

## Rates and Predictors for Influenza Vaccine Prescriptions Among HIV-infected Clinic Patients in Singapore

Poh Lian Lim,<sup>1</sup>MD, MPH, FAMS, Joanne Tan,<sup>2</sup>MBBS, Yusrina Yusoff,<sup>2</sup>MBBS, Mar Kyaw Win,<sup>3</sup>MBBS, MPH, Angela Chow,<sup>3</sup>MBBS, MMed (PH)

### Abstract

**Introduction:** Although Singapore national guidelines recommend influenza vaccination for individuals with comorbidities, the vaccine uptake remains relatively low. This study examines the rates of influenza vaccine prescriptions in a clinic population, and patient, doctor and clinic factors that could affect the vaccine prescribing rates. **Materials and Methods:** This retrospective review utilised electronic medical records from HIV-infected patients seen in an infectious disease (ID) specialist clinic. Data from 40 randomly selected patients per physician were analysed for the outcome of influenza vaccine prescriptions from 1 January to 31 December 2007. All 7 consultants and the 6 ID registrars who had spent at least 4 months in the Department during 2007 were included. Data analysed included patient, physician, and clinic characteristics, and clinically relevant outcomes of admission within a year, and the length of hospital stay. **Results:** Of the 461 HIV-infected patients analysed for this study, only 107 (23%) were prescribed influenza vaccine in 2007. Vaccine prescribing rates by individual physicians ranged from 0% to 77%. The outcome of vaccine prescribing was analysed by patient demographics (age >40 years, gender, race), physician characteristics (doctor grade, gender and training), and clinic volumes (number of patients per clinic session). Multivariate analysis demonstrated that patients with female doctors (OR 1.8, 95% CI, 1.1 to 3.0,  $P = 0.017$ ), and doctors with overseas medical training (OR 11.6, 95% CI, 6.0 to 22.2,  $P < 0.001$ ) were significantly more likely to have influenza vaccine prescribed. On univariate analysis, patients were more likely to be admitted if they were male (OR 2.1, 95% CI, 1.0 to 5.1,  $P = 0.041$ ), and over 40 years old (OR 2.1, 95% CI, 1.1 to 4.5,  $P = 0.024$ ). Patients prescribed influenza vaccine showed a non-significant trend for protection against admission (OR 0.7,  $P = 0.288$ ), and shorter length of stay (median 5 vs 9 days,  $P = 0.344$ ). **Conclusion:** Influenza vaccine prescribing for HIV-infected outpatients in 2007 was only 23%, even in an ID specialist clinic. There was substantial variability in prescribing rates by individual physicians. Neither patient demographics nor patient volumes per clinic session had an impact on the prescribing rates, but significant predictors included physician gender and medical school training. Patients prescribed influenza vaccine had fewer admissions and shorter hospital lengths of stay, although these trends were non-significant.

Ann Acad Med Singapore 2013;42:173-7

**Key words:** Asia, Influenza vaccine, HIV, Singapore, Vaccination rates

### Introduction

The national guidelines in Singapore recommend influenza vaccination for all individuals over the age of 65, as well as children and adults with comorbidities or immunosuppression such as HIV infection.<sup>1</sup> Similar recommendations have also been considered the standard of care in the United States<sup>2</sup> and many other developed countries for the past 1 to 2 decades, and have been recently extended in the US to include all persons  $\geq 6$  months of age.<sup>3</sup>

Despite these guidelines, influenza vaccine uptake remains relatively low in Singapore. Among the few studies documenting influenza vaccination rates in Singapore, vaccine uptake ranged from negligible in the general population<sup>4</sup> to 12% among patients with chronic obstructive pulmonary disease.<sup>5</sup> A knowledge, attitudes and practices (KAP) survey among 307 diabetic patients in Singapore showed that only 31% had ever been vaccinated for

<sup>1</sup>Department of Infectious Disease, Tan Tock Seng Hospital

<sup>2</sup>Faculty of Medicine, National University of Singapore

<sup>3</sup>Department of Clinical Epidemiology, Tan Tock Seng Hospital

Address for Correspondence: Dr Lim Poh Lian, Department of Infectious Diseases, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308433.

Email: pllim@post.harvard.edu

influenza, and 64.8% reported never having been advised on influenza vaccination.<sup>6</sup> Among healthcare workers (HCW) themselves, the influenza vaccination rates at a large tertiary hospital exceeded 55% in 2004, shortly after the SARS outbreak and during a period of heightened preparedness for H5N1 avian influenza.<sup>7</sup> However, HCW influenza vaccine uptake declined steadily from 78% (2003) to 21% (2009) at another hospital in Singapore.<sup>8</sup>

There are very few studies documenting the actual vaccination rates among HIV-infected patients in Asian settings. A European study utilising telephone-based, random sampling survey showed influenza vaccination coverage of approximately 21% to 24% in the general population.<sup>9</sup> The study also indicated that receiving advice from the doctor or nurse was the second most frequently cited reason by patients who were vaccinated. Only 23% of HIV-infected children received yearly influenza vaccines in a Spanish cohort.<sup>10</sup> In the United States, data from 51,021 HIV-infected persons in a longitudinal cohort study observed from 1990 to 2002 demonstrated vaccination coverage increasing from 29% (1990) to 42% (2002). In that study, predictors of influenza vaccination coverage included older age, frequent medical visits, and anti-retroviral therapy.<sup>11</sup>

The purpose of this study was to determine influenza vaccine prescribing rates among HIV-infected patients receiving regular medical follow-up in a ID specialist clinic. It is also not known if vaccination rates are due to physician factors (doctors not offering vaccination to patients), clinic factors (higher patient volumes resulting in less time to address preventive care like vaccines), or patient factors (age, gender, educational level or socio-economic factors). Previous studies have explored the effect of specialist training and patient caseloads on quality of care indicators.<sup>12</sup> We decided, therefore, to evaluate possible patient, physician, and clinic factors that could affect vaccine prescribing rates. In addition, we also looked at clinical outcomes by analysing data regarding admissions and hospital length of stay by patients' vaccination status.

## Materials and Methods

This retrospective review utilised electronic medical records from HIV-infected patients seen in an ID specialist clinic in 2007. Data from 40 randomly selected patients per physician with at least one clinic visit between 1 January and 31 December, 2007 were collected using a standardised, anonymised form, and analysed for the outcome of influenza vaccine prescribed in 2007. All 7 consultants and the 6 ID registrars who had spent at least 4 months in the Department during 2007 were included. The data analysed included patient demographics (age, gender, race), physician characteristics (gender, grade (consultant vs registrar) and training (medical degree from Singapore or

other countries)), and clinic volume (more than 12 patients per 3-hour session vs 12 or less). The cut-off for 12 patients per session was selected to reflect normal scheduling for a typical subsidised clinic; patient volumes  $\geq 12$  indicate over-booked clinics.

In addition, data on all admissions within 12 months after the influenza vaccine prescription date were also collected; for patients who were not prescribed influenza vaccine, data was collected for admissions within 12 months after the index clinic visit date. Principal or secondary diagnoses on discharge were categorised into one of 4 categories: pneumonia, influenza, other respiratory infection, or non-respiratory disease. Data collection and analysis were conducted in blinded manner as to the identity of the doctors.

## Statistical Analysis

We compared differences in influenza vaccine prescription and admission within 12 months among patient, physician, and clinic factors (all categorical variables) using chi-square test, and reported the odds ratios (ORs) and 95% confidence intervals (CIs). Multivariate models were then constructed using unconditional logistic regression. Variables that were significant in the univariate analysis were included in the multivariate analysis after checking for collinearity. A stepwise logistic regression was used and variables that did not reach statistical significance were dropped from the model. A 2-tailed  $P$  value  $< 0.05$  was considered statistically significant. All analyses were performed using Stata 9 (Stata Corp., College Station, TX).

This study was approved by the National Healthcare Group Domain Specific Review Board (DSRB E/10/041) and waiver of informed consent was approved on the basis of protection of the confidentiality of the HIV-status of the participants.

## Results

Tables 1 and 2 describe the baseline characteristics of patients, physicians and clinic patient volumes included in this study. Of the 461 HIV-infected patients analysed for this study, only 107 (23%) were prescribed influenza vaccine in 2007. Vaccine prescribing rates by individual physicians ranged from 0% to 77% (Fig. 1). The outcome of vaccine prescribing was analysed by patient demographics (age  $> 40$  years, gender, race), physician characteristics (doctor grade, gender and training), and clinic volumes (number of patients per clinic session). Univariate analysis showed that patient characteristics and high patient volumes had no significant effect on vaccine prescribing rates (Table 3). Multivariate analysis demonstrated that patients with female doctors (OR 1.8, 95% CI, 1.1 to 3.0,  $P = 0.017$ ), and doctors with overseas medical training (OR 11.6, 95%

CI 6.0 to 22.2,  $P < 0.001$ ) were significantly more likely to have influenza vaccine prescribed (Table 3).

Table 1. Baseline Characteristics of Patients and Clinic Sessions

Patient and Clinic Characteristics (n = 461)		No. of patients	%
Patient age	≥ 40 years	332	72.0
	< 40 years	129	28.0
Patient gender	Male	360	78.1
	Female	101	21.9
Patient ethnicity	Chinese	361	78.3
	Malay	33	7.2
	Indian	17	3.7
	Others	50	10.8
Clinic volumes (per 3-hour session)	> 12 patients	298	64.6
	≤ 12 patients	163	35.4

Table 2. Baseline Characteristics of Physicians and Numbers of Patients Seen

Physician Characteristics (n = 13)		No. of doctors (%)	No. of patients seen (%)
Doctor's grade	Consultants	7 (53.8)	274 (59.4)
	Registrars	6 (46.2)	187 (40.6)
Doctor's gender	Male	5 (38.5)	192 (41.6)
	Female	8 (61.5)	269 (58.4)
Medical degree	Local	6 (46.2)	215 (46.6)
	Overseas	7 (53.8)	246 (53.4)

On univariate analysis, patients were more likely to be admitted if they were male (OR 2.1, 95% CI, 1.0 to 5.1,  $P = 0.041$ ), and over 40 (OR 2.1, 95% CI, 1.1 to 4.5,  $P = 0.024$ ) (Table 4) but having had influenza vaccine prescribed did not significantly reduce admissions within the following 12 months. Multivariate analysis showed that only male gender and age >40 years were significant predictors for admission within the subsequent 12 months. Patients prescribed influenza vaccine showed a non-significant trend for protection against admission (OR 0.7,  $P = 0.288$ ) (Table 4), and shorter length of stay (median 5 vs 9 days,  $P = 0.344$ ), but no significant difference was observed for influenza-related discharge diagnoses.

**Discussion**

Influenza vaccine prescribing rates for HIV-infected outpatients in 2007 was 23%, even in an ID specialist clinic. Although this low uptake is disappointing, it is consistent with data from other developed countries. There is room for improvement, as seen by the increasing coverage in the US among HIV-infected patients from 29% to 42% over a 12-year period.

Our data indicated considerable variability in prescribing rates by individual physicians. Interestingly, consultants, as more senior specialists, did not prescribe more vaccine on average compared to registrars in training. However, consultant prescribing rates ranged more widely from 0% to 77%, whereas registrar prescribing rates varied from 9% to 33%, perhaps averaging out what they were learning from senior colleagues. The patient's gender, age and race did not have any significant effect on influenza vaccine prescribing rates. However, significant predictors for prescribing influenza vaccine included physician gender and medical education abroad. These findings may indicate that local medical training may benefit from increased educational emphasis on the importance of adult vaccination in preventive care.

Patient volumes in clinic were not significant as a predictor for influenza vaccine prescribing rates. This was a surprising negative finding because in our study, many clinics were heavily over-scheduled, with some doctors seeing 18 to 21 patients per session. Clinician complaints that very busy clinics make it difficult to address preventive care issues like vaccination probably have validity; scheduling 18 patients in 3 hours meant that these patients, many with complex AIDS-related conditions and other comorbidities to manage, had to be seen within 10 minutes each. Nevertheless, the data show that high patient volume was not the predominant factor causing low vaccine prescribing rates.

Figure 1 provides a qualitative sense of the wide variability in clinical practice. The intent was not to single

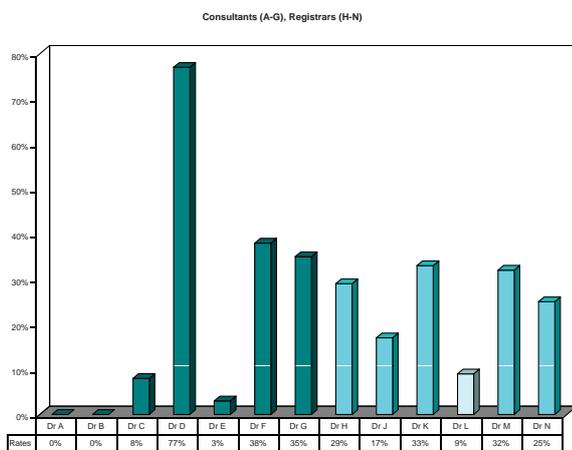


Fig. 1. Influenza vaccine prescribing rates by individual physicians.

Table 3. Predictors for Influenza Vaccine Prescription, Univariate and Multivariate Analysis

Factors	Vaccine prescribed, n = 107	No vaccine prescribed, n = 354	Univariate analysis		Multivariate analysis	
			OR (95% CI)	P value	OR (95% CI)	P value
Patient factors			1.5			
Age ≥ 40 years	77.6%	70.3%	(0.9 to 2.5)	0.144		NS
			1.4			
Male gender	81.3%	77.1%	(0.7 to 2.4)	0.359		NS
			1.4			
Chinese race	82.2%	77.1%	(0.8 to 2.5)	0.260		NS
Physician factors			1.1			
Registrar	42.9%	39.8%	(0.7 to 1.8)	0.560		NS
			1.6		1.8	
Female gender	66.4%	55.9%	(1.0 to 2.5)	0.055	(1.1 to 3.0)	0.017
			5.7		11.6	
Overseas trained	82.2%	44.6%	(3.3 to 10.4)	<0.001	(6.0 to 22.2)	<0.001
Clinic factors			0.8			
> 12 patients	49.5%	54.5%	(0.5 to 1.3)	0.365		NS

Table 4. Predictors for Admission Within Subsequent 12 months, Univariate and Multivariate Analysis

Patient Factors	Admission within 1 year from clinic date n = 71	No admission within 1 year from clinic date n = 390	Univariate analysis		Multivariate analysis	
			OR (95% CI)	P value	OR (95% CI)	P value
Patient factors			2.1		2.1	
Age ≥ 40 years	83.1%	70.0%	(1.1 to 4.5)	0.024	(1.1 to 4.3)	0.033
			2.1		2.5	
Male gender	87.3%	76.4%	(1.0 to 5.1)	0.041	(1.1 to 5.8)	0.032
			0.9			
Chinese race	76.1%	78.7%	(0.5 to 1.7)	0.617		NS
Vaccine status			0.7			
Prescribed	18.3%	24.1%	(0.3 to 1.4)	0.288		NS

out individual doctors, which was why data collection was blinded, and results presented anonymised. However, the data suggest that this variability may be due more to physician factors rather than patient or clinic factors. One implication of these findings is that increasing vaccine uptake will require implementation of a programme that does not depend upon individual physicians initiating vaccine prescribing. Subsequent to this study, our clinic put in place a nurse-initiated, opt-out influenza vaccination programme in 2010 to improve our vaccination coverage for HIV patients.

Our data showed that male gender and older age was associated with higher odds for admission, possibly indicating patients presenting with lower CD4 cell counts or a more medically fragile group for whom vaccination might be especially important. In this study, we did not show any significant reduction in admission for patients who were

prescribed influenza vaccine. As our study was primarily a descriptive analysis of vaccine prescribing practice, the sample size was not powered to show a reduction in serious clinical endpoints such as hospital admissions. Nevertheless, there were fewer vaccinated persons (18%) among those who required subsequent admission, compared to those who did not require admission (24%). Patients who were prescribed vaccine also had shorter lengths of stay in hospital, a difference of 4 days (although it did not reach statistical significance possibly due to the small sample size). One possible explanation for these findings is that patients with lower CD4 cell counts may have been prescribed influenza vaccination less frequently by their physicians, and if so, such patients would also be more likely to require longer admissions for opportunistic infections.

The efficacy of influenza vaccine in HIV-infected adults remains controversial and immunogenicity may

be reduced in those with advanced immunosuppression.<sup>13</sup> One meta-analysis of studies looking at influenza vaccine efficacy in preventing influenza in HIV-positive individuals demonstrated a pooled risk reduction of 66%.<sup>14</sup> Among patient populations other than HIV-infected individuals, there is some data indicating moderate efficacy of influenza vaccination to prevent mortality and hospital admission. A study of 35,637 vaccinated elderly individuals in Taiwan showed reductions in all cause mortality (HR 0.56)<sup>15</sup> but a case-control study of 157 hospitalised elderly patients with 639 matched controls in the UK failed to show a protective effect of influenza vaccine on emergency respiratory admissions.<sup>16</sup>

This study has several important limitations. First, these influenza vaccine prescriptions may not reflect actual vaccine administration, if patients did not fill the prescriptions at pharmacy. However, because all prescriptions are noted by the nurse as the patient leaves the consultation room, vaccines would generally be administered on the same day. Second, although this analysis included all consultants and all registrars who spent at least 4 months in the specialist clinic which serves most of the HIV-infected patients in Singapore, our data still represent a small sample size, and accordingly, our findings should be interpreted with great caution. The presence of outliers among doctors prescribing vaccines could substantially skewed the analysis of predictive factors. With the small number of doctors in this study, we are unable to adequately compensate for this particular limitation without losing a substantial portion of the analysed data. Further studies in larger settings may be required to validate these findings. Third, these findings may not be broadly generalisable to other clinics or populations. The KAP survey among diabetics in Singapore indicated that patient income levels were an important predictor for influenza vaccination. Our study did not collect patient income data, so the role of this important patient factor could not be determined.

## Conclusion

In conclusion, influenza vaccine prescribing for HIV-infected outpatients in 2007 was still low at 23%, with considerable variability in prescribing rates that appear to be more affected by physician rather than patient factors. Improving vaccine uptake for patient populations will most likely require programmes that do not rely upon individual physicians initiating vaccine prescriptions.

## REFERENCES

1. Ministry of Health Singapore. MOH Circular 10/2010, 1 April 2010. Update on influenza situation and recommendations on the use of seasonal influenza and influenza A (H1N1-2009) vaccines. Available at: [http://www.cfps.org.sg/swine\\_flu/MOH%20Circular%2010-2010.pdf](http://www.cfps.org.sg/swine_flu/MOH%20Circular%2010-2010.pdf). Accessed 2 August 2011.
2. CDC. Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010. *MMWR Recomm Rep* 2010;59:1-62.
3. CDC. Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2011. *MMWR Morb Mortal Wkly Rep* 2011;60:1128-32.
4. Ambrosch F, Fedson DS. Influenza vaccination in 29 countries: an update to 1997. *Pharmacoeconomics* 1999;16 Suppl 1:47-54.
5. Cao Z, Ong KC, Eng P, Tan WC, Ng TP. Frequent hospital readmissions for acute exacerbation of COPD and their associated factors. *Respirology* 2006;11:188-95.
6. Tan EK, Lim LH, Teoh YL, Ong G, Bock HL. Influenza and seasonal influenza vaccination among diabetics in Singapore: knowledge, attitudes and practices. *Singapore Med J* 2010;51:623-30.
7. Yang KS, Fong YT, Koh D, Lim MK. High coverage of influenza vaccination among healthcare workers can be achieved during heightened awareness of impending threat. *Ann Acad Med Singapore* 2007;36:384-7.
8. Thoon KC, Chong CY. Survey of healthcare workers' attitudes, beliefs and willingness to receive the 2009 pandemic influenza A (H1N1) vaccine and the impact of educational campaigns. *Ann Acad Med Singapore* 2010;39:307-12.
9. Muller D, Szucs TD. Influenza vaccination coverage rates in 5 European countries: a population-based cross-sectional analysis of the seasons 02/03, 03/04, and 04/05. *Infection* 2007;35:308-19.
10. Fernandez-Ibieta M, Ramos-Amador JT, Aunon-Martin I. HIV-infected children vaccination coverage and safety in a Western European cohort: a retrospective study. *Intl J STD AIDS* 2007;18:351-3.
11. Gallagher KM, Juhasz M, Harris NS, Teshale EH; Adult and Adolescent Spectrum of HIV Disease Group. Predictors of influenza vaccination in HIV-infected patients in the United States, 1990-2002. *J Infect Dis* 2007;196:339-46.
12. Landon BE, Wilson IB, Wenger NS, Cohn SE, Fichtenbaum CJ, Bozzette SA, et al. Specialty training and specialization among physicians who treat HIV/AIDS in the United States. *J Gen Intern Med* 2002;17:12-22.
13. Cooper C, Hutton B, Fergusson D, Mills E, Klein MB, Boivin G, et al. A review of influenza vaccine immunogenicity and efficacy in HIV-infected adults. *Can J Infect Dis Med Microbiol* 2008;19:419-23.
14. Anema A, Mills E, Montaner J, Brownstein JS, Cooper C. Efficacy of influenza vaccination in HIV-positive patients: a systematic review and meta-analysis. *HIV Med* 2008;9:57-61.
15. Wang CS, Wang ST, Lai CT, Lin LJ, Chou P. Impact of influenza vaccination on major cause-specific mortality. *Vaccine* 2007;25:1196-203.
16. Jordan RE, Hawker JI, Ayres JG, Tunnicliffe W, Adab P, Olowokure B, et al. A case-control study of elderly patients with acute respiratory illness: effect of influenza vaccination on admission to hospital in winter 2003-2004. *Vaccine* 2007;25:7909-13.