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The Efficacy of the Influenza Vaccine and the Implications on Vaccination Policy

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The creation of vaccines for many different illnesses has now allowed humans to live in a world where we are mostly burdened by non-communicable diseases due to lifestyle choices. Although some vaccines have almost completely eradicated some illnesses, the influenza virus continues to be a long lasting public health threat even though a vaccine has long since been created for this virus. The history of influenza epidemics and pandemics are well documented as these outbreaks can be traced back with some accuracy for the past three-hundred years (Potter, 2008). With this historical knowledge we have seen the devastation this virus can cause in pandemics such as the Spanish Influenza outbreak of 1918 and even in outbreaks as recent as the Swine Flu outbreak of 2009. As a result, study of the influenza virus is naturally significant and important because this virus has the ability to cause high rates of illness and death in humans regardless of how developed our society has become. The risk the influenza virus poses to humans has caught the focus of many different fields of professionals including researchers, epidemiologists, physicians, and the pharmaceutical industry as these groups of people have generated a vast amount of literature and knowledge in regards to this topic (Potter, 2008). The influenza virus has withstood the test of time by continuing to be a major public health problem because this virus continues to have a major worldwide impact by causing serious illness, death, and economic burden as a result of recurrent influenza epidemics that can be attributed to the viral property of antigenic drift (Carrat & Flahault, 2007).Unlike bacteria or some other agents of illness, the influenza virus has the ability to change its genetic code via antigenic drift which has caused the emergence of many different strains of the virus. The implications of this ability are significant to public health because being able to create different strains, some of which are completely novel, means that humans can continuously be infected by the influenza virus even if they have gotten this virus before as there is always the possibility of being infected by a new

strain that the immune system does not recognize (Carrat & Flahault, 2007). Therefore there is a critical need for continuously changing vaccination policies and available vaccines to keep up with the evolution of the influenza virus, and there are institutions worldwide which were created solely for this purpose. Each country has the liberty to handle their influenza vaccination policies differently, but every vaccination program must have a measureable outcome. For the United States the Advisory Committee on Immunization regularly updates why vaccination against influenza is important, and most rationales argue that the influenza vaccine reduces factors like hospital visits, mortality rates, and economic burden (Jefferson, 2006). In the United States there seems to be a new trend where people are becoming distrustful of vaccination in general, but the need for vaccination is crucial as the seasonal influenza vaccine is really our only protection against this extremely dangerous virus. Therefore there is more pressure than ever to prove to society that that influenza vaccine is important to public health and effective so the majority of people will still be motivated to get their influenza vaccine each year. Encouraging the public to get vaccinated against the influenza virus is not always an easy task as the influenza vaccine has not always had the best reputation because some people think it is ineffective or will make them sick. Unfortunately there is some truth to these reservations because some years the influenza vaccine is not as effective as it was intended to be because there is not much human control over how and when the prevalent influenza strains will evolve. The purpose of this paper is to examine the efficacy of the influenza vaccine and its implication on vaccination policy as maintaining or increasing vaccination efficacy is important to public health intervention against this virus. To achieve this purpose a literature review will be conducted based on peer-reviewed research to examine current vaccination policy, efficacy of the influenza vaccine, approaches to improve efficacy, and the gap between vaccination policy and scientific evidence.

International relations can sometimes be strained due to differences in ideology on many issues, but current influenza vaccination policy is very much dependent on a collective worldwide effort. All countries agree that the influenza virus is a danger to public health worldwide especially in an era where there is so much international travel which heightens the risk of quickly spreading illness like influenza. To get an idea of the scale of this worldwide effort, currently there are 142 national influenza centers in 113 different countries which conduct year-round surveillance for prevalent circulating influenza strains and disease trends (CDC, 2015). This part of the policy gives insight into influenza evolution because in terms of the spread of the prevalent strains seasonally, each country cannot be treated as on isolated region because geography plays an important role worldwide in which strains are most relevant at any given time. With 142 contributing laboratories a vast amount of data is produced so in order to come to a conclusion on which of the many influenza strains should be included in the vaccine for each year the World Health Organization has five collaborating centers located in five different countries which include the United States, United Kingdom, Australia, Japan, and China (CDC, 2015). These five collaborating centers help narrow down the most prevalent strains for each season, and ultimately the World Health Organization makes a worldwide suggestion on which strains they feel should be included in each country's seasonal influenza vaccine. In the United States each seasonal flu vaccine protects against three or four strains of the influenza virus based on the provided recommendations by the World Health Organization and therefore our seasonal influenza vaccine is referred to as trivalent or tetravalent. The most common circulating strains of influenza amongst humans today are Influenza A (H1N1), Influenza A (H3N2), and Influenza B therefore these strains or variations of these strains are usually included in the United States' seasonal influenza vaccine (CDC, 2015). Although the

CDC in Atlanta, Georgia is one of the World Health Organization's collaboration centers, in the United States the Food and Drug Administration makes the final decision on which vaccine viruses to include in the seasonal flu shot by February of each year (CDC, 2015). Even though the CDC does not make the final decision on the vaccine viruses, this organization is very important because they report information on influenza activity in the United States each week and conduct testing on the efficacy and ability of the seasonal flu shot to produce an immune response against the influenza virus (CDC, 2015). Another important part of the United States' current influenza vaccination policy is the prioritization of target populations for the seasonal influenza vaccine. In general the CDC continues to recommend that everyone six months and older should get vaccinated against the influenza virus, but the CDC does recognize that there are certain high risks groups that are an even higher priority for vaccination. Some of these high risks groups include adults 65 and older, young children six months to five years old, and healthcare workers (Baguelin et al., 2013). As a result, many vaccination programs target these high risk groups especially during seasons where vaccine availability is limited. Also the people who are especially vulnerable to the influenza virus fall into high risks groups, and these high risk groups are determined based on who will suffer the worst health complications from getting the influenza virus. In the United States and other countries there is recognition that the influenza vaccine is not always perfect and that vaccination programs do have limitations and do need to be revamped from time to time. Therefore the CDC is very forthcoming with the limitations of the seasonal influenza vaccine. Such as there are multiple factors which limit the influenza vaccine and contributed to the vaccine's efficacy which usually involve scientific issues and timing limitations. Although there are many different strains of the influenza virus, the influenza vaccine is limited by our scientific ability to be able to grow viable vaccine virus as vaccine

viruses can only be grown in pathogen-free chicken eggs or canine kidney cells (CDC, 2015). With these very specific criteria only certain vaccine viruses can be grown which means if a vaccine virus for a prevalent strain cannot be grown successfully then humans will have to remain unprotected. A large amount of a vaccine virus must be created in order for it to be included in the vaccine therefore time constraints sometimes limit which vaccines can be grown on time, and antigenic drift becomes a problem because even if antigenic drift is detected in some cases there just is not enough time to grown a vaccine virus that matches a variant strain which can be used in the vaccine (CDC, 2015). The importance of outlining the United States' current influenza vaccination policy is to demonstrate how seriously this virus is taken from a public health standpoint and how much effort, time, research, and money is put into creating the best seasonal influenza vaccine possible. Although it is very true that much effort is put into creating an influenza vaccine each year there still is room for improvement which makes evaluating the efficacy of the influenza vaccine valuable as this can give insight into how changes in policy could continue to increase the influenza vaccine's protective power which would benefit the humans population.

With the vast amount of influenza virus surveillance and research that is conducted year-round by many laboratories worldwide there are some key factors that have been identified which are proven to decrease the efficacy of the influenza vaccine. The singlehanded most important factor that decreases the efficacy of the influenza vaccine is the influenza virus's ability to undergo antigenic drift. The influenza virus would be simple to track and vaccinate against if there was only one strain to target, but what makes the influenza virus so dangerous to public health is that fact that antigenic drift causes mutations in the genetic code of the virus which produces many different types of strains. Therefore when creating a vaccine for the

influenza virus each year it is comparable to trying to hit a moving target because antigenic drift allows the virus to change, and we can never be completely certain which strains will be most prevalent each year. To put the problem of antigenic drift into perspective, it has been found that antigenic drift is responsible for the global change in vaccine composition and since 1968 antigenic drift had caused the influenza vaccine composition to be updated approximately every two to five years (Boni, 2008). Antigenic drift occurs as a means for the influenza virus to evade human immunity even in vaccinated individuals so clearly this ability can decrease the effectiveness of the influenza vaccine because the influenza virus is designed to change so that the human immune system cannot recognize the virus (Moldoveanu et al., 1999). Research on antigenic drift has provided information that suggests that antigenic drift occurs every two to eight years due to evolutionary pressure, and antigenic drift can occur in all strains of the A and B viruses (Kanai et al., 2010). On a biological level, changes to the genetic code of each viral strain due to antigenic drift are subtle usually only involving a point mutation of one nucleotide within antibody binding sites which occur at the hemagglutinin and neuraminidase viral proteins on the surface of the virus (Boni, 2008). As a result small changes to the virus can cause a significant impact on humans by causing an increased amount of illness and death by decreasing the efficacy of the influenza vaccine with the emergence of variant strains. Also antigenic drift causes varying evolutionary patterns as this type of biological change can causes the re-emergence of old influenza strains or the creation of new variants (Boni, 2008). Overall it is proven that antigenic drift can decrease the efficacy of the influenza vaccine, but the impact varies between seasons based on when antigenic drift is most active. Next, vaccine strain mismatching is related to and a consequence of antigenic drift and this is a factor which is also known to decrease the efficacy of the influenza vaccine. In the United States production of the

seasonal influenza vaccine can take up to nine months, and due to this lengthy production period this gives the opportunity for antigenic drift to occur and a new prevalent strain of influenza can arise while the vaccine is still in production. The consequence of this is that if a new strain arises during this production period it would be too costly and there would not be enough time to include this new strain in the vaccine that is being produced. Therefore reduce effectiveness of the influenza vaccine and a potential for an epidemic can occur as one of the circulating strains will not match one of the vaccine strains making the human immune system vulnerable (CDC, 2015). The last factor to be mentioned that decreased the efficacy of the influenza vaccine is herd immunity which occurs when the majority of the human population is vaccinated against the influenza virus. Herd immunity is significant because it is known that strong host immunity is the driving force that causes antigenic drift to occur in the influenza virus (Boni, 2008). Antigenic drift is triggered by strong herd immunity amongst a population because this causes the circulating influenza viruses to have low evolutionary fitness which in turn favors mutations to occur via antigenic drift. As a result mutations caused by antigenic drift increase the fitness of the influenza virus and allow the virus to escape the herd immunity and cause illness (Boni, 2008). This relationship between herd immunity and antigenic drift means that increasing the number of vaccinated individuals in a population increases herd immunity which in turn increases antigenic drift. In terms of vaccination strategies, vaccinating too many people can actually have negative consequences in terms of influenza virus evolution whereas vaccinating fewer people or being more selective as to who should receive vaccination would increase influenza vaccine efficacy by decreasing antigenic drift (Boni, 2008). Although it seems that vaccinating fewer people would be advantageous this is an unrealistic solution to increase efficacy because there is also danger in vaccinating fewer people, therefore it would be better to

strengthen our influenza monitoring efforts during seasons where herd immunity is high in an effort to recognize sooner when antigenic drift occurs so the human population can be warned and take extra precautions. Typically in the United States the most vaccination for the influenza virus occurs in October and November which makes herd immunity high at the beginning of the flu season which in turn would make the emergence of variant influenza strains more likely to be recognizable by the end of the same flu season so more monitoring efforts during this time period would allow for earlier recognition of variant strains which could help improve the vaccine for next season (Boni, 2008). In order to tie this section together it is important to note that factors like vaccine strain mismatching and herd immunity are indirect factors that decrease the efficacy of the influenza vaccine as these factors are either a cause or consequence of antigenic drift which again is the main factor that decreases efficacy.

Within the scientific community concerned with the influenza vaccine and vaccination policy it is undebated that the efficacy of the influenza vaccine can be decreased, but what is debated is the best approaches to try to overcome the factors that can decrease the efficacy of the influenza vaccine. Formerly mentioned in this paper were three major factors that are widely known to negatively impact the efficacy of the influenza vaccine, and there are other less significant or newly discovered factors that have not been addressed. With so many factors that can possibly negatively impact the efficacy of the influenza vaccine there are many different suggested approaches that try to overcome these factors in an effort to ensure and increase the efficacy of the influenza vaccine. With so many laboratories and research worldwide dedicated to study the influenza virus and vaccine, there is a vast amount of data related to efficacy of the influenza vaccine that has to be sifted through and interpreted for future use. In this section of the paper I will cite some of the most common and widespread approaches that are being discussed

within the scientific community currently based off of available research that has been conducted. There is naturally a worldwide problem with decreased efficacy of the influenza vaccine as this would make the human population more vulnerable to illness, therefore looking into approaches that can maintain or increase the efficacy of the influenza vaccine is important because the main goal of the influenza vaccine and vaccination programs is to protect as many people from this virus as possible to decrease illness, death, and economic burden. As a result there seems to be two categories of approaches that are predominate within current scientific research, and these categories consist of either adapting vaccination policy and monitor efforts for the influenza virus or making improvements to the content of the vaccine itself. Both categories of approaches are valuable, and the first category of approaches to be discussed is ones that suggest making adaptations to vaccination policy and monitoring efforts. One suggested approach is to increase the use of sero-epidemiological testing which means to use serum from human blood to better understand the incidence and distribution of disease (Kanai et al., 2010). In the human immune response after receiving an influenza vaccine, the human body makes antibodies against the influenza virus therefore conducting research on serum and monitoring populations periodically could give better insight into how the body reacts to the influenza virus and vaccine on a biological level (Moldoveanu et al., 1999). It is important to note that the idea of conducting sero-epidemiological testing is not a new idea as mass serological surveys worldwide are already done each year to help determine which strains should be included in the vaccine, but what is new is the suggestion for better organizing and targeting how this testing should be conducted (Kanai et al., 2010). Although there is mass serological testing that is conducted each year a noticeable trend is that there is not much of this type of testing conducted in tropical regions such as in Southeast Asian countries. Therefore it may be

advantageous to the efficacy of the influenza vaccine and monitoring efforts if sero-epidemiological is better allocated worldwide as the importance of this type of testing has been confirmed by its mass usage annually (Kanai et al., 2010). The suggestion of better allocating sero-epidemiological testing also alludes to the next approach to be discussed which is related to geography. Such as it is well known that different parts of the world play different roles in influenza virus evolution, therefore it is suggested that geographic considerations should be used to better target and monitor the emergence of novel strains of influenza and the stains that are most prevalent each year (Boni, 2008). Currently vaccine recommendations and strain monitoring are done on a global scale, but increasing monitoring on a smaller more localized scale can help indicate the regions that impact influenza virus evolution the most and target regions where the most antigenic drift occurs (Boni, 2008). Also climate plays an important role in peak influenza season and influenza virus evolution as influenza virus infection occurs throughout the year in tropical regions whereas in temperate regions infection most occurs in the winter season which is just one example of how geography can affect the influenza virus (Kanai et al., 2010). One geographic consideration that is known and valued is that it is important to have close monitoring for novel influenza variants in China and Southeast Asia, and this displays how if more attention is paid to geographic considerations there is the possibility that influenza monitoring can become more pointed and effective (Kanai et al., 2010). Another adaptation that is worth mentioning in terms of modification to influenza vaccination policy is the consideration to adjust target populations for influenza vaccination. Although the CDC recommends that everyone six months and older should get vaccinated against influenza, many vaccination programs target high risks groups like adults aged sixty-five and older or small children especially when vaccine availability is limited. Targeting these high risks groups is beneficial

because it offers protection to these groups by lowering the amount of illnesses and financial burden, but targeting other groups of people may offer a broader range of protection. Such as, children that are not young enough to be in the high risk category have been found to be the key spreaders of the influenza therefore it could be more beneficial to target children not in the high risk categories and the adults these children come in contact with in an effort to decrease the spread of the influenza virus in the first place (Baguelin et al., 2013). Specifically it has been found that the most optimal allocation of influenza vaccine would be to prioritize schoolchildren and adults aged thirty to thirty-nine as children are the key spreaders of the influenza virus and parents serve as a bridge to the rest of the population (Medlock & Galvani, 2009). Overall changes to vaccination policy and monitoring efforts are probably the fastest and most efficient routes to take in an effort to increase or maintain the efficacy of the influenza vaccine as changes to the vaccine itself would require lengthy clinical trials and testing.

Now that approaches pertaining to vaccination policy and monitoring efforts have been addressed, the next to be addressed are approaches pertaining to actual changes to the influenza vaccine itself in an effort to increase or maintain the efficacy of the influenza vaccine. Again, the approaches that will be discussed are the most current and prevalent in scientific research. In the United States all seasonal influenza vaccines either contain three or four strains that are picked to be included in each dose of the vaccine, but one approach to increasing or maintaining the efficacy of the influenza vaccine is to add more strains to the vaccine. Adding more strains to the vaccine would allow humans to be protected against a broader range of strains, but this approach also has some disadvantages to it. Such as, adding more strains to the influenza vaccine could make the vaccine too costly or make the production process too long. Also adding more strains still would not guarantee that humans would be more protected if antigenic drift occurred.

Although this approach is not perfect or foolproof, it relates to the idea behind the second approach to be addressed which is cross protective vaccines. The idea behind cross protective vaccines is the same as adding more strains to the influenza vaccine which is that cross protective vaccines could reduce the impact of antigenic drift by helping the body make more antibodies that can possibly protect the immune system against a broader range of influenza strains and variant strains (Carrat & Flahault, 2007). Therefore cross protective vaccines could provide more protection against the influenza virus than the regular seasonal influenza vaccine could provide as cross protection can evoke an immune response that provides sufficient protection against some strains even if the vaccine components are not optimally matched which would be valuable to use during seasons where antigenic drift occurs (Heckler et al., 2006). Humans can gain cross reactive antibodies from the seasonal influenza shot when variant strains are somewhat similar to the strains included in the vaccine, but most importantly specific cross protective vaccines could be made as a supplement and provide more protection during seasons when a substantial amount of antigenic drift occurs and efficacy of the seasonal influenza vaccine is lowered (Katz et al., 2009). The last approach to be addressed is the proposal for a universal influenza vaccine which would completely change vaccination policy and eliminate the need for a constantly changing seasonal influenza vaccine. Research is now moving in this direction in search of a universal influenza vaccine because it would eliminate the problem of antigenic drift, but currently a universal vaccine for the influenza virus remains in a preclinical stage as much more research needs to be done (Carrat & Flahault, 2007). Hemagglutinin and Neuraminidase are viral proteins on the surface of the virus which are the most antigenic proteins, and the current seasonal influenza vaccine is based off of these proteins even though Hemagglutinin and Neuraminidase are highly susceptible to antigenic drift (Carrat & Flahault,

2007). Therefore the goal of universal vaccine would to make a vaccine based on more conserved parts of the virus that are not heavily affected by antigenic drift so that the vaccine would remain effective and not be negatively impacted by variant strains (Carrat & Flahault, 2007). Currently there has been research conducted on a part of the influenza virus called the M2 ion channel protein which is a more conserved part of the virus, and ultimately targeting proteins like this would provide for protection across all strains of the influenza virus so there would be no need to worry about decreased efficacy of the vaccine (Carrat & Flahault, 2007). In general a lot more research needs to be conducted on improvement to the influenza vaccine itself, but some of these approaches may have a promising future if research advances to a point where these approaches are useable in creating an improved influenza vaccine for the human population.

Many approaches that are suggested to increase or maintain the efficacy of the influenza vaccine seem like valuable ideas which lead to the question as to why there is a gap between actual influenza vaccination policy and scientific evidence. Besides the fact that new approaches take time implement once they are deemed appropriate to use, there are multiple reasons why there is a gap between vaccination policy and scientific evidence. One reason which contributes to this gap is that many research studies only report data from one or two flu seasons which make the data produced from these types of studies unreliable and difficult to interpret because the circulation and incidence of the influenza virus varies greatly each year due to factors like antigenic drift (Jefferson, 2006). Another factor that contributes to this gap is based on the scale of each scientific study as studies with small numbers of participants or small data sets again make the data produced unreliable due to the limited scope of the study (Jefferson, 2006). Amongst other symptoms influenza is characterized as causing respiratory illness, and since

there are many other illnesses that cause similar symptoms it is almost impossible to differentiate actual influenza and influenza-like illness which in most cases is just considered to be influenza when it really is not (Jefferson, 2006). The confusion between influenza and influenza-like illness becomes problematic because it leads to an overestimation of the impact of influenza and unrealistic expectations of the success of influenza vaccines which can be reflected in evidence from scientific research as well (Jefferson, 2006). Besides these factors the integrity of the studies that report scientific evidence must be thoroughly scrutinized as many studies are poorly designed or biased which leads to confounders and inaccurate data that could never be used to help determine or modify vaccination policy (Jefferson, 2006). Overall the gap between vaccination policy and scientific evidence is justified because it is a lengthy process to extract scientific evidence produced by researchers that has merit and is reliable enough to include in vaccination policy. There may be pressure or temptation to use scientific evidence because it sounds good or seems like a viable way to deal with the influenza problem, but policy makers have to be very careful with which evidence they use because it would be a waste of resources like time and money to use them on improper evaluation (Miller et al., 2009). Lastly, immediate action always has to be taken against influenza in order to control this virus and hopefully there can be closer collaborations and lessons drawn from previous knowledge so that policy makers and researchers can possibly decrease the gap between policy and scientific evidence so that the human population can benefit from the outcome (Miller et al., 2009).

The influenza virus is nondiscriminatory and is a worldwide public health problem especially when pandemics and epidemics occur. Also the subject of the influenza virus is complicated because there are so many factors and collaborations that occur in an attempt to control this virus from causing illness and death. Hopefully this paper clarifies all the elements

that go into the public health intervention against the influenza virus, and above all indicates the need for continuous adaptation of both policy and vaccine composition in order to combat a continuously evolving virus that has historically been very dangerous to the human population worldwide.

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