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Original article

# Influenza and pneumococcal vaccine coverage in 584 patients taking biological therapy for chronic inflammatory joint: A retrospective study



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### ARTICLE INFO

Article history: Accepted 4 February 2015 Available online 22 December 2015

Keywords: Influenza vaccination Pneumococcal vaccination Biological therapy Chronic inflammatory joint disease

# ABSTRACT

*Objectives:* To evaluate influenza and pneumococcal vaccine coverage in patients taking biological therapy for chronic inflammatory joint disease and to identify factors associated with the decision to administer these two vaccines.

*Methods:* Retrospective cross-sectional questionnaire study of a cohort of 584 patients taking biological therapy for chronic inflammatory joint disease (rheumatoid arthritis or spondyloarthritis). We studied the influenza and pneumococcal vaccine coverage rates, information about these vaccines given to patients by the primary-care physician and rheumatologist, and reasons for not administering the vaccines.

*Results:* Overall vaccine coverage rates were 44% for influenza and 62% for pneumococcus. Factors associated with being vaccinated were patient age, previous influenza vaccination, and patient information. Concern about adverse effects and absence of patient information by the primary-care physician and rheumatologist were associated with very low coverage rates.

*Conclusion:* This study showed insufficient vaccine coverage rates, particularly against influenza, in a population at high risk because of exposure to biological therapy. Patient information by healthcare professionals about influenza and pneumococcal vaccination has a major impact and should be renewed as often as possible.

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## 1. Introduction

Patients with chronic inflammatory joint diseases, such as rheumatoid arthritis (RA) have an increased risk of death that parallels the degree of disease activity [1]. One of the main factors in this excess mortality is an increased susceptibility to infections. The risk of severe infection is a major concern when managing patients with immunosuppression related to chronic inflammatory joint disease. Compared to same-sex and same-age controls, patients with RA have a 2-fold higher risk of being admitted because of an infection [2]. The risk is slightly lower among patients with spondyloarthritis [3]. *Streptococcus pneumoniae* is among the organisms responsible for infections in patients with chronic inflammatory joint disease. Thus, in a retrospective cohort study, patients with RA had a 2fold increase in pneumococcal infections compared to patients with non-autoimmune diseases [4]. In addition to the inflammatory joint disease itself, conventional drugs and biological therapy have both been proven to increase the risk of infection [5]. When biological therapies were introduced, concern was voiced about the potential for worsening the risk of infection. In published meta-analyses, TNF $\alpha$  antagonists were associated with odds ratios of 1.3 to 2 for the risk of infection [6,7]. These findings have prompted the publication of recommendations for preventing infections in patients with inflammatory joint diseases requiring biotherapy initiation. Reviewing the vaccination history and updating the vaccines as appropriate is among these recommendations [8,9]. The French High Council for Public Health (HSCP) recommends routine administration of the pneumococcal and influenza vaccines.

http://dx.doi.org/10.1016/j.jbspin.2015.11.005

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We therefore evaluated the pneumococcal and seasonal influenza vaccine coverage rates in a cohort of patients receiving outpatient follow-up for chronic inflammatory joint disease. We also sought to identify the reasons for not administering these two vaccines.

# 2. Methods

We conducted a retrospective cross-sectional study in four hospitals in south-eastern France (Centre Hospitalier Princesse Grâce, Monaco; Hôpital Archet, Nice; Centre Hospitalier, Cannes; and Centre Hospitalier, Fréjus-Saint-Raphaël). We included consecutive patients who were taking biological therapy for inflammatory joint disease and who received outpatient or day-hospital care at one of the study centres between February and July 2013. To be eligible, patients had to be taking one of the following biological therapies: etanercept, adalimumab, infliximab, certolizumab, golimumab, rituximab, tocilizumab, abatacept, and anakinra.

A questionnaire was used to collect the study data in each patient. The questionnaire included items on the primary study objective, i.e., the history of pneumococcal vaccination during the last 5 years (without specifying whether the 23-valent polysaccharide vaccine or the new protocol combining the 13-valent conjugate vaccine and the 23-valent polysaccharide vaccine 2 months later was used) and the history of seasonal influenza vaccination during the winter of 2012-2013 and previous winters. Whether the primary-care physician and/or rheumatologist had prescribed these vaccines was also specified; as well as any reasons the patient had for not having received these vaccines (concern about adverse effects, vaccination viewed as unnecessary, unwillingness to receive the vaccination, vaccination forgotten, or other reason). The following information was recorded also: age, gender, diseaserequiring biotherapy, past and present treatment, and history of lower respiratory tract infection during biotherapy. Comorbidities were not recorded. Vaccine status was collected based on patient report. The physician completed the questionnaire during a visit, based on the patient interview and medical record data. Before study inclusion, all participants were informed about the study and signed an informed consent document, which was kept in their medical records.

Continuous data were described as mean  $\pm$  SD and categorical data as n (%). The Chi<sup>2</sup> test and McNemar test were applied to compare percentages. To identify factors associated with influenza vaccination and with pneumococcal vaccination, we first performed a univariate analysis. The factors significant in this analysis were then introduced into a multivariate logistic regression model. The odds ratios (ORs) were estimated, with their 95% confidence intervals (95% CIs) and the corresponding *P* values.

### 3. Results

During the 6-month study period, 584 patients were enrolled, including 307 with RA and 277 with spondyloarthritis. All patients accepted to participate in the study. There were 398 females and 186 males, with a mean age of  $58.3 \pm 14$  years. Table 1 reports the main patient characteristics in the groups with RA and spondyloarthritis.

#### 3.1. Influenza vaccine coverage

The seasonal influenza vaccine for the 2012–2013 winter season was given to 260 (44%) patients overall. A higher coverage rate of 62% was noted in the subgroup older than 65 years of age. Coverage was similar in the RA and spondyloarthritis groups (44% and 42%, respectively). The primary-care physician recommended the influenza vaccine to 37% of patients overall, 45% of patients with RA,

#### Table 1

Characteristics of the patients with rheumatoid arthritis (RA) or spondyloarthritis (SpA).

	RA, <i>n</i> = 307	SpA, <i>n</i> = 277
Males/Females	51/256	135/142
Age (mean $\pm$ SD)	$59\pm13$	$48 \pm 12$
Biological therapies	n (%)	
Etanercept	115 (37)	85 (31)
Adalimumab	37 (12)	121 (44)
Infliximab	19(6)	46 (17)
Certolizumab	13 (4)	5(2)
Golimumab	5(2)	14(5)
Rituximab	42 (14)	
Tocilizumab	38 (12)	1
Abatacept	24(8)	
Ustekinumab		1
Anakinra	14(5)	4(1)
Patients having received $\geq 2$ biological	151 (49)	86(31)
therapies		
Concomitant DMARD	184 (60)	78 (28)
Glucocorticoid therapy	107 (35)	14(5)

DMARD: disease-modifying anti-rheumatic drug.

28% of patients with spondyloarthritis, and 63% of patients older than 65 years of age. A recommendation to receive the influenza vaccine was given by the rheumatologist to 79% of patients overall, 82% of patients with RA, 75% of patients with spondyloarthritis, and 93% of patients older than 65 years. Overall, the influenza vaccine was recommended far more often by rheumatologists than by primary-care physicians, and elderly patients received this recommendation more often than did their younger counterparts (Fig. 1A). Of the 584 patients, 333 (56%) had not received the influenza vaccine. The main reason reported by the patients for not receiving the influenza vaccine was forgetting to get vaccinated (50%), followed by concern about adverse effects (40%) (Fig. 1B). The proportion of patients who had received the influenza vaccine was 74% among patients who had received information by both the



**Fig. 1.** The influenza vaccine was performed in 44% of patients overall. A. Proportions of patients who received information about the influenza vaccine from their primary-care physician (open bars) and rheumatologist (closed bars). B. Reasons for not receiving the influenza vaccine.

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