

BELLEVUE UNIVERISTY

A Study of Flu Vaccinations

Can Test Indicators Predict Effectiveness of Vaccines

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Abstract

Flu season takes its toll on the world every year. With so many people getting ill or even dying, an effective vaccination is critical in the fight against it. Much research has been done to this end, and this project will examine a database containing results from a number of flu studies. The first step is to analyze the data and understand the different variables and what they each represent. Examination of the data leads to several business questions, with models constructed to look for significant correlations in the data. The project seeks to see if there are predictive measures in which donors will have a high or low response to specific influenza vaccinations. It further searches for indicators as to who will respond favorably to a vaccination.

Intro/Background of the Problem

The flu, or influenza, is a contagious respiratory illness caused by viruses that infect the nose, throat, and sometimes the lungs (Thomas, 2018). Every year, 5% to 20% of the U.S. population will get the flu, with an average of 200,000 hospitalized with illness related problems (DerSarkissian, 2017). 8,200 to 20,000 Americans die each year from flu-related cases. The average cost of hospitalizations and outpatient doctor visits related to the flu are over \$10 billion (DerSarkissian, 2017). Throughout the course of history, there have been a number of flu pandemics that have made an impact worldwide. The 1889 Russian flu resulted in about 1 million deaths. The 1918 Spanish flu infected over half of the world's population, ending in over 40 to 50 million deaths. The 1957 Asian flu caused 1 million deaths, the 1968 Hong Kong flu resulted in 1 to 3 million deaths. Most recently, the 2009 H1N1 flu led to 203,000 worldwide deaths (Vincent Iannelli, 2020). The flu can be very serious, but vaccines are available to protect against some strains. For example, in 2019, the "trivalent" flu vaccine protected against two influenza A viruses and one influenza B virus (DerSarkissian, 2017).

With the flu wreaking havoc every year, the importance of finding a more effective vaccine grows stronger. A research project investigating influenza vaccine imprints on the immune system, funded by the European Commission, led to the creation of the FluPRINT database.

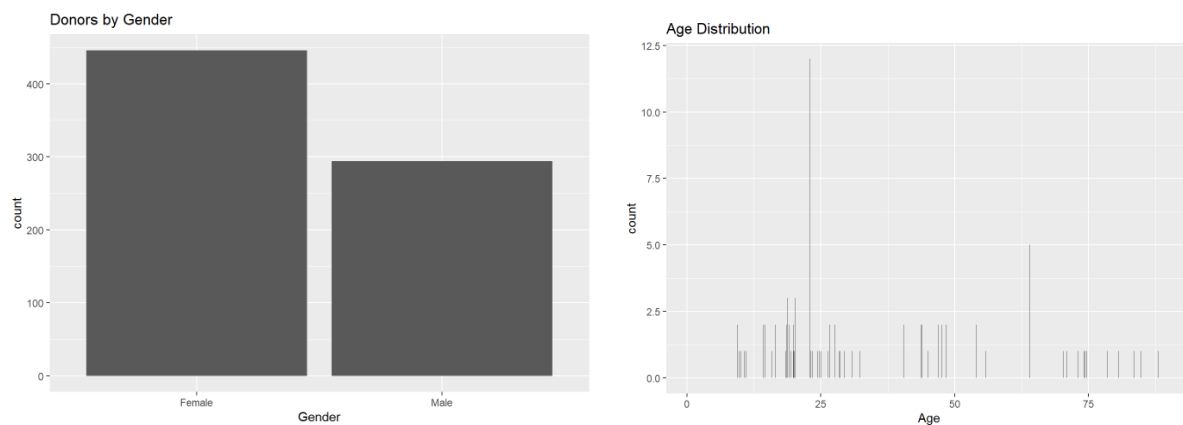
This unified database is the result of a large-scale study exploring novel cellular and molecular underpinnings of successful immunity to influenza vaccines. It contains information on more than 3,000 parameters measured using mass cytometry, flow cytometry, phosphorylation-specific cytometry (phospho-flow), multiplex ELISA, clinical lab tests (hormones and complete blood count), serological profiling with hemagglutination inhibition assay, and virological tests. The dataset represents fully integrated and normalized immunology measurements from 747 individuals from eight clinical studies conducted between 2007 to 2015 at the Human Immune Monitoring Center of Stanford University. The dataset represents a unique source in terms of value and scale, which will broaden the understanding of influenza immunity (Andriana, Tomic, Dekker, Maecker, & Davis, 2019).

The data contains information regarding different vaccine types, and the responses evoked in the donors. Various tests were performed, including tests that indicated whether the response to the vaccine was high or low. Based on these tests, are there tests that are better indicators as to whether or not a donor will respond highly? In addition, are there any indicators that would predict whether a person will still get the flu, even after vaccination?

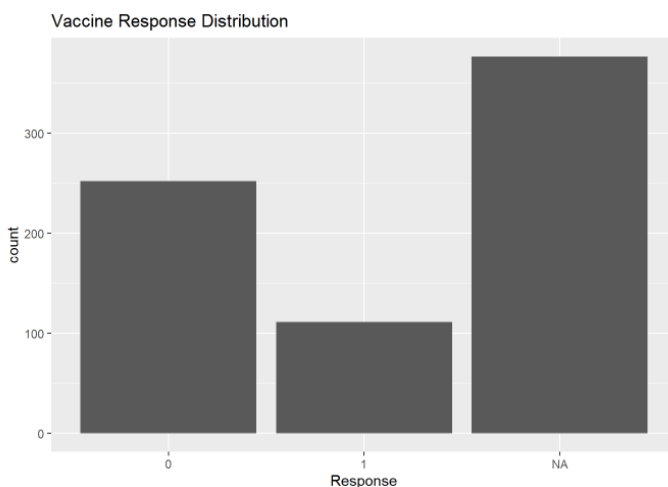
Methods

The data contains information on each donor, such as gender, race, and age. Additional information includes Body Mass Index (BMI), cytomegalovirus (CMV), Epstein-Barr virus (EBV), and the vaccine received at the visit. The outcome of the vaccine is measured as geometric mean titer (geomean), the difference in the geometric mean titers before and after vaccination (delta_geo_mean), and difference for each vaccine strain (delta_single). The vaccine_resp field is classified as high or low responder. With each visit, samples were analyzed and information about which assays were performed (assay field) and the value of the measured analytes (units and data) were recorded. Each donor's medical history was also recorded, including past influenza vaccines over the last 5 years, influenza infection history, and influenza-related hospitalization (Andriana, Tomic, Dekker, Maecker, & Davis, 2019).

Exploratory data analysis was performed using Python and R software. The data was aggregated into another file that contained one record per donor in order to capture gender, race, age, cmv status, ebv status, bmi, statin use, vaccine type, vaccine response, and influenza history and hospitalization. Both of the files will be used for further regression testing. There are 740 donors, the average age was 38, the youngest was 6 months old, while the oldest was 90 years old. Donor by gender and age distributions are charted below:



The number of donors per response type are graphed here, with a 0 indicating low response and 1 indicating high response.



Modeling and Results

Regression models were created using the aggregated donor file to test the correlations between a number of variables and outcomes. Using the aggregated dataset, the influenza infection variable was tested as a response to the type of vaccine, controlling for gender, age, and race of the donor, with no significant results. The next regression model tested the vaccine response as a response to the different vaccines administered, controlling for donor gender, age, and race. This showed a small significant correlation between vaccines 2 and 4 and a high response to the vaccine.

The next regression models were built using the entire dataset. A regression model was used to test the vaccine response variable as a response to the data variable, controlling for gender, age and race of the donor. The data variable was the measured values of the different assays tested on the donors. The model indicated a significant negative correlation between the data and the response to the vaccine. It also showed a positive correlation between the males and the age of the donors.

Because of this correlation, regression models were performed on subsets of the data, based on five different measured analytes that had the most positive vaccine responses among donors, see Appendix A. These models indicated that the analytes measured for CD8+ T cells in the assay test CyTOF phenotyping had the most significant negative correlation. CD4+ T cells and T cells analytes had minor significant positive correlation, NK cells analytes had minor negative significant correlation, while B cells analytes had no significant correlation at all.

Discussion/Conclusion

Based on the regression model performance, there is some significant correlation between vaccines 2 and 4 and having a high vaccine response. Vaccine 2 was the Fluzone Intradermal, and vaccine 4 was Fluzone. There seems to be some indication that the administration of these vaccines have a more significant impact on a recipient having a better chance for a high response to an influenza vaccination than the other types of vaccines given.

The other result that seems to be of significance is the analyte used to measure CD8+ T cells. A low data score is significantly correlated to having a high response to a vaccine. Therefore, this would seem to be a good indicator that a donor receiving a vaccine would have an improved chance of having a higher response to a vaccine, if this measure has a low data value. This test could be used to predict who will respond better to flu vaccinations. In the fight against the flu, determining who will respond favorably could be an advantage.

Acknowledgments

I would like to acknowledge the FluPRINT database and website for their extensive information. This was invaluable in understanding the research project that was conducted, as well as interpreting what the various variables represented.

References

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Appendix A

The names of analytes were counted based on having a high vaccine response. The top 5 are listed in the table below along with their frequency counts. This was the basis for determining on which analytes to conduct regression models.

CD8+ T cells	CD4+ T cells	T cells	B cells	NK cells	L50_CD40L
96	94	94	90	90	88