

Clinical trials perception in rheumatology patients

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Background: During the last decade there was a huge progress in the available therapies for chronic rheumatic conditions. The discovery, testing and implementing of the new therapies was enabled by numerous clinical trials which exposed the rheumatology patients more than ever to the challenges of clinical research. There is no evidence of previous reports which investigated the perception of rheumatology patients in relation to their willingness to participate in clinical trials. However, in certain disciplines with longer history of clinical research, such as oncology, the literature data offer suitable examples of questionnaire-based research addressing both the clinicians and patients' perceptions. We felt that there was a need to investigate the patients' self-reported views related to rheumatology clinical research in order to address unexplored areas that would hopefully facilitate in the future their involvement in research. There is a very well justified trend to involve patients in the design of clinical trials and research activities in general and also to empower them in controlling their medical condition by providing appropriate access to scientific information. The patient-centred educational programs available nowadays in many hospitals have proven the benefits of putting the patient in the driven seat of their disease control. This is possible by ensuring patients' access to suitable education about the management of rheumatologic diseases and also by enabling their access to the interdisciplinary teams that manage their condition.

Materials and methods: We conducted a cross-sectional survey of patients attending outpatient rheumatology clinics. The aim of our questionnaire-based study was to explore the patients' perception of knowledge related to clinical trials in rheumatology, targeting patients with minimal and no previous exposure to clinical trials. The questionnaire is not validated as it was used for the first time in rheumatology patients and it was adapted from version used in a recent study investigating the cancer patients' knowledge and attitudes towards clinical research (Cameron et al., 2003) (1). The survey was completed by outpatients attending University College London Hospital general rheumatology clinics from July to August 2013. The questionnaire was offered to all the patients attending randomly selected clinics. The patients were considered eligible if they were 18 years of age or older and able to understand, 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, understanding and concepts about clinical research. The study was approved as a local audit and the results of this survey were employed for designing educational activities for potential research patients and public coordinated and organised by the UCLH Clinical Research Facility, where our research activity is currently taking place.

As there are no available educational programs addressing the principles of clinical research in rheumatology in our hospital, we wanted to objectify areas where patients would have identified the need for more information. The questionnaire comprised two demographic questions, two 5-

point Likert opinion questions, 22 true/false/unsure knowledge questions, and one free space question addressing what would help the participant to the survey to understand better 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 written consent. We haven't included any of the patients' identifiable data on the data base generated by this study. The patients haven't been provided with any help or explanation when completing the questions and data were collected even from incomplete questionnaires.

The patient survey was shared with the senior members of the UCLH rheumatology department who provided feedback which optimised its simplicity and clarity. The questionnaire was also shared with rheumatologist colleagues from Addenbrooke's Hospital, Cambridge for a similar purpose.

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

Results: 85 patients returned the questionnaires and 5 declined to complete it for different reasons (response rate 94.4%). 33 questionnaires from the returned ones were incomplete (38.8%). The lowest response rate was recorded in relation to the question number 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 have a response rate of above 95.2%.

The median age of our respondents was 51 years and 25.8% were men. 25 patients (29.4%) were seen as new patients, and 60 (70.5%) are under regular follow-up for the management of rheumatoid arthritis (45.8%), osteoporosis (24.7%), osteoarthritis (14.1%) and other conditions (median duration of follow-up was 3 +/- 0.74 years). Under a quarter (21.1%) of patients had previously participated in clinical research, and 45% of patients agreed and strongly agreed that they have a good understanding about 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 (Table 1).

The biggest consensus was reached on the following points: a clinical trial is a test of an experimental drug (77.6% agreement); statistics help to decide whether an experimental treatment is better than the available treatments (76.5%); the consent explains the known risks and benefits from being in a specific clinical study (75.2%); 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 vs. experimental treatment and randomisation 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%) recognised that a standard treatment could be given in association with placebo and were aware that once the consent form is signed there is no mandatory participation until the end of the trial (n=27, 31.8%). Only 41.2% of patients (n=35) recognised 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 UK if they recruit patients in clinical trials. The main incentive for participation in research was the hope for better care and more time with the clinician (45.8%).

TABLE 1 Patients' characteristics

<i>Characteristic</i>	<i>Value</i>
Patients (n)	85
Mean age (years)	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 in the rheumatology department (years)	
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)
Post-university	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)
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	56.1+/-15.1
Median	55.3
Range	0.0-100

TABLE 2

Relationship between patient demographics, percentage of correct responses to research knowledge questions, and likelihood of participating in a clinical trial.

<i>Characteristic</i>	<i>Patients (n)</i>	<i>Mean correct answer (%)</i>	<i>p Value</i>	<i>Agree or strongly agree to join a clinical trial [n(%)]</i>	<i>p value</i>
Age					
<55 Years	49	35.4+/-13.6	0.14	23 (46.9)	0.13
+55 years	36	30.4+/-15.9		13 (36.1)	
Sex					
Men	22	38.9+/-16	0.14	9 (40.9)	0.32
Women	63	31.8+/-15		27 (42.8)	
Diagnosis					
Rheumatoid arthritis (RA)	39	40.5+/-21.3	N.S.	27 (69.2)	N.S
Osteoporosis	14	37.5+/-13.3		9 (64.2)	
Osteoarthritis (OA)	7	32.3+/-16.5		2 (28.5)	
Others	16	40.7+/-9.1		6 (37.5)	
Not known	9	28.1+/-26		3 (33.3)	
Time since first visit in the rheumatology department (years)					
<1 year	36	36.2+/-18.7	0.49	13 (36.1)	0.22
>1 year	49	36.3+/-14.7		23 (46.9)	

Education					
Trade/college/university and post-graduate	56	39.4+/-13.1	0.013	49 (87.5)	0.001
Other	29	29.8+/-20.4		14 (48.2)	
Understand clinical trials					
Agree and strongly agree	55	38.1+/-15.8		24 (43.6)	
Other	30	34.4+/-17.8	0.15	22 (73.2)	0.021
Join a clinical trial					
Agree or strongly agree	45	39.4+/-15.3	0.032	N/A	
Other	40	37.7+/-27.2			
Previous trial					
Yes	17	36.4+/-16.8	0.18	14 (82)	0.001
No	68	40.2+/-15.2		32 (47.5)	

N.S. –no significant statistical difference between any of the groups.

Patients with higher level of education (trade/college/university or postgraduate) had significantly higher knowledge scores than those with lower level of education (mean correct answers 39.4+/-13.1 vs. 29.8+/-20.4, $p=0.013$). 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” were less likely to take part in clinical trials the ones who didn’t 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 39.4+/-15.3% vs. 37.7+/-27.2%, $p=0.032$). Previous participation in clinical research wasn’t associated with higher proportion of correct answers (mean correct answers 36.4+/-16.8% vs. 40.2+/-15.2%, $p=0.18$); however patients previously recruited in clinical trials more commonly agreed and strongly agreed to take part in again 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 previous trials (n=2, 3.33%) will help them understand the principles of clinical research. Information concerning the risks and benefits of the procedures and treatments in specific studies was requested only by one patient.

Only 9.4% would consider the option of taking part in clinical research because of their poor disease control, but this correlated well with patients' previous participation in research ($r=0.71$; $p<0.05$). The lack of understanding of research principles correlated with the lack of willingness to participate in clinical trials ($r= 0.72$; $p<0.05$).

Conclusions: 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 recognised that improvement in patients' 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 extremely similar to the findings of the cancer patients' study that we adapted the questionnaire from (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 but inconsistently found in other cancer studies (3, 4). The need for more clinician time was perceived as one of the incentives to enrol in clinical research, showing that research could improve our patients' experience of care. Also, the hope for a better disease control was one of the most important incentives to take part in research.

Discussions:

There are only a few studies investigating rheumatology patients' perception related to treatments (2), telephone helpline usefulness (5) or impact of the physical environment on treatment delivery and patients' experience (6). Ethical issues related to rheumatology clinical trials design was another area of interest for rheumatologists (7); however no previous study explored the experience of rheumatology patients involved in clinical research or their knowledge about clinical trials.

The lack of systematic analysis of advantages and disadvantages for participating in clinical research was highlighted many years ago, in a study from 1985 exploring the attitudes of patients enrolled in two 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 the 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.

Previous studies investigated the recruitment experience in clinical trials, which is one of the main factors that shape patients' perception about clinical research (9-11). Our study was designed to address a group of patients with minimal experience of recruitment in clinical trials as we were interested in assessing their perception more than their experience related to clinical research activities.

Different concepts, such as general health, medical history, health and illness perceptions, attitude to clinician and information, general attitudes and expectations towards the clinical trials were included in a Health Belief Model (HBM) and were identified as determinants of patients participation in clinical studies requiring informed consent (12). If the willingness to participate in clinical research is defined as an illness coping behaviour weighted by patients own beliefs for and against the trial, the conclusion might be that patients are quite predictable in their decision to take

part in research, as observed by Verheggen *et al.*, 1998 (12). However, there is a recognised variety of psychological factors involved in every individual decision related to participation in clinical research activities, such as: personal benefits from participation in a trial, altruistic and non-altruistic motives, what do patients perceive as disadvantages of clinical research and effects of the trial medication, and previous experience of clinical research (13, 14).

Previous research identified the attractiveness to participate in clinical research as being linked to gaining personal benefit, such as access to latest research in their condition and new treatments, specialist team expertise, more frequent monitoring and active involvement in their health care (15). However, ethnical disparities in enrolment in clinical trials were noted in the past and efforts were allocated to engage diverse communities in research and incentivise the industry to help people overcome logistical barriers to participation in clinical trials (16).

Several studies exploring oncologic patients highlighted the huge impact that the pressure caused by the difficult diagnosis and perception of clinical trials as the only remaining option experienced by this category of patients (17). 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 patients understanding of the concepts of clinical research and treatment uncertainties (18).

In contrast to the results of our study, Korean cancer patients' willingness to participate in clinical trials wasn't 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 (19). 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 a positive for both, rheumatology and cancer patients.

Another similarity between these two categories of patients was found in the main reasons for participating in clinical research, which were the physician recommendation and expectation of 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 lacked with 20% of patients unable to remember the study they took part in (20). A huge proportion of patients from Kenya relies on their clinician advice as well, and tend to not scrutinise trial details when agreeing to participate in clinical trials according to Naanyu *et al.*, 2014 (21).

We didn't explore the patients' perception of the informed consent process as our cohort included only a minority of patients with previous experience of clinical research. A study from 2008, focused on the informed consent process perception indirectly suggested that patients' confidence in their physicians and drug effectiveness was also good, as they reported not wanting to withdraw from a clinical trials because of the side-effects and the conviction that research won't compromise their care (22).

Positive experience of taking part in clinical trials was also reported by another questionnaire study, where 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 (23).

In conclusion, our questionnaire study highlighted a

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