A Survey of Rheumatologists' Practice for Prescribing Pneumocystis Prophylaxis

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ABSTRACT. ***Objective.*** *Pneumocystis* pneumonia (PCP) occurs in immunocompromised hosts, in both the presence and absence of human immunodeficiency virus (HIV) infection, with substantial morbidity and a heightened mortality. We assessed practice patterns among rheumatologists for prescribing PCP prophylaxis.

Methods. Invitations to an online international survey were e-mailed to 3150 consecutive members of the American College of Rheumatology.

Results. Completed surveys were returned by 727 (23.1%) members. Among respondents, 505 (69.5%) reported prescribing prophylaxis. Factors associated with significantly higher frequency of prescribing PCP prophylaxis included female gender (OR 1.47, $p = 0.03$), US-based (OR 1.77, $p = 0.004$), academic-based (OR 2.75, $p < 0.001$), in practice less than 10 years (OR 4.08, $p < 0.001$), having previously treated PCP (OR 2.62, $p < 0.001$), and in a practice with a higher proportion of patients maintained on chronic glucocorticoids (OR 2.04, $p < 0.001$) or other immunosuppressant medications (OR 3.19, $p = 0.003$). In multivariate analysis, rheumatologists early in their careers and those with academic and US-based practices were more likely to prescribe prophylaxis. Among prescribers, the most important determinants for issuing prophylaxis were treatment regimen (68.6%), rheumatologic diagnosis (9.3%), and medication dosage (8.3%).

Conclusion. Nearly one-third (30%) of the rheumatologists surveyed reported that they never prescribed PCP prophylaxis. While the patient characteristics for which prophylaxis was prescribed varied widely, physician demographics were strongly predictive of PCP prophylaxis use. These findings suggest that development of consensus guidelines might influence clinical decision-making regarding PCP prophylaxis in HIV-negative patients with rheumatologic diagnoses. (First Release March 1 2010; doi:10.3899/jrheum.090843)

Key Indexing Terms:
PNEUMOCYSTIS PROPHYLAXIS
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Pneumocystis jirovecii (formerly *P. carinii*) pneumonia (PCP) is an opportunistic infection that occurs in immunocompromised persons and is the most prevalent opportunistic infection in patients with human immunodeficiency virus (HIV)[1]. The occurrence of PCP among HIV-negative persons with immunocompromised states of other origins has been increasingly recognized[2-8]. There are numerous reports of PCP occurring in patients with underlying rheumatologic diagnoses[9-20]. Overall, the incidence of PCP appears to be increasing[4], a rise attributed to the increasing number of patients undergoing immunosuppressive treatment for a growing number of indications[21].

While the mortality of PCP in patients infected with HIV is 10%–20%, it is substantially higher, estimated to be 30%–60%, in persons without HIV, who often present more acutely and with more severe respiratory compromise than patients infected with HIV[1]. Effective antibiotic prophylaxis for PCP is available and recommended for patients at high risk of infection, although the frequency with which prophylactic therapy is used is unknown. Consensus guidelines are well established for the use of PCP prophylaxis in HIV-infected individuals[22], but no such guidelines exist for prescribing PCP prophylaxis in HIV-negative populations. Further, a recent Cochrane review assessed the use of prophylaxis only in persons with hematologic malignancies, bone marrow transplants, and solid organ transplants[23]. We intended to review the evidence for PCP prophylaxis in HIV-uninfected persons chronically treated with corticosteroids for a variety of conditions, including rheumatologic disorders. However, no relevant studies were found addressing use of prophylaxis in this clinical context, among patients with rheumatologic diagnoses.

We surveyed an international sample of rheumatologists to assess the frequency of their use of PCP prophylaxis among HIV-negative patients with rheumatologic disorders and the factors that influenced their prophylaxis decision-making.

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MATERIALS AND METHODS

Using the online survey tool surveymonkey.com, we designed and sent a survey (Table 1) to members of the American College of Rheumatology (ACR) in November 2008. Eligible participants were physician members of the ACR who listed a working e-mail address in the online ACR directory. The e-mail addresses of 3150 consecutive eligible members selected in alphabetical order from the beginning of the ACR directory were hand-typed into the online survey tool; invitations to participate in the survey were sent by e-mail. We chose to send 3150 invitations based on an assumed response rate of ~25% and a goal to obtain at least 750 responses. A reminder e-mail was then circulated 2 weeks after the initial correspondence to those recipients who had not yet completed the survey.

We first compiled demographic data about respondents, including geographic region, sex, type of practice, and years in practice. Next we ascertained the approximate number of patients with a rheumatologic disease seen each week, approximate proportion of patients managed on chronic glucocorticoids or other immunosuppressant medications, and personal experience with a patient who developed PCP. We then gathered available demographic information for nonrespondents from the ACR directory, including geographic region, sex, and type of practice. Our survey instru-

Table 1. Questions included in the survey of US rheumatologists. Possible responses are listed in parentheses.

1. In which region of the country do you practice?
   (Southwest; Northwest; Midwest; Southeast; Mid-Atlantic; Northeast; Alaska/Hawaii; International)
2. What is your gender?
   (male/female)
3. In which type of practice do you work?
   (academic; hospital-based; solo private practice; group specialty practice; other)
4. Including fellowship, for how many years have you been practicing rheumatology?
   (< 5 yrs; 5–10 yrs; 10–15 yrs; 15–20 yrs; > 20 yrs)
5. On average, approximately how many patients with a rheumatologic diagnosis do you see each week?
   (< 5 pts; 5–10 pts; 10–15 pts; > 20 pts)
6. Approximately what percentage of the patients you care for are managed on chronic glucocorticoids?
   (< 10%; 10–25%; 25–50%; 50–75%; 75–90%; > 70%)
7. Approximately what percentage of the patients you care for are managed on other immunosuppressive agents, including cyclophosphamide, methotrexate, azathioprine, and mycophenolate?
   (< 10%; 10–25%, 25–50%; 50–75%; 75–90%; > 90%)
8. Have any of your patients ever developed *Pneumocystis jirovecii* pneumonia (PCP)?
   (no; yes; if yes, please specify how many)
9. Do you prescribe chemoprophylaxis for PCP? If yes, please specify what prophylaxis method you prefer.
   (no; yes – with trimethoprim/sulfamethoxazole once daily; yes – with trimethoprim/sulfamethoxazole 3 times per week; yes – with aerosolized pentamidine; yes – with another prophylactic medication. Please specify)
10. For which underlying conditions are you most likely to prescribe PCP chemoprophylaxis? (mark all that apply)
    (systemic lupus erythematosus; rheumatoid arthritis; psoriatic arthritis; Wegener's granulomatosis; polyarteritis nodosa; microscopic polyangiitis; other systemic vasculitides; scleroderma; dermatomyositis; polymyositis; other myositis; other. Please specify; rheumatologic diagnosis does not affect my decision to prescribe or not prescribe PCP chemoprophylaxis; I do not prescribe PCP chemoprophylaxis)
11. With which treatment regimens are you likely to prescribe PCP chemoprophylaxis? (mark all that apply)
    (prednisone alone; prednisone in combination with another immunosuppressant agent; methotrexate; cyclophosphamide; azathioprine; mycophenolate; TNF-alpha inhibitors; cyclosporine; 6-mercaptopurine; rituximab; other. Please specify; treatment regimen does not affect my decision to prescribe or not prescribe PCP chemoprophylaxis)
12. At what dose of prednisone are you likely to prescribe PCP chemoprophylaxis?
    (≥ 5 mg/day; ≥ 10 mg/day; ≥ 15 mg/day; ≥ 20 mg/day; ≥ 30 mg/day; ≥ 40 mg/day; ≥ 50 mg/day; other. Please specify; prednisone dosage does not affect my decision to prescribe or not prescribe PCP chemoprophylaxis; I do not prescribe PCP chemoprophylaxis)
13. What laboratory data do you use when deciding whether to prescribe PCP chemoprophylaxis? (please mark all that apply)
    (peripheral blood absolute lymphocyte count; peripheral blood CD4 T cell count; other. Please specify; laboratory data does not affect my decision to prescribe or not prescribe PCP chemoprophylaxis; I do not prescribe PCP chemoprophylaxis)
14. What other clinical data not mentioned above makes you more likely to prescribe PCP chemoprophylaxis? (please mark all that apply)
    (history of PCP; history of other opportunistic infection; history of interstitial pulmonary fibrosis; other. Please specify; other clinical data does not affect my decision to prescribe or not prescribe PCP chemoprophylaxis; I do not prescribe PCP chemoprophylaxis)
15. What is the most important factor in your decision as to whether or not to prescribe PCP chemoprophylaxis?
    (underlying condition; treatment regimen; dose of medication; laboratory data; history of PCP; history of other opportunistic infections; history of interstitial pulmonary fibrosis; other. Please specify; I do not prescribe PCP chemoprophylaxis)

ment also asked which clinical factors influenced a physician's prophylaxis decision-making.

Analysis. Statistical analyses were conducted using Stata 10.0 (Stata Corp., College Station, TX, USA). Chi-squared analyses were performed to analyze differences in demographic characteristics between respondents and nonrespondents. Among the respondents, univariate logistic regression analysis was first used to assess whether the demographic characteristics of those who prescribed PCP prophylaxis differed from the nonprescribers. Next, multivariate analysis, which incorporated the measurements found to be statistically significant in the univariate analyses, determined the independent contribution of these characteristics toward the decision to prescribe PCP prophylaxis. Statistical significance was defined as an α level = 0.05 using a 2-tailed test. Finally, among respondents who reported prescribing PCP prophylaxis, we calculated the proportion influenced by various clinical factors.

RESULTS

Completed surveys were returned by 727 (23.1%) individuals. Demographic characteristics of respondents and nonrespondents are summarized in Table 2. The majority of respondents practiced in the United States (80%). Almost two-thirds (63.3%) of respondents were male, and slightly more than one-third (37.3%) had been in practice for 20 or more years. More respondents described their practices as academic (42.1%) than as group specialty (28.3%), hospital-based (12.2%), or solo private (11.4%). When compared to respondents, nonrespondents were less likely to practice in an academic setting and more likely to be in private practice. There were also significant regional variations between respondents and nonrespondents, with respondents being more likely to be from the northeast, among other differences. However, demographic data for about one-fourth of nonrespondents, as well as the number of years in practice among all nonrespondents, could not be obtained from the ACR website.

Table 2. Demographic characteristics of respondents and nonrespondents to the PCP survey.

Characteristic	Survey Respondents, n = 727, n (%)	Survey Nonrespondents n = 2423, n (%)	p
Geographic region			
Southwest	74 (10.2)	235 (9.7)	< 0.001
Northwest	48 (6.6)	133 (5.5)	
Midwest	142 (19.5)	310 (12.7)	
Southeast	119 (16.4)	276 (11.3)	
Mid-Atlantic	44 (6.0)	278 (11.5)	
Northeast	152 (20.9)	144 (6.0)	
Alaska/Hawaii	4 (0.6)	2 (0.0)	
International	135 (18.6)	421 (17.4)	
No response	9 (1.2)	624 (25.8)	
Sex			
Male	460 (63.3)	1201 (49.6)	< 0.001
Female	255 (35.1)	604 (24.9)	
No response	12 (1.6)	618 (25.5)	
Type of practice			
Acedemic	306 (42.1)	395 (16.3)	< 0.001
Hospital-based	89 (12.2)	174 (7.2)	
Solo private	83 (11.4)	291 (12.0)	
Group specialty	206 (28.3)	543 (22.4)	
Other	36 (5.0)	220 (9.1)	
No response	7 (1.0)	800 (33.0)	
Years in practice*			
< 5	129 (17.7)	NA	NA
5–10	109 (15.0)		
10–15	81 (11.1)		
15–20	125 (17.2)		
> 20	271 (37.3)		
No response	12 (1.7)		

* Data not available on nonrespondents. PCP: *Pneumocystis* pneumonia; NA: not applicable.

Among the respondents, 505 (69.5%) said they prescribe antibiotic prophylaxis. In the univariate analysis, factors that were significantly associated with prescribing PCP prophylaxis (Table 3) included female sex (OR 1.47, p = 0.03), US-based practice (OR 1.77, p = 0.004), academic practice (OR 2.75, p < 0.001), practicing for < 10 years (OR 4.08, p < 0.001), a clinical practice with > 10% of patients maintained on chronic glucocorticoids (OR 2.04, p < 0.001) or other chronic immunosuppressants (OR 3.19, p = 0.003), and having previously cared for a patient who developed PCP (OR 2.62, p < 0.001). Physicians who, on average, evaluated fewer than 10 patients with a rheumatologic diagnosis each week in clinical practice were more likely than those who evaluated more than 10 patients with a rheumatologic diagnosis to prescribe prophylaxis (OR 1.48, p = 0.23), although this difference was not statistically significant. Interestingly, when US-based physicians were considered separately in a stratified analysis, all the above factors remained related to use of PCP prophylaxis; however, only the proportion of patients maintained on other chronic immunosuppressants was now of borderline statistical significance (p = 0.07; data not shown).

In a multivariate logistic regression model of the demographic characteristics found to be statistically significant in the previous univariate analyses, only sex (p = 0.97) and the proportion of patients maintained on immunosuppressant medications other than chronic gluocorticoids (p = 0.06) were no longer significant (Table 3). However, all the other demographic characteristics retained significance. Those rheumatologists relatively early in their careers, with less than a decade of practice experience, were more than 4 times as likely to prescribe PCP prophylaxis than their more senior colleagues (OR 4.13, 95% CI 2.62–6.51, p < 0.001). Moreover, American-based rheumatologists were nearly twice as likely to prescribe prophylaxis than their non-American counterparts (OR 1.97, 95% CI 1.27–3.05, p = 0.003), as were rheumatologists practicing in an academic setting (OR 1.81, 95% CI 1.23–2.66, p = 0.003) and those with a higher proportion of patients in their practice treated with chronic glucocorticoid therapy (OR 2.11, 95% CI 1.38–3.23, p = 0.001). Finally, rheumatologists who had previously treated a patient with PCP were more than 3 times as likely to prescribe PCP prophylaxis than those who had not (OR 3.04, 95% CI 1.92–4.82, p < 0.001).

Table 3. Association of demographic characteristics among 727 surveyed rheumatologists with the decision to prescribe PCP prophylaxis.

Demographic Characteristic	Prescribe PCP Prophylaxis n (%)*	Univariate Logistic Regression OR (95% CI)	p	Multivariate Logistic Regression OR (95% CI)	p
Female	191 (74.9)	1.47 (1.04, 2.08)	0.03	1.01 (0.68, 1.50)	0.97
Male	308 (67.0)				
US-based practice	420 (72.0)	1.77 (1.20, 2.61)	0.004	1.97 (1.27, 3.05)	0.003
Internationally based practice	80 (59.2)				
Acedemic practice	248 (81.0)	2.75 (1.94, 3.89)	< 0.001	1.81 (1.23, 2.66)	0.003
Nonacademic practice	252 (60.9)				
≤ 10 years in practice	206 (86.6)	4.08 (2.69, 6.18)	< 0.001	4.13 (2.62, 6.51)	< 0.001
> 10 years in practice	292 (61.2)				
≥ 10% patients on chronic glucocorticoids	414 (72.8)	2.04 (1.40, 2.96)	< 0.001	2.11 (1.38, 3.23)	0.001
< 10% patients on chronic glucocorticoids	84 (56.8)				
≥ 10% patients on other immunosuppressants	488 (70.5)	3.19 (1.48, 6.86)	0.003	2.26 (0.98, 5.26)	0.06
< 10% patients on other immunosuppresants	12 (42.8)				
Caring previously for a patient who developed PCP	159 (82.8)	2.62 (1.73, 3.98)	< 0.001	3.04 (1.92, 4.82)	< 0.001
Never caring for a patient who developed PCP	345 (64.7)				
≤ 10 patients with rheumatologic diagnosis under clinical care each week	43 (76.8)	1.48 (0.78, 2.82)	0.23	—**	—
> 10 patients with rheumatologic diagnosis under clinical care each week	455 (69)				

* Among survey respondents, the proportion with each characteristic who reported prescribing PCP prophylaxis. ** Number of patients with a rheumatologic diagnosis was not included in the final multivariate analysis because this variable did not achieve statistical significance in the univariate analysis.

Among those who responded affirmatively to prescribing PCP prophylaxis, the factors that influenced this decision (survey questions 10 to 15) varied significantly. A majority of respondents (68.6%) stated that treatment regimen was the most important factor affecting their decision (Figure 1). Other important factors included the underlying rheumatologic diagnosis (9.3%) and medication dose (8.3%). In assessing treatment regimen, most respondents reported they were likely to prescribe prophylaxis for patients treated with cyclophosphamide (75.6%), while about half (49.1%) were likely to offer antibiotic prophylaxis to their patients treated with combination therapy that included prednisone, and fewer still (12.5%) for prednisone monotherapy (Figure 2). Prednisone dose had no effect on this decision for a plurality of respondents (40.9%), while 16.6% would consider prophylaxis when prednisone dosage exceeded 20 mg daily.

Interestingly, most respondents were likely to prescribe prophylaxis for patients with Wegener's granulomatosis (WG) (68.7%; Figure 2). In addition, more than one-third of respondents furnished prophylaxis to patients with systemic lupus erythematosus (38.8%), polyarteritis nodosum (39.8%), microscopic polyangiitis (42.2%), and other systemic vasculitides (39.2%). Additionally, more than half of respondents would prescribe prophylaxis for individuals with a history of PCP (61.2%) or another opportunistic infection (54.5%).

Finally, the preferred regimen for PCP prophylaxis also varied among the surveyed rheumatologists (data not shown). Of those who reported prescribing prophylaxis, the majority (74.8%) preferred a regimen of trimethoprim/sulfamethoxazole 3 times weekly. In contrast, a regimen of once-daily trimethoprim/sulfamethoxazole was used less frequently (19.2%) but more commonly than aerosolized pentamidine (1.2%).

DISCUSSION

Despite evidence that patients with rheumatologic disorders being treated with immunosuppressive medications are at increased risk of developing PCP, nearly one-third (30%) of the rheumatologists in our study reported that they never used PCP prophylaxis. Similarly, a recent survey of US rheumatologists that specifically addressed patients with lupus who are maintained on cyclophosphamide therapy found that only 50% of rheumatologists reported using PCP prophylaxis in that clinical context[24]. In our study, rheumatologists who reported prescribing PCP prophylaxis varied in terms of the prophylactic regimen they preferred, although thrice-weekly trimethoprim-sulfamethoxazole was the predominant strategy. Wide variation was also observed among the patient characteristics that influenced the decision to prescribe PCP prophylaxis.

The risk of PCP associated with cyclophosphamide therapy in rheumatologic diseases has been widely reported[10,11,15,20,24-30]. Moreover, the majority of respondents in our study who prescribe prophylaxis reported that they use prophylaxis when their patients are receiving cyclophosphamide immunosuppressive therapy. While almost half of the respondents reported use of prophylaxis when their patients were treated with various combinations of prednisone and other immunosuppressant agents, only a small

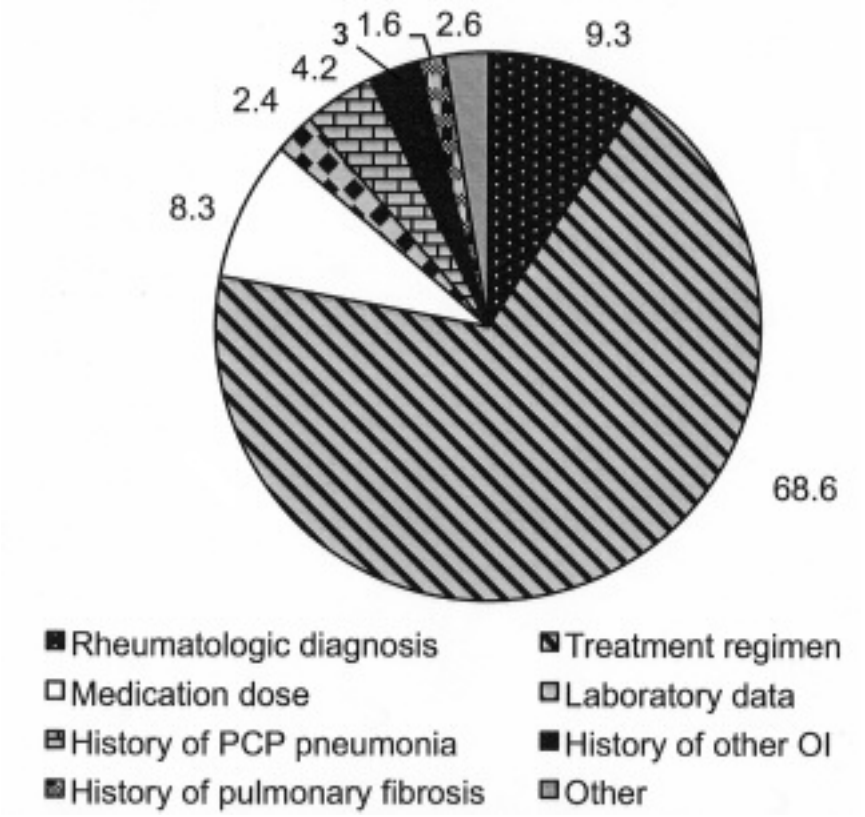

Figure 1. Among 505 rheumatologists who prescribe PCP prophylaxis, the proportions (%) reporting that a given factor was the most important influence in their decision to prescribe prophylaxis. OI: opportunistic infections.

percentage prescribe antibiotic prophylaxis for patients maintained on prednisone monotherapy or methotrexate. This finding was particularly surprising because chronic corticosteroid therapy is a commonly reported risk factor for PCP[5,9,12,14,20,23,26]. In addition, some investigators have advocated prescribing PCP prophylaxis for HIV-negative patients taking > 20 mg of corticosteroids for at least 1 month[3,31-33]. Nevertheless, only 17% of the respondents in our survey who prescribe PCP prophylaxis follow this approach. Methotrexate, even when prescribed at low doses, has also been linked to an increase in risk of PCP, especially among patients with rheumatoid arthritis[11,12,15,19,34,35]. Yet just 2% of respondents who use prophylaxis are likely to prescribe it for individuals on methotrexate therapy. However, concern about a potential drug interaction between trimethoprim (or sulfamethoxazole) and methotrexate, enhancing the toxic effects of methotrexate, may have influenced the diminished preference for PCP prophylaxis in this scenario.

Several studies have identified potential prognostic markers to distinguish which patients are at high risk of developing PCP. Viguier, *et al*[36] suggested prophylaxis for patients with peripheral lymphocyte counts < 800/μl or CD4 lymphocyte counts < 200/μl, while Li, *et al* suggested prophylaxis for CD4 lymphocyte counts < 250/μl[10]. In a retrospective analysis of 124 patients receiving at least 30 mg of daily prednisolone, Ogawa, *et al*[14] found that 2 weeks after prednisolone therapy was initiated, those patients with a peripheral lymphocyte count < 500/μl were 12.4 times more likely to develop PCP. A retrospective case-control study of patients with WG found the severity of lymphopenia both before and during immunosuppressive treatment was the best predictor of future development of PCP[26]. Several other studies also identified lymphopenia and low CD4 lymphocyte counts as significant risk factors for PCP in HIV-negative patients[5,32,37]. Notwithstanding these reports, more than three-quarters (79.6%) of the respondents in our survey who prescribe PCP prophylaxis reported that laboratory data had no effect on their prophylaxis decision (data not shown). Only 15% of respondents considered peripheral lymphocyte counts, and 7.5% monitored CD4 cell counts. This finding suggests that the predictive values of low total lymphocyte counts or of low CD4 cell counts are not well known or are not influencing prophylaxis prescribing patterns among practicing rheumatologists.

Several retrospective analyses have found that patients with WG are at higher risk of PCP than persons with other rheumatologic diseases[11,26,27,29,30]. Two-thirds of survey

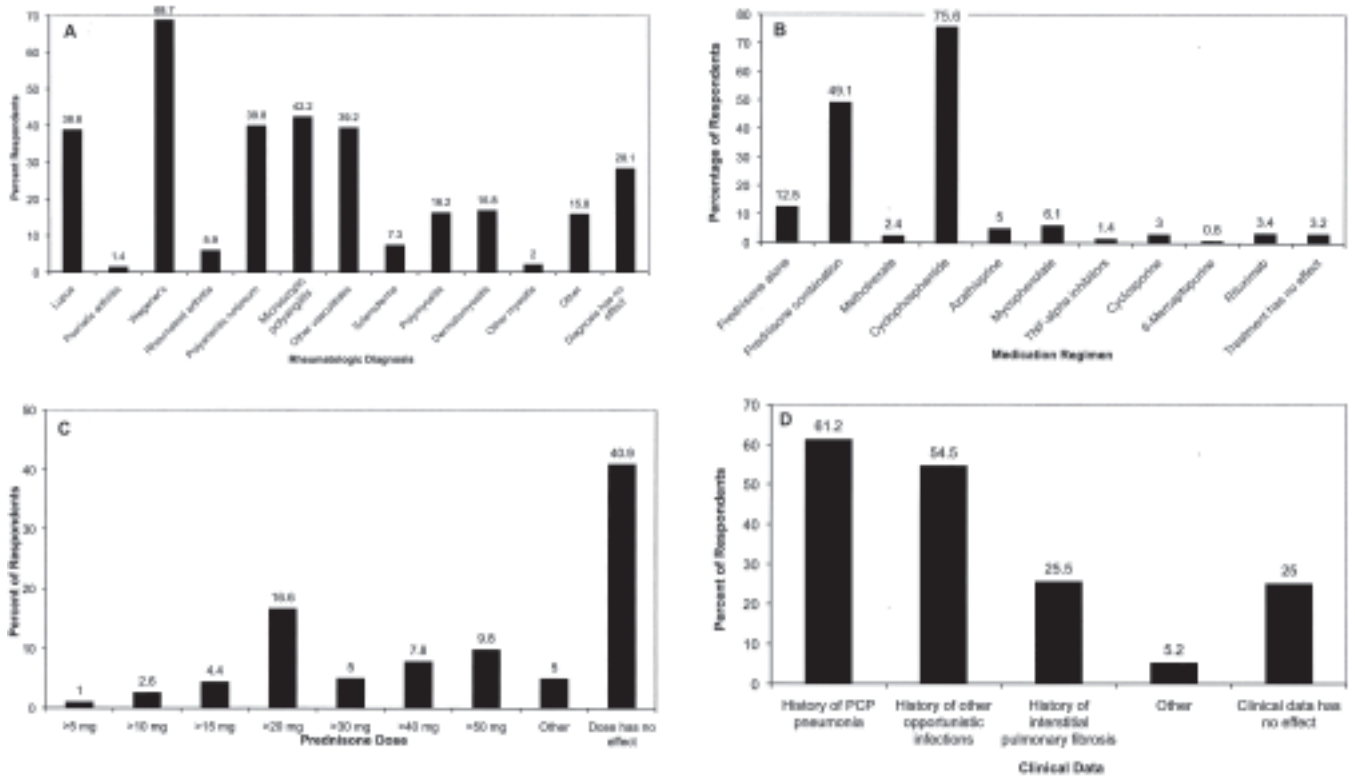

Figure 2. Among 505 rheumatologists who prescribe PCP prophylaxis, the proportion using prophylaxis according to rheumatologic diagnoses (A), medication regimens (B), prednisone doses (C), and other clinical factors (D).

respondents in our study who prescribed PCP prophylaxis indicated that they were likely to prescribe prophylaxis to patients with WG. More than one-third of respondents indicated they were likely to prescribe prophylaxis for lupus, polyarteritis nodosum, microscopic polyangiitis, and other systemic vasculitides, conditions that are also commonly associated with increased risk of PCP[9-11,18,20,24,38]. However, very few respondents reported prescribing prophylaxis for patients with rheumatoid arthritis (6%), polymyositis (16%), or dermatomyositis (17%), despite reports of their association with PCP[11,15,17,19,34,35]. In addition, more than one-fourth (28%) of respondents who prescribed PCP prophylaxis stated that a patient's diagnosis had no effect on their therapeutic decision. A disease manifestation common in individuals with inflammatory rheumatologic diagnoses that has been associated with increased risk of PCP is interstitial pulmonary fibrosis[13,39]. One-fourth of the respondents in our survey who prescribed prophylaxis reported that this was a consideration in their decision.

While our study suggests that patients for whom PCP prophylaxis is likely to be prescribed differ, even among physicians who prescribe prophylaxis, our findings further indicate that physician demographic characteristics are highly predictive of the use of PCP prophylaxis. The most highly predictive of these factors was years in practice. Rheumatologists who had been practicing medicine for 10 years or fewer were more than 4 times more likely to use prophylaxis than rheumatologists who had been practicing longer. This suggests that younger rheumatologists may be educated about this issue during postgraduate training, influencing their clinical practice thereafter. In addition, US-based physicians were nearly twice as likely to provide prophylaxis as their international counterparts. It is possible that differences in practice environment, including the more litigious American healthcare marketplace, may at least partially account for this observation.

These findings suggest that while practice patterns for prescribing PCP prophylaxis vary widely among rheumatologists, evidence exists to support the clinical efficacy of antibiotic prophylaxis when it is used in patients with rheumatologic diagnoses. In a retrospective case-control study, rheumatologic patients maintained on PCP prophylaxis were significantly less likely to develop PCP than those not on a prophylactic regimen[14]. In this study, only 2 of 46 (4.3%) patients receiving prophylaxis developed PCP, while 7 of 71 (9.9%) patients not prescribed prophylaxis developed PCP[14]. In 2 studies of hospitalized patients with rheumatologic diagnoses who were taking chronic corticosteroids, with or without PCP prophylaxis, there were no cases of PCP among persons receiving trimethoprim/sulfamethoxazole prophylaxis (n = 64)[13,39]. However, 4.3% of these patients who did not receive a prophylactic regimen

and 17% of those on a prophylactic regimen of aerosolized pentamidine developed PCP[13,39]. Other studies have shown similar results[5,10,12,23].

Despite the increased risk of PCP associated with rheumatologic disorders, the overall incidence of infection in this patient population remains relatively low. In combination with potential side effects of prophylactic regimens, this suggests that prophylaxis in all patients with a rheumatologic diagnosis may not be advantageous[14,23,24,39]. However, in principle, prophylaxis is beneficial in high-risk patients when the risk of PCP is greater than the risk of adverse events from prophylaxis[23]. In addition, a Markov model developed by Chung, *et al* suggests that prophylaxis with 3-times weekly trimethoprim/sulfamethoxazole is also cost-effective, increasing life expectancy and quality-adjusted life years in patients with WG treated with immunosuppressive therapy while decreasing direct medical costs[21].

The major limitation of our study is the modest response rate (23.1%) and the resulting potential for selection bias. Thus, while our response rate was low, it was similar to and somewhat greater than response rates recently reported in similar surveys[24,40,41]. In addition, our respondents were more likely to be from academic than community-based practices. These academic physicians were nearly twice as likely to prescribe prophylaxis as those in nonacademic practices. Therefore, our results may overestimate the true proportion of rheumatologists who prescribe PCP prophylaxis in the rheumatology community at large. In addition, only physicians with working e-mail addresses and Internet access were invited to complete the survey. A mailing option for the survey instrument was not offered. We also acknowledge that our survey methodology did not distinguish rheumatologists in training from those who had completed fellowship training. In addition, there may have been unintended ambiguity in the query of study participants as to whether they prescribe chemoprophylaxis for PCP (Table 1, Question 9); the question was not explicit regarding *typical* versus *occasional* versus *hypothetical* prophylaxis prescribing patterns. Our survey did not query participants about the HIV status of their patients. For all analyses, we assumed participants responded with regard to their prophylactic decisions in HIV-negative patients.

Despite these limitations, our study reveals that practice patterns for prescribing PCP prophylaxis and the patients for whom it is prescribed vary widely among rheumatologists. In addition, demographic characteristics of rheumatologists are highly predictive of prescribing patterns. The association between rheumatologic diseases and an increased risk of PCP has been well established[9-20], and the high rates of mortality and subsequent morbidity among HIV-negative persons with PCP are well known[1]. There is evidence that supports the clinical efficacy of primary prophylaxis in rheumatologic patients[13,39] to reduce the incidence of PCP, improve quality of life, and decrease cost[21]. Yet a rigorous risk-benefit ratio analysis of PCP prophylaxis among patients with inflammatory rheumatologic disorders has not been conducted. Moreover, there are currently no consensus guidelines to aid rheumatologists in adequately identifying patients who are at high risk of PCP infection. Published recommendations resulting from small retrospective studies and cases series are not entirely uniform. Large prospective studies are needed to investigate the clinical value and cost-effectiveness of PCP prophylaxis in HIV-negative patients with rheumatologic disorders. Once further investigations have been completed, consensus guidelines for PCP prophylaxis should be developed to establish best practices and guide clinical decision-making among practicing rheumatologists.

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