SUMMARY

	Patients', physicians, nurses' and pharmacists' preferences toward the attributes of biological agents used in the treatment of rheumatic diseases
Objective	To determine and compare patients', physicians, nurses' and pharmacists' preferences toward the attributes of treatment with biological agents used for the treatment of three rheumatic conditions in Italy: rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis
Specific Objectives	- To assess the most preferred attributes and the importance of treatment with biologic drugs for the management of rheumatic diseases in a real setting according to the different categories of study population (patients, physicians, nurses and pharmacists) and the treatments' characteristics. - To estimate the relative importance according to preferences assigned to the attributes of biological treatments and to explore differences and similarities between the different categories of participants: patients, physicians, nurses and pharmacists. - To identify other characteristics (e.g., diagnosis, having experience with treatment with biological agents) that may influence patients' preferences for the treatment with biological treatments.
Study technique	Descriptive, observational, cross-sectional, open, multicenter, stated preferences study based on the Discrete Choice Experiment, which is a technique belonging to the conjoint analysis methodologies.
Study Sample	The study sample included 1) patients, 2) rheumatologists, 3) nurses and 4) pharmacists meeting the inclusion criteria and the characteristics necessary according to the objective of the study
Statistical Methods	Conditional logit regression models were applied to analyze the DC data. These models belong to the group of probabilistic choice models and are embedded in random utility theory. From these models, the value assigned to an option and its attribute level was estimated with a linear, additive function of the attribute levels included in the health profiles.

Sample size	Considering formal statistical sample size calculations and some practical issues, we planned to involve the following number of subjects in each subgroup: 540 patients in total (180 per disease condition); 100 rheumatologists in total, 50 pharmacists and 50 nurses.
Results	The subjects were enrolled in 30 Rheumatology clinics operating in the different regions of Northern, Centre and Southern Italy from July 2014 to Decembre 2015. The mean±SD age was 50.0±13.6 for the patients, 43.7±10.5 for the rheumatologist, 46.0±7.8 for the nurses and 39.8±8.6 for the pharmacists. In the patients and rheumatologists groups, 42.5% and 40.0% were male, respectively. More than 75% of pharmacists and nurses were female.

The patients enrolled had RA in 33.9% of cases, PsA in 34.9% and AS in 31.2% of cases; the mean±SD time from symptom onset was 10.8±9.4 years and the mean time from diagnosis was 8.0±8.2. Almost 53% of patients were already receiving treatment with biologic therapy at the enrolment in the study, while the others were receiving a new prescription of biologic treatment. Adalimumab was the most used or newly prescribed drug (20.5%) and more than 56% of patients received an infusion every month or every 2 weeks. The quality of life reported with the EQ-5D VAS was on average almost 60; the level "no problem" was reported by 33.7% in mobility, 46.2% in the self-care, 22.1% in usual activities, 6.9% in pain/discomfort and 36.8% in anxiety/depression. Patients with experience with biologic therapy reported a mean EQ-5D VAS of 67.21, while naïve patients reported a mean of 52.35.

The only parameter with a statistically significant relationship with quality of life was the treatment experience with biologic agents. In the models Naïve patients reported a lower mean EQ-5D VAS and EQ-5D Utility score. As regards preferences, the Characteriatics "Hospitality, service, efficiency and courtesy of health personnel", "Frequency of reactions at the site of drug

"Frequency of administration" was the least important for patients and rheumatologists, "mode and place of administration" the least important for the pharmacists, and "mode and place of administration"and "generalized undesired reactions or allergic reactions involving the whole body" the least important for the nurses.

The four subgroups of subjects invoved in the study were consistent in preferences towards the specified levels of all characteristics except "mode and place of administration". For this characteristic, pharmacists preferred subcutaneous injection with syringe, autonomously at patient's own place, nurses preferred assisted infusion, at an infusional center close to patient's place, patients and rheumatologists preferred subcutaneously injection with pen, autonomously at patient's own place.

Further we found difference in the patients's preferences based on their experiences. Characteristics "frequency of reactions at the site of drug administration", "hospitality, service, efficiency and courtesy of health personnel" and "Additional contribution added as healthcare taxes to be paid by all the citizens to make available the treatment to target patients" were the first, second and third most important ones for every subgroup, the fourth most important characteristic was "frequency of administration" for experienced with RA, "generalized undesired reactions or allergic reactions involving the whole body" for naïve with AS, and "mode and place of administration" for the other subgroups.

Across all the subgroups, patients generally preferred very satisfactory levels of "hospitality, service, efficiency and courtesy of health personnel", infrequent "frequency of reactions at the site of drug administration", mild "generalized undesired reactions or allergic reactions involving the whole body ", and no "additional contribution". Instead, for characteristics "frequency of administration" and "mode and place of administration" the patients generally preferred the frequency, mode and place of administration that were closer to those actually experienced or prescribed.

Discussion	The study showed how different subjects have different preferences for some treatment characteristics, which together with pure clinical aspects, can play an important role in the choice and consequent success of treatments. The study showed also how the patients chracteristics, as their experiences with a biological treatment, can have a role in their treatment preferences.
	Further, the data collected on the quality of life showed a lower HRQoL in the naïve patients, suggesting that these patients need a more effective treatment than those received previously.
	In conclusion, taking into account the different opinions of patients on at least some treatment characteristics could guide the conduction of good choices aimed to optimize benefits and to allocate efficiently resources.