizontal axis), and **(C, D)** show the outputs of varying the starting confidence frequencies in the population (vertical axis) and the probability of breakthrough infection for vaccinated individuals (horizontal axis). The median average frequency of each heat map is shown.

Similarly, in the homogeneously conformist population, there does not appear to be a pattern in final confidence level in response to variations in infection probabilities (**Figure 4.7A, C**). However, unlike in the heterogeneous population, confidence and vaccination frequencies in the homogeneously conformist population roughly mirror each other (**Figure 4.7**). This population also exhibits sensitivity to initial confidence frequencies in the population (**Figure 4.7C-D**). When initial confidence frequency in the homogeneous population is varied alongside breakthrough infection probability for vaccinated individuals, average confidence frequencies at 100 timesteps remain higher at higher initial frequencies and remain lower at lower initial frequencies (**Figure 4.7C, D**). In this population, vaccination patterns correspond to confidence patterns, i.e, vaccination frequencies are higher if confidence frequencies are higher and lower when the population is hesitant (**Figure 4.7C, D**).

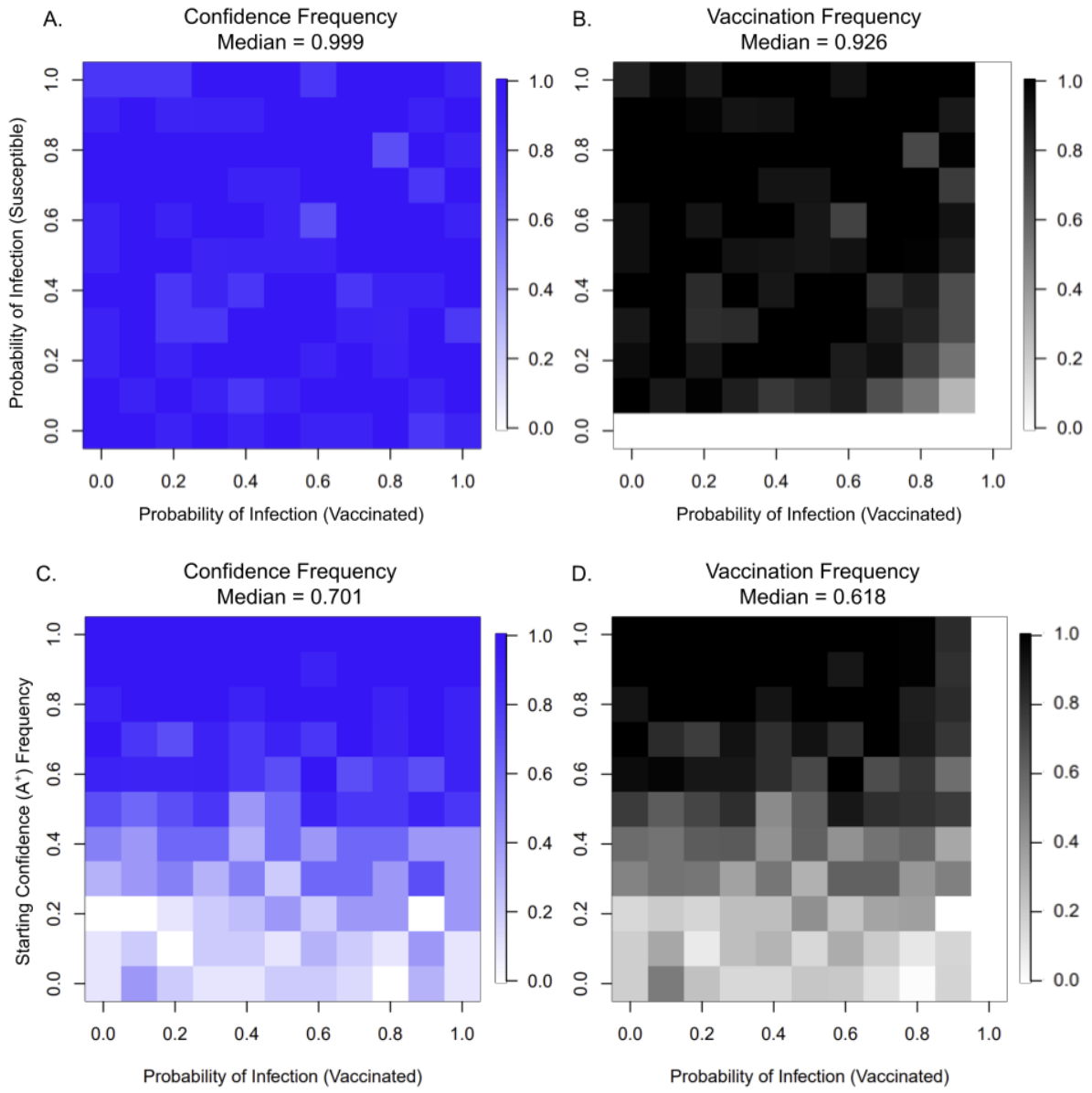

Figure 4.7: Confidence and Vaccination dynamics are sensitive to initial confidence in a homogeneously conformist population. Each heat map shows the average confidence (in blue; **A,C**) and vaccination (in black; **B, D**) frequency at the final timestep (100) of 10 simulations at each of the conditions specified on the axes in a homogeneously conformist population ($B^- = 0$, $B^0 = 0$, $B^+ = 1$). Panels **A** and **B** show the outputs at various susceptible infection probabilities (vertical axis) and probability of breakthrough infection for vaccinated individuals (horizontal axis), and panels **C** and **D** show the outputs of varying the starting confidence frequencies in the population (vertical axis) and the probability of infection for vaccinated individuals (horizontal axis). The median average frequency of each heat map is shown.

Discussion

As humans need to make many decisions each day, our conscious and subconscious minds use a variety of decision-making shortcuts (heuristics). These approaches are not without error and occasional irrational outcomes, and those shortcuts that can be predicted by the characteristics of a trait or the frequency of a trait in a population are often called cognitive or decision-making biases. Many theoretical studies have considered the effects of two frequency-dependent decision-making biases, namely conformist bias and anti-conformist bias, compared to random imitation (unbiased transmission) (Efferson et al. 2008; Denton et al. 2020; Walters and Kendal 2013; Grove 2019). Since they affect health-related decisions, it is important to understand how these decision-making biases may affect the adoption of novel health information and practices. Biases interact with the information provided by our social networks and a variety of other sources available to us. In fact, the vaccination characteristics of a parent's social network have been shown to be more predictive of parent vaccination decisions than their own vaccination characteristics (Brunson 2013a). The stochasticity created by these biases, especially when a population has heterogeneous biases, may also contribute to fluctuations in vaccination adoption rates and the lower-than-expected adoption of novel vaccines in otherwise highly vaccinated regions. In this study, we use an agent-based model to elucidate the effects of various decision-making biases on the adoption of a novel vaccine and the spread of vaccine confidence in a population.

Increasing the accessibility of accurate information about vaccines is one way of combating vaccine hesitancy (Dror et al. 2020; Jacobson, St Sauver, and Finney Rutten 2015). However, this type of approach might be less effective than expected due to the existence of anti-vaccination echo chambers—closed environments in which participants disproportionately encounter information, opinions, and beliefs that reflect and reinforce their preexisting beliefs (Diaz Ruiz and Nilsson 2023; Cinelli et al. 2021; C. T. Nguyen 2020), fueled in part by confirmation bias—the tendency to search for, interpret or remember information in a manner that confirms or supports one's existing beliefs (Nickerson 1998; Pohl 2004). The decreased vaccination and confidence frequencies in the presence of homophily likely represents an echo-chamber-like effect (**Figure 4.4**). If individuals are choosing to surround themselves with similar individuals and, at the same time, the probability of attitude transition is dependent on the attitudes of surrounding contacts, a small-scale social environment is created in which

vaccine-hesitant individuals are less likely to transition to confidence because there becomes limited exposure to individuals of the opposite attitude. As a result, the level of vaccine confidence and vaccination in a population in which individuals exhibit homophilic tendencies is lower than that in which social circles are randomly formed. This effect may also be amplified in a homogeneously conformist population, as vaccine-confident individuals who find themselves in majority hesitant circles are most likely to adopt the hesitant attitude (as opposed to if they were unbiased or anti-conformist).

We only explored the effects of frequency-dependent bias in our simulations, in so much as individual decision-making biases interact with vaccination and confidence frequencies to either drive or hinder vaccination behavior or attitude transition. However, the characteristics of cultural traits, the quality of information about those traits, and the "prestige" of the information source have all been shown to affect behavior adoption (Henrich 2001; Slater and Rouner 1996; L. L. Cavalli-Sforza and Feldman 1981; Henrich and Boyd 2002; Fogarty et al. 2017). One way in which we have accounted for the characteristics of the vaccine is via the vaccine-efficacy parameter. However, further development of the model could include, for example, a system that represents varying quality of vaccine information as vaccine frequencies increase, and/or varying prestige among agents and influencers, which would inform attitude transition probabilities.

Though the reach of the influencer is significant in this current model (30% and 40% of the population), the effect of the influencer on the outcome of the simulations is quite small (adding only 0.05 to an initially calculated probability of attitude transition of 0, such that the added effect is reduced as transition probability increases to prevent a probability of greater than 1. Incorporating more variation among agents' interactions with influencers, as well as variations in influencer effect, could reveal more interesting patterns of trait adoption and provide insight into the information–source–adoption structure surrounding health-related information.

An agent may find itself in a position that could result in possible cognitive dissonance, i.e., surrounded by mostly agents with the opposite attitude or only following a single influencer with the opposite belief. Some research suggests that being surrounded by conflicting beliefs might make individuals less likely to change their mind instead of more likely (Sharot et al. 2023). In the current framing of the model, an agent is not necessarily less inclined to adopt the opposite belief in environments in which the opposite belief is of higher frequency or presented by highly influential sources (unless anti-conformist). This creates another avenue of future

exploration with this model—the effects of cognitive dissonance. This observation also prompts the question, do social networks change to accommodate a counterintuitive response to opposing information? Are those who exhibit this obstinate response to conflicting information more or less likely to to use homophily when choosing social contacts or to have social networks of particular characteristics, for example in regards to size or distribution of beliefs?

Finally, this work prompts some larger questions about health decisions. In particular, when does a vaccine cease to be novel? Does its novelty depend on human consensus, chronological time that has passed since the introduction of the vaccine, or stability of vaccine adoption? Since vaccination beliefs and behaviors may differ between established and novel vaccines, knowing this point of transition is important to accurately modeling vaccine uptake. Overall, we predict complex short-term evolutionary dynamics when a novel vaccine is introduced to a population; these dynamics can be affected by the cultural transmission of ideas between connected individuals and from cultural influencers external to the population, but, importantly, they are meaningfully affected by the decision-making biases of individuals themselves.

CHAPTER 5. DISCUSSION

Mathematical models are essential tools in the public health toolkit. Historically, epidemiological mathematical models have primarily focused on the transmission of infectious agents, though more recently the importance of individual behaviors in predicting population-level emergent trends has become increasingly salient (Perra et al. 2011; Azizi et al. 2022). There is, however, still a need for understanding the cultural contexts driving changes in behaviors over time and the pace of these cultural evolutionary changes, both on an individual and population scale.

My dissertation work sought to expand the pool of mathematical models related to public health, particularly models that incorporate human behaviors, by integrating themes and techniques from the field of cultural evolution. Whereas behavior-change models generally examine changes in behavior within a population, cultural evolutionary theory allows behaviors to be tracked over multiple generations, which is particularly useful when examining diseases that can be prevented by childhood vaccines and thus involve inter-generational interactions. Also, the frameworks commonly employed by existing models often assume population homogeneity and rational decision making, which inaccurately characterize behavioral and belief dynamics that occur during times of uncertainty or when individuals are faced with unvetted information. Combining cultural evolutionary considerations with agent-based modeling approaches could better capture this stochasticity. Using both a discrete-time deterministic framework and agent-based modeling techniques, I mapped vaccine confidence and vaccination frequencies under various circumstances and considerations including the effects of intergenerational (vertical) and extra-parental (oblique) transmission (**Chapter 2** and **Chapter 3**), vaccination mandates and vaccine inaccessibility (**Chapter 3**), homophily and social network influences (**Chapters 2–Chapter 4**), perception of disease risk and vaccination benefit (**Chapter 2** and **Chapter 3**), and decision-making biases (**Chapter 4**). In **Chapter 2** and **Chapter 3,** I focus on childhood vaccination practices , then shift focus to self-vaccination with a novel vaccine in **Chapter 4**.

My work reveals that parental transmission of vaccine confidence drives vaccination in later generations, and preferential mate-choice (homophily) can shift population frequencies of vaccine confidence and vaccination coverage towards one extreme or the other. Cultural

selection (the overall deviation from the expected level of vaccination which can be linked to the public perception of the vaccine) is important for combatting the effects of high vaccine-hesitant homophily. I was able to model scenarios that resulted in intuitively "conflicting" outcomes: environments with vaccine mandates could produce high vaccination coverage with lower confidence frequencies, while environments with vaccine inaccessibility could produce lower vaccination coverage despite higher confidence frequencies. Finally, my model of novel vaccine adoption reveals that heterogeneity of decision-making biases in a population can differentially affect both vaccine confidence and vaccination frequencies.

As with any model, we cannot fully capture the complex interactions between beliefs, behaviors, and the environment that shape the public health landscape. Therefore, the models presented here have the necessary caveat of oversimplification. Simple models, however, are a good starting point to help researchers clarify and test assumptions about a complex system, including the effects of representing similar scenarios in multiple ways (Tedeschi 2006). Indeed, by modeling multiple interacting cultural processes, our model has the flexibility to explore the effects of altering trait dynamics through various mechanisms. For example, in **Chapter 3,** I modulated parameters that allowed parental beliefs to influence behaviors to simulate external forces affecting vaccination behaviors, focusing on vaccine exemption-seeking behavior and parental motivation to overcome barriers to vaccination; my rationale was that parents' beliefs would have less influence over their behaviors when external forces made vaccines less accessible or more compulsory. However, if I were to interpret, for example, barriers to vaccination as adding a greater cost to obtaining a vaccine (higher cultural selection against vaccination, which would result in fewer individuals vaccinated than expected), I could also modulate the cultural selection parameter to model the increasing or decreasing barriers to vaccinations. Both would result in a reduction in vaccination coverage, but via different means. Being able to model these differential effects is important especially in designing intervention strategies which can vary based on target population or healthcare intervention.

The models presented here provide a unique way of viewing vaccine belief-behavior interactions. Cultural evolutionary theory allows us to treat cultural traits as heritable, and the niche construction framework provides an avenue to explore how one cultural trait and another that affects its transmission are propagated in a population. The frameworks on which these models are based are generalizable, in that they can be used to model a variety of circumstances.

The model presented in **Chapter 2** and **Chapter 3** can be readily applied to scenarios in which the effects of a parental behavior are long-lasting and potentially influenced by beliefs. For example, other aspects of childrearing such as formula feeding, sleep training, circumcision, attachment parenting, and homeschooling could provide additional avenues of exploration with this type of model. Like vaccination, these decisions employ an assessment of social, cultural, and economic costs and benefits, both to parents and offspring. In the model discussed in **Chapter 4**, I consider, explicitly, the interplay of individual decision-making biases and external influences. This model is broadly applicable to the uptake and acceptance of novel healthcare technologies or healthcare strategies. Models like these are important to the advancement of public health, especially in an age in which technology and human interactions are quickly evolving.

Though not directly translatable to exact units of time, each model examines dynamics over varying durations. The first model structure (discussed in **Chapters 2** and **Chapter 3**) examines long-term and inter-generational dynamics. This model covers mate pairing, reproduction, and reassessing one's own beliefs during adulthood, where one iteration could be interpreted as a generation, though this interpretation is somewhat complicated by the non-overlapping generations in the model compared to overlapping generations in human populations. This type of intergenerational model is useful in understanding broadly how, for example, present conditions might shape the future, or how group characteristics change or maintain a cultural environment. The second model (discussed in **Chapter 4**), examines the effects of short-term belief and behavior dynamics within a single interconnected population. Multiple within-generation events are considered in the second model—disease transmission and recovery, social restructuring, and rapid decision-making, which may occur on a scale from days to months. This type of agent-based model is useful for understanding emergent events, and quickly identifying points of intervention for behavior modification in a heterogeneous population. These models and their foci are best considered jointly, as short-term dynamics and individual behaviors shape the present landscape from which future dynamics can be inferred. My model describing long-term dynamics (**Chapter 2** and **Chapter 3**) includes a community-influence stage in which the beliefs of adult offspring may change. This belief-transition stage is more detailed in the short-term model (**Chapter 4**), which outlines explicitly various factors that could play a role in this process. There is potential in nesting these

models to examine, perhaps, how self-vaccination practices in adulthood might affect parental childhood vaccination behavior.

Since models represent a distillation of complex processes, the representation of population heterogeneity in these models is by necessity simplified. Real populations contain a number of interacting subpopulations, each with varying characteristics that may differentially affect healthcare perceptions and disease transmission (Demongeot et al. 2022; G. Webb 2021; Reluga 2009; Thompson and Duintjer Tebbens 2017). Demographic factors shown to impact vaccination include age and gender (Babad et al. 1995; Bhattacharyya and Ferrari 2017; Edmunds et al. 2000; Ferrari, Grenfell, and Strebel 2013; Gay et al. 1995; Prada et al. 2017; Trentini et al. 2017; Magpantay, King, and Rohani 2019; Zintel et al. 2022; Hebert et al. 2005; Momplaisir et al. 2021). The effect of age on preventative health behaviors, including vaccination, is multifaceted as it may be associated with differences in adherence to tradition, values, or subjective social status; with differential risk of severe disease, which may affect the perceived vaccination value; with risk aversion, which could affect exposure to infection; and with homophily, which affects information source and belief mutability (Deeks et al. 2009; Rolison et al. 2013; Lim et al. 2019; Amarie et al. 2020; Ferrini, Edelstein, and Barrettconnor 1994; Burbank, Padula, and Nigg 2013). One hallmark of vaccination culture is experience of the vaccine-preventable disease (Dubé et al. 2013). Multiple studies have reported increased vaccine hesitancy in younger age groups (e.g. age 18-24) (Khan, Watanapongvanich, and Kadoya 2021; Lazarus et al. 2021). Today's older generations may have experienced epidemics and pandemics that younger generations have not; for example, the polio vaccine was released in 1955, serious influenza pandemics occurred in 1957 and 1968, and smallpox was eradicated in 1980 (Kayser and Ramzan 2021; J. Salk and Salk 1977). Thus, it is plausible that these age groups might perceive the risks of a current pandemic differently, thus leading to differential behaviors.

Though not tested in this work, the first model (**Chapter 2** and **Chapter 3**) has the built-in capacity to account for gender-biased transmission. The results presented in this thesis use transmission parameter settings that do not distinguish between parents, thus making the assumption that there is no difference in cultural transmission between mother and father, which is in line with a survey-based study in Italy that found most parents (~80%) reported contributing equally when deciding whether to vaccinate their child (Bertoncello et al. 2020). However, a study that more directly considered parental attitudes concluded that “mothers’, but not fathers’,

vaccine confidence predicted children's vaccination status" (Lee, Overall, and Sibley 2020), which we could readily represent in our model by relaxing the assumption that $c_1 = c_2$ (**Chapter 2**). In the agent-based model, I would account for the effects of gender and age on self-vaccination by assigning these characteristics to each agent, and having them affect vaccine adoption probabilities. Inconsistencies exist among empirical self-vaccination studies as well, with various studies reporting that women were more reluctant to get the COVID-19 vaccine than men, that men were more reluctant than women, and that both men and women had similar probabilities of adopting or rejecting the vaccine (Lazarus et al. 2021; Nery et al. 2022; Moore et al. 2021; Wu et al. 2021; Troiano and Nardi 2021; Zintel et al. 2022; Robertson et al. 2021). Similar inconsistencies in gender-biased vaccine hesitancy have been reported for influenza (lower uptake in women (Jiménez-García et al. 2010) vs. higher uptake in women (Applewhite et al. 2020)).

While representing different probabilities of cultural transmission from mothers and fathers is straightforward to implement in a cultural niche construction model, this model is quite limited in the types of family structures that can be represented. Given its basis in theoretical population genetics, structures with two primary parents (or parental decision-makers) can be easily represented, whereas representing single parent-households (household with a single parental decision-maker) may mean removing parameters unique to this type of model (e.g assortative mating frequencies), or specifying transmission probabilities for single phenotypes as well as paired phenotypes. Though we account for the effects of oblique influences (extra-parental) on attitude transition in adulthood, we did not explicitly account for oblique influences in the household or oblique influences on primary parent decisions, for example those that would exist within multigenerational or households or families with more than two parental figures. Modeling this dynamic, however, could be done similarly to my second model, in which an individual's cultural influences were spatially structured instead of generationally structured, by adding a function that scales vaccination probability based on the characteristics of influencing contacts, such as their attitudes and how much influence they have on the agent.

Cultural transmission probabilities, transition probabilities, and bias distribution in a population, were informed using empirical data whenever possible. However, much of these real-world data were limited, and thus our models are primarily based on theoretical assumptions. In the first model, we treat vaccination and vaccine attitude similarly to genetically

inherited traits; however, unlike genetic traits, which have predictable rates of transmission, cultural traits can deviate from Mendelian-like predictions of inheritance. For example, it is possible for offspring to be more likely to reject a cultural trait if both parents possess it—a form of intergenerational "rebellion" (Feldman and Cavalli-Sforza 1976). Specifically for the second model, it is difficult to parameterize the decision-making biases of a population based on real-world data since it is challenging to identify and thus quantify these decision-making biases. In real examples of cultural traits, decision-making biases that influence the adoption of a trait are likely to differ based on the type of trait being studied (Acerbi and Bentley 2014). Further, some beliefs, behaviors, and dispositions have varying rates of change depending on the perceived benefit provided to each individual within a specific environment. For example, religious beliefs might provide benefits to some because of the stress relief and social acceptance these beliefs provide (Sharot et al. 2023; Charlesworth and Banaji 2022; Kahneman, Slovic, and Tversky 1982). Also, religious beliefs might be more likely to show conformist-biased cultural transmission than, say, fashion decisions (Acerbi, Ghirlanda, and Enquist 2012)he 2019 SARs-Cov-2 pandemic sparked renewed interest in vaccine hesitancy, and vaccination data collection has begun to include various psychosocial components, for example the effect of social influences, measurements of the rates at which individuals change their minds, and vaccination intention (Meng et al. 2023; Perrin 2020). As these datasets become available, the compiled psychosocial information would be useful to more accurately fit transition probability functions and set transmission parameter values for both models.

In conclusion, the relationship between human health-related beliefs and behaviors is complex and modulated by various internal and external influences. Cultural evolution techniques and considerations assist us in gaining greater insight into these complexities. Improving and securing public health relies on acknowledging what we can and cannot change in regards to human behavior and reasoning, understanding how the things that *can* change actually *do* change over time, and knowing how to work within those confines. The work presented here should influence future models to incorporate changes in behaviors alongside epidemiological processes to better understand and improve public health.

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Supplementary Text

Text S2.1: Recursions for Vaccine Niche Construction

$$\bar{w}x_1' = (1+\sigma_1)\big(m_{11}B_{3,3}C_3 + m_{12}B_{3,2}C_2 + m_{21}B_{3,1}C_1 + m_{13}B_{2,3}C_3 + m_{31}B_{1,3}C_3 + m_{14}B_{2,2}C_2 + m_{41}B_{1,1}C_1 + m_{22}B_{3,0}C_0 + m_{23}B_{2,1}C_1 + m_{32}B_{1,2}C_2 + m_{24}B_{2,0}C_0 + m_{42}B_{1,0}C_0 + m_{33}B_{0,3}C_3 + m_{34}B_{0,2}C_2 + m_{43}B_{0,1}C_1 + m_{44}B_{0,0}C_0\big)$$

$$\bar{w}x_2' = (1+\sigma_1)\big(m_{11}B_{3,3}(1-C_3) + m_{12}B_{3,2}(1-C_2) + m_{21}B_{3,1}(1-C_1) + m_{13}B_{2,3}(1-C_3) + m_{31}B_{1,3}(1-C_3) + m_{14}B_{2,2}(1-C_2) + m_{41}B_{1,1}(1-C_1) + m_{22}B_{3,0}(1-C_0) + m_{23}B_{2,1}(1-C_1) + m_{32}B_{1,2}(1-C_2) + m_{24}B_{2,0}(1-C_0) + m_{42}B_{1,0}(1-C_0) + m_{33}B_{0,3}(1-C_3) + m_{34}B_{0,2}(1-C_2) + m_{43}B_{0,1}(1-C_1) + m_{44}B_{0,0}(1-C_0)\big)$$

$$\bar{w}x_3' = \big(m_{11}(1-B_{3,3})C_3 + m_{12}(1-B_{3,2})C_2 + m_{21}(1-B_{3,1})C_1 + m_{13}(1-B_{2,3})C_3 + m_{31}(1-B_{1,3})C_3 + m_{14}(1-B_{2,2})C_2 + m_{41}(1-B_{1,1})C_1 + m_{22}(1-B_{3,0})C_0 + m_{23}(1-B_{2,1})C_1 + m_{32}(1-B_{1,2})C_2 + m_{24}(1-B_{2,0})C_0 + m_{42}(1-B_{1,0})C_0 + m_{33}(1-B_{0,3})C_3 + m_{34}(1-B_{0,2})C_2 + m_{43}(1-B_{0,1})C_1 + m_{44}(1-B_{0,0})C_0\big)$$

$$\bar{w}x_4' = \big(m_{11}(1-B_{3,3})(1-C_3) + m_{12}(1-B_{3,2})(1-C_2) + m_{21}(1-B_{3,1})(1-C_1) + m_{13}(1-B_{2,3})(1-C_3) + m_{31}(1-B_{1,3})(1-C_3) + m_{14}(1-B_{2,2})(1-C_2) + m_{41}(1-B_{1,1})(1-C_1) + m_{22}(1-B_{3,0})(1-C_0) + m_{23}(1-B_{2,1})(1-C_1) + m_{32}(1-B_{1,2})(1-C_2) + m_{24}(1-B_{2,0})(1-C_0) + m_{42}(1-B_{1,0})(1-C_0) + m_{33}(1-B_{0,3})(1-C_3) + m_{34}(1-B_{0,2})(1-C_2) + m_{43}(1-B_{0,1})(1-C_1) + m_{44}(1-B_{0,0})(1-C_0)\big)$$

Text S3.1: Detailed Methods

Here, we expand on the model proposed in Chapter 2. We consider two cultural traits: a vaccination trait (**V**), and a vaccine attitude trait (**A**). Each individual can take one of two possible states for each trait, V^+ (vaccinated) or V^- (unvaccinated) and A^+ (vaccine confident) or A^- (vaccine hesitant), respectively. This results in four possible phenotypes: V^+A^+ (type 1: vaccinated and confident), V^+A^- (type 2: vaccinated and hesitant), V^-A^+ (type 3: unvaccinated and confident), and V^-A^- (type 4: unvaccinated and hesitant), whose frequencies in the population are denoted by x_1, x_2, x_3, and x_4, respectively, with $\sum_{i=1}^{4} x_i = 1$. (See **Table 2.2** for subscript assignments).

The four phenotypes described produce sixteen possible mating pairs. The mating frequency, $m_{i,j}$ indicates the frequency of a mating between a parent of type i and the second parent of type j where $i, j = \{1, 2, 3, 4\}$ (**Table 2.2**); for example, $m_{1,3}$ represents the mating frequency of V^+A^+ (x_1) and V^-A^+ (x_3). In this manuscript, we assume random mating, therefore individuals of different phenotypes mate with one another at a rate equal to the product of their frequencies.

Since the two traits (**A** and **V**) are transmitted vertically, for each phenotype we specify the probability that the mating produces an offspring of phenotype (V^+A^+). The vaccine confidence trait (A^+) is transmitted with probability C_n, and the vaccine hesitancy trait (A^-) is transmitted with probability $1-C_n$ (for $n = \{0, 1, 2, 3\}$ as shown in **Table S2.2**). If $C_0 = 0$, two A^- parents will always produce A^- offspring, and if $C_3 = 1$, two A^+ parents will always produce A^+ offspring. However, if $C_0 > 0$, two A^- parents can produce A^+ offspring at some probability, and similarly if $C_3 < 1$, two A^+ parents can produce A^- offspring with some probability.

Transmission of vaccination (V^+ with probability $B_{m,n}$ for $m, n = \{0, 1, 2, 3\}$; **Table S2.2**) is more complex, since parents' vaccine attitudes (**A**), in addition to their own vaccination states (**V**), can influence their behavior in vaccinating their offspring via a set of "influence parameters" that inform vaccination probabilities. The probability that each mating pair produces an offspring with the V^+ trait (i.e. vaccinates their offspring) is a scaled product of the influence of parental attitudes (c_n for $n = \{0, 1, 2, 3\}$) and the influence of parental vaccination states (b_m for $m = \{0, 1, 2, 3\}$) (**Table S2.2**). For example, for mating pair $V^+A^+ \times V^+A^-$, their combined vaccination states ($V^+ \times V^+$) will influence vaccination behavior by b_3, and their combined

attitude states, ($A^+ \times A^-$), will influence vaccination behavior by c_2. Therefore, a $V^+A^+ \times V^+A^-$ mating will produce a V^+ offspring with probability $B_{3,2} = c_2\left(\frac{1+b_3}{2}\right)$; this pair will also produce an A^+ offspring with probability C_2 based on their combined attitude states.

Transmission and influence probabilities are constant throughout a single simulation, with values ranging from 0 to 1. At baseline settings, the influence parameters b_m and c_n, and the transmission parameter C_n would take the values indicated in **Table 3.1**. In our model, vaccination probabilities are structured such that a couple's vaccine beliefs have a greater influence (c_n) on their likelihood of vaccinating their offspring than their own vaccination status (b_n). Therefore, offspring vaccination is guaranteed at some probability only if $c_n > 0$. We implement vaccine mandates and vaccine inaccessibility by modulating the influence of vaccine attitudes (c_n). We increase the influence parameter values of couples with at least one vaccine hesitant individual (c_0: $A^- \times A^-$, c_1: $A^- \times A^+$, c_2: $A^+ \times A^-$) to model a vaccine mandates or decreasing influence parameter values of couples with at least one vaccine confident individual (c_3: $A^+ \times A^+$, c_2: $A^+ \times A^-$, c_1: $A^- \times A^+$) to model vaccine inaccessibility. In other words, a vaccine mandate will make a vaccine-hesitant parent more likely to vaccinate their child, and vaccine inaccessibility will make a vaccine-confident parent less likely to vaccinate their child.

The cultural selection on vaccination is given by the parameter σ. After vertical cultural transmission has occurred, the frequency of the V^+A^+ and V^+A^- phenotypes are multiplied by 1+σ. This parameter modulates whether there are more or fewer vaccinated individuals than expected: in other words, when σ>0, vaccinated individuals are more common in a set of offspring than would be expected strictly by parental beliefs and vaccination statuses. This cultural selection coefficient is structured to encompass both biological fitness and cultural selection pressures, including perceived risks or benefits of the vaccine itself, personal cost-benefit analyses of preventative health behaviors, and the structural or societal-level factors influencing vaccination rates (Pruitt, Kline, and Kovaz 1995; L. L. Cavalli-Sforza and Feldman 1981). Under the assumption that effects of herd immunity may lead to a reduction in vaccination behaviors—for example, the belief that vaccines are unnecessary when most others are vaccinated (Omer et al. 2009)—the cultural selection coefficient function in our model is vaccine-frequency-dependent. We calculate σ in each timestep as a function of the current vaccination coverage (frequency of V^+, i.e. $x_1 + x_2$), and in each simulation we specify σ_{max} as the

maximum cultural selection pressure for getting vaccinated ($-1 \leq \sigma_{max} \leq 1$) (see the cultural selection coefficient function in **Figure 2.1**). To incorporate this relationship into the model, we constructed a function by defining our assumptions (incorporating evolutionary game theory, e.g. the "free rider" problem) and then choosing curves with a trajectories that met pre-specified conditions: with unvaccinated individuals holding baseline fitness at 0, we assume that when vaccination coverage is low, the real and perceived benefits of vaccination are highest, and thus, the cultural selection pressure is near σ_{max}, however, as vaccination coverage increases toward the level of herd immunity, the perceived benefits of vaccination decrease, represented as a reduction in the cultural selection pressure (Bauch and Bhattacharyya 2012).

The model incorporates a second phase with oblique cultural transmission (i.e. influence from non-parental adults), in which individuals can change their inherited vaccine attitudes (**A**) due to influence from other adults in the population. There are two probabilities associated with attitude modulation: the probability that an vaccine hesitant (A^-) individual adopts the vaccine confident (A^+) state (A^- to A^+ transition probability, given by $A_{\rightarrow Confident}$ in **Figure 2.2**), and the probability that an A^+ individual adopts the A^- state (A^+ to A^- transition probability, given by $A_{\rightarrow Hesitant}$ in **Figure 2.2**). As with the strength of cultural selection (σ) described previously, the probability that offspring change their vaccine attitude is a function of the V^+ frequency in the population. As the frequency of vaccinated individuals (V^+) increases in the population, vaccine-confident individuals (A^+) are more likely to become hesitant ($A_{\rightarrow Hesitant}$ probability increases) and vaccine-hesitant individuals (A^-) are less likely to become confident ($A_{\rightarrow Confident}$ probability decreases). Similarly to the cultural selection function, the belief transition functions were generated by first choosing a function with a shape that aligned with our general assumptions and then modifying the function to fit specific criteria: 1) probabilities could approach zero, but not equal zero, 2) transition to supporting belief and transition to opposing belief are equally likely at 50% vaccination frequency, and, 3) that high vaccination frequencies (e.g. above herd-immunity levels of vaccination coverage) promote the transition to vaccine hesitancy (Jacobson, St Sauver, and Finney Rutten 2015; Kennedy, Brown, and Gust 2005). The upper bound for the belief transition functions were set by calculating the percent difference between vaccine refusal rates in 1991 and 2004 in the United States to estimate transition probabilities between 1–2% (Omer et al. 2009). By modulating the attitude transition

probabilities according to the vaccination coverage in this manner, we assume that when vaccine coverage (V^+ frequency, $x_1 + x_2$) is low, disease occurrence is high and the negative effects of the disease are experienced widely, thus the benefits of being vaccinated (and the costs of not being vaccinated) are more evident (Gangarosa et al. 1998; Ozawa et al. 2012). As vaccination coverage (V^+) increases in the population, and thus disease occurrence is low, the benefits to being vaccinated are less obvious, while low-probability costs such as adverse reactions become more apparent and could be perceived as being riskier than the disease itself. Modulating both the attitude transition probabilities and the cultural selection coefficient according to the level of vaccination coverage in a population reflects that perceptions about the vaccine and its associated effects on health could be meaningfully different in a population with high vaccination coverage than in one with low coverage.

To compute the frequency of a given phenotype in the next iteration, we sum the probability that each mating pair produces offspring of that phenotype over each of the sixteen possible mating pairs. Cultural selection (σ), described above, then operates on offspring with the V^+ trait. At the end of each timestep, the frequency of each phenotype is divided by the sum of all four frequencies, ensuring that the frequencies sum to 1. The full recursions, giving x_i' phenotype frequencies in the next iteration in terms of x_i in the current iteration, are given in **Supplementary Text S2.1**. If x_i' is equal to x_i, the system is at equilibrium. Unless otherwise stated, the model is initialized with phenotypic frequencies structured to represent those of the United States: x_1 (frequency of V^+A^+) = 0.81, x_2 (V^+A^-) = 0.1, x_3 (V^-A^+) = 0.07, x_4 (V^-A^-) = 0.02. These frequencies were estimated using reports of Measles-Mumps-Rubella (MMR) vaccination rates and estimates of vaccine attitude frequencies obtained from various sources in the literature (Kennedy, Brown, and Gust 2005; Leask 2011) and the Centers of Disease Control ChildVax database (Hill et al. 2019, 2017).

Supplementary Tables

Table S2.1. Mating frequencies for all possible matings.
In this model, α_1 is the rate of assortment if the choosing parent is A^+, and α_2 is the rate of assortment if the choosing parent is A^-. The choosing parent is listed first for each mating. On the right side of the equations, the first term represents the frequency of random matings and the second term the frequency of assortative matings.

♂ × ♀	Mating Frequency	♂ × ♀	Mating Frequency
$V^+A^+ \times V^+A^+$	$m_{1,1} = x_1^2(1-\alpha_1) + \frac{\alpha_1 x_1^2}{(x_1+x_3)}$	$V^-A^+ \times V^+A^+$	$m_{3,1} = x_3x_1(1-\alpha_1) + \frac{\alpha_1 x_3 x_1}{(x_1+x_3)}$
$V^+A^+ \times V^+A^-$	$m_{1,2} = x_1x_2(1-\alpha_1)$	$V^-A^+ \times V^+A^-$	$m_{3,2} = x_3x_2(1-\alpha_1)$
$V^+A^+ \times V^-A^+$	$m_{1,3} = x_1x_3(1-\alpha_1) + \frac{\alpha_1 x_1 x_3}{(x_1+x_3)}$	$V^-A^+ \times V^-A^+$	$m_{3,3} = x_3^2(1-\alpha_1) + \frac{\alpha_1 x_3^2}{(x_1+x_3)}$
$V^+A^+ \times V^-A^-$	$m_{1,4} = x_1x_4(1-\alpha_1)$	$V^-A^+ \times V^-A^-$	$m_{3,4} = x_3x_4(1-\alpha_1)$
$V^+A^- \times V^+A^+$	$m_{2,1} = x_2x_1(1-\alpha_2)$	$V^-A^- \times V^+A^+$	$m_{4,1} = x_4x_1(1-\alpha_2)$
$V^+A^- \times V^+A^-$	$m_{2,2} = x_2^2(1-\alpha_2) + \frac{\alpha_2 x_2^2}{(x_2+x_4)}$	$V^-A^- \times V^+A^-$	$m_{4,2} = x_4x_2(1-\alpha_2) + \frac{\alpha_2 x_4 x_2}{(x_2+x_4)}$
$V^+A^- \times V^-A^+$	$m_{2,3} = x_2x_3(1-\alpha_2)$	$V^-A^- \times V^-A^+$	$m_{4,3} = x_4x_3(1-\alpha_2)$
$V^+A^- \times V^-A^-$	$m_{2,4} = x_2x_4(1-\alpha_2) + \frac{\alpha_2 x_2 x_4}{(x_2+x_4)}$	$V^-A^- \times V^-A^-$	$m_{4,4} = x_4^2(1-\alpha_2) + \frac{\alpha_2 x_4^2}{(x_2+x_4)}$

Table S2.2: Probabilities of trait transmission to offspring from cultural trait pairings. For each mating, the probability of transmitting each trait, and corresponding influence parameters, are given. The probability of vaccinating an offspring, $B_{m,n}$, depends on both the parents' vaccination state (V^+: vaccinated; V^-: unvaccinated) and their belief state (A^+: vaccine confident; A^-: vaccine hesitant). $B_{m,n}$ is informed by the influence parameter b_m that corresponds to the parents' **V** states and the influence parameter c_n that correspond to their **A** states. For each parental pairing, the probability of not vaccinating an offspring is $1 - B_{m,n}$. Each pairing transmits confidence in vaccines at a rate C_n, and hesitancy at rate $1 - C_n$. The parameters b_m, c_n, and C_n are set as constants for each simulation, and $B_{m,n}$ is calculated from these.

	Trait Transmission Probabilities				**Influence of parental vaccination and attitudes on offspring vaccination**	
Mating pair	**Offspring vaccination (V^+) probability**	**V^- offspring probability**	**A^+ offspring probability**	**A^- offspring probability**	**V influence (m)**	**A influence (n)**
$V^+A^+ \times V^+A^+$	$B_{m=3,n=3} = c_3\left(\frac{1+b_3}{2}\right)$	$1 - B_{3,3}$	C_3	$1 - C_3$	b_3	c_3
$V^+A^+ \times V^+A^-$	$B_{3,2} = c_2\left(\frac{1+b_3}{2}\right)$	$1 - B_{3,2}$	C_2	$1 - C_2$	b_3	c_2
$V^+A^- \times V^+A^+$	$B_{3,1} = c_1\left(\frac{1+b_3}{2}\right)$	$1 - B_{3,1}$	C_1	$1 - C_1$	b_3	c_1
$V^+A^- \times V^+A^-$	$B_{3,0} = c_0\left(\frac{1+b_3}{2}\right)$	$1 - B_{3,0}$	C_0	$1 - C_0$	b_3	c_0
$V^+A^+ \times V^-A^+$	$B_{2,3} = c_3\left(\frac{1+b_2}{2}\right)$	$1 - B_{2,3}$	C_3	$1 - C_3$	b_2	c_3
$V^+A^+ \times V^-A^-$	$B_{2,2} = c_2\left(\frac{1+b_2}{2}\right)$	$1 - B_{2,2}$	C_2	$1 - C_2$	b_2	c_2
$V^+A^- \times V^-A^+$	$B_{2,1} = c_1\left(\frac{1+b_2}{2}\right)$	$1 - B_{2,1}$	C_1	$1 - C_1$	b_2	c_1
$V^+A^- \times V^-A^-$	$B_{2,0} = c_0\left(\frac{1+b_2}{2}\right)$	$1 - B_{2,0}$	C_0	$1 - C_0$	b_2	c_0
$V^-A^+ \times V^+A^+$	$B_{1,3} = c_3\left(\frac{1+b_1}{2}\right)$	$1 - B_{1,3}$	C_3	$1 - C_3$	b_1	c_3
$V^-A^+ \times V^+A^-$	$B_{1,2} = c_2\left(\frac{1+b_1}{2}\right)$	$1 - B_{1,2}$	C_2	$1 - C_2$	b_1	c_2
$V^-A^- \times V^+A^+$	$B_{1,1} = c_1\left(\frac{1+b_1}{2}\right)$	$1 - B_{1,1}$	C_1	$1 - C_1$	b_1	c_1
$V^-A^- \times V^+A^-$	$B_{1,0} = c_0\left(\frac{1+b_1}{2}\right)$	$1 - B_{1,0}$	C_0	$1 - C_0$	b_1	c_0
$V^-A^+ \times V^-A^+$	$B_{0,3} = c_3\left(\frac{1+b_0}{2}\right)$	$1 - B_{0,3}$	C_3	$1 - C_3$	b_0	c_3
$V^-A^+ \times V^-A^-$	$B_{0,2} = c_2\left(\frac{1+b_0}{2}\right)$	$1 - B_{0,2}$	C_2	$1 - C_2$	b_0	c_2
$V^-A^- \times V^-A^+$	$B_{0,1} = c_1\left(\frac{1+b_0}{2}\right)$	$1 - B_{0,1}$	C_1	$1 - C_1$	b_0	c_1
$V^-A^- \times V^-A^-$	$B_{0,0} = c_0\left(\frac{1+b_0}{2}\right)$	$1 - B_{0,0}$	C_0	$1 - C_0$	b_0	c_0

Table S2.3: Probability range assignments for Figure 2.5
To vary the range of $B_{m,n}$ used in a given simulation, each probability was grouped according to default vaccination probability calculations. All probabilities in a group hold the value assigned to that group in the range, as shown. C_n probabilities were assigned values as shown, with C_0 taking the lowest value in the range and C_3 taking the highest. The lowest probability range group is given as an example of value assignment.

	Range: Low → High					
Parameters	$B_{0,0}$, $B_{1,0}$, $B_{2,0}$, $B_{3,0}$	$B_{0,1}$, $B_{0,2}$	$B_{1,1}$, $B_{1,2}$, $B_{2,1}$, $B_{2,2}$	$B_{3,1}$, $B_{3,2}$, $B_{0,3}$	$B_{2,3}$, $B_{1,3}$	$B_{3,3}$
Example value (range 0–0.49)	0	0.09	0.19	0.29	0.39	0.49

	Low → High			
Parameters	C_0	C_1	C_2	C_3
Example value (range 0.1–0.4)	0.1	0.2	0.3	0.4

Table S3.1: Quantitative differences between equilibrium frequencies with low transmission of vaccine confidence

The mean and median of vaccination coverage and vaccine confidence levels at equilibrium were calculated for the section of the heatmaps in **Figure 3.2** for which $C_1 = C_2 < 0.5$ (blue in vaccination coverage heatmaps; red in the confidence level heatmaps).

Vaccination Coverage below $C_1 = C_2 < 0.5$	**No Mandate**	**Lenient Mandate**	**Vaccine Inaccessible**
Mean	9.031%	27.723%	5.032%
Median	4.047%	25.872%	2.578%
Confidence Levels below $C_1 = C_2 < 0.5$			
Mean	10.875%	9.092%	9.927%
Median	5.262%	5.115%	5.178%

Supplementary Figures

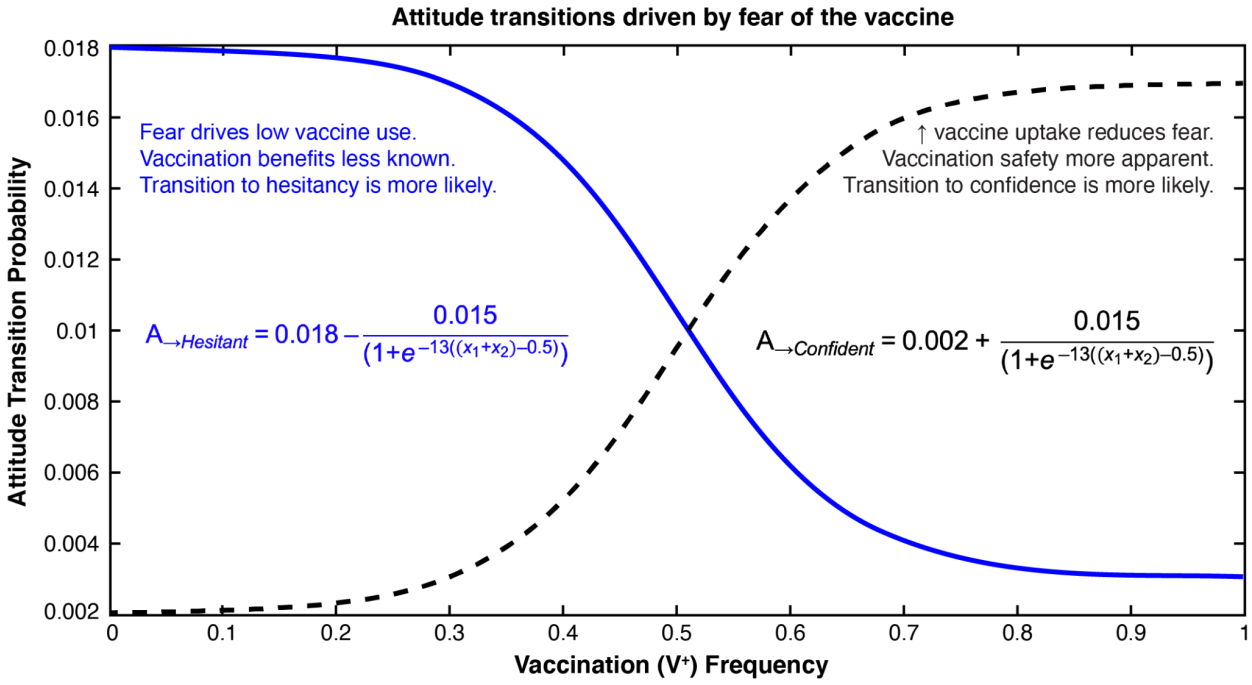

Figure S2.1: Vaccine-fear-driven attitude transition probability. Attitude transition probability (vertical axis) is a function of the vaccination frequency in the population (V^+; horizontal axis). Fear-driven hesitancy assumptions outlined on the graph: increased vaccine uptake reduces vaccine fear, thus increasing the likelihood of adopting vaccine confidence. The probability that a vaccine hesitant individual adopts vaccine confidence (A^- to A^+ transition probability, shown in dashed black) is determined by the function $A_{\rightarrow Confident}$, and the probability that a vaccine confident individual adopts vaccine hesitancy (A^+ to A^- transition probability, shown with a solid blue line) is determined by the function $A_{\rightarrow Hesitant}$. .

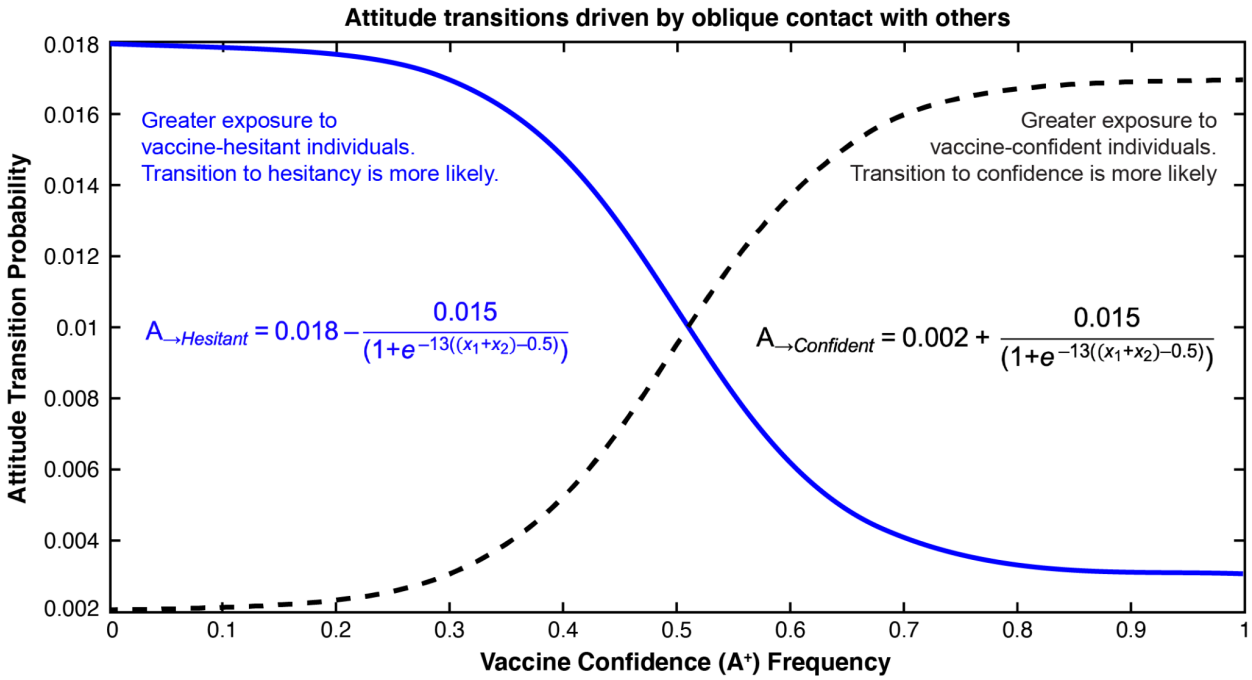

Figure S2.2: Confidence-frequency-dependent attitude transition probability function (obliquely transmitted hesitancy). We used the same equations as the belief transition functions in **Figure 2.2** to construct the confidence-frequency-dependent belief transition schema. Transition probabilities were redefined according to different assumptions outlined on the graph: Individuals are more likely to adopt the majority attitude. Attitude transition probability (vertical axis) is a function of the confidence frequency in the population (A^+; horizontal axis). The probability that a vaccine hesitant individual adopts vaccine confidence (A^- to A^+ transition probability, shown in dashed black) is determined by the function $A_{\rightarrow Confident}$, and the probability that a vaccine confident individual adopts vaccine hesitancy (A^+ to A^- transition probability, shown with a solid blue line) is determined by the function $A_{\rightarrow Hesitant}$.

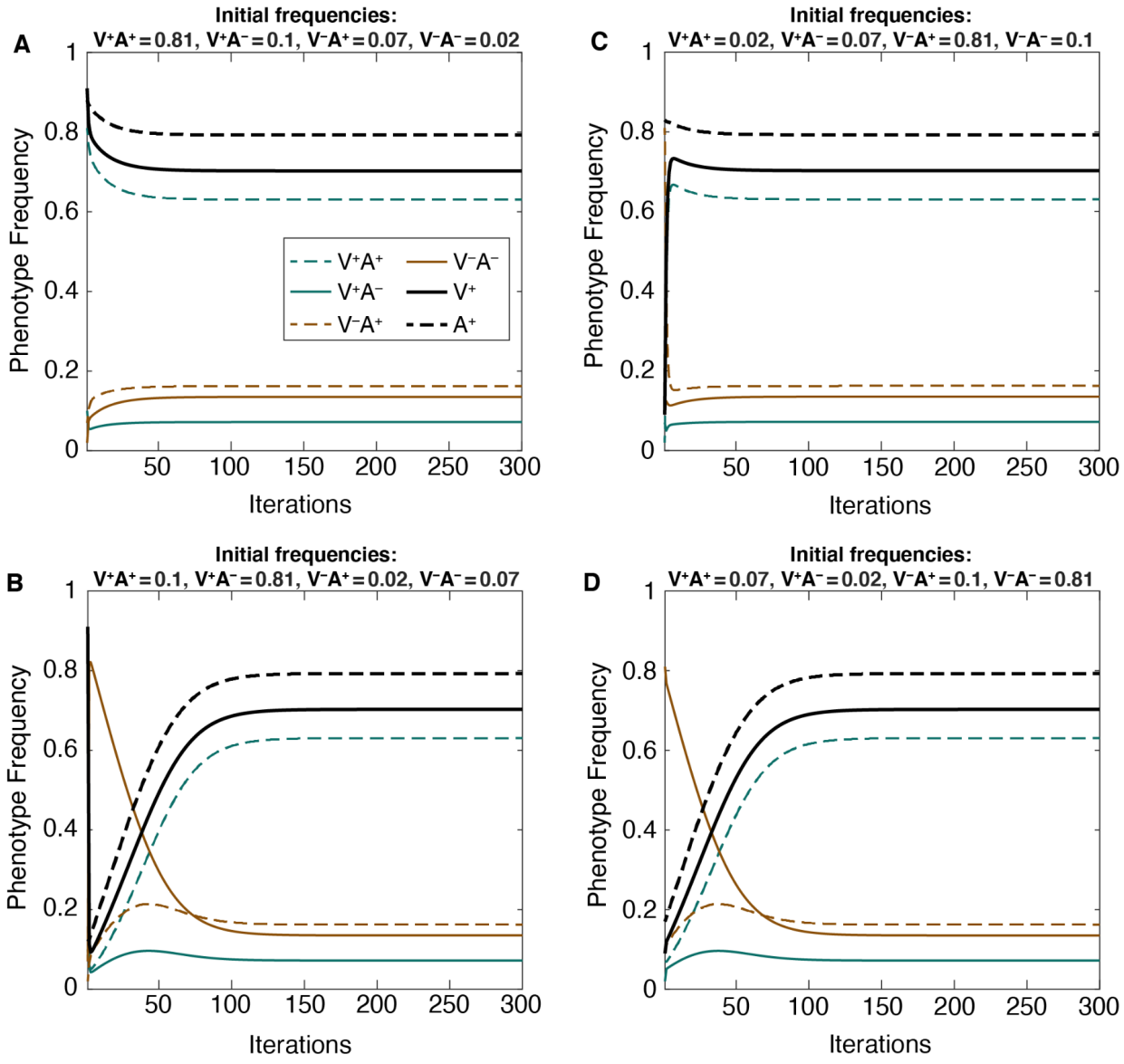

Figure S2.3: **Population frequencies reach stable equilibria determined by the parameter space, not by initial frequencies.** Each phenotype approaches the same equilibrium frequency for a given set of parameters regardless of its initial frequency in our simulations. Each of the four phenotype frequencies and the total V^+ and A^+ frequencies (vertical axis) approach equilibrium values prior to iteration 300 and remain stably at those frequencies (compare this figure with **Figure 2.3 (top row)**, which shows the first 100 iterations of the same simulations). We varied the initial frequencies, such that we begin each simulation with a different phenotype at an initial high frequency (0.81): **A)** $\boldsymbol{x_1}$ **(V^+A^+) = 0.81**, x_2 (V^+A^-) = 0.1, x_3 (V^-A^+) = 0.07, x_4 (V^-A^-) = 0.02; V^+A^-; **B)** x_1 (V^+A^+) = 0.1, $\boldsymbol{x_2}$ **(V^+A^-) = 0.81**, x_3 (V^-A^+) = 0.02, x_4 (V−A−) = 0.07; V^-A^+; **C)** x_1 (V^+A^+) = 0.02, x_2 (V^+A^-) = 0.07, $\boldsymbol{x_3}$ **(V^-A^+) = 0.81**, x_4 (V^-A^-) = 0.1); **D)** x_1 (V^+A^+) = 0.07, x_2 (V^+A^-) = 0.02, x_3 (V^-A^+) = 0.1, $\boldsymbol{x_4}$ **(V^-A^-) = 0.81**. The remaining parameters are held at default values (**Table 2.1**) and simulations were performed **with vertical transmission only (only parent-to-offspring transmission)**. These results indicate that equilibrium frequencies are determined by the parameter space, not initial frequencies.

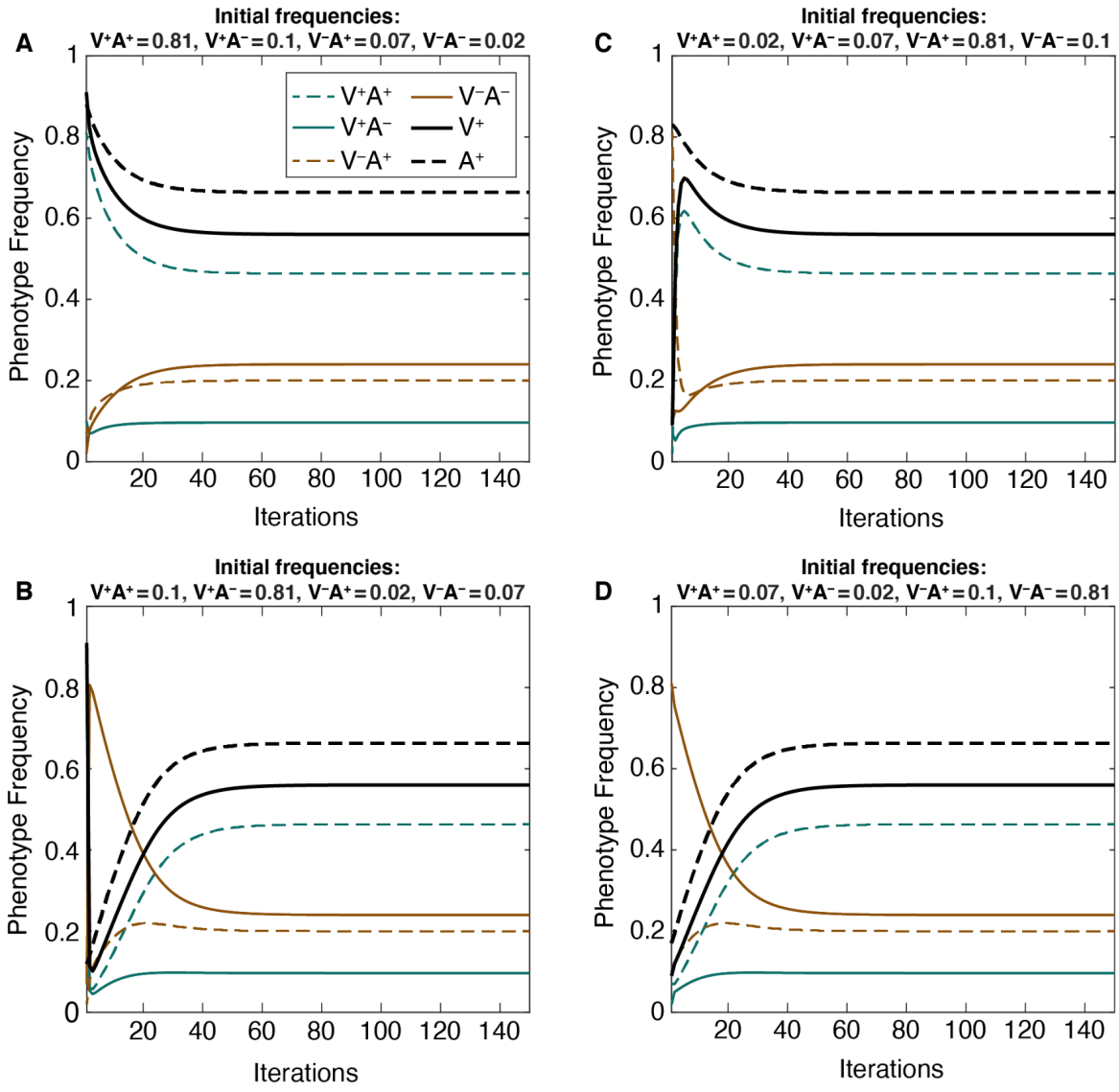

Figure S2.4: **Population frequencies reach stable equilibria determined by the parameter space, not by initial frequencies (with herd-immunity driven hesitancy).** Each phenotype approaches the same equilibrium frequency for a given parameter set regardless of its initial frequency in our simulations. Each of the four phenotype frequencies and the total V^+ and A^+ frequencies (vertical axis) approach equilibrium values prior to iteration 300 and remain stably at those frequencies (compare this figure with **Figure 2.3 (top row)**, which shows results with only vertical transmission). We varied the initial frequencies, such that we begin each simulation with a different phenotype at an initial high frequency (0.81): V^+A^+ in panel **A**, V^+A^- in panel **B**, V^-A^+ in panel **C**, V^-A^- in panel **D**; the remaining phenotypes are set to lower frequencies (0.1, 0.07, 0.02). See **Figure S1** for a full listing of these initial frequencies. The remaining parameters are held at default values (**Table 2.1**) and these simulations **included both vertical and herd-immunity-driven hesitancy**.

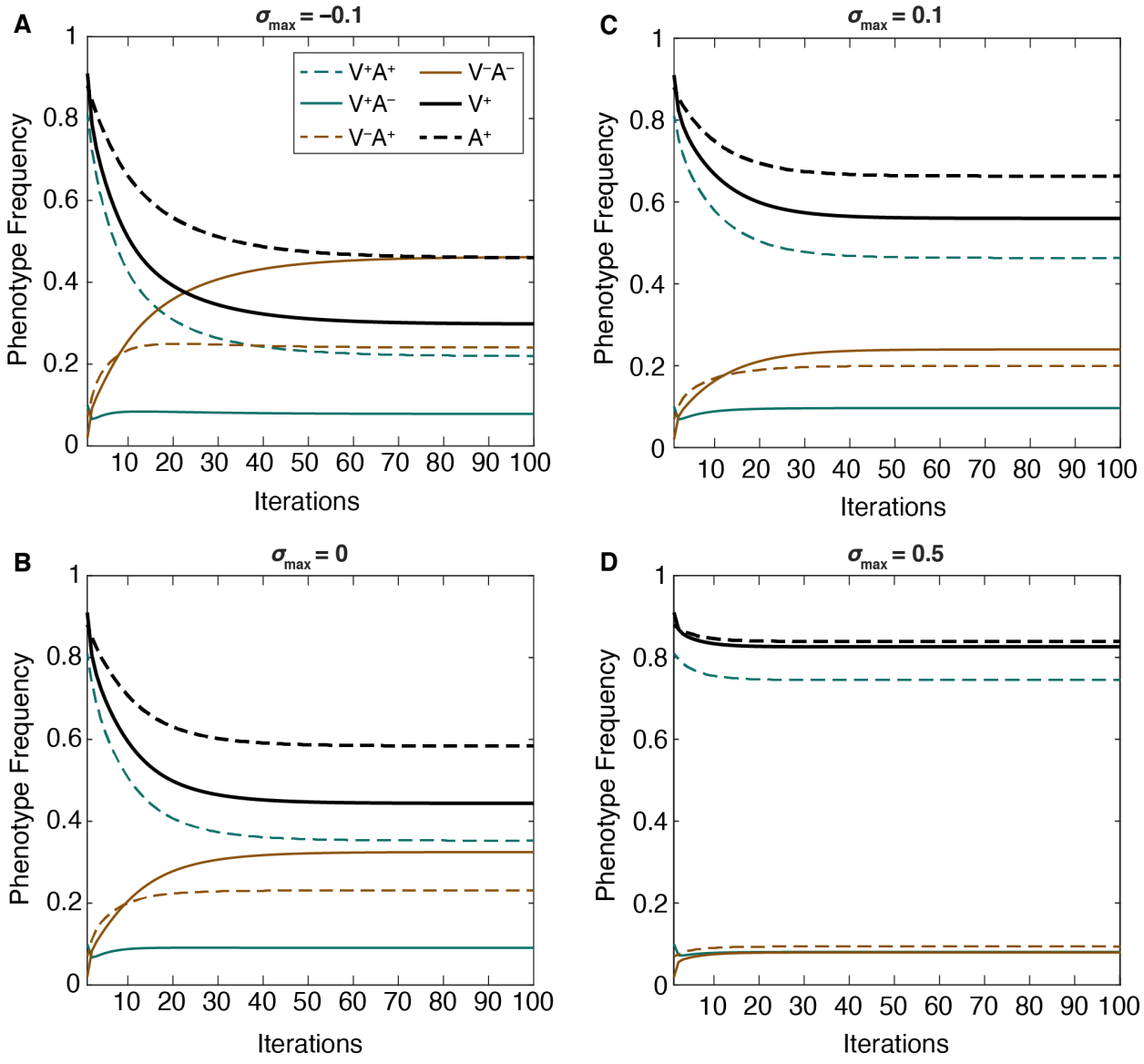

Figure S2.5: **Temporal effects of cultural selection (with herd-immunity-driven hesitancy belief transition)**. The equilibrium phenotype frequencies change as the maximum cultural selection coefficient (σ_{max}) is varied: **A.** $\sigma_{max} = -0.1$; **B.** $\sigma_{max} = 0$; **C.** $\sigma_{max} = 0.1$; **D.** $\sigma_{max} = 0.5$. Herd-immunity-driven hesitancy is included, and other parameters are held at default values (**Table 2.1**). (Compare this figure with **Figure 2.3 (bottom row)**, which shows results with vertical transmission only.) Cultural selection against vaccinated individuals increases the frequency of V^-A^-, while decreasing the other frequencies (**A**), whereas increased cultural selection favoring vaccinated individuals increases V^+A^+ frequencies while decreasing the other frequencies (**C**, **D**). The highest levels of conflicting phenotypes (V^+A^- and V^-A^+) were observed when cultural selection was neutral (**B**).

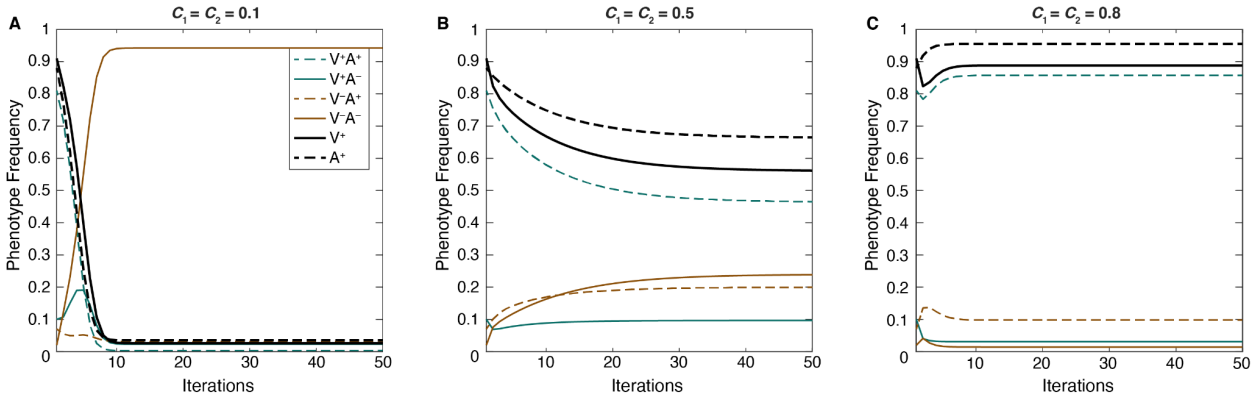

Figure S2.6: **Temporal effects of confidence transmission (with herd-immunity-driven hesitancy belief transition)**. The change in phenotype frequencies over 50 iterations as vaccine confidence transmission in mixed couples (C_1=C_2) is varied (**A**. C_1=C_2=0.1; **B**. C_1=C_2=0.5; **C**. C_1=C_2 = 0.8). Herd-immunity-driven hesitancy is included and other parameters are held at default values (Table 1). The population equilibrates at over 90% V^-A^- at low confidence transmission (**A**). Increasing the probability of confidence transmission results in higher V^+A^+ frequencies and lower V^-A^- (**B**, **C**). In comparison to simulations with only vertical transmission (**Figure 2.4**), phenotype frequencies reach equilibrium at values closer to mid-range levels (i.e. V^+A^+ levels at equilibrium are reduced while other frequencies are increased). It is also worth noting that the V^-A^- equilibrium value is higher than V^-A^+ at C_1=C_2 = 0.5 when herd-immunity-driven hesitancy is added.

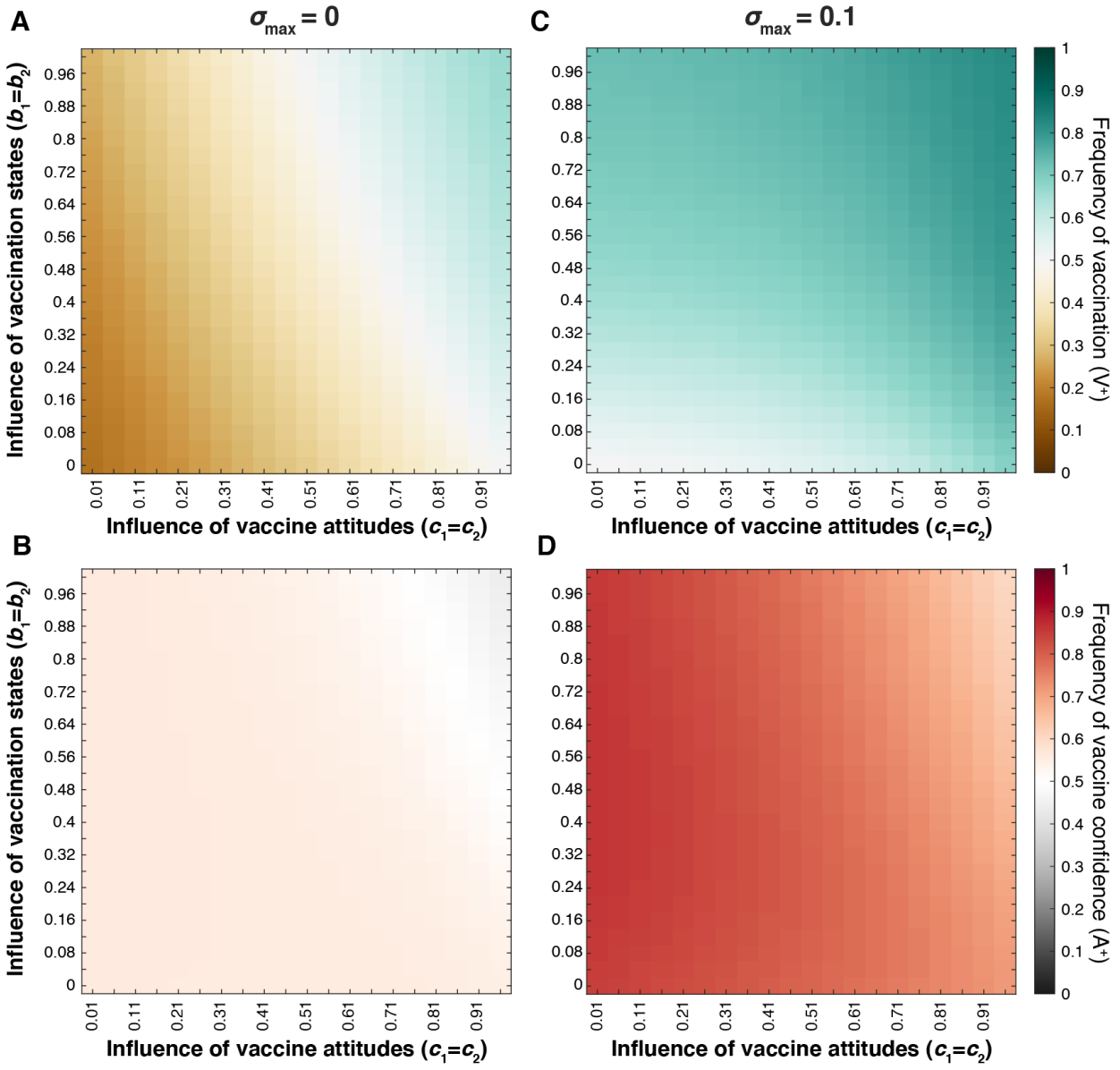

Figure S2.7: **The influence of parental traits on vaccination coverage and vaccine confidence (with vertical transmission only).** Equilibrium vaccination coverage (**A,C**) and corresponding vaccine confidence (**B, C**) after 100 time-steps **without community influence**–only parent-to-offspring transmission (Compare to **Figure 2.10** with oblique transmission). Influence of parental vaccination states (b_1=b_2; vertical axis) and influence of parent vaccine attitudes (c_1=c_2; horizontal axis) are varied at two maximum cultural selection coefficients: σ_{max}= 0 (**A, B**) and σ_{max}= 0.1 (**C, D**). Positive selection for vaccination increased vaccination coverage and vaccine confidence across parameter ranges, however, vaccine confidence is lower than expected at the intersection of high state influence parameters.

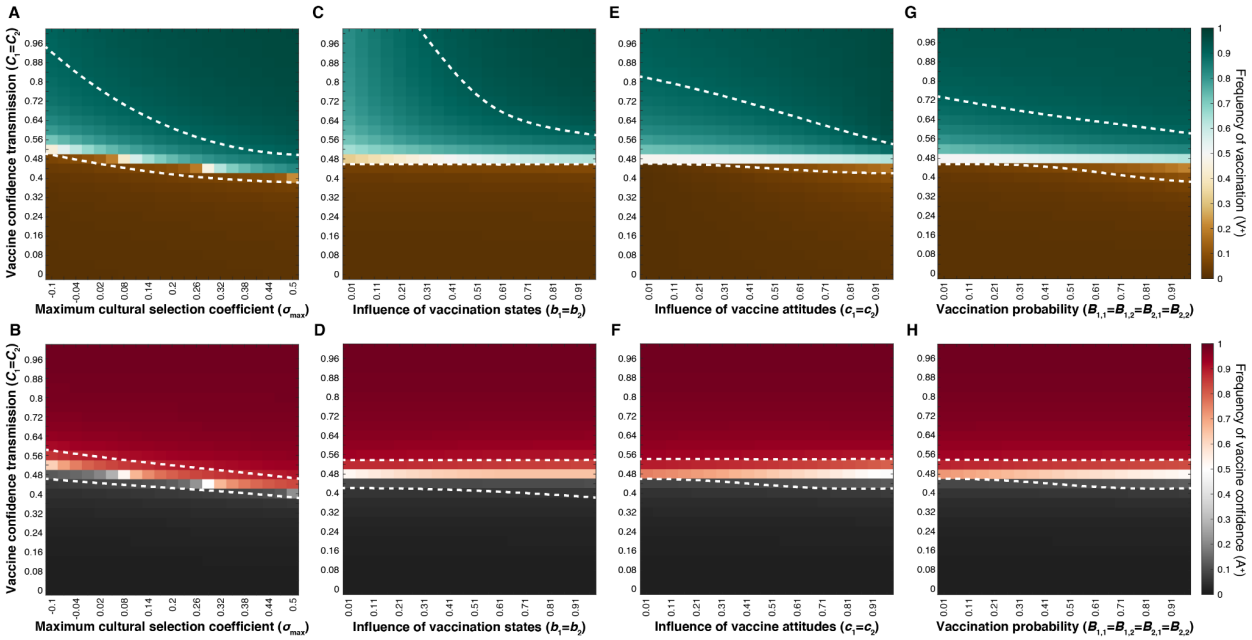

Figure S2.8: Vaccine confidence transmission dictates vaccination coverage and confidence levels (with confidence-frequency-dependent belief transition). Heatmaps showing final vaccination coverage (i.e. frequency of V^+ in the population, with low coverage in brown and high coverage in green (**A, C, E, G**)) and final vaccine confidence (i.e. frequency of A^+, with low confidence in black and high confidence in red (**B, D, F, H**)) after 100 time-steps **with obliquely transmitted hesitancy** (**Figure S2**). Unless varied on the horizontal or vertical axes, other parameters are set to the default values given in **Table 2.1**. We vary confidence transmission (C_n) of mixed trait pairs ($C_1 = C_2$) in conjunction with the maximum cultural selection coefficient, σ_{max}, (**A,B**), the influence of parental vaccination state, b_m, (**C, D**), the level of influence of parental attitudes on their vaccination behaviors, c_n, (**E,F**), and offspring vaccination probability, $B_{m,n}$ (**G,H**). Dashed white lines demarcate the region in which equilibrium frequencies are between 0.1 and 0.9.

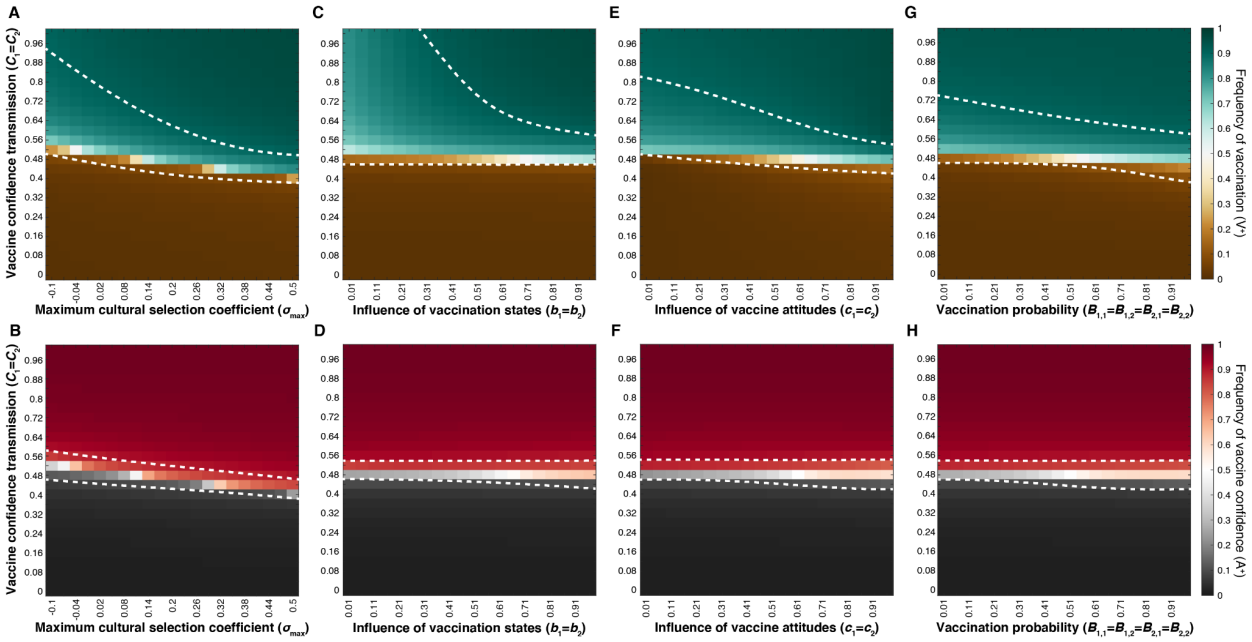

Figure S2.9: Vaccine confidence transmission dictates vaccination coverage and confidence levels (with vaccine-fear-driven belief transition). Heatmaps showing final vaccination coverage (i.e. frequency of V^+ in the population, with low coverage in brown and high coverage in green (**A, C, E, G**)) and final vaccine confidence (i.e. frequency of A^+, with low confidence in black and high confidence in red (**B, D, F, H**)) after 100 time-steps with **vaccine-fear-driven belief transition** (**Figure S2.1**). Unless varied on the horizontal or vertical axes, other parameters are set to the default values given in Table 1. We vary confidence transmission ($\boldsymbol{C_n}$) of mixed trait pairs ($C_1 = C_2$) in conjunction with the maximum cultural selection coefficient, σmax, (A,B), the influence of parental vaccination state, bm, (**C, D**), the level of influence of parental attitudes on their vaccination behaviors, c_n, (**E,F**), and offspring vaccination probability, $B_{m,n}$ (**G,H**). Dashed white lines demarcate the region in which equilibrium frequencies are between 0.1 and 0.9.

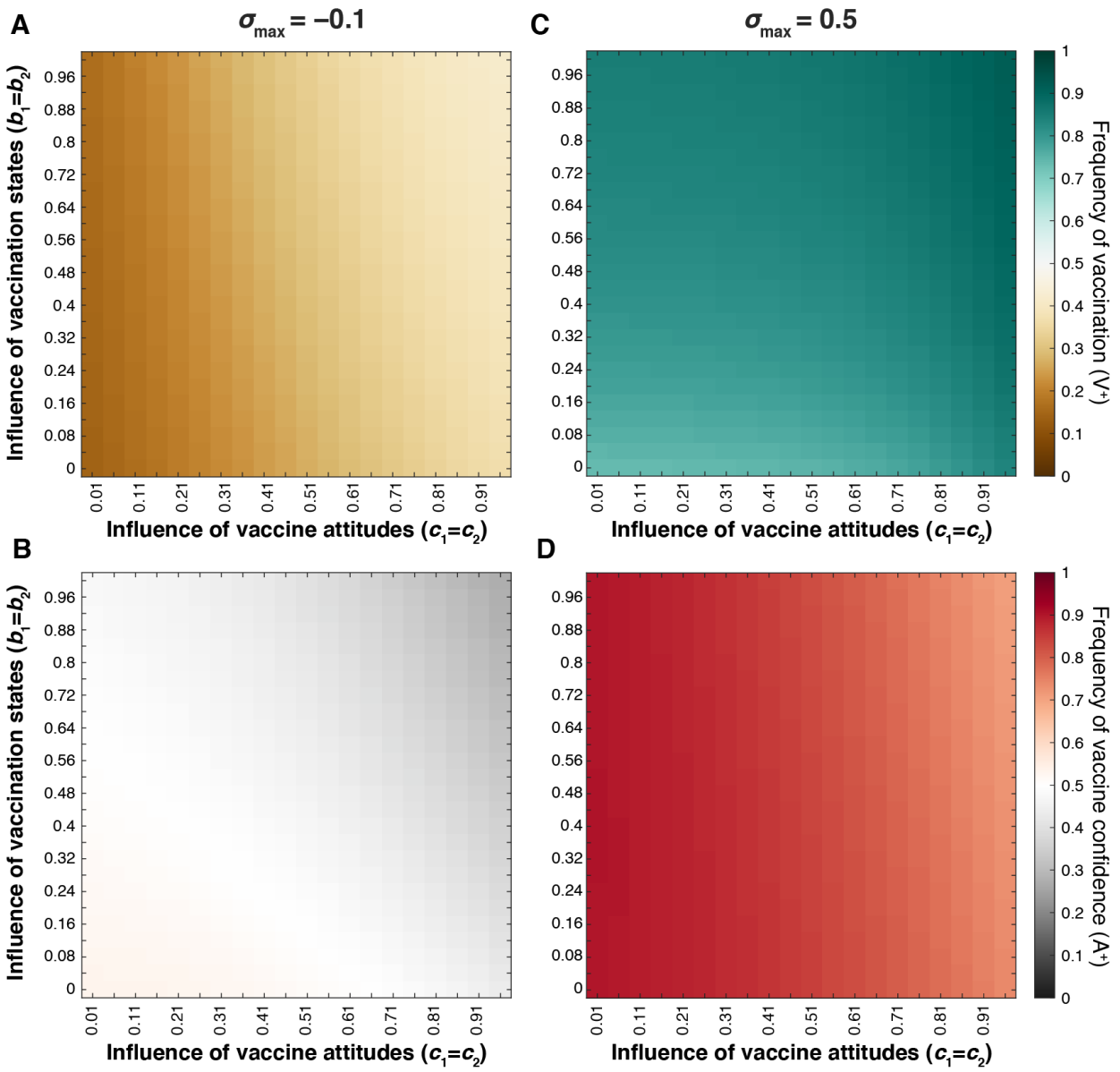

Figure S2.10: **The influence of parental traits on vaccination coverage and vaccine confidence (at extreme levels of cultural selection compared to Figure 2.10)**. Equilibrium vaccination coverage (**A,C**) and corresponding vaccine confidence (**B, C** respectively) after 100 time-steps **with herd-immunity-driven hesitancy belief transition**. Influence of parental vaccination states (b_1=b_2; vertical axis) and influence of parent vaccine attitudes (c_1=c_2; horizontal axis) are varied at two maximum cultural selection coefficients: σ_{max}= −0.1 (**A, B**) and σ_{max}= 0.5 (**C, D**). Positive selection for vaccination increases vaccination coverage and vaccine confidence across parameter ranges, however, vaccine confidence is lower than expected at the intersection of high state influence parameters.

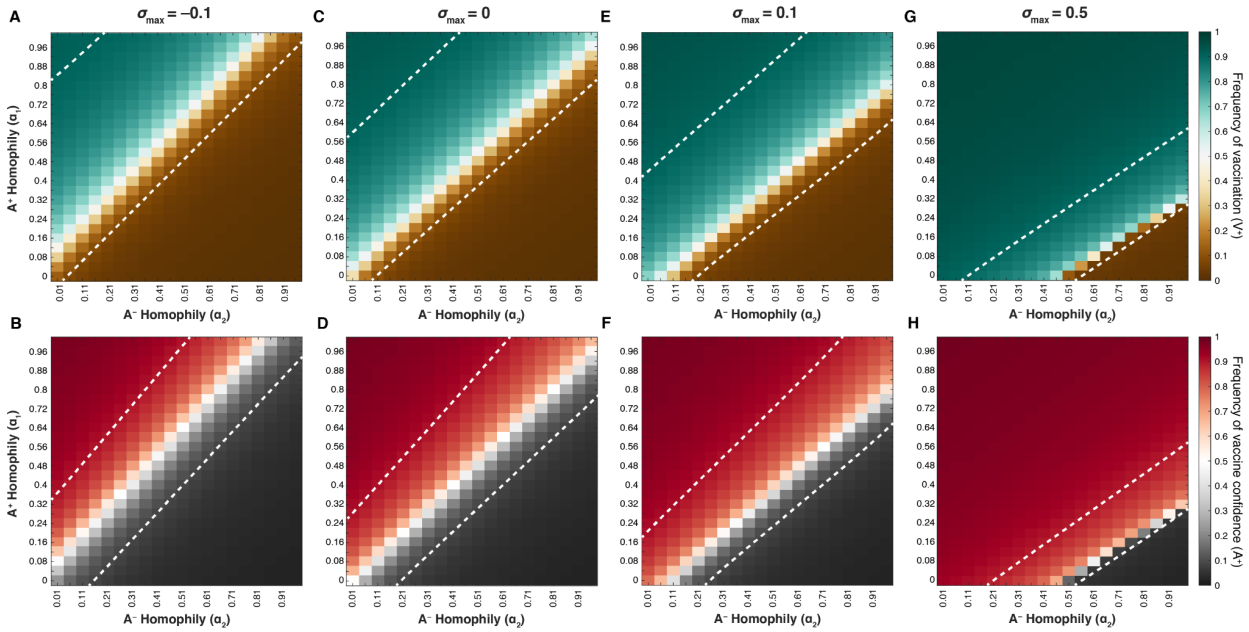

Figure S2.11: Homophily between individuals with similar vaccine beliefs can shift the equilibrium frequencies of both vaccination coverage and confidence (with vertical transmission only). Heatmaps showing final vaccination coverage **(A, C)** and final vaccine confidence **(B, D)** after 100 timesteps with only parent-to-offspring transmission (compare to **Figure 2.11**). As in previous figures, unspecified parameters are given in **Table 1**. As vaccine-hesitant individuals (A^-) increasingly prefer to pair with one another (increasing α_2; horizontal axis), vaccine-confident individuals (A^+) must also preferentially interact to maintain high vaccine coverage (α_1; vertical axis); this tradeoff is modulated by the cultural selection pressures on vaccination ($\sigma_{max} = -0.1$ **(A, B)**, $\sigma_{max} = 0$ **(C, D)**, $\sigma_{max} = 0.1$ **(E, F)** and $\sigma_{max} = 0.5$ **(G, H)**). Dashed white lines demarcate the region in which equilibrium frequencies are between 0.1 and 0.9.

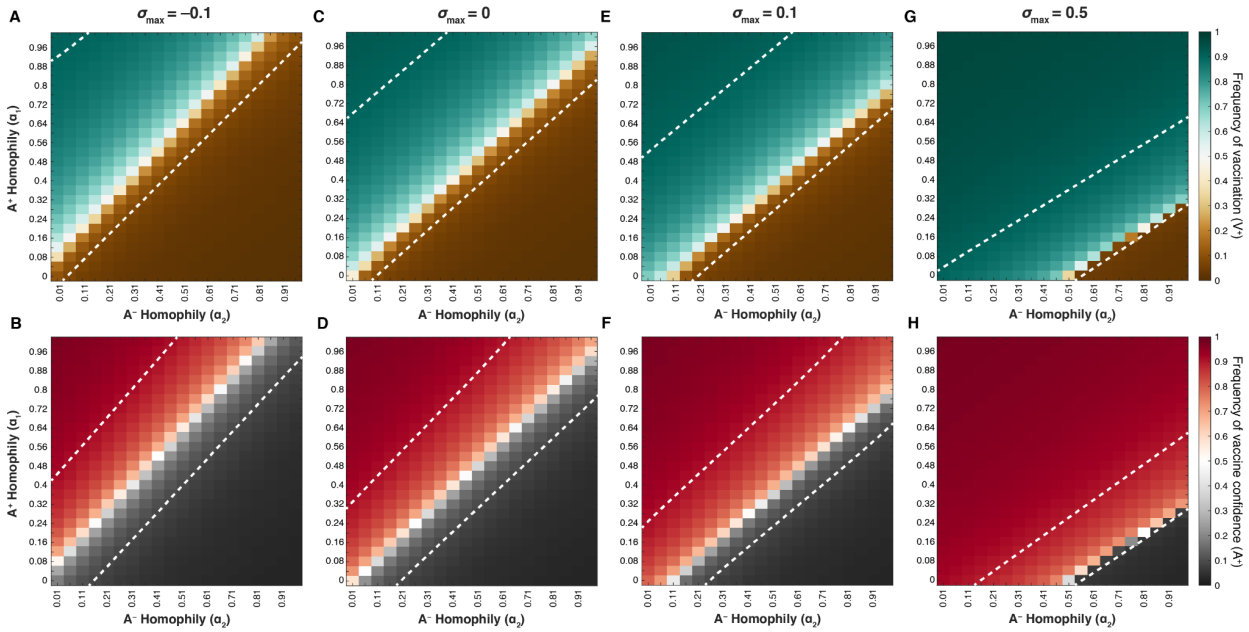

Figure S2.12: Homophily between individuals with similar vaccine beliefs can shift the equilibrium frequencies of both vaccination coverage and confidence (with confidence-frequency dependent belief transition). Heatmaps showing final vaccination coverage **(A, C)** and final vaccine confidence **(B, D)** after 100 timesteps with **obliquely transmitted hesitancy** (**Figure S2.2**). As in previous figures, unspecified parameters are given in **Table 2.1**. As vaccine-hesitant individuals (A^-) increasingly prefer to pair with one another (increasing α_2; horizontal axis), vaccine-confident individuals (A^+) must also preferentially interact to maintain high vaccine coverage (α_1; vertical axis); this tradeoff is modulated by the cultural selection pressures on vaccination ($\sigma_{max} = -0.1$ **(A, B)**, $\sigma_{max} = 0$ **(C, D)**, $\sigma_{max} = 0.1$ **(E, F)** and $\sigma_{max} = 0.5$ **(G, H)**). Dashed white lines demarcate the region in which equilibrium frequencies are between 0.1 and 0.9.

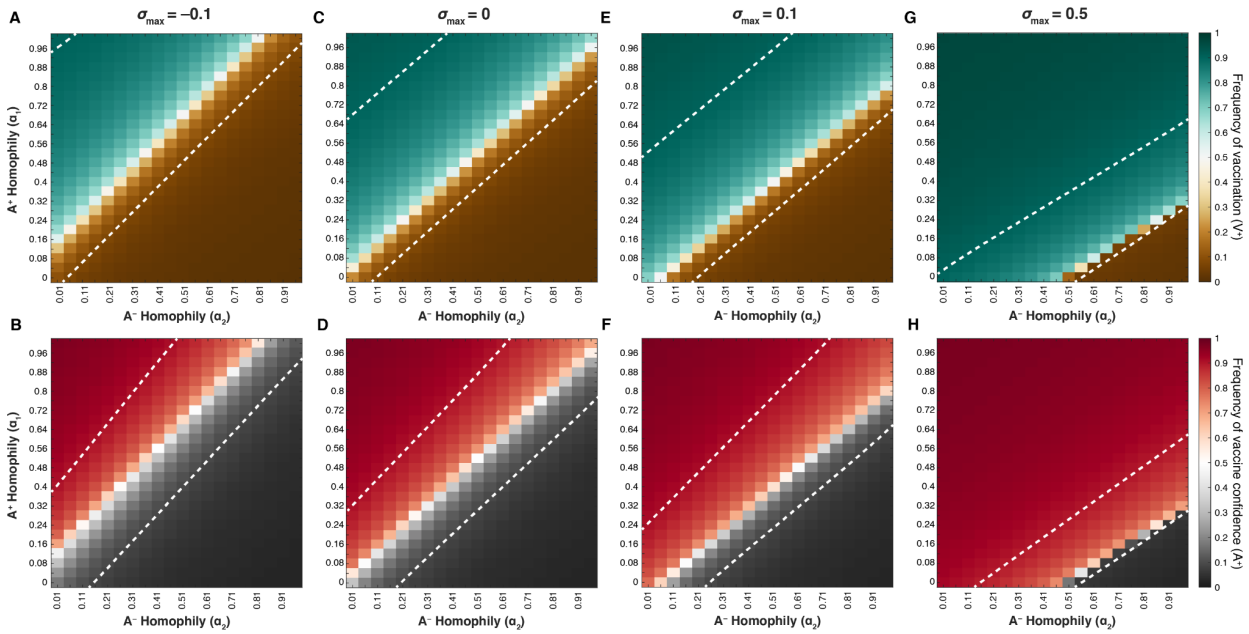

Figure S2.13: Homophily between individuals with similar vaccine beliefs can shift the equilibrium frequencies of both vaccination coverage and confidence (with vaccine-fear-driven hesitancy). Heatmaps showing final vaccination coverage **(A, C)** and final vaccine confidence **(B, D)** after 100 timesteps with vaccine-fear-driven hesitancy (**Figure S2.1**). As in previous figures, unspecified parameters are given in **Table 2.1**. As vaccine-hesitant individuals (A^-) increasingly prefer to pair with one another (increasing α_2; horizontal axis), vaccine-confident individuals (A^+) must also preferentially interact to maintain high vaccine coverage (α_1; vertical axis); this tradeoff is modulated by the cultural selection pressures on vaccination ($\sigma_{max} = -0.1$ **(A, B)**, $\sigma_{max} = 0$ **(C, D)**, $\sigma_{max} = 0.1$ **(E, F)** and $\sigma_{max} = 0.5$ **(G, H)**). Dashed white lines demarcate the region in which equilibrium frequencies are between 0.1 and 0.9.

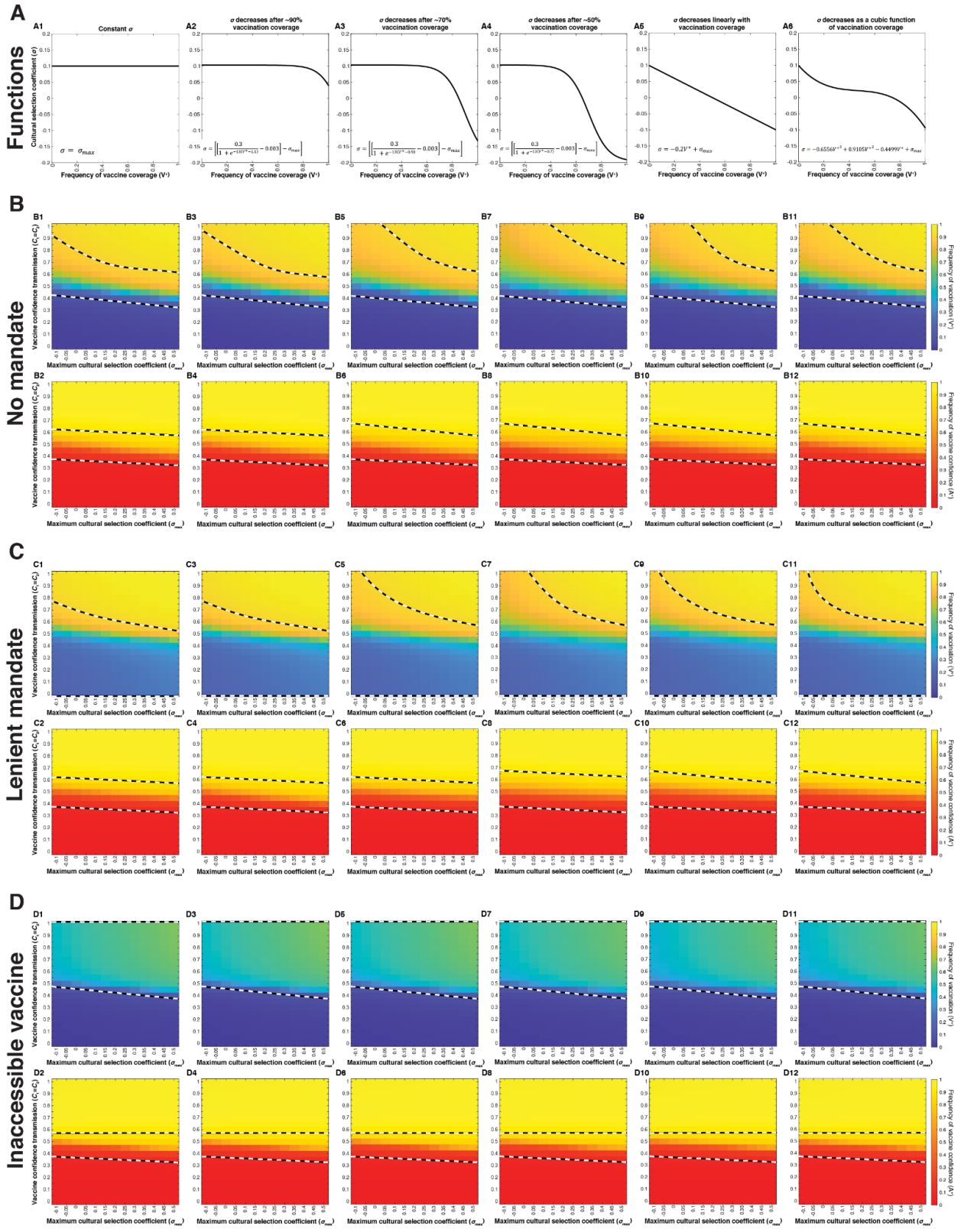
A
Functions
A1
Constant σ
A2
σ decreases after ~90% vaccination coverage
A3
σ decreases after ~70% vaccination coverage
A4
σ decreases after ~50% vaccination coverage
A5
σ decreases linearly with vaccination coverage
A6
σ decreases as a cubic function of vaccination coverage
Cultural selection coefficient (σ)
Frequency of vaccine coverage (V¹)
B
No mandate
C
Lenient mandate
D
Inaccessible vaccine
Vaccine confidence transmission (C₁=C₂)
Maximum cultural selection coefficient (σmax)
Frequency of vaccination (V¹)
Frequency of vaccine confidence (A¹)

Figure S3.1: Selection trajectories affect outcomes at equilibrium when vaccines are accessible.. Heatmaps showing equilibrium vaccine coverage and vaccine confidence levels with an accessible vaccine and no mandate (**Section B**), with an accessible vaccine and a lenient mandate (**Section C**) and an environment with vaccines somewhat inaccessible (**Section D**), employing various cultural selection (σ) functions: (**A1**) σ does not depend on vaccination coverage, (**A2**) σ decreases after a high herd-immunity threshold of ~90% coverage, (**A3**) σ decreases after a medium herd-immunity threshold of ~70% coverage (baseline function), (**A4**) σ decreases after a low herd-immunity threshold of ~50% coverage, (**A5**) σ decreases linearly as vaccination coverage increases, (**A6**) σ decreases according to a cubic function. We vary $C_1 = C_2$ (confidence transmission probability of mixed-attitude couples) on the vertical axis, and maximum selection coefficient σ_{max} (indicative of the perceived value of vaccinating offspring) on the horizontal axis. Unspecified parameters are given in **Table 3.1** with σ_{max} held at 0.1 for all functions shown in **Section A** but varied in the heatmaps in **Sections B-D**. Black and white dashed lines indicate the area of the heat maps in which vaccination and confidence frequencies equilibrate between 0.1 and 0.9.