CHEST

Original Research

INHERITED LUNG DISEASES

Predictors of Influenza Vaccination in the Cystic Fibrosis Foundation Patient Registry, 2006 Through 2007

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Background: **Influenza vaccination is recommended for all persons with cystic fibrosis (CF). Despite this recommendation, no study has been performed to determine factors associated with receipt of influenza vaccination among persons with CF.**

Methods: **We conducted a 2-year cohort study from 2006 through 2007 using the CF Foundation (CFF) Patient Registry to assess predictors of influenza vaccination with logistical regression modeling.**

Results: **In 2006, the cohort consisted of 16,435 persons with vaccination data seen at CFF care centers. Vaccination rates were high for children aged < 5 years (90.5%), children 5 to < 18 years (91.1%), and adults (87.9%). In 2006, decreased odds of vaccination were seen among adults with other or unknown insurance (0.37; 95% CI, 0.15-0.87). Among children 5 to < 18 years and adults, decreased odds of vaccination were seen among Hispanics (children, 0.74; 95% CI, 0.55-0.98; adults, 0.67; 95% CI, 0.46-0.98) and with use of oxygen therapy (children, 0.55; 95% CI, 0.38-0.78; adults, 0.68; 95% CI, 0.55-0.86), whereas four or more clinic visits annually was associated with increased odds of vaccination (children, 2.33; 95% CI, 1.92-2.84; adults, 2.05; 95% CI, 1.71-2.47). Findings associated with decreased vaccine receipt remained significant in sensitivity analyses that assumed missing vaccination data were vaccine positive.**

Conclusions: **Overall influenza vaccination rates are very high in the US CF population. Knowledge of influenza vaccination predictors among persons with CF may aid clinicians in targeting patients at greater risk for influenza infection. These data may have important implications for the evolving pandemic 2009 influenza A(H1N1).** ***CHEST 2010; 138(6):1448–1455***

Abbreviations: aOR = adjusted odds ratio; CF = cystic fibrosis; CFF = Cystic Fibrosis Foundation; CF Registry = Cystic Fibrosis Foundation Patient Registry

Cystic fibrosis (CF) is the most common inherited fatal disease in the United States.[1] Exacerbations of CF pulmonary disease are common and characterized by cough, sputum production, dyspnea, and decreases in spirometric parameters.[2] Influenza infection may contribute substantially to CF morbidity because the influenza virus has been identified during CF pulmonary exacerbations,[3-5] and there is an 8% increase in CF pulmonary exacerbation incidence during influenza seasons.[6]

There are many reasons why at-risk individuals do not receive the annual influenza vaccination.

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In non-CF populations, vaccination disparities have been identified by race and ethnicity,[7-10] socioeconomic status,[8,11] age group,[12] health insurance status,[13-15] employment status,[15] utilization of health care,[8] and smoking status.[16] We collaborated with the CF Foundation (CFF) to analyze data from the CFF Patient Registry (CF Registry) to better understand who receives and who does not receive the influenza vaccination.

Materials and Methods

Study Population

This cohort study of patients was followed in the CF Registry from January 1, 2006, to December 31, 2007. A description of the CF Registry is published in an annual report by the CFF.[1] Patient data, including demographic and clinical information, are recorded at each clinic visit, during outpatient antibiotic therapy, during hospitalizations, and at year-end reviews. The CF Registry began recording influenza vaccination in 2006.

We analyzed all patients in the CF Registry eligible to receive the influenza vaccine. The outcome of interest was influenza vaccination. Patients aged < 6 months were excluded because influenza vaccination is not approved for this age group.[12] Additionally, patients were excluded from the primary analysis during the year that they did not have influenza vaccine receipt or nonreceipt documented. However, patients with missing vaccine data were included in subsequent sensitivity analyses. The reason for vaccine nonreceipt (including refusal) is not recorded. Furthermore, verification of vaccine receipt was not possible because the data in the CF Registry are anonymous.

Study Design and Procedure

Potential demographic and clinical factors associated with influenza vaccination were determined a priori after a review of vaccine disparity and the CF literature. Continuous data were converted to categorical data at cut-points that were determined a priori and were of clinical significance.

Potential demographic factors associated with vaccination included age, sex, and race/ethnicity. Two additional variables, insurance type and median income by patient zip code, were used as indicators of socioeconomic status. Insurance included four categories: private or health maintenance organization, public, no insurance, and other. Median income during the year 2000 for the zip code in which the patient lived was categorized by quartile.

Potential clinical variables associated with vaccination included presence of pancreatic insufficiency, any use of oxygen therapy, evidence of infection by *Pseudomonas aeruginosa*, and evidence of infection by *Burkholderia cepacia*. Lung function was categorized by whether CFF goals of $FEV_1 \geq 70\%$ predicted had been achieved.[1] Clinic visit data were converted into dichotomous variables according to whether CFF visit goals of four or more clinic visits annually were achieved.[1] CF center volume where subjects received the majority of their regular care was categorized by quartile of number of patients with CF (in 2006, these were < 43, 43-67, 68-146, and > 146). Finally, a dichotomous measure of nutritional status was based on CFF body mass goals and defined the body mass goal variable.[1] The body mass goal is an aggregate of height-weight metrics that differ by age group. For children aged < 2 years, the body mass goal is > 5% of the height-weight percentile as determined by Centers for Disease Control and Prevention growth charts.[17] For patients aged 2 to 19 years, the body mass goal is BMI ≥ 50th percentile for age.[18] For patients aged ≥ 20 years, the body mass goal was BMI ≥ 23 kg/m^2 for men and ≥ 22 kg/m^2 for women.[1]

Statistical Analysis

The a priori statistical plan was to stratify analyses by adults (aged ≥ 18 years) and children (aged < 18 years) because children transition to adult CF centers at age 18. In exploratory data analyses, the relationship between influenza vaccine receipt and age differed substantially within three age groups: children < 5 years, children 5 years to < 18 years, and adults ≥ 18 years (groups subsequently called young children, older children, and adults, respectively). To account for potential confounding by age group, we stratified analyses by these three categories.

The annual percentage of persons receiving influenza vaccination was determined for the overall CF Registry and by demographic and clinical categories. Crude, annual clinical, and demographic factors associated with influenza vaccination were determined by χ^2 and Fisher exact tests comparing the ORs of vaccine receipt among categories. Multivariate logistic regression with robust standard errors adjusted the ORs for the effect of other potential predictors of vaccine receipt. Two regression analyses were performed in this primary analysis. The first model included only demographic covariates as independent variables and influenza vaccination as the dependent variable. The second model included all demographic and clinical covariates as independent variables and influenza vaccination as the dependent variable. Age- and year-specific strata were assessed using the Wald statistic. The addition of clinical covariates (second regression model) did not improve model fit in young children but did improve model fit in older children and adults. Next, clinically relevant interactions were decided a priori to their statistical assessment in the model. Sex was found to modify the effect of age on vaccine receipt for adults, so a covariate for this interaction as well as for age as a continuous variable were included in the multivariate model for this age group.

Two sensitivity analyses were performed. First, we investigated whether any factors were associated with missing vaccination data. In this multivariate analysis, the dependent variable was a dichotomous variable describing whether vaccination documentation was present, and the independent variables were the same demographic and clinical covariates as in the primary analysis. Second, the effect that missing influenza vaccination data may have on factors associated with decreased vaccine receipt was evaluated. We made the conservative assumption that all missing influenza vaccine data were vaccine positive, and the multivariate analyses were repeated. Factors associated with decreased vaccine receipt from the primary analysis that remained statistically significant after this sensitivity analysis were considered robust findings and unaffected by missing observations.

All statistical tests were two sided, and $P < .05$ was considered statistically significant. Missing data were excluded from analyses except for influenza vaccine receipt in the sensitivity analysis as described. All analyses were performed with statistical software Stata, version 10.1 (StataCorp; College Station, TX) was used for analyses. The institutional review board at the University of Washington approved this study.

Results

Baseline Characteristics

In 2006, there were 24,114 patients in the CF Registry eligible for influenza vaccination (ie, aged > 6 months). Vaccine receipt or nonreceipt was

documented in 2,184 (75.7%) of 2,884 young children, 7,565 (72.4%) of 10,444 older children, and 6,686 (62.0%) of 10,786 adults. Among those with documented vaccine receipt or nonreceipt, influenza vaccination rates were 90.5% among young children, 91.1% among older children, and 87.9% among adults (Table 1).

Vaccination rates between male and female sex were similar among young children (90.7% and 90.4%, respectively), older children (91.2% and 91.0%, respectively), and adults (87.7% and 88.2%, respectively). Among race/ethnicity groups, the lowest vaccination rate was for black race among young children (85.4%), Hispanic ethnicity among older children (87.7%), and other race/ethnicity among adults (83.1%). Among insurance types, the no insurance category had the lowest vaccination rate among young children and older children (50.0% and 51.1%, respectively), whereas other or unknown insurance had the lowest vaccination rate among adults (54.0%). Among young children, older children, and adults, the clinical factor associated with the lowest vaccination rate was the use of oxygen therapy (87.3%, 83.2%, and 82.2%, respectively), whereas the factor associated with the highest vaccination rate was four of more clinic visits per year (91.8%, 92.9%, and 91.1%, respectively). Overall and subgroup influenza vaccination rates for 2007 were similar.

Multivariate Analysis

Multivariate analyses were performed by age group and study year. Results represent significant findings from 2006 that were replicated in analyses of 2007 data.

Demographic factors associated with vaccine receipt differed by age group in 2006. Among young children,

Table 1—*Baseline Description and Univariate Analysis of Predictors of Influenza Vaccination by Age Group, Cystic Fibrosis Foundation Patient Registry, 2006*

	Vaccine Receipt by Age[a]					
	< 5 y (n = 2,184)		5 to < 18 y (n = 7,565)		≥ 18 y (n = 6,686)	
Variable	%	OR (95% CI)	%	OR (95% CI)	%	OR (95% CI)
Overall	90.5	N/A	91.1	N/A	87.9	N/A
Demographic data						
Sex						
Female	90.4	Referent	91.0	Referent	88.2	Referent
Male	90.7	1.04 (0.78-1.39)	91.2	1.02 (0.87-1.20)	87.7	1.03 (0.85-1.25)
Race/ethnicity						
White, non-Hispanic	91.1	Referent	91.4	Referent	88.3	Referent
Black, non-Hispanic	85.4	0.63 (0.38-1.03)	92.1	1.10 (0.77-1.59)	84.8	0.71 (0.57-1.55)
Hispanic	88.5	0.75 (0.49-1.15)	87.7	0.67 (0.53-0.85)	83.3	0.66 (0.45-0.97)
Other	88.7	0.76 (0.32-2.22)	92.5	1.15 (0.53-2.96)	83.1	0.65 (0.33-1.33)
Insurance status						
Private/HMO	93.4	Referent	93.5	Referent	90.8	Referent
Public	88.2	0.53 (0.39-0.72)	89.2	0.60 (0.51-0.70)	85.6	0.60 (0.51-0.70)
Other/unknown	93.3	0.99 (0.15-42.67)	87.5	0.12 (0.08-0.17)	54.0	0.12 (0.08-0.17)
No insurance	50.0	0.07 (0.01-0.40)	51.1	0.38 (0.22-0.67)	79.2	0.38 (0.22-0.67)
Mean zip code income						
Lower quartile	86.9	Referent	89.1	Referent	86.2	Referent
Second quartile	89.9	0.15 (1.11-2.15)	91.1	1.23 (0.94-1.53)	87.4	1.23 (0.94-1.53)
Third quartile	93.7	2.24 (1.46-3.43)	92.4	1.30 (0.99-1.62)	89.1	1.30 (0.99-1.62)
Upper quartile	92.7	1.93 (1.26-2.95)	93.0	1.38 (0.86-1.42)	89.6	1.38 (0.86-1.42)
CF center volume						
Lower quartile	91.3	Referent	92.0	Referent	89.2	Referent
Second quartile	93.3	1.33 (0.85-2.07)	94.4	1.48 (1.14-1.91)	86.0	0.75 (0.61-0.92)
Third quartile	90.5	0.91 (0.60-1.37)	91.9	0.99 (0.78-1.25)	87.2	0.83 (0.67-1.03)
Upper quartile	87.0	0.64 (0.43-0.94)	86.4	0.56 (0.45-0.69)	89.4	1.02 (0.82-1.29)
Clinical data						
≥ 4 clinic visits/y	91.8	1.8 (1.32-2.46)	92.9	2.20 (1.86-2.59)	91.1	2.24 (1.72-2.49)
FEV_1 > 70% predicted[b]	…	…	91.9	1.50 (1.21-1.84)	90.3	1.27 (1.08-1.49)
Pancreatic insufficiency	90.8	1.30 (0.85-2.00)	91.2	1.19 (0.89-1.60)	88.0	1.07 (0.65-1.21)
Oxygen therapy in prior year	87.3	0.70 (0.33-1.74)	83.2	0.45 (0.35-0.60)	82.2	0.55 (0.54-0.85)
Body mass goal	90.2	0.79 (0.56-1.10)	92.0	1.18 (1.00-1.38)	90.5	1.39 (1.03-1.53)
Infected by *Pseudomonas aeruginosa*	90.4	0.94 (0.68-1.29)	91.9	1.12 (0.95-1.32)	88.6	0.87 (0.68-1.07)
Infected by *Burkholderia cepacia*	85.7	0.61 (0.07-28.09)	90.6	0.90 (0.53-1.67)	84.9	0.68 (0.41-0.87)

CF = cystic fibrosis; HMO = health maintenance organization; N/A = not applicable.

[a]Includes only patients with documented influenza vaccine receipt or nonreceipt.

[b]No FEV_1 data are available for children aged < 5 y.

having no insurance was associated with decreased influenza vaccination (adjusted OR [aOR], 0.05; 95% CI, 0.01-0.28) (Table 2). In older children, Hispanic ethnicity (aOR, 0.74; 95%,CI, 0.55-0.98) and the upper quartile of CF center patient volume (aOR, 0.52; 95% CI, 0.40-0.67) were associated with decreased receipt of vaccine. Among adults, five demographic factors were associated with decreased vaccine receipt: age in years (aOR, 1.02; 95% CI, 1.00-1.03), male sex (aOR, 1.81; 95% CI, 1.04-3.17), Hispanic ethnicity (aOR, 0.67; 95% CI, 0.46-0.98), having other or unknown insurance (aOR, 0.11; 95% CI, 0.07-0.18), and second quartile of CF center patient volume (aOR, 0.73; 95% CI, 0.57-0.93). These findings remained similar and significant in 2007 (e-Tables 1-3).

Clinical factors also were associated with vaccine receipt in 2006. Patients who used oxygen therapy had significantly decreased vaccine receipt among older children (aOR, 0.55; 95% CI, 0.38-0.78) and adults (aOR 0.68; 95% CI, 0.55-0.86) (Table 2). Among adults only, an $FEV_1 > 70\%$ predicted was associated with vaccine receipt (aOR, 1.33; 95% CI, 1.09-1.63). Finally, the only clinical factor associated with increased odds of vaccination was having four or more clinic visits for older children (aOR, 2.33; 95% CI, 1.92-2.84) and adults (aOR, 2.05; 95% CI, 1.71-2.47). These findings also remained similar and significant in 2007 (e-Tables 1-3).

Sensitivity Analyses

A multivariate analysis was performed to determine whether documentation of influenza vaccination receipt and nonreceipt was randomly distributed throughout the cohort. Patients with unknown or no insurance were significantly more likely to be missing vaccination data in each age group (Table 3). Conversely, Hispanic ethnicity, four or more clinic visits annually, and use of oxygen were significantly less likely to be missing vaccination data.

To explore the effect missing influenza vaccine data had on the overall sensitivity of our primary analysis, we undertook an additional analysis that assumed that all observations with missing vaccine data were influenza vaccine positive. Even when the most conservative assumption is made, several factors associated with vaccine receipt in the primary analysis remained significant. Among older children in 2006, Hispanic ethnicity, public insurance, lack of insurance, upper quartile of CF center patient volume, and use of oxygen therapy remained significantly associated with influenza vaccination (Table 4). All of the factors associated with decreased vaccine receipt among adults in the primary analysis remained significant in the sensitivity analysis, including Hispanic ethnicity, other or unknown insurance, second quartile of CF center patient volume, and use of oxygen therapy.

Discussion

This study demonstrates that influenza vaccination rates in patients with CF followed in the CF Registry were very high in 2006 and 2007, the first 2 years vaccination data were collected. CF care providers should be commended for the high rates of influenza

Table 2—*Multivariate Predictors of Influenza Vaccination by Age Group That Are Significant in Both 2006 and 2007, Cystic Fibrosis Foundation Patient Registry*[a]

Characteristic	Referent	2006		2007	
		aOR	95% CI	aOR	95% CI
Children aged < 5 y					
No insurance	Private or HMO insurance	0.05	0.01-0.28	0.08	0.02-0.34
Children aged 5 to < 18 y					
Hispanic ethnicity	White, non-Hispanic ethnicity	0.74	0.55-0.98	0.50	0.37-0.67
CF center volume upper quartile	CF center volume lower quartile	0.52	0.40-0.67	0.64	0.47-0.88
≥ 4 clinic visits/y	< 4 clinic visits/y	2.33	1.92-2.84	2.35	1.89-2.92
Oxygen therapy in prior year	No oxygen therapy in prior year	0.55	0.38-0.78	0.55	0.38-0.81
Adults aged ≥ 18 y					
Age (each year > 18)	Age 18	1.02	1.00[b]-1.03	1.01	1.00[b]-1.03
Hispanic ethnicity	White, non-Hispanic ethnicity	0.67	0.46-0.98	0.42	0.30-0.60
Other or unknown insurance	Private or HMO insurance	0.11	0.07-0.18	0.37	0.15-0.87
CF center volume second quartile	CF center volume lower quartile	0.73	0.57-0.93	0.61	0.48-0.79
≥ 4 clinic visits/y	< 4 clinic visits/y	2.05	1.71-2.47	2.06	1.70-2.49
$FEV_1 > 70\%$ predicted	$FEV_1 \leq 70\%$ predicted	1.33	1.09-1.63	1.28	1.04-1.59
Oxygen therapy in prior year	No oxygen therapy in prior year	0.68	0.55-0.86	0.66	0.52-0.82

aOR = adjusted odds ratio. See Table 1 legend for expansion of abbreviations.

[a]The entire list of demographic and clinical predictors with aORs and 95% CIs can be found in e-Tables 1- 3.

[b]Lower end of CI is > 1.00 but presented as 1.00 because of rounding.

vaccine receipt among their patients. CFF influenza vaccination goals, CF specialty-care centers, and center-specific registry reports all contribute to increased provider awareness about the importance of influenza vaccination. Nevertheless, we identified several factors associated with decreased vaccine receipt in this study. Lessons learned about which patients are at risk to not receive the influenza vaccine among this cohort may inform caregivers for all patients with chronic lung disease to increase influenza vaccine use.

The US government has set a goal to increase influenza vaccine coverage to 60% of high-risk adults by 2010.[19] In the CF Registry, influenza vaccine receipt exceeded these goals among patients with documented vaccine status and even among the registry cohort as a whole. In 2006, vaccination rates were much lower among other high-risk populations in the United States. That year, an estimated 36.2% of persons with asthma received influenza vaccine,[20] and among adults with any high-risk indication, influenza vaccination included 30.5% of those aged 18 to 49 and 48.4% of those aged 50 to 64.[21] In 2006, children with an age indication to receive influenza vaccine also had low rates of vaccine receipt: 32.2% of children aged 6 months to 23 months and 26.4% of children aged 2 years to 4 years.[12] Despite media and government attention to avian and pandemic influenza planning[22,23] and despite the expansion of vaccination age group recommendations to include all children that year,[24] vaccination rates remained well below the *Healthy People 2010* objectives.[19]

We identified several demographic predictors of influenza vaccine receipt in the US CF population. Among all age categories and years studied, lack of insurance was most often associated with significant decreases in vaccination receipt. Other indicators of socioeconomic status were not as closely associated with vaccine receipt. Although adults had decreased vaccine receipt among the lowest income groups, this finding was not present within other age groups, likely reflecting insurance availability for children of lower income groups that is forfeited upon reaching adulthood. An additional predictor of decreased vaccine receipt was nonwhite race/ethnicity. Estimates of

Table 3—*Odds of Having Vaccine Receipt or Nonreceipt Recorded in the Cystic Fibrosis Foundation Patient Registry Among Age Groups, 2006*

	< 5 y (n = 2,884)		5 to < 18 y (n = 10,444)		≥ 18 y (n = 10,786)	
Variable	aOR	95% CI	aOR	95% CI	aOR	95% CI
Sex						
Female	Referent		Referent		Referent	
Male	1.03	0.85-1.25	1.04	0.94-1.15	1.59	1.27-1.99
Race/ethnicity						
White, non-Hispanic	Referent	…	Referent	…	Referent	…
Black, non-Hispanic	1.40	0.93-2.13	1.04	0.82-1.32	1.13	0.86-1.47
Hispanic	1.00	0.73-1.37	0.73	0.60-0.89	0.73	0.56-0.94
Other	0.78	0.42-1.47	0.83	0.51-1.34	1.15	0.76-1.74
Insurance status						
Private or HMO	Referent	…	Referent	…	Referent	…
Public	1.08	0.87-1.33	0.99	0.89-1.11	1.17	1.05-1.30
Other or unknown	4.91	2.35-10.26	9.35	5.52-15.86	2.42	1.81-3.24
No insurance	4.05	1.08-15.24	2.16	1.25-3.72	1.66	1.12-2.46
Mean zip code income						
Lower quartile	Referent	…	Referent	…	Referent	…
Second quartile	0.84	0.65-1.09	1.00	0.87-1.16	1.16	1.02-1.32
Third quartile	0.8	0.61-1.05	0.89	0.77-1.03	1.07	0.93-1.22
Upper quartile	0.89	0.67-1.19	0.88	0.76-1.02	0.98	0.85-1.12
CF center volume						
Lower quartile	Referent	…	Referent	…	Referent	…
Second quartile	0.94	0.71-1.22	0.78	0.67-0.90	0.74	0.65-0.85
Third quartile	1.11	0.85-1.44	1.05	0.91-1.21	0.81	0.71-0.93
Upper quartile	0.81	0.62-1.07	0.73	0.63-0.84	0.85	0.74-0.97
Clinical variables						
≥ 4 clinic visits/y	0.49	0.40-0.61	0.40	0.36-0.45	0.40	0.36-0.44
FEV_1 > 70% predicted[a]	N/A	…	0.85	0.73-0.98	1.03	0.92-1.15
Pancreatic insufficiency	0.88	0.65-1.19	0.93	0.76-1.12	0.87	0.75-1.01
Oxygen therapy in prior year	0.86	0.46-1.62	0.68	0.51-0.89	0.86	0.75-0.99
Body mass goal	1.02	0.82-1.28	0.88	0.79-0.97	0.81	0.66-1.00
Infection by *Pseudomonas aeruginosa*	0.94	0.75-1.17	1.03	0.93-1.14	0.84	0.75-0.94
Infection by *Burkholderia cepacia*	2.23	0.55-9.12	1.25	0.90-1.72	1.12	0.89-1.40

See Table 1 and 2 legends for expansion of abbreviations.

[a]No FEV_1 data are available for children aged < 5 y.

Table 4—*Sensitivity Analysis Demonstrating the aORs of Vaccine Receipt Assuming That All Missing Vaccine Data Are Vaccine Positive by Age Group, Cystic Fibrosis Foundation Patient Registry, 2006*

Characteristic	< 5 y (n = 2,884)		5 to < 18 y (n = 10,444)		≥ 18 y (n = 10,786)	
	aOR	95% CI	aOR	95% CI	aOR	95% CI
Age, y[a]	N/A		N/A		1.01	1.00[b]-1.03
Age-sex interaction[a]	N/A		N/A		1.00	1.00[b]-1.00
Male sex	1.01	0.74-1.37	1.08	0.90-1.29	1.89	1.10-3.25
Race/ethnicity						
White, non-Hispanic	…	…	…	…	…	…
Black, non-Hispanic	0.87	0.45-1.69	1.24	0.78-1.96	0.95	0.59-1.54
Hispanic	0.83	0.52-1.35	0.67	0.51-0.90	0.62	0.42-0.89
Other	0.76	0.31-1.85	0.77	0.35-1.68	0.67	0.34-1.31
Insurance status						
Private or HMO	…	…	…	…	…	
Public	0.59	0.41-0.84	0.64	0.53-0.78	0.76	0.63-0.92
Other or unknown	2.05	0.26-15.80	5.42	0.74-39.59	0.23	0.15-0.33
No insurance	0.25	0.05-1.30	0.37	0.18-0.79	0.65	0.33-1.28
Mean zip code income						
Lower quartile	…	…	…	…	…	…
Second quartile	1.13	0.76-1.67	1.09	0.85-1.39	1.21	0.96-1.52
Third quartile	1.69	1.07-2.67	1.13	0.88-1.45	1.26	0.99-1.61
Upper quartile	1.38	0.86-2.23	1.23	0.94-1.62	1.10	0.86-1.40
CF center volume						
Lower quartile	…	…	…	…	…	…
Second quartile	1.14	0.71-1.85	1.17	0.87-1.56	0.66	0.51-0.84
Third quartile	0.86	0.55-1.37	0.89	0.68-1.17	0.75	0.59-0.97
Upper quartile	0.56	0.37-0.87	0.47	0.37-0.61	0.93	0.71-1.20
Clinical variables						
≥ 4 clinic visits/year	1.20	0.83-1.72	1.75	1.45-2.12	1.37	1.14-1.63
FEV_1 > 70% predicted	…	…	1.25	0.96-1.61	1.32	1.09-1.60
Pancreatic insufficiency	1.62	1.01-2.62	1.05	0.73-1.50	0.65	0.48-0.88
Oxygen therapy in prior year	0.84	0.37-1.90	0.50	0.36-0.71	0.66	0.53-0.82
Body mass goal	1.04	0.71-1.51	1.09	0.91-1.32	0.85	0.58-1.25
Infection by *Pseudomonas aeruginosa*	0.93	0.65-1.31	1.20	1.00-1.45	0.80	0.64-0.99
Infection by *Burkholderia cepacia*	0.59	0.07-5.33	0.98	0.55-1.72	0.65	0.45-0.92

See Table 1 and 2 legends for expansion of abbreviations.

[a]Not included in multivariate model for children aged < 18 y.

[b]Lower end of CI is > 1.00 but presented as 1.00 because of rounding.

vaccine receipt among blacks, Hispanics, and other race/ethnicity were nearly all below white CF Registry members. Hispanic patients with CF received influenza vaccine at a significantly lower rate during the study period. Moreover, among patients aged ≥ 5 years, Hispanic ethnicity was associated with increased vaccination documentation, suggesting that although Hispanics are less likely to receive vaccine, they are more likely to have documentation of vaccine nonreceipt. Further efforts must be made to understand why more Hispanic patients are not receiving influenza vaccine recommended to them.

Clinical variables also predicted vaccine receipt. Attending four or more clinic visits per year was associated with higher vaccination rates in all age groups and years studied. This finding supports the CFF goal of at least four clinic visits annually per person and likely identifies the most adherent registry members. Improved health status as measured by lung function and weight was generally associated with greater rates of vaccine receipt. Use of oxygen therapy was consistently a significant predictor of vaccine nonreceipt, even in the sensitivity analysis that assumed all missing vaccine data were vaccine positive. These findings suggest a healthy vaccinee effect, reflecting improved health-care access and utilization by persons with decreased severity of disease. The findings also may reflect a common practice by health-care providers to withhold vaccines during clinical encounters when a patient is not clinically well and underscores the importance of caregivers arranging for subsequent vaccination whenever it is withheld.

Our study is subject to limitations. Although we assessed predictors of vaccination for the entire population in the CF Registry, our results may not be generalizable to all patients with CF or other chronic lung diseases. Influenza vaccination was recorded for each individual in the cohort, but misclassification of vaccine status may have occurred. Receipt of influenza vaccine outside of CF centers could result in underestimations of vaccine receipt in the CF Registry; however, the sensitivity analysis demonstrates

that many of the predictors of decreased vaccination persisted even after all missing vaccine data were assumed to be vaccine positive.

Although further studies are needed to better quantify the risk of influenza to persons with CF, vaccination remains the best way to prevent influenza virus infection. Physicians should pay particular attention to vaccinate patient groups that have been found to have significantly lower rates of vaccine receipt, including nonwhite patients, patients without private or health maintenance organization insurance, and patients who had received oxygen therapy during the prior year. In addition, patients should be encouraged to meet the CFF goal of four or more clinic visits per year because this was a strong predictor of vaccine receipt. All patients with CF without contraindications should receive the influenza vaccine annually. Furthermore, health-care providers and families of patients with CF should receive the influenza vaccine to decrease the risk of virus transmission in the clinic and at home.

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Dr Victor: contributed to the study concept and design, data analysis and interpretation, and the writing of the manuscript.
Dr Aitken: contributed to the data analysis and interpretation and the writing of the manuscript.
Dr Goss: contributed to the study concept and design, data analysis and interpretation, and the writing of the manuscript.
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References

1. Cystic Fibrosis Foundation. *Patient Registry Annual Data Report 2007*. Bethesda, MD: Cystic Fibrosis Foundation; 2008.
2. Goss CH, Burns JL. Exacerbations in cystic fibrosis. 1: Epidemiology and pathogenesis. *Thorax*. 2007;62(4):360-367.
3. Pribble CG, Black PG, Bosso JA, Turner RB. Clinical manifestations of exacerbations of cystic fibrosis associated with nonbacterial infections. *J Pediatr*. 1990;117(2 pt 1): 200-204.
4. Wat D, Doull I. Respiratory virus infections in cystic fibrosis. *Paediatr Respir Rev*. 2003;4(3):172-177.
5. Wat D, Gelder C, Hibbitts S, et al. The role of respiratory viruses in cystic fibrosis. *J Cyst Fibros*. 2008;7(4):320-328.
6. Ortiz JR, Neuzil KM, Victor JC, Wald A, Aitken ML, Goss CH. Influenza-associated cystic fibrosis pulmonary exacerbations. *Chest*. 2010;137(4):852-860.
7. Schneider EC, Cleary PD, Zaslavsky AM, Epstein AM. Racial disparity in influenza vaccination: does managed care narrow the gap between African Americans and whites? *JAMA*. 2001;286(12):1455-1460.
8. Rangel MC, Shoenbach VJ, Weigle KA, Hogan VK, Strauss RP, Bangdiwala SI. Racial and ethnic disparities in influenza vaccination among elderly adults. *J Gen Intern Med*. 2005;20(5):426-431.
9. Hebert PL, Frick KD, Kane RL, McBean AM. The causes of racial and ethnic differences in influenza vaccination rates among elderly Medicare beneficiaries. *Health Serv Res*. 2005; 40(2):517-537.
10. Egede LE, Zheng D. Racial/ethnic differences in adult vaccination among individuals with diabetes. *Am J Public Health*. 2003;93(2):324-329.
11. Straits-Troster KA, Kahwati LC, Kinsinger LS, Orelien J, Burdick MB, Yevich SJ. Racial/ethnic differences in influenza vaccination in the Veterans Affairs Healthcare System. *Am J Prev Med*. Nov 2006;31(5):375-382.
12. Fiore AE, Shay DK, Broder K, et al; Centers for Disease Control and Prevention (CDC); Advisory Committee on Immunization Practices (ACIP). Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2008. *MMWR Recomm Rep*. 2008;57(RR-7):1-60.
13. Schneider EC, Cleary PD, Zaslavsky AM, Epstein AM. Racial disparity in influenza vaccination: does managed care narrow the gap between African Americans and whites? *JAMA*. 2001;286(12):1455-1460.
14. Santoli JM, Huet NJ, Smith PJ, et al. Insurance status and vaccination coverage among US preschool children. *Pediatrics*. Jun 2004;113(6 Suppl):1959-1964.
15. Figaro MK, Belue R. Prevalence of influenza vaccination in a high-risk population: impact of age and race. *J Ambul Care Manage*. 2005;28(1):24-29.
16. Mayo Montero E, Hernández-Barrera V, Carrasco-Garrido P, Gil de Miguel A, Jiménez-García R. Influenza vaccination among persons with chronic respiratory diseases: coverage, related factors and time-trend, 1993-2001. *Public Health*. 2007;121(2): 113-121.
17. Centers for Disease Control and Prevention. 2000 CDC growth charts: United States. http://www.cdc.gov/growthcharts. Accessed June 19, 2009.
18. Centers for Disease Control and Prevention. About BMI for children and teens. http://www.cdc.gov/healthyweight/assessing/bmi/childrens_bmi/about_childrens_bmi.html. Accessed June 19, 2009.
19. US Department of Health and Human Services. *Healthy People 2010*. 2nd ed. *Understanding and Improving Health*. Vol 1. *Objectives for Improving Health*. Vol 2. Washington, DC: US Department of Health and Human Services; 2000.
20. Centers for Disease Control and Prevention (CDC). Influenza vaccination coverage among persons with asthma—United States, 2005-06 influenza season. *MMWR Morb Mortal Wkly Rep*. 2008;57(24):653-657.

21. Centers for Disease Control and Prevention (CDC). State-specific influenza vaccination coverage among adults aged > or =18 years—United States, 2003-04 and 2005-06 influenza seasons. *MMWR Morb Mortal Wkly Rep*. 2007;56(37):953-959.
22. US Department of Health and Human Services. *HHS Pandemic Influenza Plan*. Washington, DC: US Department of Health and Human Services, 2005.
23. Ortiz JR, Kamimoto L, Aubert RE, et al. Oseltamivir prescribing in pharmacy-benefits database, United States, 2004-2005. *Emerg Infect Dis*. 2008;14(8):1280-1283.
24. Smith NM, Bresee JS, Shay DK, Uyeki TM, Cox NJ, Strikas RA; Advisory Committee on Immunization Practices. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2006;55(RR-10):1-42.