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Vaccine Confidence, Coverage, and Hesitancy Worldwide: A Literature Analysis of Vaccine Hesitancy and Potential Causes Worldwide

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A Literature Analysis of Vaccine Hesitancy and Potential Causes Worldwide

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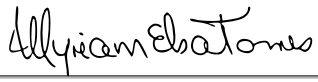

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Thesis Summary

Vaccines are one of the world's most impactful medical therapies. They are cost-effective, successfully proven, and one of the quickest treatment options available today (Clark et al., 2016). They save millions of lives every year and have eliminated certain diseases on a national and international level. However, millions of people worldwide still remain unvaccinated. In developed nations, mainly The United States (U.S.) and the European countries,

many of the unvaccinated are a result of rising vaccine hesitancy of parents in conjunction with the anti-vaccination movement. Vaccine hesitancy is defined as "a delay in acceptance or refusal of vaccines despite availability" (Macdonald, 2015, p. 34). After a thorough literature review, evidence reveals that there is a gap between perceived vaccine importance and perceived vaccine safety in developed nations as many survey respondents believe in the efficacy and importance of vaccines but lack confidence in the safety of vaccines. This gap is seemingly connected to overall health literacy. The Patient Protection and Affordable Care Act of 2010, Article V, defines health literacy as a patient's ability to "obtain, communicate, and process" health services and information needed to make health decisions (Department of Health and Human Services [HHS], 2010). However, more direct and detailed projects must be conducted before a direct connection can be made.

Inspiration

I chose this topic due to my deep interest in preventative primary care and overall wellness. I have always been passionate for global perspectives, especially in the field of healthcare. I have had the opportunity to travel to many places and that has only furthered my interest in global health. Seeing the disparities in healthcare access, healthcare literacy, and general education inspired me to choose a topic focused on how these aspects impact general health of a nation. Most global health initiatives focus on developing nations but little is done to examine disparities within developed nations.

As a firm believer in preventative care, I wanted to focus on vaccines – one of the key tools in primary care. This thesis process only furthered my interest in vaccines, and my goal is to continue this research as I move to Europe this fall for dual Public Health Masters' degrees.

As a future global Public Health professional, I chose to also emphasize the impact of health literacy on vaccine understanding. I am involved in many student organizations that inform others of health-related topics and empower them to make their own informed health decisions. This passion directly translates into the topic of this thesis.

Methods

To determine which articles should be used for this review, a thorough review of vaccine hesitancy surveys was done. Only publications that surveyed multiple countries were considered. Upon completion with article selection, the history of vaccinations and of vaccine hesitancy was researched to provide a full picture of the definition, use, and efficacy of vaccines.

Introduction

In 2017, the World Health Organization (WHO) released a surveillance survey through Global Immunization Monitoring and Surveillance to track the number of deaths and illnesses caused by vaccine-preventable diseases (VPD). A VPD is a disease for which a successful and

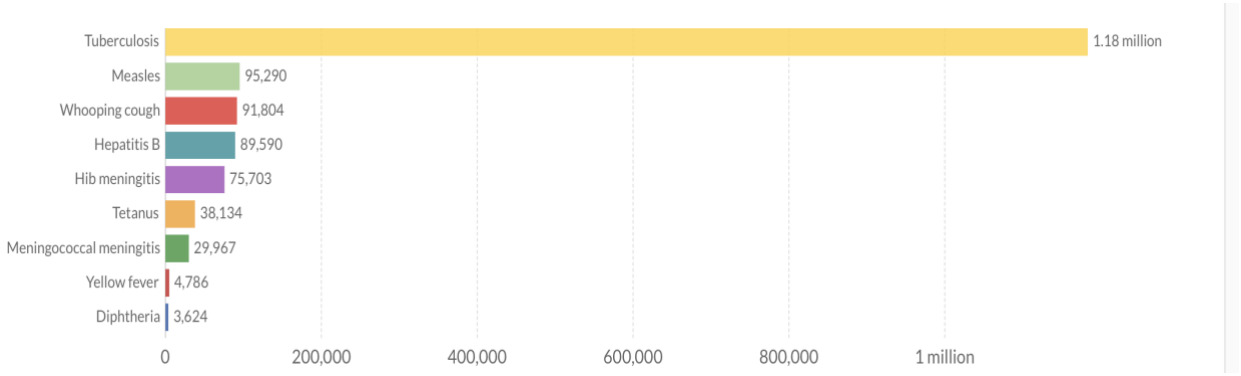

Figure 1: Deaths by the 9 Most Common VPDs Worldwide, 2017

effective vaccination exists (Australian Department of Health, 2010). Figure 1 consists of a graph showing approximate deaths from the nine most common VPDs worldwide in 2017.

Combined, the Institute for Health Metrics and Evaluation's (IHME) Global Burden of Disease study (2017) shows that over 1.6 million reported deaths worldwide could easily have been prevented with a vaccine. This is a conservative estimate considering not all cases are reported, and many of these diseases are accompanied by similarly deadly side effects. Therefore, the WHO (2018) estimates that the number is between 2 and 3 million deaths annually. These deaths generally occur in children under 35 months, which is considered to be the most vulnerable population. This is also the age range where children have most of their scheduled vaccines. The WHO collected this data in each of the 6 regions: Africa (AFR), The Americas (AMR), Southeast Asia (SEAR), Europe (EUR), Eastern Mediterranean (EMR), and Western Pacific (WPR). In their latest report, Mapping Vaccine Hesitancy (Dubé et al., 2014), data suggests that each of these regions and countries within them have different hurdles to overcome to increase the number of vaccines administered and decrease deaths due to VPDs.

The American Academy of Pediatrics [AAP] (2017) reports that only 70.4% of U.S. children ages 19-35 months have received their basic combined 7-vaccine series which includes 4 or more doses of the diphtheria, tetanus toxoids, and pertussis vaccine (DTaP); 3 or more doses of any poliovirus vaccine; at least 1 dose of a measles-containing vaccine (MCV); 4 or more doses of Haemophilus influenzae type b vaccine (Hib); 3 or more doses of hepatitis B vaccine; at least 1 dose of varicella vaccine; and 4 or more doses of pneumococcal conjugate vaccine. Compared to the 86% of children worldwide who have received their DtaP vaccines, which is the most commonly used indicator of a vaccine's immunization services, it is evident that U.S. children are behind in vaccine coverage (United Nations International Children's Emergency

Fund [UNICEF], 2019). However, both statistics demonstrate that a significant number of children globally are still not receiving their needed vaccines.

Regardless of the reasons behind the vaccination gap, it is imperative that this gap be narrowed. The Global Vaccine Action Plan focuses on tailoring vaccination strategies to individual countries, using questions from their Vaccine Hesitancy Matrix. It is evident that access to primary care is the most common reason for unvaccinated children developing nations. However, little has been researched to discover trends within more developed countries and how to counteract these potentially deadly swings in immunization rates. Through a literature review of both U.S. national and worldwide data, this thesis proposes answers to the questions: Why are people in developed countries not getting vaccinated, and what can be done to address this issue?

What is a Vaccine?

Vaccines are one of the most effective methods of avoiding disease. They are cost-effective in that they prevent VPDs from costing nations billions of dollars in disease burden annually (Centers for Disease Control and Prevention [CDC], 2019). Vaccinations are made from a small amount of weakened or dead pathogens that cause a certain disease such as viruses,

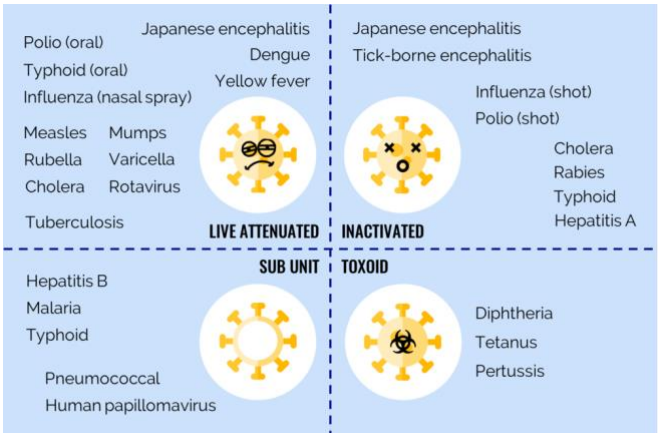

Figure 2: Vaccines by Toxin Type

bacteria, and toxins. The small dose of germs kickstarts the body's immune system into creating and replicating antibodies for an immune response for the particular disease (HHS, 2019). These vaccinations protect against more than 27 life-threatening illnesses including measles, polio, influenza, and certain types of cancer as seen in Figure 2.

When engineering a vaccine, scientists must consider how one's body may react to a germ and who needs to be vaccinated against it. There are four main divisions of vaccine types, as shown in Figure 2. Each division has benefits and drawbacks. A live-attenuated vaccine is a weakened form of a germ. As these vaccines are so similar to the natural infection process of a specific germ, they create a long-lasting, strong immune response. Usually, 1 or 2 doses of live-attenuated vaccines cover you for a lifetime. However, these vaccines have limitations because they are just weakened forms of an illness. Those who are immunocompromised are less able to receive such vaccines. These also must be kept cold so are harder to access in rural, impoverished areas such as Latin America and Asia.

Live-attenuated vaccines are used for measles, mumps, and rubella (MMR), smallpox, chickenpox, rotavirus, and yellow fever. Inactivated vaccines are dead forms of the germ so they do not spark an immune response as strong as their living counterparts. Inactivated vaccines generally require booster shots to update your immune system's response. These are more easily

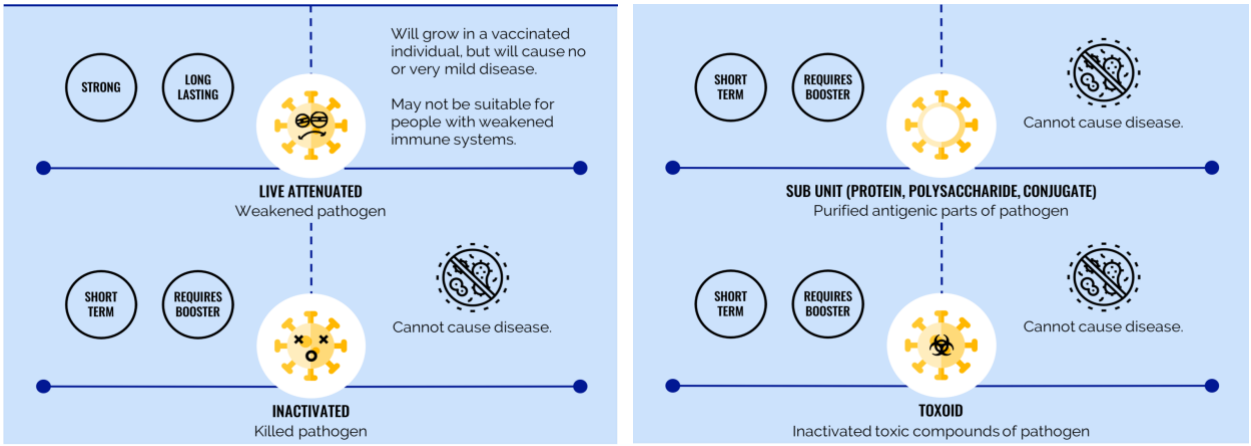

Figure 3: Four Types of Vaccines, Explained

accepted in those with weakened immune systems since the toxin is dead. Hepatitis A, influenza, polio, and rabies are protected against using this type of vaccine. Figure 3 shows the four divisions of vaccines and a summary of their positives and negatives.

Subunit, recombinant, polysaccharide, and conjugate vaccines utilize only specific pieces of the germ such as its sugars, proteins, and capsid (an external casing.) This causes one's immune system to create very strong defenses against that certain part. These vaccines are used to protect against human papillomavirus (HPV), pneumococcal and meningococcal diseases, and shingles. The final form of vaccines, called toxoid vaccines, use the germ's toxin to create immunity to the part of the germ that causes the illness, not the germ itself. Diphtheria and tetanus are the two most common diseases that are protected against using toxoid vaccines (HHS, 2020).

Why are Vaccines Important?

Along with the central idea of public health and preventative care, the CDC reminds parents and providers that it is far better to prevent a disease before it occurs rather than treating it after it infects someone (2018). As one of the most important forms of primary public health prevention, vaccines have prevented millions of cases of diseases and saved many more lives.

As defined by the CDC (2017), immunity is the human body's defense against disease with "defenders" in cells, glands, organs, and fluids. These defenders identify foreign invaders, called antigens, and produce fighter proteins called antibodies to fight them. When an antigen is introduced to the body for the first time, the body recognizes that it is not itself and begins to create antibodies to fight this foreign substance. This process often takes time so one can still get sick. Upon any subsequent exposure to this same antigen, the body "remembers" it and activates

the immune system to create a faster response of antibodies. This process of preventing disease is called immunity.

There are two divisions of immunity: acquired and innate. Innate immunity includes non-specific mechanisms of defense that come into play almost immediately when an antigen is encountered. Innate immunity mechanisms include barriers like skin, chemicals in the bloodstream, and generalized immune system cells. Adaptive immunity is the more specific response, where the immune system creates a customized plan to prevent against a certain disease (University of Arizona, 2000). There are four methods of acquired immunity, whether it is active or passive and natural or artificial. Figure 4 shows the relationship between these types. Passive natural immunity is acquired through breast milk while a fetus is in the placenta whereas passive artificial is a "quick fix" by a fabricated antibody injection which breaks down after use. Active natural immunity is acquired through getting a disease. This is the result if one is not vaccinated against the antigen. Active artificial immunity creates immunological memory so the

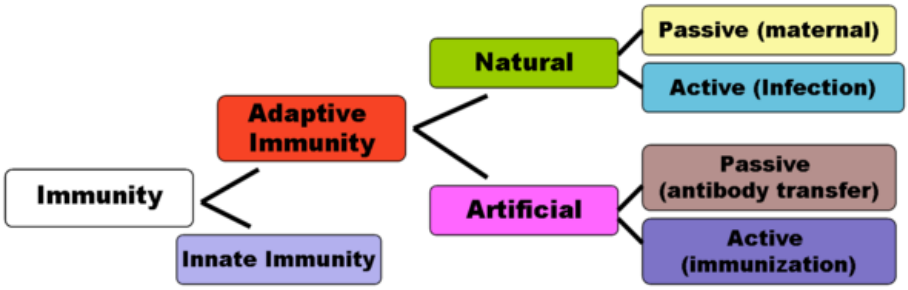

Figure 4: Relationship between Different Types of Immunity

body can better fight the antigen if it encounters it subsequently (Offit, 2019). This is the type of immunity acquired in the field of vaccinations.

To become immune to a disease, one must get the corresponding vaccine. There are currently 27 vaccine-preventable illnesses (Australian Department of Health, 2010). Getting

vaccinated not only helps the individual person, but their community as a whole through the concept of herd immunity. Herd immunity is the process by which a population is protected against or becomes immune to a disease (Sadarangani, 2016). This works by stopping the transmission of the germ between people. This way, even those who do not or are medically unable to receive the immunization, will be protected. This medical phenomenon is most

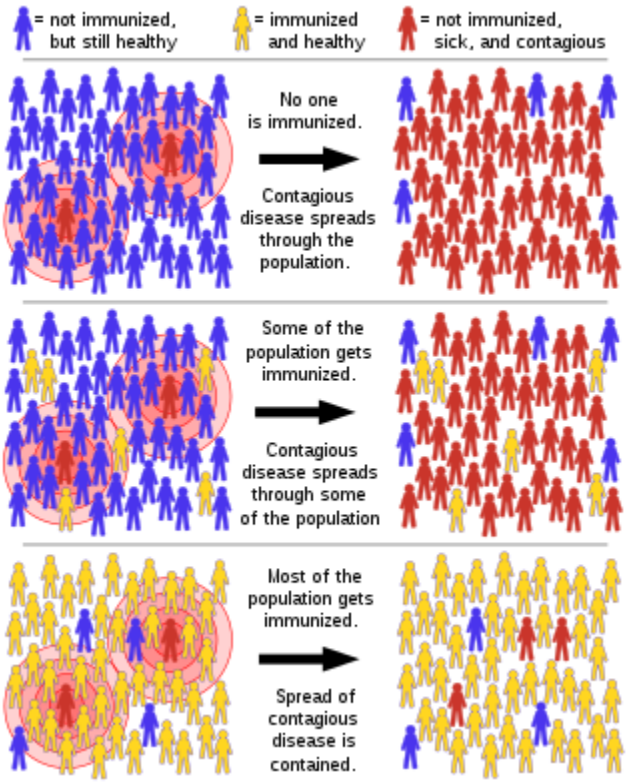

Figure 5: How does Herd Immunity work in a Population?

important for children since they are most at risk for contracting serious illnesses. Figure 5 demonstrates how immunity affects a community, using different colors to represent disease containment in herd immunity.

Because of herd immunity, diseases like polio have been eradicated in the United States (CDC, 2018). Polio was declared eradicated in the U.S. in 1979, but this is not the case for the entire globe. In 2014, the WHO stated that four of its six regions were polio-free but that still

leaves ⅓ of the globe where polio is still endemic. Developing and lower-income countries face a daily fight against these illnesses, making it more important than ever to spread the success of vaccines to other countries. Herd immunity is beneficial, and a lack of it is detrimental to a population as it puts every member at risk.

How do vaccinations impact the world, nations, and communities?

The World Health Organization's Global Vaccine Action Plan (GVAP) is the World Health Assembly's (WHA) framework to reduce vaccine-preventable deaths through the establishment of more equitable access to vaccines in all communities (2017). Endorsed by all 194 member states of the WHA, the action plan establishes immunizations as "a core component of the human right to health and an individual, community and governmental responsibility" and details how to move towards universal access to vaccines (WHO, 2017). Currently, most children in developed countries receive their childhood vaccines on time according to schedule, but there are still over 20 million children worldwide who do not get these potentially life-saving vaccines (WHO, 2019).

Globally, the only human disease to be fully eradicated is smallpox (CDC, 2016). This was declared by the WHO in 1979. Eradication is defined as the "reduction of an infectious disease's prevalence in the global host population to zero" or "extermination of the infectious agent through surveillance and containment" (Farlex Partner Medical Dictionary, n.d.). This disease only exists in laboratories thanks to vaccinations. Efforts to globally eradicate polio, malaria, and other diseases are underway. Though only one disease is no longer present anywhere in the world, many developed countries have "nationally eradicated" illnesses. This is often referred to as eradication, but is properly named regional elimination. In the U.S., polio,

rubella, and measles have been eliminated. However, with the growing international population of unvaccinated, measles has been making an appearance in Europe and in the states.

Nationally, vaccines help shift a country's demographic and epidemiologic transition model from Stages 1, 2, and 3, to Stage 4 where both birth and death rates have steadied, sanitation measures widespread, and most advanced medical technologies are readily available. Figure 6 shows the transition of a country through the five stages of both demographic and epidemiologic transition. When countries move into stage 3 and into 4, the death rate from infectious diseases decreases significantly with the introduction of vaccines and other preventative health measures.

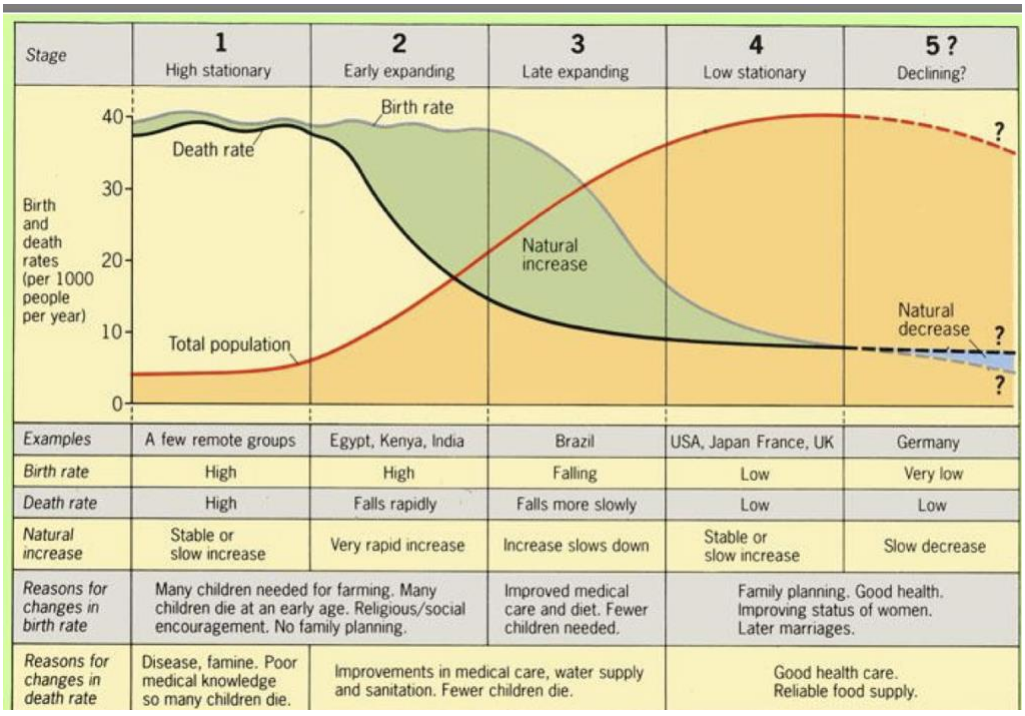

Figure 6: Demographic and Epidemiologic Transition Model

What is the Current State of Vaccination Worldwide?

Significant progress has been made worldwide with vaccine coverage. Global measles mortality has declined by 73% (WHO, 2017) and modern technologies are making vaccines more efficient and accessible, especially those considered in the childhood schedule. Still, that estimated 19.4 million infants are unprotected against these diseases. Over 60% these children live in the following 10 nations, making it timelier than ever to create plans to increase coverage: Angola, Brazil, the Democratic Republic of the Congo, Ethiopia, India, Indonesia, Nigeria, Pakistan, the Philippines and Vietnam (CDC, 2018). The main goal of the GVAP in these developing nations is to increase access to immunization, but the plan covers all 194 member countries. The anti-vaccination movement is more the focus in the developed regions, especially the United States and Europe.

History of Vaccine Hesitancy

The anti-vaccination movement has old roots. It began in France in 1763 when distrust of vaccines was warranted. Eighteenth century Europe did not have a proper quarantine procedure for those who were inoculated, and the standard of proper safety and sanitation was quite rudimentary (Measles and Rubella Initiative, n.d.). Parliament rightfully banned vaccination in Paris because inoculated patients were infecting healthy Parisians. Dr. Gatti, an Italian physician who brought the inoculation concept to Paris, needed a proper quarantine process so that those he included in his pilot study could recover from their mild cases and become immune without negatively impacting their surroundings. As time progressed, the toxins within vaccines transitioned from full-strength toxins to weakened or dead versions. However, as technology

became more advanced many people still held this old-fashioned view that vaccines did more harm than good.

Right around this time, Dr. Edward Jenner was engineering a smallpox vaccine in England (Gross & Sepkowitz, 2004). However, there was quite a lot of controversy as clergymen claimed that smallpox was God's punishment for sinners and, thus, vaccines were going against the will of God. This deep-rooted religious belief took hold in many citizens, as the 1700s was a time where people relied on the clergy more than they did on science and reason. This is yet another source of anti-vaccination beliefs, and many people have not yet shaken these antiquated tales. In 1902 as a response to a smallpox outbreak, the municipal government of Cambridge, Massachusetts passed a law requiring vaccination of all citizens. This was the first government-led effort to enforce vaccines on a large scale. They had begun to prove quite successful in creating herd immunity. However, this was met with extreme sentiments, and one case even reached the Supreme Court.

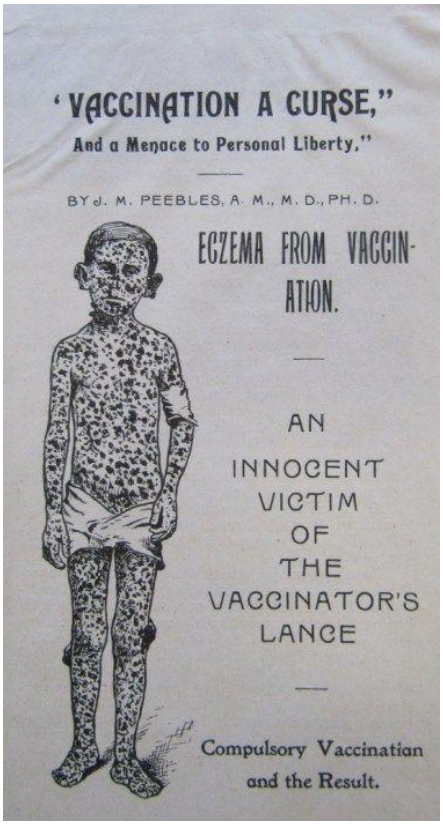

Figure 7: Advertisement for Anti-Vaccination Book, circa 1900

Biotechnology continued to grow more advanced and even more vaccines became available. Still, the American people still held those old doubts close, fighting back against U.S. public health laws to prevent communicable diseases. The turn of the century saw the formation of anti-vaccination leagues, Anti Vaccination Society of America (Wolfe and Sharpe, 2002). One of their oldest publications is seen right. The movement continued in America but few reports had been published directly citing negative outcomes until the 1998 Wakefield studies.

Modern-Day Vaccine Hesitancy

In 1998, Andrew Wakefield published his first study claiming that the MMR vaccine was linked to the development of autism (Rao & Andrade, 2011). He included 12 children in his study, 8 of which he claimed "developed" autism after receiving this vaccine. His report went viral worldwide, and what headway the U.S. had made to reverse the effects of the anti-vaccination movement was erased. However, his study is incredibly flawed for one main reason: a traditional timeline for autism diagnosis aligns directly with the MMR vaccination schedule so his observation that some patients have both, is expected. Wakefield and his team tried again in 2002 to prove this theory, and their second attempt was even more flawed. Regardless of how many holes were poked in Wakefield's findings, his studies once again ignited the anti-vaccination movement in developed nations. John Green, in his video series The Science Show, explains that it was easy for frustrated and confused parents of children with newly-diagnosed autism to find others online who felt the same way. This, once again, caused a boom in anti-vaccination sentiments. Studies now show that many parents discuss vaccination with their partner prior to giving birth and that those parents are 8 times less likely to vaccinate their children (Green, 2015). Though many unvaccinated children cannot attend public schools, the problem is perpetuated by private schools that do not have as rigid of health examinations or requirements for entering their school.

Today, the U.S. is at risk for losing its WHO designation as a measles-free country because of the increased outbreaks in 2019 due to a drop in vaccination. As a disease that requires at least a 95% vaccination rate to achieve herd immunity, drops like these can be detrimental for entire nations (Children's Hospital of Philadelphia, 2020). CDC and Health Testing Centers (2018) data suggests that between 2009 and 2018, 27 of the 50 states

experienced a reduction in vaccination rates. This is not unique to the U.S. but is far more common in developed nations than developing regions. This comparison then begs the question: why are countries with greater access to medical care and resources trending downward, almost below those countries with less money and less access?

Differences in Vaccination between Regions

When looking at vaccine confidence, coverage, and hesitancy, the discrepancies are most evident in the MMR vaccine as it is a vaccine that requires one of the highest vaccination rates to achieve herd immunity, at 95% minimum (Kwong & Ambizas, 2019). As mentioned above, the WHO threatened to remove the U.S. from its list of measles-free designated nations due to a sudden drop in MMR vaccine coverage. State MMR coverage below 90% drastically increases that state's risk for a measles outbreak which can be detrimental for the healthy and sick alike. Shown below in Figure 8, the Trust for Health documented MMR vaccine rates per state for preschool-aged children. As a developed nation, it is often assumed that the U.S. would be on the higher end of vaccination coverage.

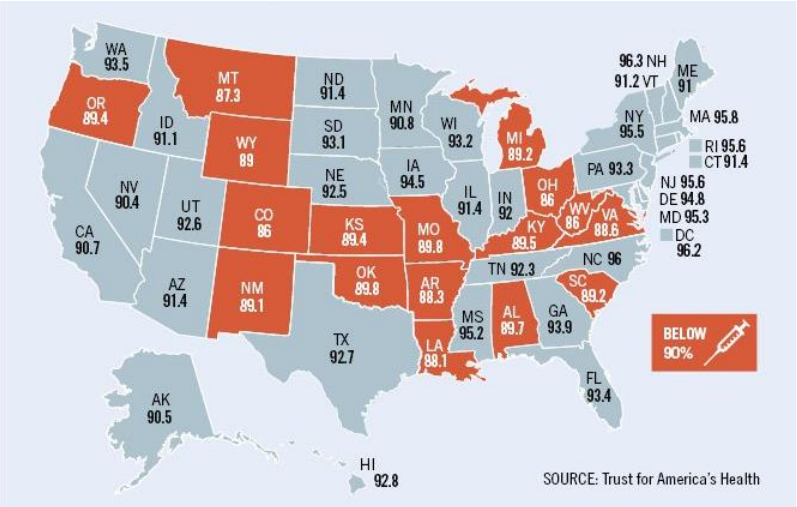

Figure 8: Measles Vaccinations per State for Preschool-Aged Children

However, that is not the case. Studies show that, within the U.S., it is actually the most affluent and educated of groups that are most hesitant to vaccines. The ones with the most money and highest education are the ones least likely to vaccinate their children or themselves with the MMR vaccine. Scientists in the past assumed that education level was directly proportional to vaccine coverage and confidence. However, recent studies have shown this is not the case. Instead, families with more money and more education are generally ones most doubting vaccines. Though there is currently little data supporting that this is exactly the trend, surveys show increased hesitancy in those with higher incomes and at least university-level education.

Though money generally leads to greater access to better healthcare, it also leads to a lack of trust in medical providers. Whereas less affluent patients generally hold more trust in providers, more affluent families seem to hold the belief that their medical knowledge has the power to counter that of their provider. They are far more likely to pick and choose medications, treatments, and procedures that appeal to them rather than trusting the medical prowess of their chosen provider. I believe that many also hold beliefs that some of the VPDs will not affect them, as many are most often found in less advantaged communities. For example, smallpox in England affected more poor people than rich people. This led many of the affluent community to think they are “immune” to the disease due to their socioeconomic status, and thus resisted the smallpox vaccine as they did not believe that this would ever come into their socioeconomic circle. Ultimately, however, this thought process backfired and left many of England’s well-to-do citizens dead or disfigured the next time the virus swept across the country. Less socioeconomically advantaged communities generally hold more trust in their providers (Lane et al., 2018). Though data has not proven the reasons behind this, it could be because disadvantaged individuals are more aware of their lack of natural immunity.

This trend is also seen within Europe, as researched by the European Union (E.U.) Vaccine Confidence Project in 2018. Some countries have decreased in both vaccination rates and confidence that vaccines, specifically the MMR vaccine, are safe and important for children to have. Both the Vaccine Confidence Project and a study conducted by the London School of Hygiene and Tropical Medicine document utilized a simple, four-question Likert-type survey to assess basic vaccine beliefs. The 4 statements were: vaccines are important for children to have; overall I think vaccines are safe; overall I think vaccines are effective; and vaccines are compatible with religious beliefs. Larson et al. (2016) notes that though any level of education increases positive views for vaccine importance, effectiveness, and religious compatibility, but the opposite occurs with perceived vaccine safety. Figure 9 shows the conglomerate results from all 67 countries polled, per region, for the four questions listed above. Looking at the U.S. in the AMR section and the 28 countries in the EUR section, there is more red (disagree or strongly

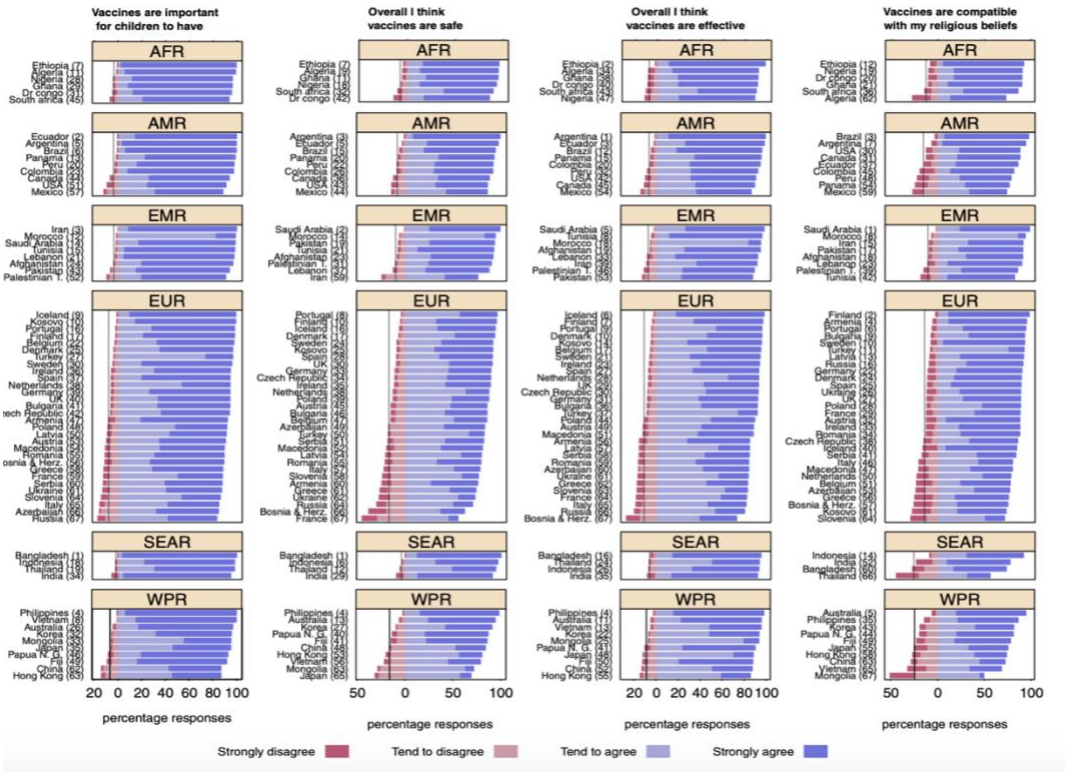

Figure 9: Poll Answers from 67-Country Survey about Vaccine Hesitancy

disagree) for the same countries for the "overall I think vaccines are safe" section than in the sections regarding vaccine importance and effectiveness. This data also supports the notion that higher income, in the case of this study, the fifth income quintile, is also not associated with more positive vaccine sentiments.

The trend is visible worldwide as well, citing that more developed regions like most of North America and most of Europe are more likely to select "tend to disagree" or "disagree" when asked if vaccines are safe. Africa, South America, and Southeast Asia are more likely, overall, to think that vaccines are safe. This also aligns with high percentages of perceived vaccine importance and effectiveness. It is opposite, however, in richer nations -- the higher incomes and more education groups reported greater perceived vaccine importance and effectiveness, but less confidence as mentioned above. A belief that vaccines are both a necessity and a proven way to reduce VPDs should seemingly be accompanied by a higher percentage of perceived safety.

Discussion and Limitations

The fact that this is not the case is puzzling. Little has been published as to why there is an increasing discrepancy in perceived vaccine safety versus perceived importance and effectiveness in affluent countries. If people in developed countries acknowledge that vaccines are important and seemingly effective, why are richer countries now vaccinating their children less? Though education is cited as both a barrier and a promoter for vaccine acceptance in developed countries, the link between an educated person's understanding of efficacy and safety has yet to be understood. Limitations of this study include a lack of full access to WHO and CDC survey data. For several surveys, country names were redacted and replace with a letter to

maintain anonymity. Therefore, many of these studies could not fully be used. For future studies, I suggest data collection to better understand personal definitions and understandings of vaccine effectiveness versus safety and where these opinions are based. Both of these variables fall under the umbrella of health literacy. While in my Master's degrees, I hope to begin a research project to determine if there is a connection between understanding of vaccines and their benefits with vaccination rates. For example, many American adults refuse the yearly flu vaccine due to a risk-benefit analysis leaning heavily towards risk, with little benefit, since the most prevalent influenza strains each season morph and become resistant to the vaccine or drugs. However, no data shows that polio, tuberculosis, or DPT diseases adapt as does the flu yet people are refusing these vaccines too. I propose that longitudinal studies across multiple developed nations to understand the key link between an understanding of vaccines and actual vaccination decisions.

Conclusion

Hopefully, once the gap between perceived effectiveness and perceived safety is understood, more individualized and targeted vaccine plans can be designed and implemented in U.S. states other high income regions, as defined by the World Bank, to reverse the decline in childhood vaccination rates and to safeguard future generations from VPD outbreaks. Currently, every one of the 50 U.S. states experiences annual outbreaks and many are affected by measles, hepatitis, and other dangerous diseases (CDC, 2019). Looking towards the future, The CDC reminds Americans of a two key elements.

1) Vaccine-preventable diseases have not disappeared. Though cases have diminished significantly, the diseases are still present.

2) If vaccine hesitancy continues to grow, these disease can become just as prevalent as they were in pre-vaccine times and will most likely be even deadlier.

They remind us that these 27 vaccine-preventable diseases are just as deadly as they were a century ago, and that without vaccines, America can once again fall victim to aggressive contagions like smallpox, measles, and polio.

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