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Andres Chang, Emory University
Mallory K Ellingson, Emory University
Christopher Flowers, Emory University
Robert Bednarczyk, Emory University

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Influenza Vaccination Rates Among Patients With a History of Cancer: Analysis of the National Health Interview Survey

Andres Chang,1,2,*, Mallory K. Ellingson,3,*, Christopher R. Flowers,4,5,6, and Robert A. Bednarczyk1,7,8

1Department of Hematology and Medical Oncology, Winship Cancer Institute, Emory University School of Medicine, Atlanta, Georgia, USA, 2Department of Microbiology and Immunology, Emory University School of Medicine, Atlanta, Georgia, USA, 3Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, Georgia, USA, and 4Cancer Prevention and Control Program, Winship Cancer Institute, Emory University, Atlanta, Georgia, USA.

**Background.** Annual influenza vaccination is recommended for all patients with cancer, but vaccine uptake data by cancer type and time since diagnosis are limited. We sought to estimate vaccination rates across different cancer types in the United States and determine whether rates vary over time since diagnosis.

**Methods.** Vaccination rates in individuals with solid tumor and hematological malignancies were estimated using data from 59,917 individuals obtained by the 2016 and 2017 National Health Interview Survey conducted by the Centers for Disease Control and Prevention.

**Results.** An average of 64% of the 5053 individuals with self-reported cancer received the influenza vaccine. Vaccination rates in men and women with solid tumors (66.6% and 60.3%, respectively) and hematological malignancies (58.1% and 59.2%, respectively) were significantly higher compared to those without cancer (38.9% and 46.8%, respectively). Lower rates were seen in uninsured patients, those younger than 45 years of age, and in African Americans with hematological malignancies but not with solid tumors. Vaccine uptake was similar regardless of time since cancer diagnosis.

**Conclusions.** Influenza vaccination rates are higher in men and women with cancer but remain suboptimal, highlighting the need for additional measures to improve vaccine compliance and prevent complications from influenza across all cancer types.

**Keywords.** cancer; immunization; influenza; prevention; vaccine.

Influenza infections in individuals with cancer have an estimated case fatality rate surpassing 10% [1]. Influenza is also a significant cause of morbidity such as bacterial pneumonia, respiratory failure, and deconditioning, oftentimes resulting in delays in cancer care that can produce inferior cancer-related outcomes. Given the significant burden of influenza on cancer patients, multiple organizations—including the Centers for Disease Control and Prevention (CDC) [2], the American Society of Clinical Oncology [3], the National Comprehensive Cancer Network [4], and the German Society for Hematology and Medical Oncology [5]—have instituted guidelines recommending annual influenza vaccination for all individuals with cancer. It is also recommended that caregivers, family members, and health care providers also get vaccinated as the vaccine effectiveness in patients undergoing active cancer treatment remains unclear [6].

Despite recommendations from multiple societies, prior studies showed that the influenza vaccination rate in adults with cancer is similar to that in the United States (US) general population at approximately 40% [7–9]. However, these studies were limited by small sample sizes and cover only few specific cancer diagnoses [10]. Understanding vaccine uptake among individuals with different types of cancer is important because different cancers cause different degrees of immunosuppression. Furthermore, the management of cancer differs significantly based on cancer type, treatment course, response to therapy, and time from cancer diagnosis. Ensuring adequate vaccination coverage may therefore be of higher priority in patients whose cancer or cancer treatment actively causes significant immunosuppression. However, how vaccine uptake varies over time in individuals with different cancer types is unknown. In this report, we used data from the National Health Interview Survey (NHIS) to determine the influenza vaccination rate based on a history of cancer diagnosis by type and time since most recent cancer diagnosis for 2016 and 2017 across the US.

**METHODS**

**Study Population and Data Collection**

We analyzed data from the 2016 and 2017 NHIS [11, 12], a nationally representative, face-to-face household interview survey.
conducted annually by the CDC. The NHIS collects data on a variety of health-related topics from the US population. Survey administrators utilize a multistage area probability design to gain a representative sample of the noninstitutionalized, civilian population [13, 14]. All variables are self-reported.

Patient Consent Statement
Participant consent for the original NHIS was obtained at the time of data collection [13, 14]. The team conducting this analysis used publicly available, deidentified data and no direct patient or participant contact was conducted for this analysis. The Emory University Institutional Review Board determined that this analysis was not human subjects research, as the project utilized only secondary analysis of deidentified publicly available data.

Data Analysis
The 2016 and 2017 survey datasets were combined for this analysis. The primary outcome of interest was influenza vaccine receipt in the 12 months prior to survey administration. We evaluated vaccine receipt by history of cancer diagnosis. Participants were first asked “Have you ever been told by a doctor or other health professional that you had ... cancer or a malignancy of any kind?” If respondents answered yes, they were then asked to specify what kind of cancer. Further information related to the cancer diagnosis such as stage or treatment history was not available in this dataset. We evaluated vaccine receipt by specific cancer types (breast, colon, etc) and major cancer groups (genitourinary, gastrointestinal, etc), and compared vaccine receipt among participants with a history of hematological malignancies, solid tumors, and no history of cancer. Participants with a history of “unspecified cancers” were considered separately because no further information was available on the specific cancer type. Non-melanoma skin cancers and unspecified skin cancers were excluded. Cancer-type categories were not mutually exclusive; participants with a history of multiple cancer types were counted in multiple categories. If participants had a history of >1 cancer categorized in different major cancer groups (eg, breast and genitourinary cancer) within the same category (eg, solid tumor), they were counted in both major cancer groups but only once in the main category. Therefore, the sum of the individuals in each specific cancer type (eg, stomach) or major cancer group (eg, gastrointestinal) may be equal to or exceed the total of the major cancer group or category.

Additional covariates of interest included age, sex, race/ethnicity, insurance status, region of residence, presence of any comorbidities, and time since diagnosis. Potential comorbidities were grouped into 4 categories—cardiovascular/metabolic disease, lung disease, weak/failing kidneys, and liver disease. Differences in influenza vaccine receipt by history of cancer stratified by age, insurance status, sex, race/ethnicity, and time since diagnosis were evaluated. Time since most recent cancer diagnosis was calculated by subtracting the age at most recent diagnosis of cancer from the participant’s age at the time of survey administration and grouped into 4 categories: <1 year, 1–5 years, 5–10 years, and >10 years.

Statistical Analysis
All analyses were conducted using SAS version 9.4 software (SAS Institute, Cary, North Carolina). All proportions presented were weighted according to the specifications provided in the NHIS Survey Description, using SAS procedures for analysis of complex survey data (eg, PROC SURVEYFREQ, PROC SURVEYMEANS), with sampling weights divided by the number of years of data pooled (2), as suggested by the National Center for Health Statistics [13, 14]. Number of events presented are unweighted. Wald confidence intervals were calculated. Proportions presented represent a weighted average of responses across the 2 years. χ2 tests were used to evaluate the association of a history of cancer with influenza vaccine receipt with α = .05.

The prevalence of influenza vaccination, by cancer type, may be confounded by the demographic characteristics named above. We stratified our analysis of influenza vaccination by cancer type by these demographic characteristics to generate vaccination prevalence estimates stratified by these key demographics. Given the associations between age and other demographic characteristics, cancer diagnosis, and influenza, we attempted a multivariate analysis to adjust our vaccination prevalence estimates for these factors; however, due to small sample size in some categories, the multivariable models did not converge to give adjusted prevalence estimates.

RESULTS
There were 5053 individuals who reported a history of cancer (cancer group) among the 59917 individuals surveyed by the NHIS during the 2016 and 2017 periods: 4503 with solid tumors, 342 with hematological malignancies, and 355 individuals who did not specify the type of cancer (Table 1). Among the cancer group, 566 participants reported a history of >1 cancer (Supplementary Table 1), most of which were solid tumors (75.6%; Supplementary Table 2). Participants in the cancer group were older and had significantly more comorbidities than those without cancer (Table 1). Breast cancer (40.9%) and prostate cancer (28.6%) were the most prevalent cancers in women and men, respectively (Supplementary Table 3). Within the cancer group, only 5.6% of women and 8.7% of men reported a hematological malignancy.

Overall, 63.8% of patients with a history of cancer and 43.3% without a history of cancer received the influenza vaccine during the 2016–2017 and 2017–2018 seasons. Higher influenza vaccination rates were reported by men and women with a history of solid tumors (66.6% and 60.3%, respectively),
hematological malignancies (58.1% and 59.2%), and unspecified cancers (54.2% and 62.0%) compared to individuals without cancer (cancer-free group, 38.9% and 46.8%) (Figure 1 and Supplementary Table 4). Rates were significantly higher in men and women across genitourinary, gastrointestinal, lung, breast, melanoma, and hematological malignancies. Notably, a statistical difference in influenza vaccination rate was observed in only 1 sex for participants with a history of cancers in the esophagus, liver, pancreas, stomach, head/neck, bone, leukemia, and lymphoma (Figure 1 and Supplementary Table 4).
Interestingly, unlike the cancer-free group, vaccination rates were higher in men with solid tumors compared to women.

The higher vaccination rates in the cancer group were partly due to higher vaccine uptake in middle-aged and elderly adults (Figure 2A and Supplementary Table 5). Although individuals 65 years and older had higher influenza vaccination rates regardless of diagnosis of cancer, 72.5% of participants with solid tumors reported being vaccinated compared to 66.5% of the cancer-free group in that age group. Higher vaccination rates were also observed among middle-aged adults with a history of solid tumors (51.3% vs 42.5%, respectively).

Vaccination rates in African American and white individuals with a history of solid tumors were similar (57.2% vs 63.8%, not significant) despite lower vaccination rates among African Americans in the cancer-free group (35.6% vs 46.0%; Figure 2B and Supplementary Table 5). Rates in African Americans with a history of hematological malignancies were not statistically different from the cancer-free group (27.4%) and was significantly lower than whites with hematological malignancies (60.9%). Significantly higher vaccination rates for individuals with solid tumors compared to individuals without cancer were also observed in Asians (66.6% vs 46.4%) and Hispanics (57.5% vs 35.1%), and in Hispanics with a diagnosis of hematological malignancies (81.0% vs 35.1%).

While uninsured individuals had lower vaccination rates overall, rates were higher in those with a history of solid tumors compared to those without a history of cancer (26.3% vs 16.1%; Figure 2C and Supplementary Table 5). Of the privately insured, vaccine uptake was higher in the cancer group. No difference was observed among participants receiving Medicare as all individuals receiving Medicare had significantly higher vaccination rates.

**Figure 1.** Influenza vaccine receipt by history of cancer (stratified by sex). *Significant for both men and women at \( \alpha = 0.05 \). *bSignificant for women but not men at \( \alpha = 0.05 \). *cSignificant for men but not women at \( \alpha = 0.05 \). Error bars = 95% confidence interval.
Individuals with cardiac, lung, or liver comorbidities showed higher vaccination rates regardless of the presence of cancer, but rates were further increased when these patients were diagnosed with solid tumors. Interestingly, this was not observed in patients with underlying kidney comorbidities (Figure 2D and Supplementary Table 5), though individuals with kidney comorbidities and no cancer had significantly higher vaccination rates compared to those with other comorbidities.

Given that cancer management changes throughout the course of the disease, we performed a cross-sectional comparison of influenza vaccination rates across participants diagnosed with cancer at different times. Vaccination rates for men and women diagnosed with solid tumors were similar regardless of time since cancer diagnosis (62.2%–69.9% for men and 56.9%–63.8% for women, across time since diagnosis categories). Vaccination rates in the hematological malignancies group also remained similar regardless of time since diagnosis (54.5%–60.2% for men and 55.9%–64.5% for women, across time since diagnosis categories) (Tables 2 and 3).

**DISCUSSION**

This is the first report to our knowledge where vaccination rates were determined for individual malignancies, major cancer groups, and at different times in the continuum of cancer care. Additionally, we provide vaccination data based on sex, race, and insurance status in individuals with a history of cancer. Although influenza vaccination in the cancer group was significantly higher compared to previously published results [7, 8] and to the cancer-free group, rates remain suboptimal as <70% of individuals with solid tumors and <60% of those with hematological malignancies were vaccinated. The proportion of individuals receiving the influenza vaccine varied by age, race, insurance status, and the type of cancer.

In addition to providing novel and important information on influenza vaccination trends among patients with cancer over time, our analysis also validates prior reports on vaccine uptake and disparities based on age, race, and insurance status in the general population [7–9, 15–21]. Our report also supports the previously reported prevalence of the most common cancer diagnoses and the distribution of cancer over time since diagnosis [22].

**Figure 2.** Influenza vaccine receipt by cancer type and age (A), race/ethnicity (B), insurance status (C), and comorbidity (D). All racial groups are non-Hispanic. Hispanics can be of any race. Native American, Alaska Native, and individuals self-defined as multiracial are not shown due to low numbers within the cancer categories. Other insurance status includes the Children’s Health Insurance Program (CHIP), other public insurance, other government insurance, and military insurance. Maroon, solid tumor (n = 4503); orange, hematological malignancies (n = 342); blue, unspecified cancer (n = 355); white, no history of cancer (n = 5,717). Error bars represent 95% confidence intervals of weighted percentages. *P ≤ .05. ‡Cell sizes too small to compute p-values. Abbreviation: AA, African American.

Despite the recommendations on vaccinating cancer patients, there are conflicting data on the effectiveness of the vaccine at mounting an immune response in individuals with cancer, particularly while receiving cancer-directed therapies [23–25]. For instance, some studies reported low vaccine responses in lymphoma patients after rituximab therapy [26–28], but recent data show that individuals treated with rituximab mount an immune response despite the lack of peripheral CD20+ B cells [29, 30]. Studies in patients with solid tumors are limited but appear to elicit an adequate response [31]. Little is known about vaccine responses in patients receiving novel anti-cancer therapies.
including immune checkpoint inhibitors. Thus, determining the influenza vaccine effectiveness and the optimal vaccination schedule in cancer patients remain important research areas.

There are several factors at the practice, provider, and patient level that could result in suboptimal vaccination rates in cancer patients [32]. Areas of improvement at the practice and provider levels include enhancing access to care, as uninsured participants had lower vaccination rates, and expanding the opportunities to educate patients and caregivers about importance of vaccines. Indeed, a recent review of National Cancer Institute–designated cancer center websites showed that only 8 centers provided vaccine-related content to patients and caregivers through that platform [33]. Additionally, systems that alert and remind the many providers that care for cancer patients (primary care, oncology, surgeons, radiation oncologists, etc) about offering the vaccine may be lacking [34]. Ensuring that state-level vaccine registries are functional, capable to interphase between states, and are easily accessible to health care providers would also facilitate coordinating efforts between providers. Perceptions about low risk of influenza infection, concerns about vaccine safety, low efficacy, and lack of cues and pressure from health care providers and relatives are some of the factors at the patient level that impact vaccination rates [35]. Many of these factors, however, appear to be modifiable as suggested by the higher vaccination rates in African Americans with solid tumors.

Several strategies have been proposed and tested to increase influenza vaccination rates in the general population including

### Table 2. Influenza Vaccine Receipt Stratified by Time Since Most Recent Diagnosis (Women)—National Health Interview Survey, 2016–2017

<table>
<thead>
<tr>
<th>Type of Cancer</th>
<th>&lt;1 y Since Diagnosis</th>
<th>1–&lt;5 y Since Diagnosis</th>
<th>5–&lt;10 y Since Diagnosis</th>
<th>≥10 y Since Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Weighted % (95% CI)</td>
<td>No.</td>
<td>Weighted % (95% CI)</td>
</tr>
<tr>
<td>Solid tumor cancers</td>
<td>113</td>
<td>63.8 (55.7–71.8)</td>
<td>386</td>
<td>56.9 (52.4–61.4)</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>25</td>
<td>61.4 (45.9–76.9)</td>
<td>92</td>
<td>48.7 (40.0–57.4)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>24</td>
<td>75.5 (59.6–91.4)</td>
<td>49</td>
<td>60.2 (48.2–72.2)</td>
</tr>
<tr>
<td>Head/neck</td>
<td>4</td>
<td>54.6 (16.0–93.2)</td>
<td>5</td>
<td>78.3 (48.6–100.0)</td>
</tr>
<tr>
<td>Lung</td>
<td>10</td>
<td>63.6 (37.4–89.7)</td>
<td>42</td>
<td>70.4 (50.1–83.8)</td>
</tr>
<tr>
<td>Breast</td>
<td>43</td>
<td>56.4 (43.0–69.0)</td>
<td>178</td>
<td>59.1 (52.7–65.6)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>11</td>
<td>64.5 (32.6–96.4)</td>
<td>26</td>
<td>59.6 (43.5–75.8)</td>
</tr>
<tr>
<td>Other solid tumors</td>
<td>16</td>
<td>74.6 (53.9–95.6)</td>
<td>46</td>
<td>58.9 (45.6–72.3)</td>
</tr>
<tr>
<td>Hematological malignancies</td>
<td>11</td>
<td>64.5 (32.4–96.6)</td>
<td>26</td>
<td>59.6 (43.2–76.1)</td>
</tr>
<tr>
<td>Unspecified cancers</td>
<td>10</td>
<td>50.7 (25.7–75.7)</td>
<td>22</td>
<td>50.9 (33.8–70.0)</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.

*a*Includes cancers of the bladder, cervix, kidney, ovary, prostate, testis, and uterus.

*b*Includes cancers of the colon, esophagus, gallbladder, liver, pancreas, rectum, and stomach.

*c*Includes cancers of the larynx, mouth/tongue/lip, and throat.

*d*Includes bone cancers, brain cancer, soft tissue cancers, thyroid cancer, and other cancers.

*e*Includes blood cancer, lymphoma, and leukemia.
home visits, incentives/subsidies, implementation of standing orders, vaccine screening protocols, and reminders to patients and providers [34, 36, 37]. Implementing some of these strategies, particularly reminder systems to patients and providers, are predicted to result in vaccination rates exceeding 80% with a modest increase in cost [36, 37]. To provide a framework to systematically identify factors associated with poor uptake of prevention activities and the potential interventions to address these factors at the practice, provider, and patient levels, we have recently developed the P3 Model [32]. This model provides a comprehensive path to address the complex interactions involved in the delivery of preventive services at the 3 levels.

This study has several strengths. First, our analysis used recent data collected from a representative sample of the US population, facilitating the generalizability of our findings. Second, reporting vaccine uptake over time since diagnosis among major cancer subgroups increases the relevance of these findings for subspecialties that participate at different times in the multidisciplinary approach to cancer care or practices that focus on a specific cancer type. Additionally, we report data on vaccine uptake based on age, race/ethnicity, and insurance status. Each of these variables may be an important independent factor affecting vaccination rates and thus should be further studied.

This study has some limitations. First, the data are self-reported and thus are subject to misreporting or recall bias. Second, this dataset lacks detailed cancer-specific information such as cancer subtype (eg, type of lung cancer, lymphoma), stage, treatment history, or whether individuals were receiving anti-cancer treatment at the time of interview. Thus, although the proportion of patients with a recent diagnosis of cancer (<1 year) receiving cancer-directed therapy is likely high, this assumption cannot be made for individuals with more remote diagnoses, potentially limiting its applicability in the population receiving anti-cancer therapies. Third, although the NHIS has been considered the most representative source for estimates [11], the ethnic composition of the cancer group differed from the cancer-free group and from data from the US Census Bureau [38]. This could be due to differences in incidence and cancer-related mortality between ethnic groups [39] and may partially explain some of the differences in vaccine uptake between cancer types. We attempted to conduct a multivariate analysis, but due to small sample size in some cancer types, the multivariable models did not converge to give adjusted prevalence estimates. Nonetheless, our results would support the conclusion achieved by a recent meta-analysis by Okoli et al in that socioeconomic factors may also affect influenza vaccine uptake among cancer patients [10]. However, further studies are needed to determine how disparities related to age, sex, race, and insurance status operate differently among patients with specific solid or hematologic malignancies.

In summary, vaccination rates in men and women with a history of cancer are higher compared to those without cancer, but rates across all major cancer subgroups are still suboptimal. Increasing the use of the influenza vaccine in this vulnerable population is particularly important this season as our society continues to battle with the COVID-19 pandemic. Understanding the factors associated with suboptimal vaccine uptake and applying a systematic approach to design interventions that address these factors will be key to allow for the design of optimal strategies to improve vaccine uptake, thereby protecting cancer patients against a potentially fatal infection.

Supplementary Data
Supplementary materials are available at Open Forum Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes
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