

# Attitudes of Patients in Developing Countries Toward Participating in Clinical Trials: A Survey of Saudi Patients Attending Primary Health Care Services

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## ABSTRACT

**Objectives:** Clinical trials are experimental projects that include patients as subjects. A number of benefits are directly associated with clinical trials. Healthcare processes and outcomes can be improved with the help of clinical trials. This study aimed to assess the attitudes and beliefs of patients about their contribution to and enrolment in clinical trials. **Methods:** A cross-sectional study design was used for data collection and analysis. A questionnaire was developed with six categories to derive effective outcomes. **Results:** Of the 2000 participants approached to take part in the study, 1081 agreed. The majority of the study population was female, well educated, and unaware of clinical trials. Only 324 subjects (30.0%) had previously agreed to participate in a clinical trial. The majority (87.1%) were motivated to participate in clinical trials due to religious aspects. However, fear of any risk was the principal reason (79.8%) that reduced their motivation to participate. **Conclusions:** The results of this study revealed that patients in Saudi Arabia have a low awareness and are less willing to participate in clinical trials. Different motivational factors and awareness programs can be used to increase patient participation in the future.

Clinical trials refer to behavioral or biomedical research projects based on patients who fulfill the role of subjects. The objective of a clinical trial is to evaluate specific aspects of a particular intervention. Another goal of clinical or non-clinical research projects is to improve the standard of care based upon evidence-based medicine. Randomized controlled trials (RCT) have remained the foundation for medical advances since the first RCT was published in 1949.<sup>1</sup> Clinical research has the potential to provide the most advanced treatments and diagnostic approaches. Participation and enrollment of patients in clinical research, especially clinical trials, is the leading challenge for the investigators. Having an inadequate number of participants seriously affects the cost and outcomes of the trial. Similarly, reduced selection and participation can also reduce the statistical strength of a project, which will certainly result in inconclusive findings.<sup>2,3</sup>

The scale of the problem has not been determined. Benson<sup>4</sup> stated that the rate of recruitment of eligible

participants was less than 3%. Haidich and Ioannidis further explained that 17% of RCT have never achieved a 50% target recruitment rate.<sup>4,5</sup> Moreover, the recruitment rates of suitable patients for surgical RCTs are less than 50%.<sup>6</sup> A recruitment-based survey was conducted in which 41 RCTs were investigated in the United States of America. In this study, only 75% of the planned sample was recruited in 34% of the trials.<sup>3</sup> The attitudes of potential participants toward clinical research are still being evaluated. Certain studies have determined that participation can be affected by many factors, which depend on the culture and methodology. Numerous studies have identified certain barriers toward the enrolment within clinical trials. These studies focused on oncology and cardiology groups. However, the studies have not investigated the standpoints of the participants within society. Some previous studies have concentrated on the attitudes of outpatients regarding involvement in the trials. Two previous studies described contradicting findings related to the patients' attitudes during participation. One of

these studies was conducted in Denmark and showed positive behavior and attitudes of the participants. However, a second study, from Germany, identified a lower willingness to participate.<sup>7,8</sup> Another survey conducted in the Mayo Clinic in an internal medicine outpatient setting showed that 68% of participants were interested in taking part in clinical trials.<sup>9</sup>

The patient participation rate has been identified by different studies within different countries, and every country has its own results and outcomes. The New Mexico Cancer Care Alliance determined that reduced information related to clinical trials delayed participation.<sup>10</sup> Thus, lack of awareness has a direct impact on participation. Among 6,000 cancerous individuals within a survey, 85% were unaware about enrolling in clinical trials. After educating them, the rate of participation increased to 75%.<sup>11</sup>

This research project aimed to evaluate and investigate the beliefs and attitudes of patients in Saudi Arabia regarding participation and enrolment in the clinical trials. We assume that by identifying the reasons behind patients agreeing or refusing to enroll in trials will help to improve participation in the future.

## METHODS

This cross-sectional study used a self-administered questionnaire to obtain the results. The questions were written and administered in Arabic and translated into English for analysis. Two experts in the research methodology field reviewed the survey and provided their feedback. The Institutional Review Board approved this project before data collection. Patients gave their informed consent before completing the questionnaire. Pilot testing of the questionnaire was conducted on 100 subjects to ensure good reliability and validity of the instruments. The survey was revised according to all inputs. The questionnaire included the following six sections:

1. Demographic information (general questions).
2. Patients' knowledge of clinical trials and their experiences in participating (five questions).
3. General attitude regarding participation in clinical trials (three questions).
4. Recruitment preference (two questions).
5. Beliefs on research integrity (four questions).
6. Attitude associated with participation in the clinical trial (single question).

To identify a relationship between the general attitude toward participating in a clinical trial and the level of difficulty in reaching the hospital, one-way analysis of variance (ANOVA) was used. ANOVA was also utilized to determine the effects of the difficulty of reaching a hospital and the general attitude toward participating in a clinical trial.

Correlation was used to identify relationships between the participants' attitudes toward taking part in a clinical trial and their age, marital status, and education level [Table 1]. This question was rated on a 3-point scale while the three variables each had four groups. The three variables were significant, meaning that the relationships found in the sample also likely exist in the population. However, the correlation coefficients were all  $< 0.20$  and represented very weak relationships. The independent sample *t*-test was used to find a relationship between the general attitude toward participating in a clinical trial and the independent variable (gender). The level of significance for the statistical tests was set at 0.050 by convention, as mentioned by Sood et al, in 2009.<sup>9</sup>

The participants were recruited from adult primary care clinics in King Khalid University Hospital. Consecutive patients who attended the outpatient clinics were invited to participate. The study coordinators approached the patients in the waiting area and explained the study, and then asked them to complete the questionnaire. Illiterate patients or those who could not read Arabic were given assistance. Incomplete questionnaires were excluded from the analysis. Incapacitated individuals were not included. The sample size was chosen by convenience.

## RESULTS

Two-thousand participants were approached by the study coordinators to participate. Of these, only 1081 (54.1%) filled the questionnaire. The majority of the respondents were female (76.5%) and had a high education level (53.7%). Table 1 shows the age, gender, education level, and accessibility to the health care facility of the respondents.

Most of the respondents had never participated in a clinical trial (82.7%). However, the majority (72.7%) of participants agreed on their importance. Only 324 subjects (30.0%) agreed to participate in clinical trials previously. A small percentage of participants (29.3%) were aware of the advantage of

**Table 1:** Participants' characteristics and accessibility to the hospital (n = 1081).

Variable	Frequency	Percentage
<b>Age</b>		
20–30 years old	485	44.9
30–40 years old	285	26.4
≥ 41	311	28.2
<b>Gender</b>		
Male	254	23.5
Female	827	76.5
<b>Education Level</b>		
None	56	5.2
Less than high school	447	41.4
More than high school	581	53.7
<b>Area</b>		
Within Riyadh	822	76.0
Outside Riyadh	259	24.0
<b>Accessibility to hospital</b>		
Difficult	237	21.9
Not easy	522	48.3
Sometimes difficult	322	29.8

clinical trials to assess medication benefits and the majority of patients (68.9%) lacked fundamental information regarding clinical trials. Over half (n = 618, 57.2%) of the respondents did not know that clinical trials need the approval of an ethics committee before enrollment.

**Table 3:** Reasons that would discourage patients from participating.

Reasons	Responses, n (%)
Fear of risks	863 (79.8)
Religious reasons	463 (42.8)
Takes a long time	725 (67.1)
Takes multiple appointments	777 (71.9)
Fear of treatment toxicity	817 (75.6)
Medical reasons (poor health)	711 (65.8)
No financial compensation	550 (50.9)

The factors that were directly associated with improved participation within clinical trials are given in Table 2. The most important factor was religious motivation (87.1%) followed by being approached by their primary physician (70.6%) and receiving special medical care (67.1%).

The most significant factors that discouraged participation were fear of any risk or complication (79.8%) and the personal commitment to additional clinical appointments and follow-up (71.9%) [Table 3].

Of the 1081 patients, 809 (74.8%) reported that they wished to know the results of the study once complete. When asked about the methods for improving knowledge about the importance of clinical trials, most of the respondents thought that social media and the internet were the best ways to increase public awareness of clinical research.

**Table 2:** Motivating factors to participate in clinical trials.

Questions	Positive response, n (%)
Knowing that there is a reward from God (religious)	942 (87.1)
Helping in developing new medications	857 (79.3)
Being part of scientific knowledge	765 (70.8)
Willing to participate if you were provided with a good consent form explaining the benefits and risks of the clinical trial	786 (72.7)
Willing to participate if you were approached in a completely private setting	748 (69.2)
Willing to participate if you were approached by your physician	741 (68.5)
Knowing there are religious representatives in the clinical trial and an ethics committee will make you more likely to participate in the study	718 (66.4)
Belief that they will receive the best medical care	729 (67.4)
Access to free medications	728 (67.3)
Willing to participate if you were with a family member when approached	472 (43.7)
Willing to participate if you had more time to think about it	616 (57.0)
Willing to participate if you could obtain information from your physician	194 (17.9)

## DISCUSSION

Clinical studies are the cornerstone of medical development, and trials are the most important way of evaluating innovative medical treatments. Medical studies have shown that the failure to recruit the needed sample size is a major threat to the validity of clinical research and more so in RCTs.<sup>12,13</sup>

This study revealed that a smaller percentage (30.0%) of patients, who attended primary health care clinics, were willing to participate in clinical research. Nonetheless, the study found that most participants (67.8%) were unaware of the basic concepts of clinical trials.

Numerous studies have focused on the barriers related to patient enrollment in clinical studies in different patient groups such as those with cancer or cardiovascular diseases.<sup>14</sup> Additionally, there was a greater focus on the preferences and attitudes of patients toward clinical studies. Findings from developed countries have reported appropriate patient attitudes and behaviors related to clinical trials.<sup>15</sup> However, limited data are present in developing countries about patient attitudes. Nabulsi et al,<sup>16</sup> focused on the attitudes of parents in Lebanon toward the inclusion of their children in clinical trials and research projects. The study clearly determined that the risk/benefit ratio assessment was a major determinant of parental consent. Additionally, fear of painful processes or adverse events were major concerns of the selected sample. Misconceptions about clinical trials were another factor that inhibited participation. The investigators of this research project concluded that improving communication with parents and building trust between researchers and parents is important for successful recruitment.

Another study conducted in Jordan, focusing on patients with sickle cell disease (SCD), illustrated that many planned clinical trials ended early due to insufficient enrollment.<sup>17</sup> The study findings revealed that the patients expressed positive attitudes about clinical trial participation and that specific factors attached to particular clinical trial opportunities may play a greater role in their decision to participate than a general unwillingness.

A Malaysian study focused on the barriers to clinical trial participation. The study identified that patient participation in cancer clinical trials is extremely low. Various factors were identified as participation barriers by the patients including lack

of transportation, lack of interest, job commitment, and medical problems.<sup>18</sup>

An Egyptian study sought to identify which factors can influence parental consent of their children in clinical trials.<sup>19</sup> The study mentioned that the attitudes and beliefs of the parents should be positive to increase patient participation. An extensive explanation of benefits, increased benefits for children, and increased knowledge about the child's health status were three factors that increased the participation of children. On the other hand, the use of certain drugs, use of new procedures, and fear of adverse event were amongst factors that negatively influenced the parental decisions.

A study conducted in the UK focused on the participation of patients from South Asia in clinical trials.<sup>20</sup> While there were motivators to participate, such as to help society, improve one's own or the family's health, and increase scientific knowledge, deterrents included concerns about the side effects of drugs, bad experiences, mistrust, language barriers, and a feeling of not belonging to British society. Furthermore, another study also looking at South Asian patients' views and experiences of clinical trial participation also mentioned mistrust of healthcare professionals, trial burden, and language problems as common barriers to participation.<sup>21</sup> Catania,<sup>22</sup> investigated Italian patients, who identified fear of any complication as the leading reason for limited participation in clinical trials.

The studies about the willingness of subjects to participate in clinical research conducted in almost all Asian countries indicate that the populations of these countries are unaware of the significance of clinical trials. Their perspectives, knowledge, and attitudes are impaired in relation to the clinical trials. Reduced recruitment of patients in the clinical trials has emerged as the major factor in the low rates of clinical trials in Asia.<sup>23</sup> Racial and ethnic minorities have shown much less enrollment in many published trials.<sup>24-26</sup> For instance, Joshi et al,<sup>27</sup> showed that the awareness of clinical trials was very low among Indian patients.

Even the well-educated participants of this study were unaware of clinical trials. Therefore, it is extremely necessary to focus on public awareness.

A significant number of patients showed reduced interest levels in participating. Highlighting the religious and spiritual benefits and participation as a good deed may help the researchers to motivate

participants to enroll in studies. The majority of the participants declared that phone contact is a vital approach to invite participation. This study also highlighted that different types of media can be used to deliver appropriate knowledge and information.

One of the limitations of this study was that it was conducted in a single tertiary care center. Additionally, the population was relatively homogenous.

## CONCLUSION

The study found that the beliefs and attitudes of the participants toward clinical trials were diverse and varied. A fear of complications was the leading reason for the reduced rate of participation. However, highlighting religious benefits can be used to motivate participants. Despite that the majority of the participants were well-educated, they were unaware of basic information related to clinical trials. Increased awareness of clinical trials, the use of motivational factors, and reducing the impact of discouraging factors will increase the participation of individuals in research projects.

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