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Vaccine hesitancy: a systematic literature review on the rationale behind parental vaccine hesitancy and its effects on pediatric medicine

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VACCINE HESITANCY: A SYSTEMATIC LITERATURE REVIEW ON THE RATIONALE BEHIND PARENTAL VACCINE HESITANCY AND ITS EFFECTS ON PEDIATRIC MEDICINE

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ABSTRACT

Vaccine hesitancy remains a constant threat to global health despite the release several public health initiatives aimed at targeting and reducing vaccine hesitancy. The aftermath of the COVID-19 pandemic and rapid release of the SARS-CoV-2 vaccine resulted in increased vaccine hesitancy amongst individuals. Within pediatric medicine, concerns over the doubt and efficacy of vaccines has led to a significant decrease in the number of children receiving vaccines. Parental delay or refusals of vaccines, termed vaccine hesitancy, has resulted in a recurrence of vaccine preventable diseases such as measles, pertussis, and diphtheria. This review of the literature attempts to understand the parental reasons for continued vaccine hesitancy, examine the effects of the COVID-19 pandemic on vaccine hesitancy, and examine how continued vaccine hesitancy is affecting healthcare. An analysis of the literature revealed that health education, geographic location, and economic status are all contributing factors of vaccine hesitancy. More information is needed on this topic to better address and education vaccine hesitant parents.

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LIST OF ABBREVIATIONS

CDC .....Centers for Disease Control and Prevention

COVID-19..... Coronavirus Disease 2019

DPT .....Diphtheria, Pertussis, and Tetanus

DTaP ..... Diphtheria, Tetanus, and Pertussis Vaccine

EEG..... Electroencephalography

FDA .....Food and Drug Administration

H1N1..... Hemagglutinin Type 1 and Neuraminidase Type 1 (influenza virus)

HBV .....Hepatitis B Vaccine

Hep B ..... Hepatitis B

HCPs .....Healthcare Providers

HPV ..... Human Papillomavirus

IPV .....Inactivated Polio Vaccine

MIS-C .....Multisystem Inflammatory Syndrome in Children

MMR.....Measles, Mumps, and Rubella

MRI..... Magnetic-Resonance Imaging

MS..... Multiple Sclerosis

NHS ..... National Health Service (UK)

PHAs.....Public Health Advocates

RBB ..... Risk Benefit Balance

SAGE ..... Strategic Advisory Group of Experts

SARS-CoV-2 ..... Severe Acute Respiratory Syndrome Coronavirus 2

UNICEF ..... United Nations Children's Fund

US ..... United States

VH ..... Vaccine Hesitancy

VHPB ..... Viral Hepatitis Prevention Board

VPD ..... Vaccine Preventable Diseases

WHO ..... World Health Organization

INTRODUCTION

Defining Vaccine Hesitancy

Vaccine hesitancy (VH) is a well-known concept amongst healthcare providers (HCPs) and public health advocates (PHAs) that has challenged the practice of immunization since Edward Jenner's 1798 discovery of the smallpox vaccine (Plotkin 2014). The increasing practice of VH among parents and individuals resulted in the World Health Organization (WHO) naming VH as a top-ten threat to global health in 2019 (Benzian et al. 2023). With the recent COVID-19 global pandemic and the addition of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) vaccine, and its many variants, these sentiments towards VH have not changed and if any, have become increasingly common practice among individuals (Cascini et al. 2021, Dror et al. 2020). Considering the egregious potential that VH can have on global health, the WHO established a strategic advisory group of experts (SAGE) with the sole purpose of defining VH, monitoring it, and creating tactics to address it. After review of the literature and field reports, the SAGE Working Group on Vaccine Hesitancy (WG) broadly defined VH as a delay in acceptance or refusal of vaccination despite the availability of such services. Within this definition the SAGE WG also noted that VH is complex, context-specific, vaccine specific, and varies across place and time (MacDonald 2015).

Despite the SAGE WG providing a broad definition of VH in 2011, there have since been discrepancies among publications on the definition of VH. This can be attributed to the multifaceted nature of VH and the determinants that fall under the

umbrella of vaccine hesitancy (Dube et al, 2013). There has been discussion by the SAGE WG on whether 'hesitancy' is an appropriate term to describe this phenomenon however its broad terminology allows for a myriad of concerns to be covered within this term and avoids grouping individuals into pro vs anti vaccination factions (McAteer 2020). This is especially crucial considering that previous terms used to describe VH, such as vaccine avoidance, vaccine refusal, non-compliance, etc., were more judgmental and held punitive connotations. Since the 2011 SAGE WG definition, there have been numerous publications that suggest different definitions for VH, such as considering it as a 'kind of decision-making process' (Peretti-Watel 2015). In 2020, McAteer, Yildirim, and Chahroudi noted that the term 'hesitancy' heavily implies that an individual's decision can be swayed towards acceptance during said period of contemplation (McAteer 2020). In 2021 VH was defined as 'an attitude of ambivalence' (Goldenberg 2021). Recent literature has shown support for the idea that VH is an attitude or sentiment, rather than an action. In conceptualizing VH in this manner, VH is becoming more defined as a period of indecision or uncertainty preceding the decision to become or not become vaccinated (Larson 2022).

It is important to note that VH and the term 'anti-vax' are two separate and distinct concepts. Although the term 'anti-vax' has been used in context to describe vaccine skepticism, its usage in this connotation is incorrect as the term describes opposition to the use of all or some vaccines (Merriam-Webster dictionary). As of recent, the term 'anti-vax' represents a broader issue that has become politicized and represents an issue of individual freedom. Due to their distinct and differing definitions, VH and

‘anti-vax’ should not be used interchangeably. One final consideration when defining VH is that VH will continue to evolve in response to the continued evolution of vaccine science.

SPECIFIC AIMS

Despite the numerous scientific and technological advancements, parents are still hesitant to vaccinate their children, leading to a significant decrease in the number of children receiving vaccines and a resurgence in VPD.

The first aim this review is an overview of the history of vaccine hesitancy and vaccine specific controversies, reports of increased VPD outbreaks, and an overview of different vaccine specific hesitancies.

A secondary objective of this review is to describe the parental reasons for vaccine hesitancy given the current literature supporting the use of vaccines.

The third objective of this review is to examine the effect of the SARS-CoV-2 pandemic on VH. Given that social media played a significant role in the public perception and response of the Covid-19 vaccine, the third objective of this review will also analyze how social media has, if any, affected the VH movement.

The final objective of this review is to examine how VH is affecting healthcare, specifically pediatric healthcare, and the repercussions of continued VH in pediatric medicine.

LITERATURE CITED

History of Vaccine Hesitancy and Vaccine Related Controversies

Doubt and concern over the efficacy of vaccines is not a new phenomenon. Since the discovery of the vaccine, individuals have questioned whether the proposed benefits of vaccines pose a significant advantage to the health of the individuals who are receiving them. Aversion towards vaccines originated as early as the eighteenth century. In 1772, Reverend Edmund Massey delivered a sermon, in England, berating the use of vaccines as an attempt to reject the sufferings placed on man for his sins (Hussain et al. 2018). Similar views were seen in the writings of Reverend John Williams where he claimed vaccines to be the Devil's work. In addition to being rejected for theological beliefs, vaccines were also opposed for political and legal reasons during that time period. In Britain during the mid-nineteenth century, a set of laws were passed that enforced mandatory vaccination for children. However, after public outcry and the pressure exerted by the formation of the Anti-Vaccination League in London, Parliament passed an act in 1898 that withdrew the punishment for not abiding by the vaccination law and allowed parents to determine whether or not their child would be vaccinated (Hussain et al. 2018). Since the early eighteenth-century, opposition towards vaccines has never fully quieted however it has increased in scope and scale, due in part to controversies and vaccination scares.

In 1998, physician and researcher Andrew Wakefield published a now-retracted article in the *Lancet* suggesting a connection between autism, gastrointestinal disease and the Measles, Mumps, and Rubella vaccine (MMR) in children. The publication of this

article further fueled the anti-vaccine movement and led to a subsequent drop in vaccination rates for the MMR vaccine and a resurgence of measles throughout different parts of the Western world. In his study, Wakefield examined twelve children with a history of chronic enterocolitis, or inflammation of the digestive tract, along with regressive developmental disorder, or normal development followed by a regression in developmental skills such as language, social function, and motor skills. These children, ranging from ages three to ten, underwent numerous tests, some of which included electroencephalography (EEG), magnetic-resonance imaging (MRI), and developmental assessments (Wakefield et al. 1998). In his findings, Wakefield argued that onset of these behavioral symptoms, that are classified as regressive developmental disorder, were noticed by the parents after their child received the MMR vaccine. Wakefield found no evidence of neurological abnormalities, EEG and MRI testing results were negative, and cerebrospinal-fluid profiles were normal. It was also noted that many of the children experienced early adverse reactions towards vaccinations. Upon reviewing these findings, Wakefield and colleagues (1998) determined that there was a causal association in children with autism-spectrum disorders and intestinal dysfunction, occurring after the MMR vaccine was administered.

Wakefield's research was used as a catalyst for vaccine conspiracy theories and the anti-vaccine movement (Gagnon 2023). Using the misinformation provided in Wakefield's study, individuals were convinced that vaccination with the MMR vaccine, or any immunization, could lead to the development of autism. The theory of vaccines

causing autism, that developed based on the Wakefield study, not only threatened public health and collective immunity, but also acted as a proponent of VH (Gagnon 2023).

Since the publication of Wakefield's article, his idea of an association between the MMR vaccine and autism has not only been debunked, but researchers have also not been able to replicate his findings, which is due in part to the many limitations of his study, including the use of parental recollections and ideologies, the small size of his case study, and the lack of controls throughout the study. Thirteen years after its initial publication, journalists discovered that Wakefield had received funding from anti-vaccine manufacturers (Husain et al. 2018). The paper was ultimately retracted in 2010, yet the retraction did nothing to alleviate public distrust of vaccines or diminish the VH movement.

Vaccine controversies, such as the Wakefield controversy, are not new phenomena and have been prevalent throughout history since the introduction of the vaccine. These controversies have had varying effects on public perception, vaccine acceptance, and vaccination programs and efforts (Dube 2013). Between 1995 and 1997 there were several reports of individuals developing Multiple Sclerosis (MS) after receiving the Hepatitis B vaccine (HBV) in France during a mass immunization campaign. Reports of an association between the HBV and MS resulted in the temporary suspension of the school-based vaccination program by the French government (Ascherio 2001). The initial temporary termination of the program was due to the preliminary results of one case-control study which did not reveal a significant increase in risk of MS for vaccinated versus unvaccinated individuals. By 1998, the Viral Hepatitis Prevention

Board (VHPB) had reviewed the safety of the HBV using several studies that investigated a causal relationship between the HBV and demyelinating or other neurologic disorders. These studies have reported no evidence of a causal association between MS and the HBV or have shown support of biologic plausibility of such a link (Francois 2005). Although the HBV and MS controversy occurred in 1998, recent research has shown that despite the risk-benefit balance (RBB), and the numerous studies that have been conducted since the controversy, parents in France are still vaccine hesitant towards the HBV (Rey 2018).

Controversies, vaccine scares, and radical associations between vaccines and disorders have commonly occurred since the introduction of the first vaccine and will unfortunately continue to occur in response to the continued evolution of vaccine science. Prior to research being conducted to either prove or disprove these controversies, vaccine scares, and radical associations, a public fear and distrust of vaccines arises, further fueling the VH movement. Although much work has been done to try to disseminate information from studies to debunk some of these vaccine controversies and scares, it has proven difficult. According to reports by Rutjens et al. (2021, p. 29), conspiratorial thinking was the predominant rationale for individuals with anti-vaccination beliefs. This report found that anti-science skepticism was shared on social media more often than factual science data, further contributing to VH (Rutjens et al. 2021). Despite research studies reporting evidence that combats these negative connotations, continued fear and public distrust of vaccines remains, as is noted by the continued distrust of the MMR vaccine and most recently, the SARS-CoV-2 vaccine.

Increased Cases of Disease Outbreaks

Despite advances in technology, multiple research efforts, and scientific evidence, VH remains a prevalent and constant threat to global health. This period of indecision or uncertainty towards vaccines has resulted in a significant decline of vaccination rates worldwide and has led to the reappearance of diseases that are preventable and can be eradicated with the use of vaccines. Additionally, increased VH among parents has resulted in an increase in school immunization exemptions and pediatric dismissal rates which further increases the risk of the spread of vaccine preventable diseases (VPD) such as Diphtheria, Measles, and Pertussis, to name a few.

In the year 2000 the United States (US) had achieved measles elimination status however; increased cases of measles outbreaks threaten to jeopardize this status. Most notable was the 2017 measles outbreak that occurred in Minnesota and the 2015 measles outbreak that was linked to Disneyland in California, which resulted in a multi-state outbreak (Cadena et al. 2019). Since reports of these outbreaks, the occurrence of measles outbreaks has not diminished with a total of 1282 confirmed cases of measles in the US in 2019 alone. The amount reported in 2019 has been the greatest number reported in the US since 1992 (McAteer 2020). Similarly in Europe, reported incidences of measles increased by 300% during the first quarter of 2019 when compared to the first quarter of 2018 (Wilder-Smith & Qureshi 2019). This is of great concern considering that Measles is one of the most highly contagious diseases and requires very high levels of immunization to prevent spread. Many researchers believe that the infrequency of vaccine-preventable diseases and the ramifications of these diseases have enabled the

parental belief that vaccines are unnecessary and, as a result, have led to a decrease in vaccination rates (Hough-Telford et al. 2016).

Similar reports of increased outbreaks have been noted with other VPDs such as pertussis. Although pertussis is one of the most common VPDs, a dramatic resurgence in pertussis cases are occurring with a total of 2388 confirmed cases in the US in 2022 and 3 confirmed deaths from pertussis infection (Hartzell 2014, CDC 2022 Provisional Report). From the reported 2388 confirmed cases in 2022, only 39.1% of children were confirmed to have completed their primary DTaP vaccination series (Figure 1 and 2). Although pertussis incidence reports have seen a slight decrease between 2015 and 2021 (Figure 3), recent declines in trend between 2020 and 2021 have been associated with the implementation of face masks (Zamir 2023).

The efforts that are required to respond to VPD outbreaks have a detrimental effect on public health resources and economic burden both in the US and throughout the world. In 2011 it was estimated that the US spent between $2.7 million and $5.3 million to respond to 16 measles outbreaks (Ortega-Sanchez et al 2012). Similarly for a 2012 measles outbreak in England, the NHS spent an estimated 3.9 million to 5.2 million pounds to respond to the outbreaks. It was further estimated that it would have only cost the NHS 182,909 pounds to achieve herd immunity and potentially prevent the outbreaks, just 4% of the total cost of the outbreak (Ghebrehewet et al 2016). Similar reports of economic burden and strain on public health resources following VPD outbreaks were reported in the Netherlands in 2013, estimated cost of $4.7 million; Ethiopia in 2011,

estimated cost of $758,869; and China in 2017, estimated cost of $214,774 (Suijkerbuijk et al 2015, Wallace et al 2014, & Zou et al 2021).

Reported Pertussis Cases and Percent Hospitalization by Age Group

Age	No. of Cases (% of total)	Age Inc /100,000	% Hospitalized by age**
< 6 mos	139 (5.8)	7.8	17.1
6-11 mos	130 (5.4)	7.3	4.9
1-6 yrs	622 (26.0)	2.7	1.9
7-10 yrs	176 (7.4)	1.1	0.0
11-19 yrs	231 (9.7)	0.6	1.2
20+ yrs	1,089 (45.6)	0.4	11.2
Unknown Age	1 (0.0)	N/A	N/A
Total	**2,388 (100)**	**0.7***	**6.9**

*Total incidence per 100,000 calculated from 2,387 cases with age reported.
**Calculated from those with known hospitalization status.

Reported Pertussis Deaths

Age	Deaths*
Cases, aged < 1 yr	1
Cases, aged ≥ 1 yr	2
Total	**3†**

*Deaths reported through NNDSS
Confirmation of deaths is ongoing and may result in changes to the final count for 2022.

Figure 1: CDC Reported Pertussis Cases, Hospitalization, and Reported Deaths. Figure taken from the Centers for Disease Control and Prevention, (2022).

Reported DTaP Vaccine Status of Children with Pertussis, Ages 6 months through 6 years

Age	Vaccine History Unknown	Unvaccinated	Undervaccinated (1-2 doses)	Completed Primary DTaP Series (3+ doses)	Total
	No. (%)	No. (%)	No. (%)	No. (%)	No.
6-11 mo	75 (57.7)	8 (6.2)	10 (7.7)	37 (28.5)	130
1-4 yrs	230 (50.1)	26 (5.7)	30 (6.5)	173 (37.7)	459
5-6 yrs	61 (37.4)	10 (6.1)	8 (4.9)	84 (51.5)	163
Total	**366 (48.7)**	**44 (5.9)**	**48 (6.4)**	**294 (39.1)**	**752**

Figure 2: CDC Confirmed Completed DTaP Series Report. Figure taken from the Centers for Disease Control and Prevention, (2022).

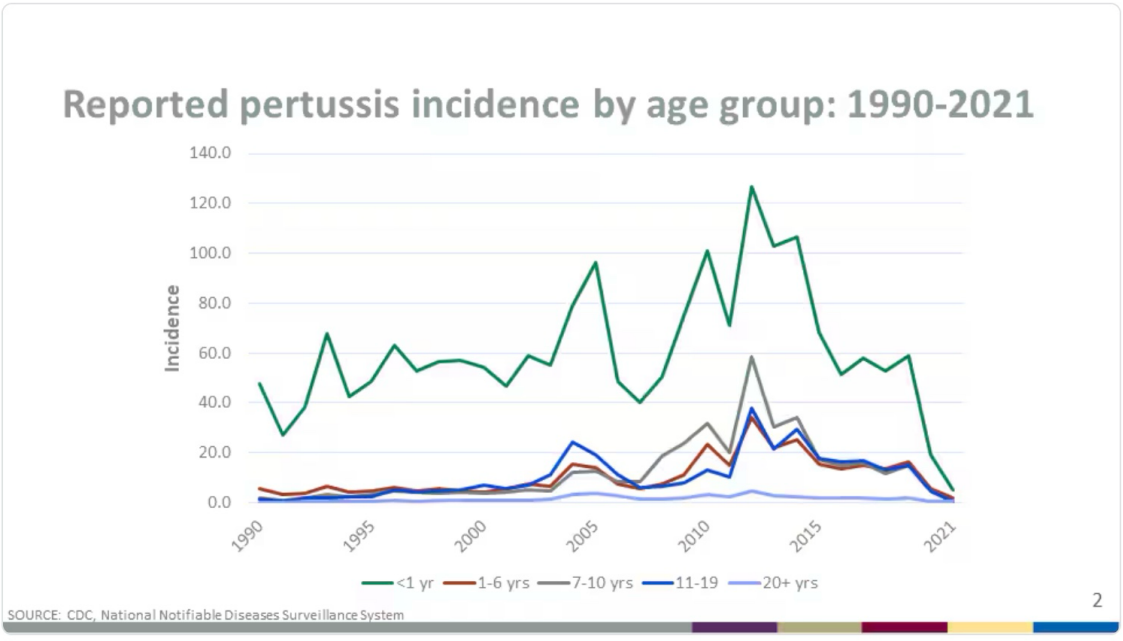

Figure 3: CDC Reported Incidences of Pertussis Between 1990 and 2021. Figure taken from the Centers for Disease Control and Prevention, (2024).

Vaccine Specific Hesitancy

As previously discussed, there is a distinct difference between the term ‘anti-vax’ and ‘vaccine hesitant.’ Individuals who are perceived to be ‘anti-vax’ have an opposition towards the use of all or some vaccines, whereas an individual who is vaccine hesitant may exhibit uncertainty or indecision towards specific vaccines, which could be subject to change. Although every vaccine that has ever been discovered, introduced, and implemented into public health society has been subject to hesitancy and scrutiny, there are a few vaccines that are constantly and more commonly associated with VH; these include the Influenza vaccine (flu vaccine), the Human Papillomavirus vaccine (HPV), the MMR vaccine, the Diphtheria Pertussis and Tetanus vaccine (DTP), and most recently the SARS-CoV-2 vaccine.

Although hesitancy towards vaccines is heavily associated with the Wakefield-autism vaccine controversy, the fear of mercury-based thimerosal in vaccines further elicited hesitancy towards immunizations. Historically, the incorporation of organomercurials into pediatric vaccines was due to their preservative and germicide-like properties. Previous organomercurials that were used in vaccines as preservatives, such as Phenol and Cresol, would decrease the potency of the vaccine. After the discovery of Thimerosal in 1928, researchers found that thimerosal did not have this effect and it inhibited bacterial growth in vaccines (Baker 2008). Due to this, the use of thimerosal in pediatric vaccines became standard practice because of the ability to provide vaccines in multi-dose vials. Thimerosal allowed for the immunization of large groups of individuals, an essential aspect for remote areas and areas where single-dose vaccines would be too

costly and leading to greater collective-immunity. In the year following the Wakefield controversy, the US Food and Drug Administration (FDA) conducted a food and drug review of all products containing mercury. In doing so, pediatric vaccines that contained thimerosal, a compound that contained trace amounts of ethylmercury, were assessed and thimerosal was ultimately removed from pediatric vaccines as a precaution (Larson et al 2022). Although the reports indicated no evidence of harm, removal of the compound from pediatric vaccines reinforced VH and public concern of a causal association between vaccines and autism (Larson et al 2022). It should be noted that the MMR vaccine, the Varicella vaccine (chickenpox), inactivated polio vaccine (IPV) and the pneumococcal conjugate vaccines have never contained thimerosal (CDC Vaccine Safety).

Fear and concern about the contents in immunizations has been a growing concern amongst parents and VH individuals and it will likely continue to be a subject of great concern as the VH movement continues, further resulting in vaccine-specific hesitancy. Fear and concern about the contents in the DPT vaccine is the influential contributor of hesitancy towards this vaccine. In 1982, after the women's health movement, parents, and patients began to question the use of Thimerosal and mercury-containing components in vaccines, a novel investigative news report was aired entitled 'DPT: Vaccine Roulette' (Conis 2014). This broadcast reported on the hazards of the Pertussis component of DPT and included reports from physicians and government scientists that implicated that DPT was no longer necessary and was causing harm. This broadcast inspired the formation of the group 'Dissatisfied Parents Together', which

advocated for safer vaccines and compensation for families of children who had been harmed by vaccines (Conis 2014). Although the efforts of the Dissatisfied Parents Together group led to the passing of the National Childhood Injury Act of 1986, it incited a lack of distrust towards vaccines, further fueling the VH movement.

Similar to the DPT and MMR vaccine, the flu vaccine has been subject to scrutiny and public distrust. Despite the severity of the Influenza virus and an estimated 290,000 to 650,000 deaths globally per year due to Influenza, hesitancy towards the flu vaccine remains high (WHO Fact Sheet 2020). Between 2009-2010, during the Hemagglutinin Type 1 and Neuraminidase Type 1 (H1N1) pandemic, it was estimated that there was low flu vaccine uptake with a reported less than 50% expected coverage in target populations globally (Schmid et al 2017). Similar statistics were observed in the 2018-2019 flu season in pediatric patients in which only 62.6% of children were covered with at least one dose of the flu vaccine. Furthermore, when compared to other pediatric vaccines, the flu vaccine habitually lags behind other pediatric vaccines and has reduced coverage rates (Santibanez et al 2020). The decline in both adult and pediatric flu vaccine coverage rates is the result of flu vaccine specific hesitancy. Qualitative research has found that reasons for flu vaccine hesitancy are attributable to a myriad of considerations and that many flu vaccine hesitant individuals view the flu vaccine differently than other vaccines. One consideration that flu vaccine hesitant individuals noted was the varied effectiveness of the flu vaccine. Flu vaccine hesitant individuals also noted annual requirement as a concern (Schmid et al 2017 and Quinn et al 2019). However, markedly, one of the major considerations that plague flu vaccine hesitant individuals is the myth that the flu vaccine

will result in an individual contracting the influenza virus. Claims such as these may lead individuals to believe that the flu vaccine is unsafe and thus result in vaccine-specific hesitancy (Nyhan & Reifler 2015). The reasoning behind these claims could be attributed to a lack of understanding of vaccinology as well as an error in the physicians understanding of the patient's knowledge of the flu vaccine. Considering that some vaccines, such as Measles, help to prevent the disease from occurring, patients expect the same from the flu vaccine and this unfortunately may not be explained by their physicians. Further research is needed to qualitatively assess this.

In comparison, research has shown that access to contradictory and potentially inaccurate information is one of the driving forces behind parent VH of the HPV vaccine (Patel & Berenson 2013). Although the HPV vaccine is one of two cancer-preventing vaccine with high efficacy to be introduced, the other being the Hepatitis B vaccine (Hep B), uptake rates in the US have been less than favorable. In 2019 the CDC found that only 54.2% of adolescents aged 13-17 completed the HPV vaccination series (Elam-Evans et al 2020). In a 2013 National Teen Immunization Survey parents reported that reasons for HPV VH were due to lack of knowledge, concerns about vaccine safety, that the vaccine was not recommended by providers, or that the vaccine was unnecessary (Szilagyi et al 2020). Concerns for vaccine safety, most notably after a vaccine controversy or scare, have resulted in declined uptake of vaccines. After an HPV vaccine scare in Denmark, coupled with negative media portrayal, vaccine uptake of the HPV vaccine declined from 95% to about 30% (Gortz et al 2020). The fallout from the HPV vaccine scare in Denmark was the result of increased reports of adverse effects following

vaccination, specifically reported symptoms of dizziness, fatigue, and fainting. Similar symptom episodes were reported in Japan, triggering VH towards the HPV in Europe (Larson et al 2022). Concerns for the safety of the HPV vaccine culminated in an anti-HPV vaccine movement on Twitter which resulted in the Japanese government temporarily suspending its recommendation of the HPV vaccine in 2013. This suspension lasted for about nine years until 2022 (Haruyama, Obara & Fujita 2022). Despite the Japanese governments re-enactment of active recommendation, the repercussions from the initial suspension and vaccine scare have prompted global VH towards the HPV vaccine.

The most recent example of vaccine-specific hesitancy can be observed with the SARS-CoV-2 vaccine. The 2019 Coronavirus global pandemic resulted in an estimated 18.2 million deaths worldwide (Larkin 2022) and complications, due to infection, that are still being studied. Although the effects from infection were detrimental and the aftereffects from the pandemic were witnessed globally, there was immense hesitancy towards the introduction of the SARS-CoV-2 vaccine. According to CDC data, only 57% of US adults were immunized against SARS-CoV-2 during the period between December 2020-May 2021 (Diesel, 2021). Of the 57% of individuals that were immunized, 80% of individuals were greater than or equal to 65 years of age. Despite early availability of the vaccine, weekly initiation rates remained less than 4% and decreased amongst age groups (Diesel, 2021). Furthermore, reports of vaccine safety concerns from the AstraZeneca covid-19 vaccine did little to diminish VH towards the vaccine. Consequently, the European Medicines Agency's decision to declare the AstraZeneca vaccine safe, despite

early reports of safety concerns due to anaphylaxis and blood clots, further fueled feelings of VH towards the SARS-CoV-2 vaccine and an unwillingness to immunize. Contradictory reports such as these cause confusion and result in public mistrust of medical information and hesitancy towards immunization. This hesitancy towards specific vaccines or newly introduced vaccines, such as the SARS-CoV-2 vaccine(s), can result in increased hesitancy towards other vaccines, further fueling the VH movement.

Parental Reasons and Motivations for VH

Since the implementation of vaccines in routine medical care, there have been several reasons as to why individuals, specifically parents, have opposed the idea of vaccines. These reasons have changed over the years as the evidence that supports vaccines continues to grow. Many studies that have analyzed parental motivations behind vaccine hesitancy cite location and economic status as a factor that could contribute to the decline in vaccination rates. One study in particular examined the spatial clusters of under-vaccinated children across the United States. In their study, Cadena et al. (2019) used population models for the state of Washington and Minnesota along with immunization data from public schools. Using this information, they were able to analyze vaccine coverage among children and found significant clusters of under-immunized children based on demographics. In their study Cadena et al. (2019) found that there were two significant under-vaccinated clusters in Minnesota and three significant clusters in Washington. The first of the two areas that were found in Minnesota was an urban area, St. Paul and Minneapolis; and a rural area, west of Minneapolis. They found that the first cluster, the urban area, contained mostly low-income households while the second

cluster, the rural area, contained mostly high-income households. The three areas that were discovered in Washington were classified as major metropolitan areas that then spread out to rural areas. The observations for demographics in Washington state were similar to those seen in Minnesota. They also found that the number of unvaccinated children was significantly higher in Washington than in Minnesota, with the MMR vaccine named as a vaccine with significant under-immunization rates in both states (Cadena et al. 2019). These clusters showed that under-vaccinated children and unvaccinated children tended to reside in the same location, cementing the theory that location is a contributing factor in parental reasons for VH.

Similarly, a study conducted in Shanghai, China analyzed decreases in vaccine rates in urban and rural areas. In addition to analyzing demographic conditions, Ren et al. 2018 reviewed vaccine educational literacy and its correlation to location. They identified two groups of residents, locals and non-locals. The non-local group of residents were then subdivided into two sub-groups: rural non-locals, people who moved from rural areas to urban cities, and urban non-locals, people who moved from one urban city in China to another urban city. The Chinese government, in an effort to control infectious diseases, provides all non-local children with the means to receive free vaccinations (Ren et al. 2018). The article notes that due to the inaccessibility of public services, health quality in suburban areas were expected to be lower than those in urban areas. Using this information, the researchers compared vaccine hesitancy between the different demographic groups, specifically the locals and non-locals. The population that was studied contained 48.3 percent of locals and the remaining 51.7 percent were non-locals.

Of the 51.7 percent of non-locals, 15.8 percent resided in urban areas and 35.9 percent resided in rural areas (Ren et al. 2018). According to the article, the researchers found that the area where one resides is a significant factor in predicting vaccination beliefs. Their research found that individuals living in rural areas, who were also non-locals, were more likely to refuse vaccines than individuals living in urban areas.

Ren et al. (2018) also noted that many parents living in rural or outer suburb areas were less confident in the effectiveness and ability of vaccines. Their study found that about 71.6 percent of parents were concerned about adverse effects specifically. Ren et al. (2018) found that parents who were not educated on vaccines had more concerns about newer vaccines and that exposure to VPDs did not encourage individuals to vaccinate themselves. Similar results were noted in a study that analyzed the reasons cited to pediatricians for parental VH. After analyzing surveys conducted by the American Academy of Pediatrics on VH, researchers found that the location of a pediatric practice had a significant effect on VH. Researchers noted that pediatricians located in urban-inner cities were less likely to come across a request for a vaccine delay or refusal. Furthermore, researchers observed that pediatric offices located in the Southern region were more commonly experiencing vaccine refusals than pediatric offices located in the Midwestern region (Hough-Telford et al. 2016). The results from these studies indicates the significance of location in regard to parental reasons for VH. Pediatric offices and individuals in rural areas express increased VH when compared to individuals and pediatric offices located in urban areas.

While these results are based on demographics in Shanghai, China and the United States, similar responses towards VH are expressed globally. A survey distributed by the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) was designed to better understand the reasons behind vaccine hesitancy and to oversee the increasing number of vaccine hesitancy reports throughout the world in 2014. This standardized questionnaire was sent to 194 WHO and UNICEF member states (Marti et al. 2017). These states were then asked two questions that were both indicators related to vaccine hesitancy: the reasons for vaccine hesitancy, and whether there has been an assessment of vaccine hesitancy within the previous five years at a national or subnational level. The survey also considered demographics and focused on low and lower-middle income countries since they are priority countries for WHO. There were 185 out of the 195 WHO member states that completed the survey form. Each country, grouped together by region, had a different response rate with the region of the America's having an 89 percent response rate. The survey noted that the most commonly cited reason for vaccine hesitancy among the member states was the concern of the risk and benefits of vaccines, as well as the safety of vaccines, specifically adverse reactions. This reason was most commonly associated with countries in the European region, the Southeast Asian region, and the Western Pacific region (Marti et al. 2017). The most frequently cited reasons in the region of the Americas were religion, culture, and socio-economic status. No specific religion was cited. The reported reasons in the African region and in the Eastern Mediterranean region was a lack of education and awareness of vaccines and vaccine importance. The causes behind these reasons were similar in a

majority of the regions except for the region of the Americas. WHO and UNICEF cited communication and media coverage as a big factor whereas other regions named the design of the vaccination program and low risk of obtaining vaccine-preventable diseases as causes. Evidence found in the survey also supported the idea that demographics play an important role in the vaccine hesitancy movement. Research found that low income and lower-middle income countries' reasons behind vaccine hesitancy revolved around a lack of knowledge and awareness of vaccines. However, in upper-middle income countries, reasons for vaccine hesitancy included the risk/benefits of vaccines particularly relating to adverse reactions. This reason was reported in high-income countries as well (Marti et al. 2017). Likewise, one study noted that pediatricians who cared for wealthier families that were more educated, experienced more vaccine hesitancy amongst parents and an increase in vaccine refusal rates (Leib et al. 2011).

Although each country cited different reasons for vaccine hesitancy, parental health education and health literacy was a common reason cited in most countries. Many parents are either unaware or uncertain of the benefits of vaccines and are quick to assume the risks of such vaccines that are often presented in the media. Many researchers have suggested that the negative portrayal of vaccines in the media has affected parental health education (Facciola et al. 2019). In a study conducted in Italy, researchers analyzed parental attitudes of vaccines and specific vaccines based on their health education and past experiences. Much importance was placed on the various sources of information that affected the parents' decision to vaccinate their children. Questionnaires were distributed to parents of lower secondary school children in the city of Messina in

Sicily, Italy. The researchers distributed 1,300 questionnaires and received an 84 percent response rate, about 1,093 questionnaires. Parents were asked about their opinions towards vaccines, their education levels, their opinions of their physicians, their reasons of opposing vaccines, and a number of other questions related to vaccine hesitancy. Of the parents who responded, a majority of them, 42.6 percent of fathers and 45.7 percent of mothers, had an upper secondary school diploma, which is equivalent to a high school diploma in the United States (Facciola et al. 2019). Less than half of the parents who responded to the questionnaire had a university degree; 21 percent of fathers and 24.3 percent of mothers. When asked about their personal opinions about vaccinations, 86 percent of parents had favorable views towards vaccines, 6.6 percent had indifferent views, and 7.4 percent had contrary views. The researchers noted that the number of vaccinations that were implemented correlated negatively with the education levels of the parents. Facciola et al. (2019) found that 32 percent of parents received negative information about vaccines from the internet and television, and 27 percent of parents received such information either by word of mouth from friends or from books and journals. Additionally, the reasons for parental vaccine hesitancy were from fear of adverse reactions, with 91.5 percent of parents reporting this. The contrary opinion of parents was related to direct or indirect knowledge of individuals who were affected by vaccines. Facciola et al. (2019) concluded that lack of knowledge and misleading information from the media greatly affects parents' decisions about vaccinating their child. Furthermore, parents with a reduced education were more inclined to vaccinate their children whereas parents with a secondary level education were more likely to be

VH and were four times as likely to have more concerns about adverse reactions than parents with reduced education levels (Facciola et al. 2019; Opel et al. 2011).

Similar results have been noted in other studies where researchers have found that parental refusals of childhood vaccines were generally associated with parents of secondary level education as opposed to parents with lower education levels (Smith et al. 2004). Although this study was conducted in Italy, similar sentiments have been expressed amongst parents in other countries. Researchers discovered that concerns of parents in Melbourne, Australia towards vaccines was due in part to their lack of knowledge and education levels. Researchers found that 23 percent of parents cited insufficient knowledge as a factor in their decisions to vaccinate their children (Costa-Pinto et al. 2018).

Despite the health education of parents being a considerable reason for VH, other factors that contribute to parental reasons for VH include the age at which children are immunized and its effect on their immune system. Many parents believe that their children receive too many vaccines at such a young age and that this could be potentially harmful to their child's immune system. In one study, researchers analyzed vaccine coverage in Australian children and the vaccine concerns that many parents have. Using two different surveys, targeting two different groups of parents, 461 parents were surveyed. The first survey, the Parental Immunization and Needs survey, was intended for parents with children under five years of age. The second survey, the Community survey, was intended for mothers with children under nineteen months of age (Costa-Pinto et al. 2018). The researchers based their survey questions on earlier studies that

focused on vaccine hesitancy amongst parents. Although a majority of the parents surveyed, 97 percent, believed vaccines to be important and necessary, a significant number of parents, 14 percent, still held doubts about the safety of vaccines. Costa-Pinto et al. (2018) found that of the many concerns that parents had, 25 percent had concerns over the number of vaccines given in the first two years of their child's life. Researchers also noted that 17 percent of parents were worried about the outcome that vaccines may have on their child's immune system. Parents feared that vaccines could potentially cripple their child's immune system (Costa-Pinto et al. 2018). The survey results also indicated similar parental concerns that were found in other studies, such as the risk/benefits of vaccines, the harmful side effects of vaccines, and whether vaccines cause autism. Additionally, 41 percent of parents claimed that their child's immune system was more delicate than most children's immune systems. Other important reasons for VH included the belief that vaccines cause their child too much pain and the idea that their children did not need to be immunized since other children were vaccinated (Costa-Pinto et al. 2018).

The responses from Costa-Pinto et al. (2018) study were similar responses found in other studies conducted in other countries. Utilizing pediatrician survey results from the American Academy of Pediatrics, between 2006 and 2013, Hough-Telford et al. (2016), found that the reasons for VH cited to pediatricians from parents included: concern over their child's discomfort and fear of too many vaccines at a young age, 75 percent of parents and 22 percent of parents respectively. Pediatricians also cited parent concerns their children were too small to be receiving such a large quantity of vaccines.

Other concerns that were cited included the risk/benefits of vaccines, fear of adverse reactions, concerns about autism, and the idea that vaccines are unnecessary (Hough-Telford et al. 2016). In response to these parental concerns, the Institute of Medicine reported that the number of foreign antigens that an infant is exposed to poses more of a concern than vaccines. They argued that it is unlikely that the antigens found in vaccines would harm or burden the immune system of infants (Blackford 2001). Although there is plenty of data to refute these claims and concerns of VH parents, VH rates continue to increase globally and have led to a subsequent decrease in vaccination coverage rates. This decline in vaccination rates and the increase in VH has had detrimental effects on the human population. Reasons for this could be attributed to the use of social media in propagating vaccine misinformation and anti-vaccine sentiments.

Effects of the COVID-19 Pandemic and Vaccine on VH

As witnessed during the H1N1 pandemic and the implementation of the flu vaccine, attitudes towards vaccination tend to change during the midst of a public health crisis. Although past research has suggested that the increased prospect of a disease threat may improve attitudes towards the overwhelming value of immunization, the recent SARS-CoV-2 pandemic has proven otherwise. Prior to the implementation of the SARS-CoV-2 vaccine, reports indicated increased hesitancy and skepticism towards the vaccine. In a preliminary study focused on identifying factors associated with Covid-19 VH, researchers found that several factors were associated with both the refusal and delay in receiving the SARS-CoV-2 vaccine. These reasons included age, loss of income during

the pandemic, non-receipt of a flu vaccine that year, a low confidence in the vaccine being developed, a disappointment in government response during the pandemic, and distrust of the health information provided by healthcare personnel (Saores et al. 2021). The correlation of non-receipt of a flu vaccine the year prior and hesitancy towards the SARS-CoV-2 vaccine could be attributed to an individual's perception of disease risk versus vaccine uptake. Saores et al. (2021) also found that only 35% of the 1,943 individuals surveyed planned to receive the SARS-CoV-2 vaccine when it became readily available however, VH towards the SARS-CoV-2 vaccine was higher prior to information about the safety and efficacy of the vaccine being released (Saores et al. 2021).

Although this study noted a decrease in VH towards the SARS-CoV-2 vaccine with the release of the safety and efficacy information, the SARS-CoV-2 also resulted in declination trends of other immunization rates. In a longitudinal study conducted during the COVID-19 pandemic, researchers found a decrease in pro-vaccination attitudes and noted that VH towards the SARS-CoV-2 vaccine had a positive correlation to increased VH towards the flu vaccine (Fridman, Gershon, & Gneezy 2021). Similarly, research conducted by Machado et. al. found that there was an increase in Google searches of anti-vaccine terms during the COVID-19 pandemic. These peaks in Google searches often occurred following various WHO announcements (Machado et al. 2021). The COVID-19 pandemic dissuaded many parents' intentions of vaccinating their children. In a group of previously VH parents, 50% of parents were still reluctant to vaccinate during the pandemic (Yilmazbas, Terzi, & Ozceker 2021).

During the COVID-19 pandemic, there was a reported decline in the number of vaccines administered, resulting in increased cases of VPDs in endemic countries. Due to decreased access to routine healthcare and a growing fear of the safety and efficacy of vaccines, the COVID-19 pandemic adversely affected routine immunization administration (Machado et al. 2021, Lassi et al. 2021). Immunizations, such as the Measles vaccine, were postponed in 23 countries, resulting in the potential of a large Measles outbreak (Lassi et al. 2021). Moreover, there was an increased belief that vaccines were unnecessary during the COVID-19 pandemic, further hindering and decreasing routine immunization administration. A multi-methods approach study in England found that parents believed that their child was at a low risk of developing severe outcomes, such as multisystem inflammatory syndrome in children (MIS-C), from SARS-CoV-2 infection. This belief was one of the many deciding factors in parent's choosing to refuse SARS-CoV-2 vaccination for their children (Machado et al. 2021). This belief that vaccines are unnecessary due to low risk of disease has existed prior to the COVID-19 pandemic and has been a key factor in VH however, the COVID-19 pandemic further reinforced this ideology. Parents not only questioned the necessity of the SARS-CoV-2 vaccine, but other routine immunizations as well based on the belief that VPDs are no longer a threat to public health and low risk perception (Troaino and Nardi 2021).

Rapid development of the SARS-CoV-2 vaccine, which incited questions about the safety and necessity of the vaccine, and government oversight during the pandemic, further contributed to VH towards the SARS-CoV-2 vaccine and overall vaccines. The

unique expedited development of the SARS-CoV-2 vaccine and the misinformation surrounding its development, approval, and distribution process lessened confidence in healthcare administrations and increased distrust in immunizations. This, coupled with existing VH and anti-vaccine rhetoric contributed to factors that created further doubts about the need for immunization (Lin, Tu, & Beitsch 2020). In addition to this, partisan divides during the COVID-19 pandemic further contributed to VH and SARS-CoV-2 specific VH.

Reports from a longitudinal study conducted during the COVID-19 pandemic found that political ideology correlated to a decrease in pro-vaccination attitudes and SARS-CoV-2 vaccination. Researchers found that party affiliation resulted in differing risk perception of SARS-CoV-2 infection and coincidentally, VPDs, leading to varying motivations to take preventative measures (Fridman, Gershon, & Gneezy 2021). Troaino and Nardi (2021) found that individuals who leaned towards radical parties, individuals that did not vote, or individuals that identified with a specific political affiliation, the Republican party, were significantly more likely to refuse the SARS-CoV-2 vaccine. Previous analysis conducted by Kennedy et al. (2019) found that support for populist political parties could serve as an indicator for VH, and increased backing for such parties should alert public health officials to remain vigilant. Yasmin et al. (2021) found that endorsement of public health campaigns by political or government figures were perceived as politicizing a current necessity. Government oversight in mandating vaccination in workplaces and prohibiting unvaccinated individuals from entering public

spaces further influenced SARS-CoV-2 VH and overall VH (Vergara, Sarmiento, & Lagman 2021).

Effects of Social Media on VH

The continued proliferation of anti-vaccination information and misinformation of vaccine safety and effectiveness on social media has undoubtedly caused significant decline in public vaccination efforts and is a contributing factor in VH. Although this has been an ongoing concern, it become more prevalent and increased in urgency during the COVID-19 pandemic and the rapid development and deployment of the SARS-CoV-2 vaccine. With the improvement of technology and media outlets, social media has become widely accessible globally. In contrast to traditional media, social media has allowed for the rapid creation and sharing of content globally without editorial oversight (Puri et al. 2020). In doing so, individuals generate an algorithm that selects content aligning with their beliefs and may not contain factual information, resulting in ideological isolation. As a result, there is significant public health concern regarding vaccine misinformation on these platforms and its implication on the effect of VH.

VH groups have a significant presence on social media, with research from the early 2000s to now indicating that a large portion of vaccine-related content on social media platforms are anti-vaccine related (Wilson & Wiysonge 2020). This poses a significant question of whether the effects of social media usage or disinformation campaigns increases VH. In 2017, Bach et al. analyzed 87 YouTube videos containing the words ‘vaccine safety’ and ‘vaccines and children’. Their analysis found that 65% of these videos conveyed anti-vaccine sentiments. Notably, only 5.6% of the videos

analyzed were created by government professionals and 36.8% lacked scientific evidence (Bach et al. 2017). When analyzing YouTube videos containing the words 'COVID-19' and 'Coronavirus', 27.5% of the videos contained non-factual information and had collectively amassed over 60 million views (Li et al. 2020).

This trend appears to reinforce itself, as research suggests that anti-vaccine content tends to attract more user interaction. Blankenship et al. (2018) analyzed tweets containing the hashtag 'vaccine' from 2010 and 2016 and found that anti-vaccine tweets were re-tweeted 4.13 times more often than neutral tweets. Similarly, Basch et al. (2019) analyzed 150 Instagram posts featuring the hashtag 'HPV' and noted that the anti-vaccine posts received a significantly greater average number of likes. Interestingly, research has shown that discussions about vaccines on social media have evolved with time and are often influenced by real-world events (Puri et al. 2020). Significant increases in anti-vaccination discussions on Facebook, Twitter, and Instagram, were found to coincide with the release of documentaries, novel vaccines, and news of VPD outbreaks. During the 2014-2015 Measles outbreak, there was a significant increase in anti-vaccine discussions on Twitter, which coincided with the release of the anti-vaccine book 'Vaccine Whistleblower' (Gunaratne et al. 2019). Similarly, Piedrahita-Valdes et al. (2021) found that negative vaccine tweets increased in frequency during April 2016 following the release of a documentary that linked vaccines and autism.

Increase in anti-vaccination discussion on social media was also noted during the COVID-19 pandemic and following the release of emergency use authorization of the SARS-CoV-2 vaccine. The hashtag 'coronavirus' emerged as the second most used

hashtag in 2020, with Twitter data reporting that a COVID-19 related tweet occurred every 45 milliseconds (Josephson & Lamb 2020, Cinelli et al. 2020). During the initial phase of the COVID-19 pandemic, Cinelli et al. (2020) investigated the false and misleading information about SARS-CoV-2 that was shared across different social media sites to measure the 'transmissibility' of posts on each platform. Their findings showed that regardless of the social media platform, there was no significant difference in the spreading of false and misleading information compared to reliable information. This finding demonstrates that there is no one specific social media platform that promotes anti-vaccines misinformation over another, rather social media as a whole. There is growing concern that distrust towards vaccines and vaccine misinformation stems from non-human-run accounts, or 'bots' (Puri et al. 2020). Due to this, some researchers propose that existing public health and vaccine initiatives could lead to increased VH and instead recommend using hashtags and keywords that are frequently searched by VH individuals (Piedrahita-Valdes et al. 2021).

Furthermore, several studies have noted that even minute exposure to anti-vaccine social media rhetoric can result in a previously pro-vaccine individual becoming VH (Al-Uqdah et al. 2022, Betsch et al. 2010, Nan et al. 2012). Betsch et al. (2010) found that just five to ten minutes of exposure to vaccine-critical websites heightened VH amongst users when compared to individuals who visited control websites. Al-Uqdah et al. (2022) emphasized this notion by noting that just a few minutes of exposure to disinformation on social media platforms can impact VH, especially considering that the majority of adults (98%) use social media. Social media tends to propagate vaccine misinformation and

anti-vaccine rhetoric by employing the use of vivid narratives and powerful imagery. These techniques have proven successful and social media posts containing these methods are shared more. Alarmingly, certain social media users, including older adults, individuals with lower literacy levels, and those with limited digital literacy, are more vulnerable to the emotional narratives propagated on social media (Puri et al. 2020). These social media users may find it challenging to distinguish the credibility of vaccine information sources, further affecting VH amongst individuals.

Effects and Repercussions of Continued VH in Pediatric Healthcare

Increased VH amongst parents has led to an increased risk of VPDs, increased school immunization exemptions, an increase in pediatricians dismissing patients and families from their practice (pediatric dismissal rates), and a number of other effects that negatively impact the human population. However, one of the main concerns of vaccine hesitancy is the increased risk VPDs on public health, as noted by several studies and outbreaks. Many researchers believe that the infrequency of VPDs and the lack parental health literacy on the severe outcomes of these diseases have enabled the parental belief that vaccines are unnecessary and, as a result, have led to a decrease in vaccination rates (Hough-Telford et al. 2016). In 2015 the Center for Disease Control and Prevention (CDC) conducted an analysis in the US of recent measles outbreaks, in an effort to better understand why these outbreaks were occurring. Of the 159 cases that were reported during the months of January to April, 80 percent of the cases involved individuals who were unvaccinated (Clemmons et al. 2015). The CDC reported that only 28 individuals,

18 percent, out of the 159 patients had received a measles vaccination. The remaining 82 percent of patients were either unvaccinated or had unknown vaccination statuses. The reasons cited amongst the unvaccinated patient cases included religious conflict, medical opposition, and other reasons. Comparable results were found in a study that analyzed the exposure of the measles infection during 1985 to 1992 (Salmon et al. 1999). The study found there to be a 35 times greater risk of measles in children who were unvaccinated when compared to children who were vaccinated, within the US. The transmission of diseases such as measles from unvaccinated individuals not only increases the possibility of future outbreaks but also increases the likelihood of transmission of these diseases to groups of individuals that are more susceptible to these diseases, such as infants that are too young to receive vaccines and individuals who cannot receive vaccinations due to medical conditions (Clemmons et al. 2015).

Feiken et al. (2000) found similar results during an independent study of the effects of personal immunization exemptions and the risks of measles and pertussis outbreaks. In their study, researchers analyzed whether personal immunization exemptions, regardless of the reason, was associated with an increased risk of pertussis and measles outbreaks. Using school immunization summary reports from the state of Colorado, researchers evaluated children between the ages of 3 and 18, whose parents refused vaccination. The children were then subdivided into four different age groups, matching their school levels (preschool and kindergarten, elementary school, middle school, and high school) and then separated into two categories: vaccinated children and unvaccinated children (Feiken et al. 2000). The incidence rate for measles and pertussis

outbreak cases were then calculated. After calculating the incidence rate for measles and pertussis cases, researchers found that there were 202 confirmed cases of measles in children from 1987-1998. Children whose parents were vaccine hesitant were 22 times more likely to develop measles than children who were vaccinated. Researchers also noted that 541 cases of pertussis were recorded during 1996-1998. Much like the measles results, pertussis outbreaks were reported to be 5.9 times more likely to occur in unvaccinated children than in vaccinated children. For both pertussis and measles outbreaks, the risks of acquiring said diseases were higher in younger-aged children, specifically between the ages of three and ten (Feiken et al. 2000). Researchers also noted that 22 percent of children obtained measles while at school and in four different counties in Colorado, eight measles outbreaks occurred at school. Similarly, 21 percent of children obtained pertussis while at school and in five different counties in Colorado, 17 pertussis outbreaks occurred at school. These schools with measles and pertussis outbreaks had higher immunization exemption rates than schools without outbreak (Feiken et al. 2000).

Increased risk of the spread of VPDs, due to VH, is a severe concern amongst the human population and the spread of such diseases could be linked to an increase in school immunization exemptions. Parental reasons for these school exemptions can be grouped into two different categories: religious exemptions and philosophical exemptions. Philosophical exemptions include the parental belief that vaccines are unnecessary, that vaccines pose more harm than good, and that vaccines are harmful to their child's immune system. In one study (Feiken et al. 2000) researchers found there to be a 0.85 percent increase in philosophical school exemptions in the state of Colorado

during 1987-1998, and a slight decrease in religious school exemptions, 0.04 percent. Comparable results were found in a study that analyzed spatial clusters of vaccine refusals and high-school exemption rates.

Although the United States has laws that require certain vaccinations for entry into public schools, many states, twenty states in particular, allow parents to exempt their child from vaccines. National reports show that the state of Arizona ranked eighth in the highest exemption rates in the United States. During the academic school of 2012-13 and 2013-14, there was a 0.7 percent increase in the number of school immunization exemptions in the state of Arizona. Recently, reports show that school immunization exemptions in Arizona have nearly tripled within the past decade (Pottinger et al. 2018). Consequently, the number of vaccine-preventable diseases have also increased, with an average of over 200 outbreak cases per year. Researchers have indicated that low vaccination rates, coupled with increased exemption rates, are to blame for the increase in outbreak cases. Researchers also noted that the reasons parents exempt their children from school immunizations are because of parental concerns of the risk/benefits of vaccines and skepticism of the value of vaccines (Pottinger et al. 2018; Kumar et al. 2016).

Due to increases in school immunization exemptions, states like California have begun to pass bills that remove non-medical exemptions for school entry. In June 2015 the California State Senate passed a bill that eliminated school immunization exemptions in response to the 2015 Disneyland measles outbreak. With the passing of State Senate 277, both religious and philosophical exemptions are no longer granted. Following its

passage, researchers noted an increase in vaccine rates and a significant decline in non-medical vaccine exemptions (Mohanty et al. 2017). Researchers analyzed the changes that occurred after passing State Senate 277 by surveying 40 health professionals. Researchers first noted that during the first year of its implementation the vagueness of State Senate 277 left much open to interpretation and resulted in the law not being used as it was intended. Researchers also found that, in light of its implementation, many health professionals believed that medical exemptions should be reviewed under the state level as opposed to at the pediatric level. However, many argue that the passing of State Senate 277 is a direct violation of a parent's constitutional right and this has caused an increase in suspicious medical exemptions (Mohanty et al. 2017).

Parental VH has also placed considerable strain on the patient-physician relationship and is resulting in increased pediatric dismissal rates of patients. A study conducted by the American Academy of Pediatrics surveyed pediatricians to gain insight into their experiences with VH parents and parental non-compliance with the proposed immunization schedule. The study analyzed data collected from the American Academy of Pediatrics Survey in 2006 and in 2013. The results showed that 87.6 percent of pediatricians have experienced a parental demand to delay or refuse vaccines (Hough-Telford et al. 2016). Pediatricians cited a number of reasons as to why parents have requested vaccine delays or refusals and many of the reasons were similar to those found in previous studies. In response to these continued requests for vaccine delays and in some cases refusals of all vaccines, pediatricians have dismissed patients and families from their practice. Researchers found that there was a 5.6 percent increase in the number

of pediatric dismissals between 2006 and 2013. The reasons stated by pediatricians for these dismissals were due to a disturbance in the patient-physician relationship, specifically the lack of trust between the physician and the patient (Hough-Telford et al. 2016). Other reasons that were noted for patient dismissals included the concern for the risk of transferable VPDs between patients while they are in the waiting room.

Similarly, other studies have found that nearly 30 percent of pediatricians are dismissing patients due to requests for delays in vaccination or refusal of all vaccines. Reports have shown that 28 percent of pediatricians that have experienced parental VH have experienced a negative impact in patient-physician relationships (Leib et al. 2011). As a consequence, researchers argue that the negative effect on the patient-physician relationship can hinder the health care provider's ability to properly communicate with VH parents about the benefits of vaccines and can impede on their ability to form trusting relationships with VH parents. Studies have noted that this fractured patient-physician relationship and increased pediatric dismissal rates have resulted in 91 percent of parents placing higher trust in alternative medical practitioners and VH parents seeking medical advice from naturopaths (Costa-Pinto et al. 2018; Pottinger et al. 2018).

DISCUSSION

Vaccine hesitancy continues to challenge the practice of immunization and presents a serious threat to global health if continued. There are several factors that contribute to VH and due to the multifaceted nature of VH, there is no one factor that greatly contributes to VH over another. Understanding these factors that drive VH is crucial in preventing increased risks of VPDs and is essential for developing targeted interventions to improve vaccine acceptance rates. In understanding parental reasons for VH, research has pointed to parental education and awareness, media influence, demographics, economic and political status, and concerns over vaccine safety as reasons for delay or refusal in vaccination.

It is evident that current methods being used to combat VH have proven unsuccessful and PHA's are finding it difficult to compete with the vaccine misinformation and anti-vaccine sentiments that are propagated on social media. One solution to this problem would be to implement public health campaigns on social media with the focus of educating the public on vaccine safety and efficacy. Several studies have found that some of the contributing factors of parental VH is a lack of health literacy regarding vaccines, parental education level, and targeted anti-vaccine misinformation on social media (Hough-Telford et al. 2016). Although public health campaigns have been implemented in the past and have proven unsuccessful, potentially utilizing similar methods that anti-vaccine groups use in their social media posts may prove successful in helping to disseminate factual vaccine information.

The literature has found that anti-vaccine sentiments are shared more frequently on social media and one reason is due to their use of vivid narratives and powerful imagery (Puri et al. 2020). Combining factual vaccine information with vivid narratives and powerful imagery could help to educate the public on vaccine safety and efficacy. Vivid narratives and powerful imagery are learning models that can transmit to all individuals regardless of their education level, health literacy, or age. This is especially convenient given that certain social media users, including older adults, individuals with lower literacy levels, and those with limited digital literacy, are more vulnerable to the emotional narratives propagated on social media by anti-vaccine groups (Puri et al. 2020). The literature notes that increases in anti-vaccine conversations on social media tend to coincide with real world events, the COVID-19 pandemic is a great example of this. If PHA's can integrate into these social media conversations at the start of these real-world events it could help to promote factual vaccine information across social media platforms.

One effort that might prove difficult would be identifying, tracking, and removing false vaccine information and social media accounts. Given that there is a plethora of anti-vaccine accounts and the use of non-human-run accounts or 'bots' has increased in frequency, it may be difficult for PHA's to combat this. However, if a solution was implemented to combat this, it would greatly aid in generating algorithms that contain factual information, resulting in decreased ideological isolation.

Despite VH being a global phenomenon, studies conducted within the US cite geographic location and economic disparity rates as factors contributing to VH and

decline in vaccination rates. Identified clusters of under-vaccinated children in both urban low-income areas and rural high-income area suggest that VH is not confined to a specific economic group but can manifest in diverse settings and is influenced by local conditions and access to healthcare services (Cadena et al. 2019). Though it may be easy to confine this reasoning to the US alone, similar decreases in vaccine rates in urban and rural areas identified in Shanghai China, highlight the significant impact of migration and the resultant socio-economic challenges on vaccine acceptance (Ren et al. 2018).

One solution to this would be to implement mobile vaccination clinics in rural and underserved areas to reduce geographical barriers to access. Considering that the literature finds that VH individuals tend to cluster in a single area, focusing vaccination efforts in these cluster areas could help in reducing VH. Unfortunately, reducing geographical barriers to access is only one part of the issue when it comes to geographical location-related vaccine hesitancy. For this solution to work, PHA's would first need to educate families on vaccine safety and efficacy in the form of vaccine health literacy campaigns. Most notably, educating parents on the risk of increased VPDs and the severe outcome of acquired VPDs is important as most VH parents believe vaccines are unnecessary due to the near eradication of these VPDs. If families are lacking in vaccine and health literacy, any effort to increase vaccination rates, even in the form of mobile vaccination clinics, would be unfruitful.

Parental education levels play a crucial role in influencing VH. Notably, studies by Facciola et al. (2019) and Smith et al. (2004) found that parents with lower education levels were more likely to accept vaccines compared to parents with higher education

levels, who exhibited greater hesitancy. This paradox suggests that higher education levels among parents may be associated with increased exposure to misinformation about vaccines, leading to heightened scrutiny over vaccine safety.

This is a prominent opportunity for physicians to educate parents on factual vaccine information as many of these parents with higher education levels are receiving their vaccine information from non-factual sources. By spending a few minutes informing parents about the importance of immunization and providing information about the safety of vaccines, physicians can reduce VH significantly. This is especially crucial considering that literature has found that even minute exposures to anti-vaccine rhetoric on social media can significantly increase VH among parents (Al-Uqdah et al. 2022, Betsch et al. 2010, Nan et al. 2012). This can also help to foster trust between parents and physicians which is of great importance, considering that lack of trust between parents and physicians is also a contributing factor in VH and a determinant in parents seeking vaccine information elsewhere. Clear and transparent communication about the benefits and risks of vaccines from PHA's, physicians, and government officials is essential in reducing VH and building trusting relationships.

Consequently, pediatric dismissals due to the request for alternative vaccine schedules or refusal of all vaccines is affecting the patient-physician relationship. Literature cites that 87.6% of pediatricians have encountered vaccine refusals or alternative schedule demands (Hough-Telford et al. 2016) however, dismissing patients from practices is not the appropriate solution. In doing so, physicians instill a negative connotation towards vaccines/pediatric medicine and drive parents to seek alternative

medical practitioners that may not follow evidence-based medical guidelines. This both reduces public health efforts to increase vaccination rates and further fragments the healthcare system and pediatric medicine. It is understandable that physicians want to protect their vaccinated or medically vulnerable patients in the waiting room from unvaccinated patients by dismissing them from their practice. However, continuity of care may prove to be more successful in addressing VH over time.

Although alternative vaccination schedules go against medical guidelines, they could be beneficial in reducing VH. It is important for physicians to note that hesitancy towards vaccines is not a definite refusal of vaccines but rather a period of indecision or uncertainty preceding the decision to become or not become vaccinated (Larson 2022). Considering this, it may be beneficial for physicians to initially adhere to an alternative vaccine schedule, while maintaining adherence to recommended guidelines, when interacting with VH families who are concerned about simultaneous vaccinations. This can help to alleviate concerns about overwhelming their child's immune system or adverse events. During this initial phase of alternative vaccination schedule adherence, physicians can work towards building a trusting relationship with VH families, educating them on the importance of immunizations, and directing them to online resources where they can find reliable information about vaccines. In time, these VH families may develop a tolerance towards immunizations, gain a better understanding of vaccine health literacy, and may decide to adhere to normal vaccination schedules.

The consequences of VH extend beyond affecting individual patient/parent-physician relationships and impact the broader healthcare system. Rising incidences of

VPDs are creating additional burdens on healthcare facilities, resulting in increased hospitalizations and higher healthcare expenses. Managing these outbreaks demands significant resources and requires public health resources to be reallocated. This involves extensive efforts in tracking contacts, organizing vaccination campaigns and public awareness initiatives, and in certain instances, establishing quarantine centers. These measures divert attention and funding from other vital healthcare services such as chronic disease management, maternal and child health programs, and preventative care initiatives. The financial implications of VH are significant and influences the overall quality of care and the availability of resources for non-outbreak-related health issues.

CONCLUSION

Continual decline of vaccination rates is detrimental to public health due to the increase in resurgence of diseases that were near eliminated. In particular, evidence is accumulating that further decline in vaccination rates can lead to greater outbreaks of diseases and a greater mortality rate. Vaccine education and strategies to address vaccine hesitancy are needed to reduce the amount of vaccine hesitant parents. Research has found that misinformation and the negative portrayal of vaccines in the media is a factor that affects parental health education. Studies have shown that parents are eager for more information regarding vaccines and that vaccine education provided by pediatricians has significantly decreased vaccine hesitancy amongst parents. This period between hesitancy and indecision towards vaccines is a vulnerable time and can present as an opportunity for physicians and providers to provide support and information that can help to dispel vaccine myths and misinformation. More information is needed to better address and educate vaccine hesitancy amongst parents.

LIST OF JOURNAL ABBREVIATIONS

Child Care Health Dev ..... Child: Care, Health and Development

Eur J Publ Health ..... European Journal of Public Health

Health Commun ..... Health Communication

Hum Vaccin Immunother ..... Human Vaccines & Immunotherapeutics

Isr J Health Policy Res ..... Israel Journal of Health Policy Research

J Health Psychol ..... Journal of Health Psychology

J Public Health ..... Journal of Public Health

JAMA ..... JAMA: The Journal of the American Medical Association

Perm J ..... The Permanente Journal

PNAS ..... Proceedings of the National Academy of Sciences of the United States of America

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