Flu Vaccine Ethical Debate

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Abstract

The finest and the most effective approach that has been confirmed to prevent influenza infection is vaccination. However, despite the advantages of administering the influenza vaccine, various limitations arise from the use of the vaccine. Relatively, there are a number of challenges that need to be addressed to improve the effectiveness of the influenza vaccine. For instance, the current market of influenza vaccine formulation and production need to address safety issues and matters to do with facilitating universality of the vaccines. This paper, therefore, gives an overview of the types of influenza vaccines and the process that they undergo in their formulation. The study further suggests solutions that could aid the development of more advanced and universal influenza vaccine.

Flu Vaccine Ethical Debate

Influenza virus is characterized by negative strands of RNA viruses that belong to the Orthomyxoviridae family. Influenza viruses are in three distinct classes including A, B, and C of which type A and B are the most common that affect humans. People with influenza infection usually exhibit symptoms like a headache, fever, fatigue, and coughs. At an advanced stage, infections from influenza can result in complicated conditions like cardiovascular issues, respiratory distress, and pneumonia that can cause death. Influenza infections are more prevalent and severe among individuals with weak immune systems like young children and the elderly are more vulnerable.

Influenza fairly varies from the common cold. Colds are more of the illness that results from viruses that infect the upper part of the respiratory tract. On the other hand, influenza is a version that is more severe and has the ability to infect both the upper and lower respiratory tracts. Both cold and influenza viruses are prevalent during the winter, fall, and early period of spring, especially in the north. Risks of contracting the infections are increased by poor nutrition, stress, and inadequate sleep. Washing of hands has proven to be the best means of reducing the prevalence of these infections.

Background

Influenza infections, most of the times, occur during winter of the southern and northern hemispheres. According to the United Nations' World Health Organization, the global influenza epidemics affect an estimated three million people in the world. Of the many cases during the winter, an average of 500,000 people succumbs to the infection [4.] The occurrence and prevalence

of the H1N1, H7N9, and H5N1 viruses indicate that influenza remains to be a global epidemic to date.

Scientific research has shown that vaccination is one of the most effective means of preventing influenza infection. The spread of the influenza vaccine has been used as one of the best ways to counter the wrath of the virus and the global epidemic. Despite the presence of the influenza virus for quite a long time, since the 1930s, the debate on ethics in using the virus still continue. This is due to the limitations concerning the safety to patients, effectiveness, and availability of remote healthcare facilities.

Immune system and influenza

The success of most of the vaccines used for influenza today is facilitated by the presence of sufficient hemagglutination inhibition (HI) titers that are present in individuals before they are vaccinated. The hemagglutination inhibition titers represent the responses of antibodies against the influenza virus but do not shield unvaccinated individuals from the virus itself. Virus neutralization (VN) titers also almost perform the same function as the HI in individuals who are not vaccinated. Ideally, the influenza vaccines should be able to protect vaccinated individuals against all mismatched strains of influenza without being influenced by changes in antigens. On the other hand, virus neutralization titers represent the responses of antibodies that can be used for development of cross-reactive vaccines. The responses are able to neutralize the influenza vaccines in vaccinated individuals[1.] Additionally, universal influenza vaccines can be developed from alternative CoPs like crossreactive responses of T cell or antibodies.

Consequently, inducing immune reactions against conserved epitopes, as opposed to the variable epitopes of HA is the trend in the present vaccine world. The conserved epitopes can

result in vaccines that prompt antibodies that act on the stalk regions of the HA. In addition, the resulting vaccine has the ability to prompt cellular responses that act in the internal proteins of the influenza virus. Such vaccines could form part of the solution of developing a universal vaccine for the influenza virus.

Influenza Virus Antibodies

HA, antibodies can be classified into two major categories. These include those that are reactive to the stalk area of the virus and those that act on the globular head domain. The current vaccines used against the influenza virus mainly consist of antibodies that are reactive to the head domain. This is very variable considering antigenic drifts. In the contrary, the stalk domain lacks the antigenic drifts that make it more conserved and therefore an attractive target for the cross-reactive humoral response.

Influenza Vaccines

Currently, the seasonal influenza vaccines either have live-attenuated viruses or inactivated influenza antigens gotten from a combination of influenza A and B strains in the ration of 2 to 1. Apart from the seasonal trivalent influenza vaccine, there are the quadrivalent vaccines that have appeared in the vaccine market. The quadrivalent influenza vaccine combines an additional influenza B to the two influenzas A and one influenza B strain that characterizes the seasonal trivalent influenza vaccine. Apart from the two vaccines mentioned above, several other pandemic vaccines have been constructed in anticipation of attacks by highly pathogenic influenza viruses that might rise in future. Some of the vaccines are explained in the following section.

Inactivated vaccines. This group of influenza vaccine either consists of split or subunit antigen. Notably, the inactivated influenza vaccine as well consists of complete inactivated viruses. All these components of the inactivated influenza virus all differ in some way; either in viral or structural components. The inactivated influenza vaccines were the first type of vaccines to be applied in the world for the annual influenza campaigns. The inactivated influenza viruses, however, upon administration caused adverse effects to vaccinated individuals. The unwanted effects were attributed to the impurity components like egg proteins that were present in the vaccine. Consequently, when split vaccines got into the market, the inactivated influenza vaccines were abandoned. This was because the split vaccines were less reactogenic. Current technologies that are used in the production of the inactivated vaccines, however, result in pure vaccines that exhibit lower levels of side effects than the previous ones.

In the current vaccine market, influenza vaccines either contain subunit antigens or split influenza viruses. Split influenza vaccines are made up of particles of influenza viruses that are disrupted by detergent treatment. Despite the fact that the current split influenza vaccines still contain the viral proteins; the immunogenicity of the virus has been lost through the elimination of the organization of the original viral particulate. Currently, in the vaccine world, split viruses are widely used in the formulation of trivalent influenza vaccine. This owes to their ease of production and their adequate immunogenicity. In addition to the standard intramuscular split vaccines, a new advanced split vaccine has been licensed. The advanced intradermal influenza has the ability to induce a non-inferior immune response at a lower dose than the standard intramuscular split vaccine. The elderly, however, still require a standard dosage even for the advanced intradermal influenza split vaccine.

The trivalent influenza vaccines are also formulated from subunit antigens that include the NA and HA proteins. The subunit antigens are extracted from lipids and nucleocapsid through detergent splitting. However, for the purposes of attaining the required immunogenicity in elderly individuals, it becomes necessary to add adjuvants to the antigens. This has seen the entry of a recombinant subunit vaccine that contains a higher dose if antigens compared to non-recombinant subunit vaccines. Compared to the non-recombinant trivalent influenza vaccines, the administration of the recombinant subunit vaccine results to a higher rate of seroconversion in adults and elderly [4]. However, the administration of the recombinant subunit vaccines among healthy children leads to lower efficacy rates compared to the non-recombinant trivalent influenza vaccines. As a result, the vaccine needs an additional formulation with adjuvants to improve immunogenicity in children.

In addition to the two vaccines mentioned above, virosomal trivalent influenza vaccines are also widely used especially in European Union countries from as early as 1997[2.] . Virosomal trivalent influenza vaccine formulation is only reconstituted formulations that consist of HA, NA, and additional phospholipids. The particulate structures of the virosomal trivalent influenza vaccine formulations enable retention of the fusion of the viral membrane and the capabilities of the cells to bind. This will consequently improve the level of immunogenicity compared to the split and subunit vaccines.

Current literature on vaccines indicates that there is a disparity in the level of safety and immunogenicity of the three formulations of influenza vaccine. However, meta-analyses point in a different direction. Meta-analyses of the influenza vaccines show that the difference in the levels of immunogenicity and safety of the vaccines is insignificant. However, studies

concerning vaccines have largely concentrated on comparing vaccines of a single season of an epidemic.

Live-attenuated vaccine. Contrary to the inactivated vaccines, the live-attenuated vaccines are administered through the nose. This induces a mucosal immune response to the influenza virus that infects the body through the nose. In addition to the strong mucosal response induced by the live-attenuated influenza vaccines, they also induce cell-mediated immune responses that are quite effective in the prevention of influenza infection. Despite the proven effectiveness of the live-attenuated influenza vaccine, there are issues that have been raised concerning its safety for use among both adults and children. Firstly, the live-attenuated influenza vaccine can theoretically go through the process of genetic reconversion and become a transmissible strain of influenza. This scenario is however quite unlikely to happen and is yet to be proven. The second concern involves the use of the live-attenuated influenza vaccine in young children. This is because the vaccine has been proven to cause wheezing in children who are below two years. Consequently, it is explained that the use of the live-attenuated influenza vaccine has been limited for children above two years and adults below the age of forty-nine [4].

Quadrivalent Vaccines. More efforts have been recently invested in adding a second influenza B strain to the seasonal influenza vaccine. Since 1985, there have been two influenza lineages going round. Studies have showed that this has led to the decreased efficacy of the trivalent influenza vaccine that includes only one strain of influenza B [3]. Five strain mismatches between 2001 and 2011 have been documented, which necessitates the addition of influenza B strain to the trivalent influenza vaccine. To minimize the chances of the strain mismatches, an additional influenza B strain is needed to build an advanced quadrivalent influenza vaccine. The first quadrivalent influenza vaccines were launched in 2012. Several other formulations of the

quadrivalent influenza vaccines that are made from inactivated vaccine formulations have been licensed since the first appearance in the market. The market share for the quadrivalent influenza vaccines has continually expanded due to their efficiency in preventing influenza infection.

Pandemic Vaccine. The demand for pandemic influenza vaccines has been on the rise since outbreaks of H1N1 and H5N1 viruses. The formulation of the pandemic influenza vaccine involves the usage of whole inactivated virus and split antigens in combination or without adjuvants. The application of the whole inactivated virus in the pandemic influenza vaccine is because of its high intrinsic immunogenicity. Several pandemic vaccines have been used in combination or without adjuvants to fight the H1N1 pandemic since 2009[2]. For instance, the high number of cases reported at the healthcare facilities in the United States between 2008 and 2009 necessitated the need for the vaccine for the H1N1 viruses (See graph 1). Currently, additional H5N1 pandemic vaccines have been licensed. The H5N1 mock-up vaccines are mainly formulated to generate a registration dossier that is used in the licensing of the actual vaccine once a pandemic strain of vaccine has been included. Such moves would aid in speeding up the process of regulation in case a pandemic occurs.

Since the live-attenuated influenza vaccines stimulate strong cellular along mucosal immune responses in individuals, they are the best candidates for pandemics. The live-attenuated influenza vaccines are however less effective against heterosubtypic strains since they lack cross-reactivity.

Methods

This paper will review various works of literature and other previous research to come up with information concerning the pros and cons of vaccination with reference to the influenza

vaccines. The information from the reviewed literature will further be analyzed to give light to the major issues of the influenza vaccine debate. This paper will finally weigh the advantages and disadvantages of the administration of influenza vaccine on children, adults, and elderly. Additionally, recommendations to the challenges and outstanding issues in the debate will further be provided to allow for improvements in the field of vaccines especially influenza vaccine formulation, production, and administration.

Findings

Medical personnel recommend the administration of influenza vaccines to people who are above six months annually to minimize the risks of contracting the influenza virus. Most of the time in many countries, especially in the southern and northern hemispheres, influenza vaccines are most of the time administered from the beginning of the month of September to winter. While the influenza vaccines have proven to be advantageous especially in the prevention of influenza infection, various disadvantages have resulted in the low administration of the vaccine among healthcare workers and the public. Some of the pros and cons of the administration of the influenza vaccine are highlighted below.

Pros of Influenza Vaccine

The major benefit of influenza vaccine is the protection of users from the infection by the virus. This lowers the cost of health and saves people money. The administration of the influenza vaccine is less costly compared to seeking medical attention and taking care of sick members of a family or friends. For instance, children below the age of five infected with the influenza virus take plenty of time of their parents. Studies indicate that such infected children consume up to seventy-three hours of wages of their parents to look after[3].

Additionally, influenza vaccines help in the protection of future generations. Pregnant mothers are able to protect their infants from influenza virus infection. This is quite advantageous especially owing to the fact that the vaccine cannot be administered to children who are under the age of four months. Generally, vaccinated parents are able to guard their unborn babies against viruses like the influenza virus that can lead to birth defects. Such moves can help in eradicating the influenza virus especially with the current efforts geared at developing a longer lasting influenza vaccine.

Cons of Influenza Vaccine

Firstly, the current influenza vaccines in the vaccine world have a short protection period and as a result, have to be administered annually. Research show that the current influenza vaccines in use only stimulate immunity in patients for a period of four to six months. The vaccine only protects the patients from the infection be the influenza virus for as long as the duration of a single influenza season. In addition, the influenza vaccines, once administered, do not offer an instant protection of the patients against influenza. After the administration of the influenza vaccine, patients will have to wait for averagely two weeks before their immune system is enhanced. This leaves the patients exposed even after taking the influenza shots that still gives the virus a window for infecting them.

Secondly, another study indicates that the current influenza vaccines are not universal and as a result, cannot be administered to everyone[5]. For instance, the administration of the vaccine to infants below six months can lead to adverse effects on them. Additionally, individuals with egg allergy cannot receive the influenza vaccine shots since they are formed and developed on eggs. The vaccine, therefore, can lead to serious reactions when injected into people who are allergic to eggs. The influenza vaccine cannot also be administered to people

who are ill from diseases that are accompanied by fever until they have fully recovered from the illness.

Influenza vaccines may also have adverse side effects in some individuals. The side effects that may occur from the administration of the influenza vaccine could be as simple as allergic reactions or permanent neurological damage. The occurrence of these effects are however rare and may occur in one out of one hundred thousand individuals. Further side effects which are come after the issuance of influenza vaccine comprise soreness at the place of infection, body pain, as well as low-grade fever.

Discussion

Seasonal vaccination of influenza remains suboptimal in many countries in the world. The confidence of users and providers of influenza vaccines remain confused concerning the effectiveness of the vaccines in the prevention of the virus. The challenge in the vaccine coverage is also compounded by the lack of tangible evidence concerning the burden of the virus. However, studies indicate that an increased coverage of the influenza vaccination would lower the disease burden and the cost of health in many parts of the world. Despite the evident benefits of having influenza vaccination, the healthcare sector still needs multifaceted and country-oriented approaches to address the hesitancy issues that are exhibited among healthcare workers and the general population. One of the major means of improving the influenza vaccine coverage is through the formulation of better influenza vaccines that address some of the challenges of the current types of vaccines. Issues like the effectiveness of the vaccines, longer periods of immunity, and the need for vaccines that do not require annual administration should be considered in the development of better influenza vaccines.

Since the influenza virus undergoes continuous antigenic evolutions, in order to maintain a good level of immunology, an annual revaccination must be administered among healthcare providers and the public. Annual influenza vaccination programs require adequate information including the disease burden, coverage of vaccination, and the associated risk/benefit analysis of the undertaking.

The sector of influenza vaccine formulation has seen a number of changes of the past few years. Apart from the improvements the levels of production and formulation of traditional vaccines, there are also developments to come up with universal vaccines. For instance, the vaccine formulation sector has seen the addition of novel antigens for influenza and the novel correlates that constitute some of the most advanced additions. Before the invention of the universal influenza vaccines, it is likely that the novel antigens could be used to supplement the immune response of the traditional vaccines through a combination of cellular and humoral responses. The good news is that the production of the novel antigens is easier and flexible than the traditional influenza vaccines. While the currents methods of production of the novel influenza vaccines are much faster, reagents availability is still an obstacle and should, therefore, be deeply looked at. In addition, the production of universal vaccines could be continuous and would greatly contribute to a wider coverage and capacity of the influenza vaccines. The next few years is therefore expected to be quite exciting in the field of vaccine formulation and production.

Conclusively, the single most effective solution to the influenza menace is vaccination. Improving the effectiveness of influenza vaccination programs should, therefore, be the major focus of healthcare providers in the world. The coverage of influenza vaccination programs should, as a result, be closely monitored through vaccination registries in combination with other

country-specific methods and periodic survey of populations. Such methods would enable healthcare providers to know the regions that are not well covered by the vaccination program and their reasons for being unvaccinated. This would further inform interventions aimed at increasing the coverage of influenza vaccination in the world in the bid to kick out the virus out of the world.

In addition, the healthcare surveillance system should also be improved to provide adequate information concerning the burden of the disease according to risk groups and age. The effectiveness and safety of the influenza vaccines also should be frequently and closely monitored against the rising population to enable researchers to design various interventions that can be used to improve the performance of the vaccine. Lastly, to improve the level of acceptance of the influenza vaccines among the public and healthcare providers, research on immunology is needed to aid the formulation of more advanced and effective influenza vaccines. The studies on immunological correlates of protection are quite expensive and require combined efforts from both the private and public sectors. Producers of influenza vaccines should consequently consider such collaborations as research priorities in the field of influenza vaccine production.

Annotated Bibliography

Linn, S. T., Guralnik, J. M., & Patel, K. V. (2010). Disparities in Influenza Vaccine Coverage in the United States, 2008. *Journal of the American Geriatrics Society*, *58*(7), 1333-1340. doi:10.1111/j.1532-5415.2010.02904.x. Retrieved from http://onlinelibrary.wiley.com/doi/10.1111/j.1532-5415.2010.02904.x/full.

In this study, the authors analyze vaccination patterns across the United States. The study focuses on adults who are more than fifty years old. The study was mainly informed by the seasonal influenza especially among older adults. Previous studies show that ninety percent of fatalities that result from influenza virus are the elderly. The research acknowledges the ongoing controversy in the debate about the effectiveness of influenza vaccines in the prevention of the infection of the virus among the elderly. The study, however, remains quite objective in the in assessing the coverage of the influenza vaccine across the United States. The authors found out that close to 42 percent of adults between the ages of fifty to fifty-four were vaccinated in the past twelve months. The study also noted that more than seventy percent of adults in the same age group have been vaccinated against influenza virus infection. The authors also indicated that race, income, and education had roles to play in the coverage of the influenza vaccine. The study discovered that individuals who had lower levels of education and incomes were less vaccinated compared to their other counterparts. This data and information is important to this research since it shows the percentage of coverage of the vaccine and the need for further drives for influenza vaccination.

Molinari, N. M., Ortega-Sanchez, I. R., Messonnier, M. L., Thompson, W. W., Wortley, P. M., Weintraub, E., & Bridges, C. B. (2007). The annual impact of

seasonal influenza in the US: Measuring disease burden and costs. *Vaccine*, *25*(27), 5086-5096. doi:10.1016/j.vaccine.2007.03.046. Retrieved from http://www.sciencedirect.com/science/article/pii/S0264410X07003854.

The observational study of the authors assessed the long-term effectiveness of the vaccine especially among the elderly in the United Kingdom. The data and information that results from this study in necessary in the studies and programs that focus on the influenza vaccine administration among the elderly in the community. The report involves the study of long-term effectiveness of influenza vaccine in the prevention of the flu to rule out the impact of possible mismatch of the vaccine and the influenza virus strains. The long-term study indicates that those who were vaccinated with the influenza vaccine were almost 28% less likely to find themselves in hospitals due to the pneumonia or influenza. The research also showed that the vaccinated individuals were 48% less likely to succumb to infection by the influenza virus. This article is important to my research since it supplies information concerning the effectiveness of the influenza virus among the elderly individuals in the society. The study acknowledges that vaccination against influenza is quite beneficial in the reduction of hospitalization and deaths.

Osterholm, M. T., Kelley, N. S., Sommer, A., & Belongia, E. A. (2012). Efficacy and effectiveness of influenza vaccines: a systematic review and meta-analysis. *The Lancet Infectious Diseases*, *12*(1), 36-44. doi:10.1016/s1473-3099(11)70295-x. Retrieved from http://www.sciencedirect.com/science/article/pii/S147330991170295X.

This study is a meta-analysis of the influenza vaccines concerning their effectiveness and efficacy tracing from 1969 to 2010. The authors supply the first meta-analysis with tests that confirm the virus. This is more accurate since when studies apply methods that do not confirm influenza virus to value the effectiveness on the influenza vaccine; they tend to overestimate the value. This study was quite selective in the selection of trials for the effectiveness on the influenza virus and discovered that the vaccine was sixty percent effective in adults. However, the meta-analysis also indicated that there is little evidence concerning the effectiveness of the influenza vaccines among infants below six years and the elderly who are over 65 years of age. This research is important in my study because it shows that despite the advancements in the market of vaccines, the currently used vaccines are not effective enough. However, despite the flaws in the current influenza vaccines, it is better to administer them instead of giving no vaccine.

Ottenberg, A. L., Wu, J. T., Poland, G. A., Jacobson, R. M., Koenig, B. A., & Tilburt, J. C. (2011). Vaccinating Health Care Workers Against Influenza: The Ethical and Legal Rationale for a Mandate. *American Journal of Public Health*, *101*(2), 212-216. doi:10.2105/ajph.2009.190751. Retrieved from http://www.sciencedirect.com.ezp1.lib.umn.edu/science/article/pii/S1473309907702360.

This study was conducted to further give insight to the debate concerning the effectiveness of the current influenza vaccines in the prevention of the infection by the influenza virus. The study mainly focuses in the effectiveness on the influenza vaccine in lowering the mortality rate among the elderly. This is relevant to this study since the elderly in the society

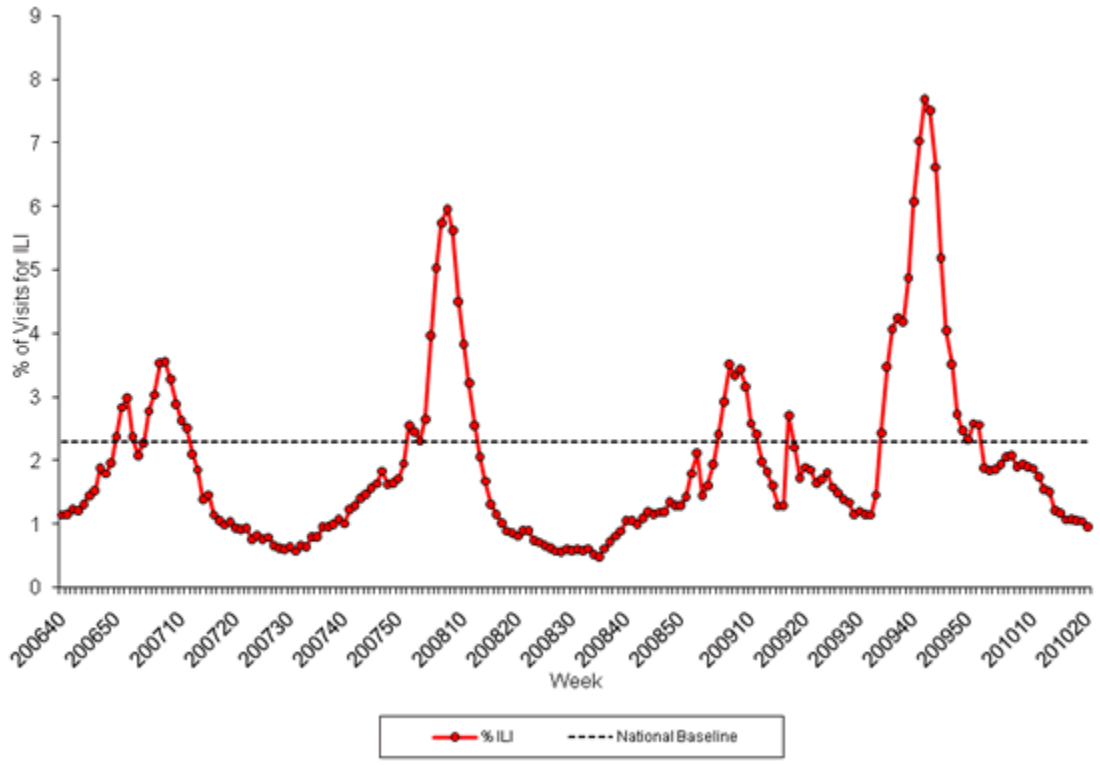
comprise a group of people who are targeted in the promotion of the influenza vaccines. The study indicates that there are little data to support the argument concerning the effectiveness of influenza vaccine among this age group. The study further explains that the effectiveness of the vaccine especially among the elderly is overestimated because of selection bias. Simonsen et. al also explain that cohort studies have exhibit a lot of selection bias and as a result cannot be trusted[4]. This study is therefore important to this study since it supplies the needed information that aids the assessment of the efficacy and effectiveness of the traditional influenza vaccine.

Simonsen, L., Taylor, R. J., Viboud, C., Miller, M. A., & Jackson, L. A. (2007). Mortality benefits of influenza vaccination in elderly people: an ongoing controversy. *The Lancet Infectious Diseases*, *7*(10), 658-666. doi:10.1016/s1473-3099(07)70236-0. Retrieved from http://www.sciencedirect.com.ezp2.lib.umn.edu/science/article/pii/S0264410X0801030X.

This paper suggests that influenza vaccination should be compulsory among healthcare workers to aid the fight against the virus. Although there are plenty of objections to the compulsory administration of the vaccine, the authors suggest that the advantages of administering the vaccine outweigh the arguments that are laid against it. The proposal argues that healthcare workers should be the first line of defense in the fight against the virus and should therefore remain as healthy as possible. The proposal goes on to shed light on some of the ethical concerns that arise from the compulsory administration of the virus. This paper is important in this study since it provide evidence and data that support the need for vaccination against influenza virus. It is also important for this paper to acknowledge the issues that are raised by

those who are opposed to the administration of the influenza vaccine. The proposal also presents data that show the implications of the influenza vaccines in various groups of people.

Graph 1



Graph for the number of patient visits for influenza related illness in the United States between 2008 and 2009. Reported by the United States Outpatient Surveillance Network.

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Simonsen, L., Taylor, R. J., Viboud, C., Miller, M. A., & Jackson, L. A. (2007). Mortality benefits of influenza vaccination in elderly people: an ongoing controversy. *The Lancet Infectious Diseases*, *7*(10), 658-666. doi:10.1016/s1473-3099(07)70236-0.

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