Clinical Trials Perception in Rheumatology Patients: Experience from a Single Rheumatology Tertiary Center

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ABSTRACT. ***Objective.*** To investigate the perception and willingness of rheumatology patients to participate in clinical trials. No previous similar studies are available.

Methods. We conducted a cross-sectional survey of rheumatology patients using a questionnaire, which comprised 2 demographic questions, two 5-point Likert opinion questions, 19 true/false/unsure knowledge questions, and 1 open question addressing what would help the participant to gain a better understanding about clinical trials.

Results. Eighty-five patients returned the questionnaires (response rate 84.1%). The mean number of correct answers to the 19 knowledge questions was 10.5 ± 2.87. Patients with higher versus lower levels of education had significantly higher knowledge scores (mean correct answers 59.4 ± 13.1 vs 39.8 ± 20.4, $p = 0.013$). They also expressed greater willingness to take part in research (87.5% vs 48.2%, $p < 0.001$). The patients who agreed to participate in research provided significantly more correct answers (59.4 ± 15.3% vs 47.7 ± 27.2%, $p = 0.032$). Poor disease control as the main reason to join a clinical trial correlated well with patients' previous participation in research ($r = 0.71$; $p < 0.05$) and the lack of understanding of research principles (defined as less than 50% correct answers to the knowledge questions) correlated with the lack of willingness to participate in clinical trials ($r = 0.72$; $p < 0.05$).

Conclusion. The results of our study revealed that patients lack information about clinical trials (the correct response rate was only slightly above 50%), and that they had a moderate willingness to take part in clinical trials. The need for educational programs about clinical research was highlighted by the participants to the survey. (J Rheumatol First Release April 1 2015; doi:10.3899/jrheum.141091)

Key Indexing Terms:
CLINICAL TRIALS PATIENT EDUCATION QUESTIONNAIRE

Over the last decade there has been a huge increase in the available therapies for chronic rheumatic conditions. The discovery, testing, and implementing of these therapies was enabled by numerous clinical trials that exposed rheumatology patients more than ever to the challenges of clinical research. To our knowledge, no previous reports have investigated the perceptions that rheumatology patients have about clinical trials or their willingness to participate in them. However, in certain disciplines with longer histories of clinical research, such as oncology, there are good examples in the literature of questionnaire-based studies addressing both the clinicians' and patients' perceptions. There was a need to investigate the patients' self-reported views related to rheumatology clinical research to address unexplored areas that would facilitate their future involvement in research.

There is a positive trend to involve patients in the design of clinical trials and other research activities and also to empower them in controlling their medical condition by providing appropriate access to scientific information. The patient-centered educational programs available in many hospitals have proven the benefits of putting more disease control in the patient's hands. This is possible by ensuring patient access to suitable education about the management of rheumatologic diseases and also by enabling their access to the interdisciplinary teams that manage their condition. This study aimed to explore our rheumatology patients' knowledge and perception of clinical trials, to identify how we can improve their willingness to take part in research.

MATERIALS AND METHODS

We conducted a cross-sectional survey of patients attending general rheumatology outpatient clinics at University College Hospital, London, UK, in July

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and August 2013. The aim of our questionnaire-based study was to explore the patients' perception of clinical trials in rheumatology, targeting those patients with minimal or no previous exposure to clinical trials (questionnaire available from the authors on request). The questionnaire is not formally validated and it was used for the first time in rheumatology patients. However, it was adapted from a version used in a recent study investigating cancer patients' knowledge and attitudes toward clinical research[1]. The questionnaire was offered to all patients attending randomly selected clinics. The patients were considered eligible if they were 18 years of age or older and able to speak and read English. They were approached in person by their rheumatologist and asked if they wanted to complete a questionnaire described as addressing the knowledge and understanding of concepts about clinical research. The study was approved as a local audit and the results of this survey were used for designing educational activities for potential research patients organized by the University College London Hospitals (UCLH) Clinical Research Facility, where our research activity occurs.

Because there are no available educational programs addressing the principles of clinical research in rheumatology in our hospital, we wanted to clarify areas where patients would have identified the need for more information. The questionnaire comprised 2 demographic questions, two 5-point Likert opinion questions, 19 true/false/unsure knowledge questions, and 1 open question addressing what would help the participant completing the survey to gain a better understanding of clinical trials. We collected demographic information about sex, age, date of the first visit to the rheumatology department, previous exposure to clinical trials, and level of education. The participation was voluntary and implied consent. We did not include any of the patients' identifiable data on the database generated by this study. The patients were not guided when completing the questions.

The patient survey was shared with the senior members of the UCLH rheumatology department who provided feedback, which optimized the survey's simplicity and clarity. The questionnaire was also shared with rheumatologist colleagues from Addenbrooke's Hospital, Cambridge, UK, for a similar purpose. The survey was registered as a local audit, aiming to optimize the quality of patient research educational programs available in our department based on the identified areas where improvement was needed.

Statistical analysis. Descriptive statistics were used to assess the proportion of correct answers and to assess patient knowledge and characteristics. We calculated a questionnaire score for each participant by giving 1 point to every correct answer and 0 points to each "unsure" and incorrect answer. T-test, Pearson correlation coefficients, and ANOVA statistical techniques were used to investigate patient characteristics associated with questionnaire scores. Logistic regression was used to explore whether the questionnaire score was related to the willingness to participate in clinical research. Statistical significance was defined at the $\alpha = 0.05$ level.

RESULTS

Eighty-five patients returned the questionnaires and 16 declined to complete it for various reasons that we did not explore (response rate 84.1%). Thirty-three questionnaires from the returned ones were incomplete (38.8%). The lowest response rate was recorded in relation to the question 22, where patients have to complete a free-text space asking what would help them in understanding clinical trials better (response rate 70.6%), followed by the question regarding the date of their first visit to our rheumatology clinics (response rate 92.9%), and the one about their diagnosis (response rate 94.1%). The rest of the questions had a response rate above 95.2%.

The patients' age had a normal distribution and the median age of our respondents was 51 years. Twenty-two were men (25.8%; Table 1). Twenty-five patients (29.4%) were seen as new patients, and 60 (70.5%) were under regular followup for the management of rheumatoid arthritis (45.8%), osteoporosis (24.7%), osteoarthritis (14.1%), and other conditions (18.8%). Median duration of followup was 3 years (interquartile range 0.0-35 years). Less than one-quarter (21.1%) of the patients had previously participated in clinical research, and 45% agreed or strongly agreed that they have a good understanding of clinical trials; 27% were neutral about this statement, and 28% disagreed.

The mean number of correct answers to the 19 research knowledge questions was 10.5 ± 2.87 (56.1 ± 15.1%) with a median number of correct answers of 11 per questionnaire (55.3%, range 0–100%; Table 1).

The biggest consensus was reached on the following points: a clinical trial is a test of an experimental drug (77.6%

Table 1. Patient characteristics.

Characteristics	Value
Patients, n	85
Mean age, yrs, ± SD	50.9 ± 16.3
Sex, n (%)	
Men	22 (25.8)
Women	63 (74.2)
Diagnosis, n (%)	
Rheumatoid arthritis	39 (45.8)
Osteoporosis	14 (16.4)
Osteoarthritis	7 (8.2)
Others	16 (18.8)
Not known	9 (10.6)
Time since first visit to the rheumatology department, yrs	
Median	3
Range	0.0–35.0
No response, n (%)	3 (3.5)
Education, n (%)	
No formal education	8 (9.4)
Grade school	2 (2.4)
Secondary school	16 (18.9)
Trade/college/university	37 (43.5)
Postgraduate	19 (22.3)
No response	3 (3.5)
Understand clinical trials, n (%)	
Strongly disagree	4 (4.7)
Disagree	7 (8.2)
Neutral	27 (31.8)
Agree	28 (32.9)
Strongly agree	17 (20)
Missing	2 (2.4)
Would join a clinical trial, n (%)	
Strongly disagree	3 (3.5)
Disagree	8 (9.4)
Neutral	35 (41.2)
Agree	20 (23.6)
Strongly agree	16 (18.8)
Missing	3 (3.5)
Correct answers (% of total)	
Mean ± SD	56.1 ± 15.1
Median	55.3
Range	0.0–100

agreement); statistics help to decide whether an experimental treatment is better than the available treatments (76.5%); the consent form explains the known risks and benefits from being in a specific clinical study (75.2%); and proving the efficacy of a drug *in vitro* is not enough to enable its use in humans (74.2%). Specific questions about definitions of placebo, standard versus experimental treatment, and randomization generated a significant degree of uncertainty (52.9%, 52.9%, and 50.5%, respectively, of patients replied "I don't know"). Only a small proportion of patients (n = 23, 27%) recognized that a standard treatment could be given in association with placebo and were aware that even though the consent form is signed, there is no mandatory participation to the end of the trial (n = 27, 31.8%). Only 41.2% of patients (n = 35) recognized that a clinical trial might require more visits to the hospital than patients receiving usual treatments, and 54.1% of patients (n = 46) considered that doctors personally received money in the United Kingdom if they recruited patients for clinical trials. The main incentive for participation in research was the hope for better care and more time with the clinician (45.8%).

Patients with higher levels of education (trade/college/university or postgraduate) had significantly higher knowledge scores than those with lower levels of education (mean correct answers 59.4 ± 13.1 vs 49.8 ± 20.4, p = 0.013; Table 2). They also expressed in a higher proportion the willingness to take part in clinical trials (87.5% vs 48.2%, p < 0.001). Patients who agreed or strongly agreed with the statement "I have a good understanding about how clinical trials work," irrespective of their level of education, were less likely to take part in clinical trials, compared to those who did not agree with this statement (43.6% vs 73.2%, p = 0.021). The patients who agreed to participate in clinical trials provided significantly more correct answers to the questions related to research knowledge (mean correct answers 59.4 ± 15.3% vs 47.7 ± 27.2%, p = 0.032). Previous participation in clinical research was not associated with higher proportion of correct answers (mean correct answers 56.4 ± 16.8% vs 50.2 ± 15.2%, p = 0.18); however, patients previously recruited in clinical trials more commonly agreed or strongly agreed to take part in the future (82% vs 47.5%, p = 0.001).

In response to the question, "What would help you in understanding clinical trials better?", 60 patients (70.6%) provided text comments. The most frequent requirement was for more information including leaflets, discussions with the research team, and Website information (n = 52, 86.7%). A small proportion of patients stated that taking part in a clinical trial (n = 3, 5%) and being provided with clinical data from

Table 2. Relationships between patient demographics, percentage of correct responses, and likelihood of participating in clinical trials.

Characteristic	Patients, n	Mean Correct Answer, %	p	Agree or Strongly Agree Would Join a Clinical Trial, n (%)	p
Age, yrs					
< 55	49	55.4 ± 13.6	0.14	23 (46.9)	0.13
≥ 55	36	50.4 ± 15.9		13 (36.1)	
Sex					
Men	22	58.9 ± 16	0.14	9 (40.9)	0.32
Women	63	51.8 ± 15		27 (42.8)	
Diagnosis					
RA	39	60.5 ± 21.3	0.42 (ANOVA)	27 (69.2)	0.072 (ANOVA)
Osteoporosis	14	47.5 ± 13.3		9 (64.2)	
OA	7	42.3 ± 16.5		2 (28.5)	
Others	16	50.7 ± 9.1		6 (37.5)	
Not known	9	38.1 ± 26		3 (33.3)	
Time since first visit in the rheumatology department, yrs					
< 1	36	56.2 ± 18.7	0.49	13 (36.1)	0.22
≥ 1	49	56.3 ± 14.7		23 (46.9)	
Education					
Trade/college/university and postgraduate	56	59.4 ± 13.1	0.013	49 (87.5)	0.001
Other	29	49.8 ± 20.4		14 (48.2)	
Understand clinical trials					
Agree and strongly agree	55	58.1 ± 15.8		24 (43.6)	
Other	30	54.4 ± 17.8	0.15	22 (73.2)	0.021
Would join a clinical trial					
Agree or strongly agree	45	59.4 ± 15.3	0.032	N/A	
Other	40	47.7 ± 27.2			
Previous trial					
Yes	17	56.4 ± 16.8	0.18	14 (82)	0.001
No	68	50.2 ± 15.2		32 (47.5)	

N/A: not applicable; RA: rheumatoid arthritis; OA: osteoarthritis.

previous trials (n = 2, 3.33%) would help them understand the principles of clinical research. Information concerning the risks and benefits of the procedures and treatments in specific studies was requested by 1 patient.

In our study, according to the multiple choice selection, patients perceived these as the most important incentives for enrolling in clinical research: the poor response to previous treatments (n = 48, 56.4%), the altruistic reason "for helping research" (n = 47, 55.3%), and the need for more clinician time (n = 15, 17.6%). The evidence of poor disease control as the main reason to join a clinical trial correlated well with patients' previous participation in research ($r = 0.71$; $p < 0.05$). The lack of understanding of research principles, expressed as a proportion of correct answers below 50%, correlated with the lack of willingness to participate in clinical trials, expressed by a negative response to the statement "If I had the option, I would definitely consider joining a clinical trial" ($r = 0.72$; $p < 0.05$).

DISCUSSION

The results of our study revealed that patients lack information about clinical trials and have difficulty understanding the principles of medical research. It is widely recognized that improving patient understanding of the principles of clinical research could improve interest in and recruitment to clinical trials. Our questionnaire revealed that the correct response rate to the knowledge questions was only slightly better than pure chance (56.1%), which is similar to the findings of the cancer patients' study from which we adapted the questionnaire[1]. Significant correlation of higher proportion of correct answers with higher level of education and previous participation in clinical research was evident in our study, despite being inconsistently found in other cancer studies[2,3].

There are very few studies investigating rheumatology patients' perception of treatments[4], telephone helpline usefulness[5], or influence of the physical environment on treatment delivery and patient experience[6]. Ethical issues related to rheumatology clinical trial design was another area of interest for rheumatologists[7]; however, no previous study, to our knowledge, explored the experience of rheumatology patients involved in clinical research or their knowledge about clinical trials.

The lack of systematic analysis of the advantages and disadvantages of participating in clinical research was highlighted 30 years ago, in a study of the attitudes of patients enrolled in 2 clinical trials[6]. The patients reported that the time spent with the clinician and additional medical monitoring, as well as the access to a "second opinion" and reassurance received during participation in a clinical trial, were more important than the actual benefit of the trial intervention[8]. In the same study, altruistic motivation to participate was reported by 65% of the patients recruited in both clinical trials, while in our questionnaire study only 55% of patients stated this reason. If the willingness to participate in clinical research is defined as an illness coping behavior weighted by patients' own beliefs for and against the trial, the conclusion might be that the decision of a patient to participate in research is predictable, as observed by Verheggen, *et al*[9]. However, there are a variety of psychological factors involved in every individual decision related to participation in clinical research activities, including personal benefits from participation in a trial, altruistic and nonaltruistic motives, what patients perceive as disadvantages of clinical research and the effects of the trial medication, and previous experience of clinical research[10,11].

Several studies of oncology patients highlighted the huge influence of the pressure caused by the difficult diagnosis, with the perception of clinical trials as the only remaining option for this category of patients[12]. On the other hand, oncology patients expressed positive expectations in relation to cancer treatments when enrolled in early phase clinical trials, suggesting that optimism and positive thoughts and expectations are more influential than patient understanding of the concepts of clinical research and treatment uncertainties[13].

In contrast to the results of our study, Korean cancer patients' willingness to participate in clinical trials was not influenced by the patients' level of education, despite the good correlation between higher level of education and economic status with patients' awareness of clinical trials[14]. However, patients with previous experience in clinical trials had a greater willingness to participate in clinical research, similar to our study, suggesting that the experience of taking part in clinical trials was positive for both rheumatology and cancer patients.

Another similarity between these 2 categories of patients was found in the main reasons for participating in clinical research, which were the physician's recommendation and expectation of the effectiveness of a new drug. An Indian study published in 2013 revealed that physician advice and access to free medication along with family advice were the main reasons for taking part in a clinical trial, but otherwise the knowledge about clinical research was lacking, with 20% of patients unable to remember the study they took part in[15]. A large proportion of patients from Kenya relied on clinician advice as well, and tended not to scrutinize trial details when agreeing to participate, according to Naanyu, *et al*[16]. In our study, the dominant incentive for participation in research was more personal, related to the need for better control of the disease and a desire to provide altruistic help. No ethnic analysis was performed in our study because 94% of patients were white.

Our paradoxical finding that patients' impressions of having good knowledge about research correlated with less willingness to take part in research merits particular attention. Our previous experience with patients whom we approached to participate in clinical trials suggested that by providing

explanations about research principles (such as the rationale of placebo medication, randomization process, strictness of inclusion criteria, additional treatment restrictions, lack of availability of the treatment after the trial ends, etc.), we observed a decreased willingness of an informed patient to take part in research and to accept the risks associated with it. However, there are no studies, to our knowledge, that assess whether the patients who had explanations or were provided with information about clinical research retain this information over the long term. They might retain the impression that they know about research, without being able to provide correct answers to strict knowledge questions, as assessed by our survey. They might react in a way that is influenced by their previous impression when exposed to information about research principles, and it is recognized that the explanations about the risks associated with research activities usually have a more prominent psychological effect than those highlighting the benefits of research. Interestingly, in our cohort, only a small proportion of the interviewed patients have previously participated in clinical trials, and they expressed willingness to participate in research in the future, suggesting that their experience was beneficial. We concluded from our data that the majority of patients describing themselves as having good knowledge about research did not participate in the past in clinical trials; their perception might have been influenced by the way in which they were informed about research. Investigating this aspect was beyond the purpose of our study.

We hypothesized that the general perception about taking part in research is a positive one, and many participants have an altruistic attitude toward clinical research; this could explain why they want to take part in research even if they do not understand or know too much about it. Because our questionnaire is a subjective assessment of a limited population sample, we accept that there are many other personal reasons that are difficult to explore or explain that might drive the responses of the participants. The authors do not claim that the results of the study should be generalized, and further research using a bigger patient group is definitely needed.

Positive experience in clinical trials was also reported by another questionnaire study[17], in which patients stated that they were given more time to ask questions and discuss the treatment options in the research setting than in the usual clinical setting. People taking part in clinical trials also reported that appropriate information about the study was provided[17]. In our study, patients who agreed with the statement that they have a good understanding about research were less likely to take part in clinical trials, compared to those who did not agree with this statement ($p = 0.021$), suggesting that better knowledge about research risks or the randomization process might be a limiting factor in the decision to take part in research.

Our study has several limitations. It was performed in a single academic center and the data were collected only from patients willing to complete the questionnaire, which may skew the generalizability of the results. The relatively small sample of patients is not representative of a larger population; therefore the results must be considered exploratory. In addition, we have not examined the patients' perception of the informed consent process, because our cohort included only a minority of patients with previous experience of clinical research. This questionnaire was not validated for use in rheumatology studies. However, its ability to collect data efficiently was proven by the results of the oncology study from which we adapted it[1]. Considering that our study took place in a similar setting (hospital outpatient clinics), and recorded similar variables of interest that correlated with our study hypothesis, we can conclude that our questionnaire does not need to be tested for reliability in rheumatology studies and its results can be compared with other similar studies. The use of such a questionnaire is considered acceptable according to the current guidelines for optimal study design and administration of questionnaires[18]. The limitations of our study results are better explained by the relevance of the population surveyed (single-center study, limited number of participants) than by the questionnaire used.

A study from 2008 that focused on perception of the informed consent process indirectly suggested that patients' confidence in their physicians and drug effectiveness was good, because they reported not wanting to withdraw from a clinical trial because of the side effects and the conviction that research would not compromise their care[19].

Our questionnaire study revealed the perception of and knowledge about clinical research of a group of rheumatology patients. It showed that their understanding of research principles is generally poor, but that they have a moderate willingness to take part in clinical trials. The need for educational programs and accessible information about clinical research was highlighted by the patients' preference to gain more knowledge about research. If we want to increase recruitment of rheumatology patients to our clinical research programs, we should invest in educational programs to give them a better understanding about research relevant to their pathology and to help them understand better the risks, and more importantly, the benefits of participating in clinical trials.

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