

Predictors for and Coverage of Influenza Vaccination Among HIV-Positive Patients

A Cross-Sectional Survey

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HIV Medicine. 2017;18(7):500-506.

Abstract and Introduction

Abstract

Objectives Influenza vaccination is recommended for HIV-infected patients, but limited data about vaccination rates are available. The aim of this study was to evaluate the coverage of and predictors for influenza vaccination among HIV-positive patients.

Methods All HIV-positive patients who visited the HIV out-patient department of the University Hospital of Vienna, Austria, between June and August 2015 were asked to participate in this survey by completing a questionnaire.

Results A total of 455 HIV-positive patients completed a questionnaire, with 359 male and 96 female participants with a mean age of 46 years. The influenza vaccination rate for the previous season (2014/2015) was 11.9% [$n = 54/455$; 95% confidence interval (CI) 9.2–15.2%]. Older age was significantly associated with a positive influenza vaccination status. Obtaining information through a medical consultation or receiving a direct recommendation for vaccination by a physician had a significant impact on vaccination behaviour. The probability of being vaccinated against influenza was about 13 times higher among patients who received a recommendation for vaccination by their family physician or by their HIV specialist ($P < 0.001$). Important reasons for declining vaccination were fear of side effects (39%), not considering influenza as a severe disease (36%) and reasons related to HIV: 17% were worried that the vaccine could worsen the course of HIV infection and 16% believed vaccination would fail because of their compromised immune system.

Conclusions A low influenza vaccination rate of 11.9% was detected in this HIV-positive cohort. The most effective impact for a positive vaccination status was direct recommendation of the influenza vaccine by the attending physician.

Introduction

Influenza is a viral respiratory infection which leads to an average of 1300 deaths per influenza season in Austria.^[1] Notably, patients with immunosuppressive conditions experience an increased risk for respiratory complications such as bacterial pneumonia.^[2] Although nowadays the mortality of HIV-infected patients attributable to influenza is lower than in the era before antiretroviral therapy (ART),^[3] influenza is still a common respiratory illness among these patients.^[4] Therefore, annual vaccination against influenza is recommended for HIV-positive patients in international guidelines.^[5–7]

Considering the impairment of T lymphocytes by HIV, a reduced effect of the influenza vaccine might be expected. Several studies have shown that HIV-infected patients have a weaker antibody response than healthy persons^[8] and in particular patients with low CD4 counts might experience a limited response. Nonetheless, there is sufficient evidence that vaccination against influenza significantly reduces the clinical occurrence of this disease in HIV-positive patients.^[9] Thus, it can be assumed that, despite a reduced antibody response, sufficient protection against influenza is achieved by vaccination in most HIV-positive individuals.^[10] Furthermore, influenza vaccination appears to be safe in HIV-infected patients, although a transient rise in plasma HIV RNA has been observed. However, these values return to baseline after a short period of time and have no effect on the clinical outcome of the patient.^[11,12] Therefore, vaccination against influenza is considered to be a safe and effective preventive measure against influenza infection in this group of patients.^[10,13] However, only limited data are available on vaccination rates in HIV-positive cohorts in Europe.

The aim of this study was to evaluate the influenza vaccination coverage among HIV-positive patients and to determine predictors for influenza vaccination.

Patients and Methods

Study Population

This survey was conducted in the HIV out-patient ward of the Department for Dermatology at the Medical University of Vienna, Austria. Most patients visit the out-patient ward for routine follow-up and prescription of ART. All HIV-positive patients who visited the out-patient department between June and August 2015 were asked to participate in this survey by completing a questionnaire.^[14]

Questionnaire

The questionnaire consisted of a total of nine questions which asked about demographics (age and sex), duration of HIV infection, influenza vaccination status for the previous influenza season (2014/2015), sources of information about influenza vaccination and reasons for not receiving the influenza vaccine.

Ethical Considerations

The Ethics Committee of the Medical University of Vienna approved the study (No. 1364/2013). Participation was voluntary and completion of the questionnaire implied consent for study participation. All gathered information was anonymized and kept confidential.

Statistical Analysis

Continuous data are presented as mean $\pm$ standard deviation (SD), and categorized data as absolute count and relative frequency. We calculated proportions together with exact binomial 95% confidence intervals (CIs). For further analyses, we categorized age and duration of infection into quintiles. To identify predictors of vaccination, we used contingency tables and used the chi-squared test to test the hypothesis of no difference. We used a score test to assess linear relationships between increasing categories of predictors and vaccination. For estimation, we used logistic regression models with vaccination as the outcome and the predictors as covariates. To assess the influence of age and sex on

the estimates, we included these as other covariables in these models. We used the likelihood ratio test to test for deviation from linearity and to test for interactions with age and sex. We used MS Excel 2011 and stata for Mac (Stata Corp, College Station, TX, USA) for data management and analyses. Generally, a two-sided *P*-value < 0.05 was considered statistically significant.

Results

Study Population and Influenza Vaccination Coverage

A total of 455 HIV-positive patients completed the questionnaire, with an influenza vaccination rate for the previous season of 11.9% (*n* = 54/455; 95% CI: 9.2–15.2%). Overall, 359 male (78.9%; 95% CI: 74.9–82.4%) and 96 female (21.1%; 95% CI: 17.6–25.1%) patients participated in this study. Of these, 13.1% (*n* = 47/359) of male patients and 7.3% (*n* = 7/96) of female patients claimed to be vaccinated, showing no significant association between gender and vaccination rate [odds ratio (OR) 1.9; 95% CI: 0.8–4.4; *P* = 0.1].

The mean (±SD) age of participants was 45.9 years (±12.3 years) and older age was significantly associated with being vaccinated against influenza (.). In the oldest age group (55–86 years), 20.8% (*n* = 21/101) were vaccinated compared with 6% (*n* = 5/83) in the youngest age group (15–34 years). Therefore, patients between 55 and 86 years old were 4 times more likely to be vaccinated than patients between 15 and 34 years of age (OR 4.1; 95% CI: 1.5–11.4; *P* < 0.01).

Table 1. Number of HIV-positive patients vaccinated against influenza according to age (*n* = 453; missing data *n* = 2)

Age (years)	Number vaccinated/total number (%)	Odds ratio (95% confidence interval)	<i>P</i> -value
15–34	5/83 (6)	Reference	–
35–41	8/94 (9)	1.5 (0.5–4.6)	0.5
42–47	7/76 (9)	1.6 (0.5–5.2)	0.5
48–54	13/99 (13)	2.4 (0.8–6.9)	0.1
55–86	21/101 (21)	4.1 (1.5–11.4)	< 0.01

A significant *P*-value is shown in bold.

The mean (±SD) duration of HIV infection was 11.2 years (±8 years). There was no significant association between duration of HIV infection and influenza vaccination (.).

Table 2. Number of HIV-positive patients vaccinated against influenza according to duration of HIV infection (*n* = 454; missing data *n* = 1)

Duration of HIV infection (years)	Number vaccinated/total number (%)	Odds ratio (95% confidence interval)	<i>P</i> -value
0.5–3.5	10/89 (11)	Reference	–
4–6.5	6/75 (8)	0.7 (0.2–2.1)	0.5
7–11	12/97 (12)	1.0 (0.4–2.4)	0.9
12–18	15/98 (15)	1.0 (0.4–2.6)	0.9
19–35	11/95 (12)	0.7 (0.3–1.8)	0.4

Fourteen per cent (65/455) stated that their close contacts were vaccinated against influenza, while 51% (230/455) stated that their contacts were not vaccinated and 35% (160/455) had no information about vaccination status. HIV-positive patients whose close contacts were vaccinated against influenza were significantly more likely to be vaccinated themselves (OR 6.4; 95% CI: 3.0–13.6; *P* < 0.001).

Predictors for Acceptance of Influenza Vaccination: Information Through Media

Predictors for acceptance of influenza vaccination with crude ORs and ORs adjusted for age and sex are depicted in .

Table 3. Predictors for acceptance of influenza vaccination among HIV-positive patients with crude odds ratios (ORs) and ORs adjusted for age and sex

Sources of information on flu shot				
Information on flu shot obtained from	Not vaccinated [<i>n</i> (%)]	Vaccinated [<i>n</i> (%)]	Crude OR (95% CI)	Adjusted OR (95% CI)
Physician				
No information (<i>n</i> = 292)	275 (94)	17 (6)	Reference	Reference
Information (<i>n</i> = 163)	126 (77)	37 (23)	4.8 (2.6–8.8)	4.6 (2.5–8.5)
Friends				
No information (<i>n</i> = 397)	348 (88)	49 (12)	Reference	Reference
Information (<i>n</i> = 58)	53 (91)	5 (9)	0.7 (0.3–1.8)	0.7 (0.2–1.7)
Radio				
No information (<i>n</i> = 389)	341 (88)	48 (12)	Reference	Reference
Information (<i>n</i> = 66)	60 (91)	6 (9)	0.7 (0.3–1.7)	0.7 (0.3–1.8)
Television				
No information (<i>n</i> = 327)	283 (87)	44 (13)	Reference	Reference
Information (<i>n</i> = 128)	118 (92)	10 (8)	0.5 (0.3–1.1)	0.5 (0.2–1.1)
Newspapers				

No information (<i>n</i> = 362)	317 (88)	45 (12)	Reference	Reference
Information (<i>n</i> = 93)	84 (90)	9 (10)	0.8 (0.4–1.6)	0.7 (0.3–1.6)
Internet				
No information (<i>n</i> = 409)	358 (88)	51 (12)	Reference	Reference
Information (<i>n</i> = 46)	43 (93)	3 (7)	0.5 (0.1–1.6)	0.5 (0.2–1.8)
Other				
No information (<i>n</i> = 423)	373 (88)	50 (12)	Reference	Reference
Information (<i>n</i> = 32)	28 (88)	4 (12)	1.1 (0.4–3.2)	1.2 (0.4–3.6)
No information received				
No (<i>n</i> = 373)	322 (86)	51 (14)	Reference	Reference
Yes (<i>n</i> = 82)	79 (96)	3 (4)	0.2 (0.1–0.8)	0.3 (0.1–0.9)
Information on flu shot obtained from physicians				
Information on flu shot obtained from	Not vaccinated [<i>n</i> (%)]	Vaccinated [<i>n</i> (%)]	Crude OR (95% CI)	Adjusted OR (95% CI)
Family physician				
No information (<i>n</i> = 353)	323 (92)	30 (8)	Reference	Reference
Information (<i>n</i> = 102)	78 (76)	24 (24)	3.3 (1.8–6.0)	3.1 (1.7–5.7)
Internist				
No information (<i>n</i> = 449)	397 (88)	52 (12)	Reference	Reference
Information (<i>n</i> = 6)	4 (67)	2 (33)	3.8 (0.7–21.4)	2.9 (0.5–17.0)
HIV specialist				
No information (<i>n</i> = 386)	346 (90)	40 (10)	Reference	Reference
Information (<i>n</i> = 69)	55 (80)	14 (20)	2.2 (1.1–4.3)	2.2 (1.1–4.4)
Company physician				
No information (<i>n</i> = 414)	372 (90)	42 (10)	Reference	Reference
Information (<i>n</i> = 41)	29 (71)	12 (29)	3.7 (1.7–7.7)	3.6 (1.7–7.6)
Other physician				
No information (<i>n</i> = 441)	388 (88)	53 (12)	Reference	Reference
Information (<i>n</i> = 14)	13 (93)	1 (7)	0.5 (0.1–4.4)	0.6 (0.1–4.7)
Recommendation for flu shot obtained from physicians				
Recommendation obtained from	Not vaccinated [<i>n</i> (%)]	Vaccinated [<i>n</i> (%)]	Crude OR (95% CI)	Adjusted OR (95% CI)
Family physician				
No recommendation (<i>n</i> = 287)	277 (97)	10 (3)	Reference	Reference
Recommendation (<i>n</i> = 65)	44 (68)	21 (32)	13.2 (5.8–29.9)	11.9 (5.2–27.2)
Advised against vaccination (<i>n</i> = 7)	5 (71)	2 (29)		
No data (<i>n</i> = 96)	75 (78)	21 (22)		
Internist				
No recommendation (<i>n</i> = 234)	223 (95)	11 (5)	Reference	Reference
Recommendation (<i>n</i> = 6)	3 (50)	3 (50)	20.3 (3.7–112.2)	15.2 (2.7–86.4)
Advised against vaccination (<i>n</i> = 0)	0 (0)	0 (0)		
No data (<i>n</i> = 215)	175 (81)	40 (19)		
HIV specialist				
No recommendation (<i>n</i> = 242)	233 (96)	9 (4)	Reference	Reference
Recommendation (<i>n</i> = 67)	45 (67)	22 (33)	12.7 (5.5–29.3)	11.7 (5.0–27.4)
Advised against vaccination (<i>n</i> = 2)	2 (100)	0 (0)		
No data (<i>n</i> = 144)	121 (84)	23 (16)		
Company physician				
No recommendation (<i>n</i> = 229)	218 (95)	11 (5)	Reference	Reference
Recommendation (<i>n</i> = 22)	14 (64)	8 (36)	11.3 (3.9–32.7)	10.0 (3.4–29.1)
Advised against vaccination (<i>n</i> = 1)	1 (100)	0 (0)		
No data (<i>n</i> = 203)	168 (83)	35 (17)		

Other physician				
No recommendation (<i>n</i> = 239)	229 (96)	10 (4)	Reference	Reference
Recommendation (<i>n</i> = 11)	8 (73)	3 (27)	8.5 (2.0–37.4)	8.1 (1.8–35.5)
Advised against vaccination (<i>n</i> = 2)	2 (100)	0 (0)		
No data (<i>n</i> = 203)	162 (80)	41 (20)		

CI, confidence interval.

HIV-positive patients who gathered information on influenza vaccination through the radio (14.5%), television (28.1%), newspapers (20.4%), the internet (10.1%) or friends (12.7%) demonstrated no significant association between source of information and vaccination status. Patients who claimed that they had not received any information about the influenza vaccine (18%) were significantly less likely to be vaccinated [adjusted OR (AOR) 0.3; *P* = 0.03].

Predictors for Acceptance of Influenza Vaccination: Information Through Medical Consultation

A total of 35.8% (*n* = 163/455) of HIV-positive patients stated that they had received information on influenza vaccination during a medical consultation. Patients who received advice from a physician were significantly more likely to be vaccinated (*P* < 0.001). Most patients were informed by their family physician (22.4%) or their HIV specialist (15.2%). The OR for being vaccinated against influenza was 3.3 for patients informed by their family physician (*P* < 0.001) and 2.2 for patients informed by their HIV specialist (*P* = 0.02). Patients who received information from their company physician were also significantly more likely to be vaccinated (AOR 5.8; *P* < 0.001), while for information obtained from a specialist in internal medicine or from other doctors there was no significant association with vaccination.

Predictors for Acceptance of Influenza Vaccination: Recommendation in a Medical Consultation

Patients for whom influenza vaccination was recommended by a physician during a medical consultation were significantly more likely to be vaccinated. Sixty-five patients (14.3%) declared that influenza vaccination had been recommended by their family physician. These patients were 13.2 times more likely to be vaccinated than patients who did not receive such a recommendation (*P* < 0.001). Sixty-seven patients (14.7%) were advised by their HIV specialist to receive the influenza vaccination. Among this group of patients, the OR for influenza vaccination was 12.7 (*P* < 0.001). Six patients (1.3%) received a recommendation from a specialist in internal medicine, 22 patients (4.8%) from their company physician and 11 patients (2.4%) from another physician. All recommendations were found to be significantly associated with a positive influenza vaccination status (.

Table 3. Predictors for acceptance of influenza vaccination among HIV-positive patients with crude odds ratios (ORs) and ORs adjusted for age and sex

Sources of information on flu shot				
Information on flu shot obtained from	Not vaccinated [<i>n</i> (%)]	Vaccinated [<i>n</i> (%)]	Crude OR (95% CI)	Adjusted OR (95% CI)
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No data (<i>n</i> = 203)	162 (80)	41 (20)		

CI, confidence interval.

Reasons for Nonvaccination

Of 455 HIV-positive patients, 401 (88.1%; 95% CI: 84.8–90.8%) had decided not to receive the influenza vaccination. Their reasons for nonvaccination are shown in .

Table 4. Reasons for HIV-positive patients to decline vaccination against influenza (*n* = 401; multiple answers possible)

Reason for declining influenza vaccination	Number (<i>n</i> = 401)	Percentage (95% CI)
In doubt because of information from		

Press reports	84	21 (17–25)
Television reports	62	15 (12–19)
I do not watch television	24	6 (4–9)
Internet reports	40	10 (7–13)
I do not have access to internet	22	6 (4–8)
Relatives	33	8 (6–11)
Medical reasons		
Afraid of side effects	155	39 (34–44)
Influenza is not such a severe disease	145	36 (32–41)
Vaccination could worsen HIV illness	66	17 (13–20)
Vaccination would fail because of compromised immune system	63	16 (12–19)
Vaccination would fail because of HIV therapy	20	5 (3–8)
Vaccination is painful	24	6 (4–9)
Organizational reasons		
Vaccination would have resulted in an additional appointment	94	23 (20–28)
No vaccine available	9	2 (1–4)
Attitude towards vaccination		
Generally against vaccines	69	17 (14–21)
Vaccination efficacy is a fabrication of the pharmaceutical industry	79	20 (16–24)
Negative experience with flu shot in the previous year	41	10 (8–14)
Generally negative experiences with vaccinations	28	7 (5–10)

Seventeen per cent ($n = 69/401$) of the 401 patients claimed that they were generally against vaccines. The main reasons for not receiving vaccination were the fear of side effects ($n = 155/401$; 39%) and not considering influenza as a severe disease ($n = 145/401$; 36%). Several reasons for not receiving vaccination were related to HIV: 17% ($n = 66/401$) were worried that the vaccine could worsen the course of HIV infection, while other patients believed that vaccination would fail either because of their compromised immune system ($n = 63/401$; 16%) or because of their ART ($n = 20/401$; 5%). Patients stated that negative reporting by the media influenced them not to get vaccinated. Twenty-one per cent of participants ($n = 84/401$) were negatively affected by reports in newspapers, 15% ($n = 62/401$) by information obtained through television and 10% ($n = 40/401$) by internet reports. Other important reasons for nonvaccination were avoiding an additional doctor's appointment ($n = 94/401$; 23%), the belief that vaccines are a fabrication by the pharmaceutical industry ($n = 79/401$; 20%) and negative experiences with vaccines in general ($n = 28/401$; 7%) or with the flu shot in the previous year ($n = 41/401$; 10%). Eight per cent ($n = 33/401$) declared that they had been negatively influenced by their relatives, 6% ($n = 24/401$) avoided vaccination because of the pain and 2% ($n = 9/401$) claimed that the influenza vaccine had not been available.

Discussion

Insufficient vaccination coverage for seasonal influenza in the general population has been reported in recent years, despite the fact that influenza causes about 15.5 deaths per 100 000 inhabitants per influenza season in Austria.^[1] A recent health survey showed that only 8.5% of Austrians claimed to be vaccinated against influenza in the year 2014 and about two-thirds of Austrians have never received an influenza vaccination.^[15] Even among health care workers, an insufficient vaccination rate of 42% was recently reported.^[16] Considering that immunosuppressed patients have an even higher risk for hospitalization and severe complications resulting from influenza infection, which are associated with increased mortality,^[2] it appears essential to gather more information on vaccination rates among such populations. A recent study conducted at the Oncology Department of the Vienna University Hospital showed that 18% of patients with a malignant disease were vaccinated against seasonal influenza.^[17]

The present study focused on patients living with HIV and showed an even lower vaccination rate of 11.9% in this group of patients. The data were collected at a single study site in Vienna, but can be considered representative as the HIV-infected cohort of the Medical University of Vienna is the largest in Austria. The vaccination rate of 11.9% is substantially lower than reported vaccination rates from other countries. Multicentre cohort studies in the USA showed vaccination rates between 28 and 43%^[18,19] among HIV-infected patients or even 57%^[20] in a female HIV-positive cohort. In Europe, only limited data are available concerning the influenza vaccination status of persons living with HIV. In France, two single-centre studies reported vaccination rates of 21%^[21] and 31%^[22] among adult HIV-positive patients. Another study from Spain focusing on HIV-infected children reported that only 23% had a yearly influenza vaccination documented.^[23] Based on the available data, it appears that influenza vaccination rates among HIV-positive patients in Europe are lower than in the USA.

The particularly low influenza vaccination rate in Austria cannot be easily explained. Negative reporting in the media might play a crucial role. In this survey, negative reporting in newspapers or on television was a reason for not receiving vaccination for 21% and 15% of patients, respectively. The media were commonly used as a source of information on vaccination, but there was no significant association between use of media and vaccination status. The most common reason for declining vaccination was the fear of side effects. It appears that a majority of persons have limited confidence in the effectiveness and usefulness of influenza vaccination. Scepticism about the pharmaceutical industry was also often named as a reason for refusing vaccination.

Thirty-six per cent of HIV-positive patients claimed that they do not perceive influenza as a serious disease. There might be a shift in risk perception towards considering side effects of the vaccine as a higher risk than contracting an influenza infection. Similar to other studies, older age was a significant predictor for influenza vaccination.^[17,22] Influenza vaccination is generally recommended for people over the age of 60 years.^[24] It is possible that elderly people consider themselves more at risk for complications resulting from influenza infection and are therefore more willing to accept vaccination. Moreover, other comorbidities such as respiratory or heart disease might influence the patient's decision to

receive vaccination. It is certainly important to sensitize patients with immunosuppressive conditions to the risks of an influenza infection to ensure that influenza vaccination is not declined because of a skewed risk perception.

A possible interaction between HIV infection and the influenza vaccine was another important issue. Seventeen per cent feared that the course of HIV disease could worsen because of vaccination and 16% believed that the vaccine would not be effective because of their immunosuppressed condition. These fears are not completely ungrounded as there is evidence of an interaction between HIV and the influenza vaccine. However, increases in viral RNA appear to be transient and have no apparent clinical effect.^[11,12] Despite possible interactions there is evidence that the influenza vaccine is safe and effective in HIV-infected patients.^[10]

There was no significant association between duration of HIV illness and vaccination status. However, as a consequence of the study design, no information on the immune status of the participants in terms of CD4 counts was obtained, which represents a limitation of this study. Several studies have demonstrated that patients with low CD4 counts or high viral loads are at risk not to be vaccinated against influenza.^[19,20,22] However, previous studies performed at the same HIV centre in Vienna showed that only 5% of HIV-infected patients had CD4 counts of < 200 cells/ μ L.^[25,26] A recent report of the Austrian HIV Cohort Study stated that 88% of HIV-positive patients in Vienna showed viral loads of < 50 HIV-1 RNA copies/mL.^[27] Therefore, it can be assumed that the immune reconstitution of the majority of patients in our study cohort was sufficient.

The most significant outcome of this study was the fact that HIV-positive patients who received information on vaccination from the attending physician were more likely to be vaccinated against influenza. Directly recommending vaccination to the patient was even more effective than only informing the patient about the influenza vaccine. It seems that if doctors inform their patients about the importance of vaccination and help them to overcome certain hindering factors, such as the fear of side effects, this will effectively increase the vaccination rate. Therefore, physicians should be aware of the importance of making a direct recommendation for influenza vaccination especially for patients with immunosuppressive conditions, including HIV infection.^[28]

In conclusion, a low influenza vaccination rate of 11.9% was detected in this HIV-positive cohort in Vienna. Direct recommendation of the influenza vaccine by the attending physician had the most effective impact on vaccination behaviour. The focus should be on improving information on vaccination for HIV-positive patients during medical consultations. Based on the present findings, providing educational material or even offering influenza vaccination for patients during their regular follow-up at the HIV clinic are approaches that could be recommended to increase influenza vaccination coverage. However, to confirm this conclusion, prospective studies measuring the impact of such interventions on vaccination behaviour of HIV-positive patients are necessary.

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