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Prescription of *Pneumocystis jiroveci* pneumonia prophylaxis in HIV-infected patients

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Abstract

U.S. treatment guidelines recommend *Pneumocystis jiroveci* pneumonia (PCP) prophylaxis for all HIV-infected persons with CD4+ T-lymphocyte (CD4) counts <200 cells/μl (i.e. eligible for PCP prophylaxis). However, some studies suggest PCP prophylaxis may be unnecessary in virally suppressed patients. Using national data of HIV-infected adults receiving medical care in the United States during 2009–2012, we assessed the weighted percentage of eligible patients who were prescribed PCP prophylaxis and the independent association between PCP prophylaxis prescription and viral suppression. Overall, 81% of eligible patients were prescribed PCP prophylaxis. Virally suppressed eligible patients were less likely to be prescribed PCP prophylaxis (prevalence ratio, 0.84; 95% confidence interval, 0.80–0.89). Although guidelines recommend PCP prophylaxis for all eligible patients, some HIV care providers might not prescribe PCP prophylaxis to virally-suppressed patients. Additional data on the risk for PCP among virally-suppressed patients are needed to clarify this controversy.

Keywords

HIV; *Pneumocystis* pneumonia prophylaxis; viral suppression

Introduction

The incidence of *Pneumocystis jiroveci* pneumonia (PCP) among HIV-infected persons in the United States has declined dramatically in the era of antiretroviral therapy (ART). A large U.S. cohort study shows that PCP incidence has been below one case per 100 person-years since 2000. However, PCP remains the second most frequently diagnosed AIDS-

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defining opportunistic illness.[1] It is still a life-threatening disease even in developed countries with high-quality medical care. [2,3]

U.S. treatment guidelines recommend PCP prophylaxis for all HIV-infected persons with a $CD4^+$ T-lymphocyte (CD4) count <200 cells/μl or a history of oropharyngeal candidiasis.[4] Recent data suggest that PCP prophylaxis may be unnecessary for virally suppressed patients even if their CD4 counts are <200 cells/μl.[5–7] In this report, we present the national percentage of HIV-infected persons with a CD4 count <200 cells/μl who were prescribed PCP prophylaxis, and evaluate socio-demographic and clinical characteristics that may be associated with PCP prophylaxis prescription, in particular, durable viral suppression.

Methods

The Medical Monitoring Project (MMP) is a supplemental surveillance system designed to produce nationally representative estimates of behavioral and clinical characteristics of HIV-infected adults receiving medical care in the United States and Puerto Rico.[8] MMP utilizes a three-stage, complex sampling design in which US states and territories are sampled, followed by facilities providing outpatient HIV medical care in those jurisdictions, then HIV-infected adults (aged 18 years and older) receiving care in those facilities. Data were collected by interviews and medical record abstractions. The surveillance period included the 12 months prior to interview. We combined data from the 2009 through 2012 cycles for this analysis. All sampled states and territories participated and the facility response rates were 76% – 85% across all years. Approximately 50% (ranging from 47% to 53% across years) of eligible persons sampled from these facilities completed an interview and had their medical records abstracted. Data were weighted to account for unequal selection probabilities, and both facility and patient nonresponse.

MMP is a public health surveillance activity and not subject to federal institutional review board (IRB) review.[9] However, some jurisdictions obtained local IRB approvals. All participants provided informed consent to participate.

We analyzed data on 2143 patients who had at least one CD4 count <200 cells/μl during the first 6 months of the surveillance period to allow adequate opportunity for providers to prescribe PCP prophylaxis. We excluded 154 patients who were diagnosed with PCP during the surveillance period to avoid potential misclassification of PCP treatment as prophylaxis.

CD4 count, HIV plasma viral load, and prescription information were abstracted from medical records. Durable viral suppression was defined as all viral load results <200 copies/ml during the surveillance period. Provider prescription of PCP prophylaxis was ascertained via medical record documentation of PCP “prophylaxis”, or documentation that the patient was either prescribed or continued on medical regimens typically provided for prophylaxis. Brief antibiotic prescriptions for two weeks or less were likely treatment of an acute infection and therefore were not considered as prophylaxis. Medications included atovaquone, aapsone, leucovorin, pentamidine, pyrimethamine, and trimethoprim-sulfamethoxazole. Medical record abstractors received training on how to identify and abstract PCP prophylaxis for quality assurance. We assessed the weighted percentage of

HIV-infected patients with a CD4 count <200 cells/μl who were prescribed PCP prophylaxis. We also assessed the association between selected characteristics and PCP prophylaxis prescription using bivariate analysis (Rao-Scott chi-square test). Durable viral suppression was of particular interest so we employed a multivariable logistic regression model to elucidate its independent association with PCP prophylaxis prescription. In this multivariable modeling process, we considered socio-demographic and clinical factors that were associated with both durable viral suppression and PCP prophylaxis prescription, including race, education, poverty, homelessness, length of HIV diagnosis, and hospitalization, as potential confounders. Only potential confounders that changed the association by at least 10%, as measured by the prevalence ratio, were retained in the final model.

All analyses accounted for the complex sample design by using the survey procedures in SAS 9.3 and SUDAAN 10.0.1.

Results

The socio-demographic and clinical characteristics of patients who had at least one CD4 count <200 cells/μl are shown in table 1. Among them, 64% had durable viral suppression, and 81% were prescribed PCP prophylaxis. Patients with a PCP prophylaxis prescription were not significantly different from patients without a prescription with regards to gender, age, education, homelessness, illicit drug use (excluding marijuana), or hospitalization ($p>0.05$). Patients of white or Hispanic race/ethnicity, those above poverty level, or diagnosed with HIV for 5 years or more were less likely to be prescribed PCP prophylaxis ($p<0.05$).

During the logistic regression model selection process, the change in the association between durable viral suppression and PCP prophylaxis prescription by potential confounders ranged from 0% to 2% so no confounders were included in the final model. Therefore, we used the unadjusted prevalence ratio to measure the independent association between durable viral suppression and PCP prophylaxis prescription. Virally suppressed patients were 16% less likely to be prescribed PCP prophylaxis (prevalence ratio= 0.84; 95% confidence interval, 0.80–0.89) compared with patients who were not virally suppressed.

Of note, among patients with a CD4 count <200 cells/μl who were not virally suppressed, 14% were not prescribed PCP prophylaxis (Table 1). In addition, 13% of the patients with a CD4 count <100 cells/μl were not prescribed PCP prophylaxis, regardless of viral loads (Table 1).

Discussion

Using nationally representative data of HIV-infected adults receiving medical care in the United States during 2009–2012, we estimated that 81% of patients who had at least one CD4 count <200 cells/μl were prescribed PCP prophylaxis. Our estimate indicates improved adherence to guidelines compared with the 2003 estimate of 76% produced using the Centers for Disease Control and Prevention's Adult/Adolescent Spectrum of HIV Disease,

which assessed trends in receipt of PCP prophylaxis among HIV-infected persons in the United States during 1994–2003.[10]

We also found that among patients indicated for PCP prophylaxis, virally suppressed patients (viral loads <200 copies/ml) were less likely to be prescribed PCP prophylaxis compared with patients with HIV viral loads ≥ 200 copies/ml. Several recent studies have found a low incidence of PCP in HIV-infected persons with CD4 count < 200 cells/μl if they are on ART and virally suppressed, and this may explain why providers in our analysis were less likely to prescribe PCP prophylaxis to virally suppressed patients. A large European cohort study and a case series found that PCP prophylaxis may be safely discontinued for patients who had plasma viral loads <400 to 500 copies/ml and had CD4 counts 100–200 cells/μl, but not for patients who had CD4 counts <100 cells/μl, regardless of viral suppression status.[6,11] One clinical trial and two case-series revealed that PCP prophylaxis may be unnecessary for virally suppressed patients, regardless of CD4 count; however, they did not compare PCP incidence among virally suppressed patients with CD4 counts <100 cells/μl and patients with CD4 counts 100–200 cells/μl.[7,12, 13]

Patients with advanced immunosuppression are more likely to be diagnosed with PCP.[14] In our analysis, we found that >10% of HIV-infected patients with CD4 counts < 100 cells/μl were not prescribed PCP prophylaxis. Given the lack of evidence to support discontinuation of PCP prophylaxis for patients with CD4 counts <100 cells/μl, prophylaxis is warranted in these individuals.

The major strengths of our analysis are that we generated national estimates on percentages of HIV-infected patients who were prescribed PCP prophylaxis by characteristics. There are at least two limitations to this analysis. First, while current treatment guidelines recommend PCP prophylaxis for all patients who have a CD4 count <200 cells/μl, a history of oropharyngeal candidiasis, CD4 cell percentage of <14%, or a history of an AIDS-defining illness, we used CD4 count <200 cells/μl as our sole criterion for inclusion. Per treatment guidelines, CD4 count <200 cells/μl has the strongest evidence to support use of PCP prophylaxis compared to the other criteria and should cover the majority of patients eligible for PCP prophylaxis. Second, given the cross-sectional nature of the analysis, we may have failed to capture PCP prophylaxis prescriptions provided after the end of the data collection period. To minimize this concern, we limited the analysis to participants who had at least one CD4 count <200 cells/μl during the first 6 months of the surveillance period to allow providers opportunities to prescribe prophylaxis if warranted.

In summary, 81% of HIV-infected persons with at least one CD4 count < 200 cells/μl were prescribed PCP prophylaxis. Compared with patients who had detectable HIV viral loads (≥200 copies/ml), virally suppressed patients were less likely to be prescribed PCP prophylaxis. While recent data suggest that PCP prophylaxis may be safely discontinued in virally suppressed patients with CD4 counts between 100–200 cells/μl, the Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents has determined that evidence is insufficient to change current recommendations.[4] Additional data on patient characteristics associated with PCP incidence in the ART era are needed to determine which individuals are at the highest risk for PCP and would benefit most from PCP prophylaxis.

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http://www.cdc.gov/hiv/pdf/research_mmp_studygroupmembers_2009.pdf; http://www.cdc.gov/hiv/pdf/research_mmp_studygroupmembers_2010.pdf; http://www.cdc.gov/hiv/pdf/research_mmp_studygroupmembers_2011.pdf; http://www.cdc.gov/hiv/pdf/research_mmp_studygroupmembers_2012.pdf.

References

1. Buchacz K, Baker RK, Palella FJ Jr, et al. AIDS-defining opportunistic illnesses in US patients, 1994–2007: a cohort study. AIDS. 2010; 24(10):1549–59. [PubMed: 20502317]
2. Mocroft A, Sterne JA, Egger M, et al. Antiretroviral Therapy Cohort Collaboration (ART-CC). Variable impact on mortality of AIDS-defining events diagnosed during combination antiretroviral therapy: not all AIDS-defining conditions are created equal. Clin Infect Dis. 2009; 48(8):1138–51. [PubMed: 19275498]
3. Kovacs JA, Masur H. Evolving health effects of Pneumocystis: one hundred years of progress in diagnosis and treatment. JAMA. 2009; 301(24):2578–85. [PubMed: 19549975]
4. Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. [Accessed August 2016] Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf. Published May 2013
5. Costiniuk CT, Fergusson DA, Doucette S, et al. Discontinuation of *Pneumocystis jirovecii* pneumonia prophylaxis with CD4 count <200 cells/microL and virologic suppression: a systematic review. PloS one. 2011; 6(12):e28570. [PubMed: 22194853]
6. Opportunistic Infections Project Team of the Collaboration of Observational HIV Epidemiological Research in Europe (COHERE), Mocroft A, Reiss P, Kirk O, et al. Is it safe to discontinue primary *Pneumocystis jiroveci* pneumonia prophylaxis in patients with virologically suppressed HIV infection and a CD4 cell count <200 cells/microL? Clin Infect Dis. 2010; 51(5):611–9. [PubMed: 20645862]
7. Chaiwarith R, Praparattanapan J, Nuntachit N, et al. Discontinuation of primary and secondary prophylaxis for opportunistic infections in HIV-infected patients who had CD4+ cell count <200 cells/mm(3) but undetectable plasma HIV-1 RNA: an open-label randomized controlled trial. AIDS patient care and STDs. 2013; 27(2):71–6. [PubMed: 23373662]
8. Centers for Disease Control and Prevention. [Accessed August 2016] Behavioral and Clinical Characteristics of Persons Receiving Medical Care for HIV Infection — Medical Monitoring Project, United States, 2011; HIV Surveillance Special Report. p. 10http://www.cdc.gov/hiv/library/reports/surveillance/#special. Published January 2015
9. Centers for Disease Control and Prevention. [Accessed August 2016] Distinguishing public health research and public health nonresearch. http://www.cdc.gov/od/science/integrity/docs/cdc-policy-distinguishing-public-health-research-nonresearch.pdf. Published in 2010
10. Teshale EH, Hanson DL, Wolfe MI, et al. Reasons for lack of appropriate receipt of primary *Pneumocystis jiroveci* pneumonia prophylaxis among HIV-infected persons receiving treatment in the United States: 1994–2003. Clin Infect Dis. 2007; 44(6):879–83. [PubMed: 17304464]
11. Soriano V, Dona C, Rodriguez-Rosado R, et al. Discontinuation of secondary prophylaxis for opportunistic infections in HIV-infected patients receiving highly active antiretroviral therapy. AIDS. 2000; 14(4):383–6. [PubMed: 10770540]
12. D'Egidio GE, Kravcik S, Cooper CL, et al. *Pneumocystis jiroveci* pneumonia prophylaxis is not required with a CD4+ T-cell count < 200 cells/microl when viral replication is suppressed. AIDS. 2007; 21(13):1711–5. [PubMed: 17690568]

13. Cheng CY, Chen MY, Hsieh SM, et al. Risk of pneumocystosis after early discontinuation of prophylaxis among HIV-infected patients receiving highly active antiretroviral therapy. BMC Infec Dis. 2010; 10:126. [PubMed: 20492660]

14. Wolff AJ, O'Donnell AE. Pulmonary manifestations of HIV infection in the era of highly active antiretroviral therapy. Chest Dec. 2001; 120(6):1888–93.

Table 1

Socio-demographic and clinical characteristics of HIV-infected persons with a CD4 cell count <200 cells/μl and receiving medical care in the United States, Medical Monitoring Project, 2009–2012.

Characteristic	Total (n=2143) Weighted % (95% CI)	Prescribed PCP prophylaxis (n=1753) Weighted % (95% CI)	Not prescribed PCP prophylaxis (n=390) Weighted % (95% CI)	*P* for Rao-Scott chi-square test
Total (n=2143)		**81 (79–84)**	**19 (16–22)**	
All viral loads < 200 copies/ml[a,e]				
Yes	**64 (61–66)**	**73 (69–77)**	**27 (23–31)**	**<0.001**
No	**36 (34–39)**	**86 (84–89)**	**14 (11–16)**	
Gender				
Male	73 (71–76)	81 (78–84)	19 (16–22)	0.925
Female	27 (24–29)	82 (77–86)	18 (14–23)	
Age (years)				
18–29	6 (5–8)	88 (82–94)	12 (6–18)	0.128
30–39	18 (16–20)	83 (78–89)	17 (11–22)	
40–49	38 (36–41)	82 (78–85)	18 (15–22)	
≥50	38 (35–40)	79 (75–83)	21 (17–25)	
Race and ethnicity				
White, non-Hispanic	27 (21–32)	77 (72–82)	23 (18–28)	0.001
Black, non-Hispanic	49 (42–57)	85 (82–88)	15 (12–18)	
Hispanic or Latino	19 (14–24)	78 (73–83)	22 (17–27)	
Other	5 (4–7)	82 (74–91)	18 (9–26)	
Education				
<High school	27 (25–30)	84 (80–87)	16 (13–20)	0.054
High school	30 (27–32)	83 (79–87)	17 (13–21)	
>High school	43 (40–46)	79 (76–82)	21 (18–24)	
Poverty level[a,b,e]				
Above poverty level	44 (41–48)	79 (76–83)	21 (17–24)	0.022
Below or at poverty level	56 (52–59)	83 (80–86)	17 (14–20)	
Experienced homelessness[a]				
Yes	12 (11–14)	86 (81–91)	14 (9–19)	0.073
No	88 (86–89)	81 (78–84)	19 (16–22)	
Any illicit drug use[a,c]				
Yes	15 (13–17)	84 (80–89)	16 (11–20)	0.167
No	85 (83–87)	81 (78–84)	19 (16–22)	
Length of time HIV diagnosed[e]				
<5 years	26 (24–29)	86 (82–89)	14 (11–18)	0.015
5–9 years	18 (16–19)	81 (77–86)	19 (14–23)	
≥10 years	56 (53–59)	80 (76–83)	20 (17–24)	
Hospitalized[a,d]				
Yes	22 (20–25)	84 (80–88)	16 (12–20)	0.071

Characteristic	Total (n=2143) Weighted % (95% CI)	Prescribed PCP prophylaxis (n=1753) Weighted % (95% CI)	Not prescribed PCP prophylaxis (n=390) Weighted % (95% CI)	*P* for Rao-Scott chi-square test
No	78 (75–80)	81 (78–83)	19 (17–22)	
Lowest CD4 count (cells/μl)[a]				
0–99	48 (46–50)	87 (82–91)	13 (9–18)	0.001
100–199	52 (50–54)	77 (74–80)	23 (20–26)	

Abbreviations: CI, confidence interval; DHHS, Department of Health and Human Services; PCP, *Pneumocystis jiroveci* pneumonia.

[a]The surveillance period, 12 months before interview..

[b]This measure uses the DHHS Poverty Guidelines to determine whether respondent's household is above or below the poverty level.

[c]Any illicit drug use excluding marijuana.

[d]Hospitalized at least once in the 12 months prior to interview; based on both interview and medical records.

[e]Missing n: all viral loads < 200 copies/ml, 39; poverty, 69; length of HIV diagnosis, 2.