

**CANCER PATIENT ATTITUDES TOWARDS INFLUENZA VACCINATION AND THE PREVALENCE
OF VACCINATION IN CANCER PATIENTS**

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Abstract:**Introduction:**

Thousands of people die from influenza or its complications each year despite the fact that it is one of the few vaccine preventable diseases. Immunocompromised cancer patients are among the most vulnerable to this infection and flu-related complications, and therefore vaccination is highly recommended in these patients; however, current vaccination rates and attitudes towards vaccination remain unknown. We hypothesize that immunization rates are lower than the 100% recommendation rate, and hope to understand the reasoning behind the discrepancy. The purpose of this study is to assess cancer patient attitudes towards influenza vaccination in an effort to minimize barriers to vaccination and eventually increase vaccination rates in this immunocompromised population.

Methods:

Cancer patients enrolled in phase I clinical oncology trials at the Virginia G Piper Cancer Center at Scottsdale Healthcare were invited to participate in a voluntary survey. The 15-item survey consisted of demographic information, knowledge regarding the flu vaccine, vaccination status after cancer diagnosis and while on treatment, and general attitudes towards vaccination. A total of 84 cancer patients completed the survey. Results were stratified by age, gender, education level, and vaccination status. As this was a descriptive study, no statistical analyses were performed.

Results:

A total of 84 (n=84) advanced cancer patients enrolled in phase I clinical oncology trials completed the survey. Results indicate that although 71% of patients received the vaccine prior to cancer diagnosis, only 58% of patients have received the vaccine since their cancer diagnosis, and only 48% have been vaccinated while on cancer treatment. Of those vaccinated since cancer diagnosis, 94% reported doctor recommendation of the vaccine and most vaccinate to protect themselves from the virus. Of those not vaccinated since cancer diagnosis, only 37% report their doctor recommends the vaccine and the majority avoid vaccination because they believe the vaccine can cause the flu, they do not feel at risk of infection, and they do not believe the vaccine is effective.

Conclusion:

Our findings suggest that although the CDC strongly recommends influenza vaccination in cancer patients due to the risk of secondary complications and even death in these immunocompromised individuals, vaccination rates remain low. Our data demonstrates that patients who receive a doctor recommendation for the vaccine are more likely to be vaccinated, but not all doctors recommend the vaccine. Furthermore, false information regarding the vaccine, its efficacy, and its ability to cause infection continues to deter patients from vaccination. Together, this information offers profound insight into the cancer patient population and suggests the need for increased physician and patient education regarding the benefits of annual influenza vaccination to improve vaccination rates and decrease influenza infection and complications in the future.

Table of Contents

Introduction	1
Research Methods	4
Results	7
Discussion.....	15
Future Directions	17
Conclusions	19
References	20

List of Figures and Tables (In order of presentation)

Figure 1: Example of Survey: Cancer Patient Attitudes Towards Influenza Vaccination 5

Table 1: Demographic Information..... 8

Figure 2: Knowledge and Perceptions of the Flu Vaccine Based on Vaccination Status..... 10

Figure 3: Patient Reasons for Vaccination in those Vaccinated 12

Figure 4: Patient Reasons for Avoiding Vaccination in those not-vaccinated 14

Introduction

The influenza virus is one of the most common vaccine-preventable diseases that affects a large portion of our population every year. The CDC's Advisory Committee on Immunization Practices (ACIP) currently recommends "Universal" vaccination to every person greater than six months of age to maximize the effect of Herd Immunity;¹ however, it is particularly important to immunize populations at high-risk of developing complications associated with the flu receive the vaccine. These populations include pregnant women, children younger than five years of age, adults older than 50 years of age, anybody with chronic medical conditions (such as asthma, kidney disease, diabetes, lung disease and/or with a weakened immune system), people who live in nursing homes and long-term care facilities, and people who live with or care for high risk populations, (such as healthcare workers or family members of at-risk individuals.² Common complications from the flu include dehydration, sinus or ear infections, bacterial pneumonia, and associated worsening of chronic health conditions.³ High risk groups are more likely to develop these adverse symptoms due to their relative immunosuppression. Vaccination, however, does not guarantee immunity, and level of protection from infection varies with age and health status.

Not only do vaccine recipients vary, but the influenza virus, itself, mutates regularly; therefore, the vaccine must be reformulated every year via estimation of the specific viral strains that will be circulating each year, and a single vaccination is only protective for that year. Each year, the World Health Organization (WHO) recommends a trivalent vaccine that contains the three most likely influenza virus strains, and develops the vaccine in two forms: 1) a nasal spray that contains a live-attenuated vaccine for non-pregnant healthy populations between the ages of 20-49; and 2) Three forms of a killed (inactivated)-virus: a) regular short-acting for all people over 6months of age; b) high dose vaccine for ages 65+, and c) an intradermal vaccine for healthy individuals between 18-64.¹ Though vaccination confers significant protection from infection, other viral strains, not predicted to circulate, can arise, and vaccinated individuals may still become infected. Furthermore, individual immune systems develop different quantities of antibodies, which alter degrees of immunity as well. Because high-risk populations are prone to greater flu-related complications, vaccine supply is prioritized and highly recommended to these populations, particularly when infection rates increase.

Of particular interest, are the immunocompromised cancer patients undergoing anti-neoplastic treatments.

Yet, while cancer patients are likely to suffer complications from infection with influenza and are recommended to get the vaccine for protection, their immunosuppression begs the public health question of whether or not these patients can develop a sufficient response to vaccination to provide benefit. Because there are risks associated with vaccination, itself, it is important to consider the benefits of immunization in comparison to the risks associated with the procedure and vaccine formula.

Several studies have previously attempted to evaluate the benefit of influenza vaccination in specific cancer patient populations. Because the vaccine composition varies from year to year, however, and because the extent of cancer patient immunosuppression varies widely, there is still a great deal to learn regarding patient response to annual vaccination. In a study analyzing the effect of the monovalent 2009 influenza A (H1N1) vaccine, Xu et al. (2012) demonstrated that cancer patients taking myelosuppressive chemotherapy or non-myelosuppressive chemotherapy are equally able to generate an immune response to the H1N1 vaccine similar to that of healthy controls.⁴ This study, however, only evaluated immunogenic response to the single H1N1 strain.

Interestingly, not all anti-cancer treatments are myelosuppressive, so the effects of vaccination must be considered in patients undergoing different treatment regimes. In a more specific patient study, performed by Mulder et al. (2011), the authors explored the effects of influenza vaccination in metastatic renal cell carcinoma patients treated with one of two tyrosine kinase inhibitors (TKIs), sorafenib and sunitinib, which have been shown to affect the immune system. The authors determined that all patients treated with these drugs developed seroprotection rates similar to controls, and therefore recommended that cancer patients treated with these TKIs should be vaccinated.⁵ Moreover, in a study analyzing immune responses in advanced melanoma patients treated with Ipilimumab, a monoclonal antibody which blocks cytotoxic T-lymphocyte antigen-4, Weber et al. (2012) demonstrated that patients who received ipilimumab generated increased humoral responses relative to baseline titers, as well as increased various T-cell populations. The treatment, in this case, actually enhanced

vaccine response.⁶

The results from these studies suggest that in general, cancer patients on anti-neoplastic therapy should seroconvert and receive beneficial protection from the vaccine. Unfortunately, however, many individuals are opposed to vaccination. Many myths exist regarding vaccines and their effects on the body which has decreased vaccination rates over the years. Because of this, it is important to understand barriers to vaccination. In a 2010 survey of cancer patients on radiation therapy, Yee et al. found that 30% of the 204 surveyed patients had never received the flu vaccine, and only 7% reported that their oncologist educated them about the flu vaccine.⁷ In another similar study in 2013, researchers surveyed 359 patients with solid or hematologic malignancies and found that the overall influenza vaccination rate was only 17%.⁸ Furthermore, the most common reasons for not getting vaccinated included lack of knowledge for indication, currently on chemotherapy, fear of side effects, lack of efficacy, and because the vaccine was not advised by the physician.⁸ These surveys suggest that influenza vaccination rates are significantly lower than desired in cancer patient populations, and the most significant reasons for not being vaccinated can all be improved via public health education efforts.

Influenza immunization is highly encouraged in all cancer patients undergoing cancer treatment. However, little is known regarding actual current vaccination rates among the local cancer patient population. Because many individuals are opposed to annual influenza vaccination, we also evaluate patient knowledge and behaviors regarding immunization by conducting a survey of patient attitudes towards vaccination. We hypothesize that immunization rates will be significantly lower than the 100% population recommendation, and that beliefs regarding the efficacy of vaccination will vary; however we hope to gain greater knowledge regarding attitudes to determine barriers to vaccination and identify specific targets for public health intervention.

Overall, increased knowledge regarding current vaccination rates and attitudes towards immunization will help healthcare professionals and public health workers improve education efforts to increase vaccination rates and subsequently decrease influenza infection and complications in the immunocompromised cancer patient population.

Research Methods

Survey of Cancer Patient Attitudes Towards Influenza Vaccination

Patient attitudes and knowledge of vaccination were evaluated via a survey. The 15-item survey consisted of multiple choice questions regarding general demographic information, knowledge about the flu vaccine, vaccination status after cancer diagnosis and while on cancer treatment, and general attitudes towards vaccination (Figure 1).

Upon Scottsdale Healthcare and University of Arizona IRB approval, all cancer patients enrolled in a phase I clinical oncology trial at the Virginia G Piper Cancer Center at Scottsdale Healthcare were invited to complete the in-person, 2-sided, printed survey. Generally, to be enrolled in a phase I clinical oncology trial (testing new anti-cancer therapeutics in humans for the first time), an individual's cancer must have progressed despite all conventional/standard chemotherapy and radiation treatments. Eligibility criteria for the survey included any consenting cancer patient greater than 18 years of age who was actively involved in a phase I anti-cancer therapeutic clinical trial at the Virginia G. Piper Cancer Center. Exclusion criteria included any individual without a cancer diagnosis or not involved in a clinical trial at the Virginia G Piper Cancer Center.

The surveys were voluntary and anonymous, and no protected health information was collected. Surveys were not assigned a subject number so that no completed survey could be traced back to its original author. Surveys were offered to patients when they checked into the clinic for a scheduled appointment. Each patient was advised to only complete the survey once so as not to duplicate answers.

Surveys were collected over a three month period. Partially completed (i.e. only one side of the 2-sided form) were discarded. A total of n= 84 complete surveys were collected and analyzed. Individual surveys were each logged into SurveyMonkey (survey production and analysis software) to facilitate comprehensive data collection. Given the qualitative nature of the questions asked and descriptive nature of the study, no statistical analyses were performed. Results of the study were stratified by age, gender, education level, and vaccination status. (Figure 1: Sample Survey)

Figure 1: *Example Patient Survey - Attitudes Towards Influenza Vaccination (2-sides)*

Survey: Attitudes Towards Influenza (Flu) Vaccination

- What is your Gender?
 - Male
 - Female

- What is your Ethnicity?
 - Caucasian
 - Hispanic
 - African American
 - Asian
 - Other

- What is your highest completed education level?
 - ~~Highschool~~
 - College
 - Graduate School

- What age group are you in?
 - 20-40
 - 41-50
 - 51-60
 - 61-70
 - 71-80
 - >80

- How did you hear about the flu (influenza) vaccine?
 - Doctor recommended
 - Newspaper
 - Advertisements
 - Friends/Family
 - Self

- Does your physician recommend the flu vaccination every year?
 - Yes
 - No

- Have you received the flu vaccine since you were diagnosed with cancer?
 - Yes
 - No

- If yes, where do you get vaccinated?
 - Doctor's office
 - Pharmacy (ex: CVS, Walgreens)

- **If yes, what is your primary reason for being vaccinated?**
 - To protect myself. It is safer to get the vaccine than the flu.
 - To protect other patients (because I'm in a health care environment)
 - To protect my family/friends from getting infected
 - The vaccine is free of charge
 - My doctor told me to

- **If no, what is your primary reason for not being vaccinated?**
 - Fear of needles
 - Not feeling at risk of infection
 - I believe it is safer to get the flu than get the vaccine.
 - No convenient clinic for vaccination
 - I have alternative protection (immune system supplements)
 - I do not believe the vaccine is effective
 - Influenza is neither serious nor common
 - Vaccination can cause influenza infection

- **Have you received the flu vaccine within the last five years?**
 - Yes
 - No

- **Have you received the flu vaccination while on cancer treatment?**
 - Yes
 - No

- **Have you ever felt side effects related to the flu vaccine?**
 - Yes
 - No
 - If yes, describe the reaction: _____

- **Do you think you are at greater risk of getting the flu because you are on cancer treatment?**
 - Yes
 - No

- **Do you think it is more important for you to get the vaccine because you are on cancer treatment?**
 - Yes
 - No

We sincerely thank you for participating in this anonymous survey.

Results

Demographics

A total of 84 (n=84) advanced cancer patients enrolled in phase I clinical oncology trials completed the survey. The demographic distribution of participants is described in Table 1. Overall the majority of participants were female (62% females in comparison to 38% males), and the majority were Caucasian. Because these patients are enrolled in phase I clinical oncology trials, which suggests that their cancer had progressed on standard chemotherapy and radiation treatments, the population was generally older with the majority of patients between 61-80 years of age. Furthermore, in regards to education level, the majority of participants completed high school as their highest level of education (48%), While 32% completed college and 20% received a graduate degree.

Table 1: Demographic Data

Demographic	n = number (total = 84)	% of total respondants (n/84)
<i>Gender</i>		
Women	52	62%
Men	32	38%
<i>Ethnicity</i>		
Caucasian	69	82%
Hispanic/Latino	5	6%
African American	4	<5%
Asian	2	<3%
<i>Education Level</i>		
High School	40	48%
College	27	32%
Graduate Degree	17	20%
<i>Age</i>		
20-24 yrs	2	<3%
41-50 yrs	9	11%
51-60 yrs	17	20%
61-70 yrs	28	33%
71-80 yrs	23	28%
>80 yrs	4	< 5%

Vaccination Rates

Results demonstrate that of all patients evaluated, 71% had received the influenza vaccine within the last five years; however, only 58% had been vaccinated since cancer diagnosis, and only 48% had been vaccinated while on cancer treatment. When stratified by gender, ethnicity, education level, or age, there were no significant differences between those vaccinated since cancer diagnosis and those not-vaccinated since diagnosis.

Knowledge Regarding the Influenza Vaccine

The majority of respondents heard/learned about the flu vaccine via a Doctor's recommendation (52%). Otherwise, patients were made aware of the vaccine via Advertisements (22%), Friends/Family (17%), Newspaper (10%), or claimed that they just knew about the vaccine themselves (16%). Of those who do get vaccinated, most receive the vaccine at the Doctor's office (59%) vs. a Pharmacy or other location (ex: CVS/Walgreens) (41%). Results indicate that overall, 70% (n=59) of patients reported that their physician recommends the flu vaccine every year; however, when stratified by vaccination status, of those vaccinated since cancer diagnosis, 94% report their doctor recommends the flu vaccine every year, while only 37% of those not vaccinated since diagnosis report doctor recommendation of the vaccine (Figure 2). Interestingly, of those vaccinated since diagnosis, 55% believe they are at greater risk of getting the flu because I'm on cancer treatment, but 89% believe it is more important for them to get vaccinated because they are on cancer treatment (Figure 2). On the other hand, 34% of non-vaccinated participants believe they are at greater risk of getting the flu because they're on cancer treatment, but only 26% believe it is more important to get vaccinated because of this (Figure 2). Of note, only 14% and 12% of those vaccinated and non-vaccinated, respectively, report a history of experiencing side effects from the vaccine (Figure 2). There were no significant differences when stratified by demographics.

Figure 2: Knowledge and Perceptions of the Flu Vaccine Based on Vaccination Status

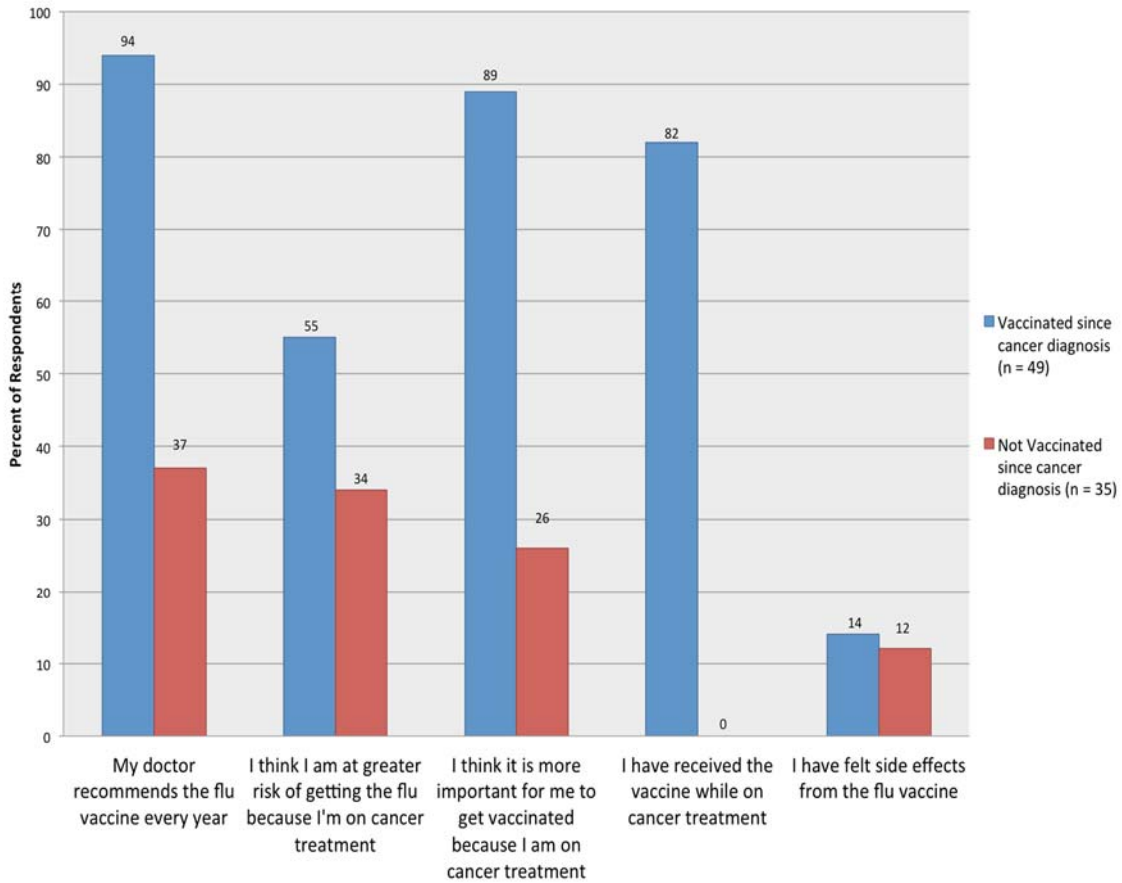


Figure 1: Comparison of knowledge and perceptions regarding influenza vaccination between patients who have been vaccinated since cancer diagnosis vs. patients who have not been vaccinated since cancer diagnosis.

Attitudes Towards Influenza Vaccination

Patient attitudes towards vaccination varied widely between those who have been vaccinated since cancer diagnosis (n = 49) vs. those patients who have not been vaccinated since diagnosis (n = 35). When asked for the primary reason for vaccination, the majority of those who get vaccinated do so to protect themselves from the influenza virus (88%). They also choose to vaccinate to protect friends and family (14%), because their doctor told them to (12%), and to protect other patients because they are around other immunocompromised patients while receiving treatment (8%) as demonstrated in Figure 3. Patients do not report choosing to be vaccinated because the vaccine is free. Vaccinated patient attitudes did not differ by age, gender, ethnicity, or education level.

Figure 3: Reasons for Vaccination in Those Vaccinated Since Cancer Diagnosis

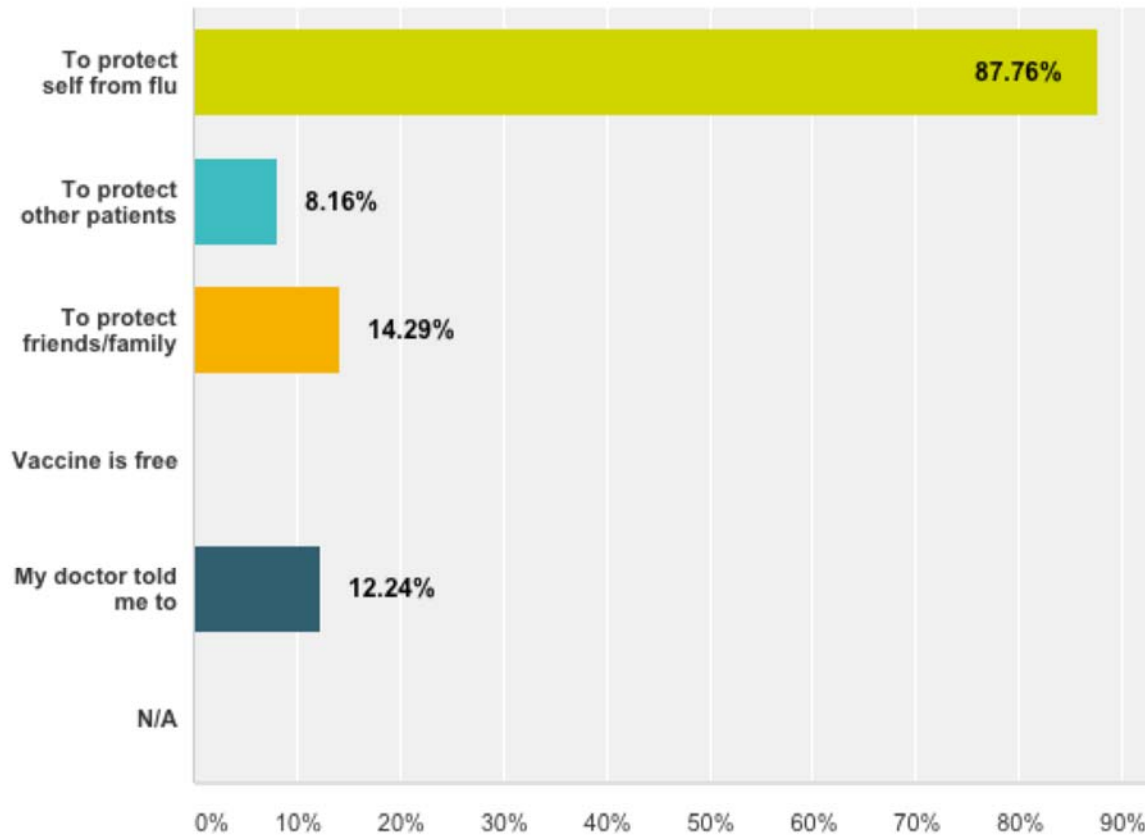


Figure 3: Patient reasons for vaccination in those who have been vaccinated since cancer diagnosis. Most vaccinated individuals do so to protect themselves and others, with a small subset of the population responding to doctor recommendations to vaccinate.

On the other hand, the reasons for avoiding vaccination in those who have not been vaccinated since cancer diagnosis are even more variable and diverse. Of those not vaccinated, 20% report avoiding vaccination because they “do not feel at risk of the flu.” Other reasons for avoiding vaccination include the belief that the “vaccine is not effective,” (17%), “the vaccine can cause the flu,” (11%), and the “flu is safer than the vaccine,” (9%) (Figure 4). Again, there were no significant differences between stratification by gender, age, ethnicity, or highest level of education.

Figure 4: Reasons for Avoiding Vaccination in Those Not Vaccinated Since Diagnosis

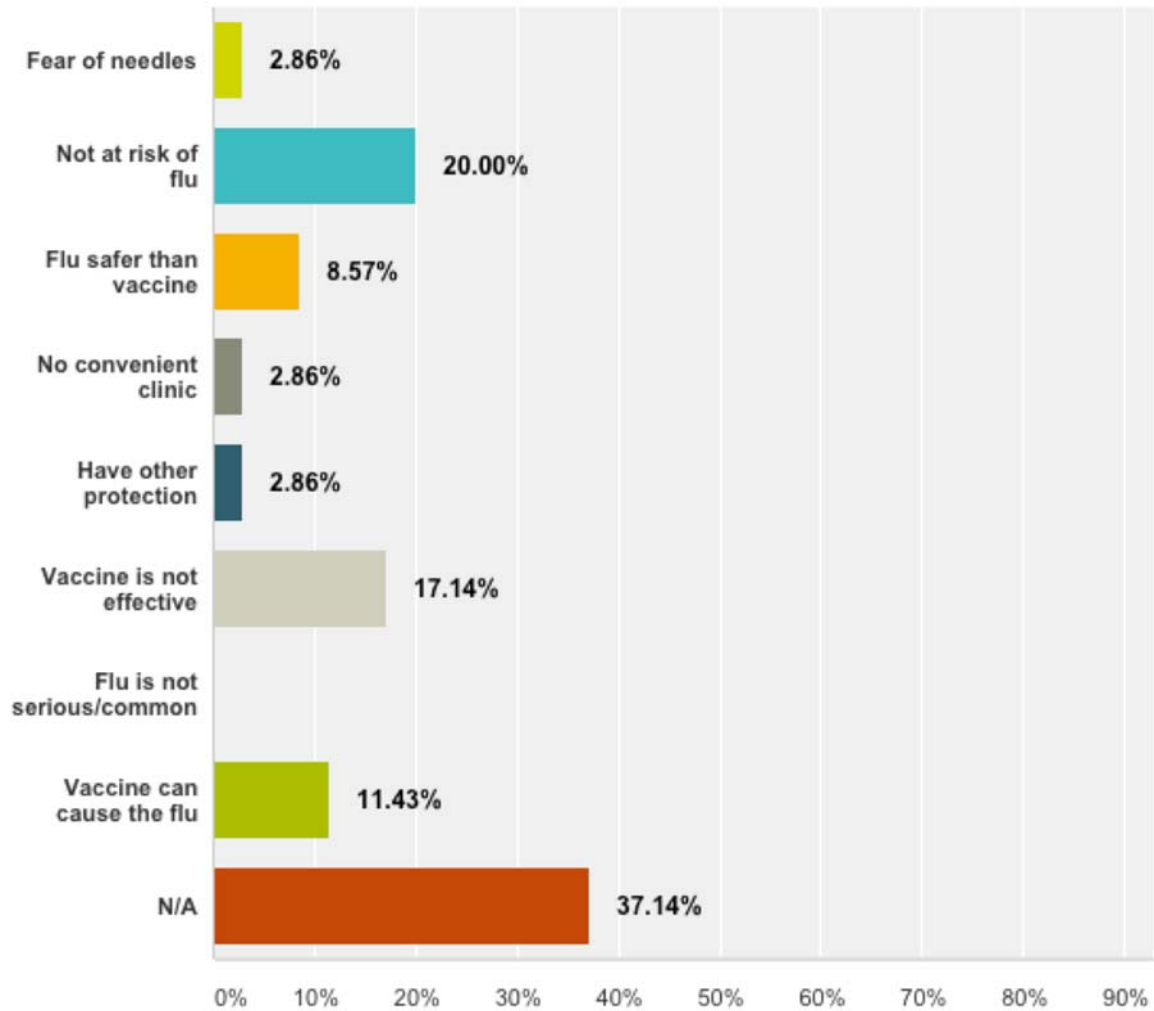


Figure 4: Patient reasons for avoiding vaccination in those who have not been vaccinated since cancer diagnosis. Though 37% did not participate in this question on the survey, the majority of the remaining 63% report beliefs in “not [feeling] at risk of the flu,” (20%), and that the “vaccine is not effective”

Discussion

Overall, our results demonstrate that vaccination rates are significantly lower than the 100% CDC recommended goal for this immunocompromised population; however, the vaccination rates at the Virginia G Piper Cancer Center (VGPCC) (58% vaccinated since diagnosis) are higher in comparison to rates in cancer patients described in previous studies (17% & 30% in other surveys).⁸ This suggests that the VGPCC staff may be encouraging influenza vaccination more readily than other oncologists. On a similar note, of those who have been vaccinated since cancer diagnosis, 94% reported that their doctor recommended the vaccine, in comparison to the 37% reported by those who have not been vaccinated since diagnosis. This positive correlation suggests that doctor recommendations for vaccines may truly play an influential role in whether patients get vaccinated or not, which thus provides an opportunity for intervention.

Interestingly, there was no difference between gender, ethnicity, age distribution, or educational background in regards to vaccination status or positive vs. negative attitudes towards vaccination. This lack of disparity between demographic groups suggests that these independent variables do not have a significant influence on attitudes towards vaccination. For example, there is no difference in vaccination rates or attitudes between those who have completed high school vs. a graduate education, suggesting higher education does not influence attitudes towards vaccination or vaccination behaviors. Though the lack of difference makes it more difficult for public health efforts to target a specific population for intervention, it is reassuring to know that those factors that cannot be changed have little influence on vaccination behaviors.

In regards to attitudes towards vaccination, 55% of vaccinated patients vs. 34% of non-vaccinated patients believe they are at greater risk of getting the flu because they are on cancer treatment, while 89% of those vaccinated vs. 26% of non-vaccinated believe it is more important for them to get vaccinated because they are on treatment. This demonstrates a very stark difference in background knowledge regarding risks of both an immunocompromised state and the vaccine itself. This drastic difference suggests education regarding vaccines and their purpose may significantly increase vaccination rates because there is a significant positive correlation between perception of vaccine importance and positive vaccination status. This

further highlights poor health literacy as a barrier to vaccination and the need for increased patient education regarding cancer, cancer treatment, influenza, and the flu vaccine.

The survey demonstrated that the majority of patients who receive the vaccine do so to protect themselves or others from the infection, and interestingly, most recall their doctors recommending the vaccine. On the other hand, the primary reasons for avoiding vaccination (in order of prevalence) are as follows: not feeling at risk of infection > disbelief that the vaccine is effective > the belief that vaccination can cause influenza > the influenza infection is safer than the vaccine. These reasons for non-vaccination are very similar to those noted in the literature. Many of these reasons and historical myths have been debunked by various studies; therefore, patient-directed educational efforts have the potential to enlighten the mindset of those who have learned from elsewhere in the past. Increased educational efforts regarding the truth about vaccines could help these patients make a better-informed decision regarding their interest for or against vaccination.

Overall, the results of the study demonstrate that although the CDC strongly recommends influenza vaccination in cancer patients due to the risk of secondary complications and even death in these individuals, vaccination rates remain suboptimal. It is important to note that the small sample size ($n = 84$) of this survey population limits the power and generalizability of our data. However, our data demonstrates that patients who receive a doctor recommendation for the vaccine are more likely to be vaccinated; however, not all doctors recommend the vaccine to patients. Furthermore, false information regarding the vaccine and its ability to cause infection continues to thrive and deter patients from vaccination. Together, this information offers profound insight into the cancer patient population and provides guided direction regarding both physician and patient directed educational efforts that may improve vaccination rates and decrease influenza infection and complications in the future.

Future Directions

Given that vaccination rates are lower than desired at the VGPC, it would be interesting to determine current national influenza vaccination rates in cancer patients. A dataset from the SEER-Medicare linked database was obtained to evaluate national vaccination rates. The SEER-Medicare database is a unique database consisting of linked data between the SEER (Surveillance, Epidemiology, and End Results Program = the National Cancer Institute's source of current cancer epidemiology in the United States), and the Medicare database, which allows researchers to link specific cancer patient data with their Medicare-specific data. This crossed database allows researchers to correlate cancer epidemiology with Medicare data. Unfortunately lack of time limited the data analysis for flu vaccination in Medicare cancer patients during this study; however, future analysis of the database is warranted to determine national vaccination rates in cancer patients. Furthermore, with hundreds of thousands of patients in the database, this portion of the study also has the potential to determine statistically significant differences between demographic factors and vaccination status. This would offer very directed targets for public health intervention.

Furthermore, because the primary reasons for opposition to vaccination are all secondary to poor understanding of influenza infection, the vaccine, and its safety, it would be interesting to determine how individuals ascertain their attitudes/beliefs. This would enable public health workers to best target media campaigns to improve public knowledge via those avenues that the public looks to for information and education.

As a starting point, because our data shows that vaccination recommendation by a physician is associated with increase vaccination rates, it is essential to evaluate current vaccination protocols at the Virginia G Piper Cancer Center (and other institutions) in an effort to determine how to increase physician recommendation to patients. Furthermore, public health workers should educate physicians on the importance of and strength of physician recommendations in their patients' eyes, and encourage them to increase their recommendation rates.

It would also be beneficial to develop educational materials regarding the flu, its complications, the vaccine and the vaccine's effectiveness for patients to read while waiting for the doctor. It is important to demystify the myths associated with vaccination as general media

has not been successful in this arena. Large-scale media educational campaigns could also be considered to reach a larger audience.

Lastly, given the resistance to vaccination, it is important to determine how beneficial the vaccine actually is in these cancer patients undergoing experimental therapy. It would be interesting to look at influenza serum titers before and 6 weeks after vaccination to determine if these patients are able to seroconvert and confer immunity. If they do not seroconvert, it would be valuable to look at the strength of vaccine boosters vs. no vaccination. This would require a prospective study with significant funding and IRB approval to physically work with human subjects administering vaccines and drawing titers.

Conclusions

Our findings suggest that although the CDC strongly recommends influenza vaccination in cancer patients due to the risk of secondary complications and even death in these immunocompromised individuals, vaccination rates remain low. Barriers to vaccination include flawed perceptions of the vaccine, its efficacy and its ability to cause infection. Though frustrating, each of these barriers offer opportunities for public health intervention, particularly in the form of patient-focused educational initiatives. Our data also demonstrates that patients who receive a doctor recommendation for the vaccine are more likely to be vaccinated, but not all doctors recommend the vaccine to patients; therefore, increased physician-directed education regarding vaccine recommendation may be beneficial as well. Together, this information offers profound insight into the cancer patient population and provides direction regarding possible patient and physician directed educational interventions to improve vaccination rates and decrease influenza infection and complications in the future.

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