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Public motives and willingness to participate in first-in-human clinical trials in Saudi Arabia: A new era in the making

Adel F. Almutairi[*], Badriah M. Almutairi, Abdullah S. Alturki, Abdallah A. Adlan, Mahmoud Salam, Majed I Al-Jeraisy, Hanan H. Balkhy

King Abdullah International Medical Research Center, King Saud bin Abdulaziz University for Health Sciences, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia

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ABSTRACT

Background: Participation in first-in-human (FIH) clinical trials is a valuable contribution to science. This study aims to investigate the Saudi public's attitude toward FIH clinical trials, identify their willingness to take part in it, and their preferences for participating in these kinds of trials, given the fact that the Saudi FDA has never approved such studies in Saudi Arabia.

Methods: This was a cross sectional study conducted in February 2018. It was based on a self-reported survey distributed by convenience among Saudi adults visiting a national festival in Riyadh and through social media. Data were analysed using descriptive and bivariate statistics, as well as linear and binary logistic regression.

Results: Study participants who were invited and completed the survey were 657. The percentage mean score of participants' attitudes and concern was 70.1 ± 16.4 and 58.3 ± 15.3 respectively. Almost 71.5% expressed their intention to enroll in such trials. Higher attitudinal scores were reported by those who perceived healthcare services as good/excellent (adj.P < 0.001), and by those who had less concerns (adj.P = 0.005). Less educated participants were 1.75 [1.04–2.93] times more likely to enroll in future clinical trials, adj.P = 0.035. For every one unit increase in the attitudinal score, study participants were 1.03 [1.02–1.04] more likely to enroll in future trials, adj.P < 0.001. In contrary, for every one unit increase in concern scores, the odds of enrollment decreased among study participants by 0.98 [0.97–0.99], adj.P = 0.017. The factors causing people to decline participation were mainly fear of the unknown, social reasons, religious reasons, moral reasons, and the concern over human beings being treated as animals. The preferred duration for participation was 1–3 days (n = 268, 57%). Participants revealed their preferences of clinical trial studies were in favor: (a) vaccines (n = 209, 44.5%); (b) treatment drugs (n = 232, 49.4%); and (c) medical devices (n = 310, 66.0%).

Conclusion: The Saudi public community showed a high level of enthusiasm for participation in future FIH clinical trials, yet they had some reservations. Increasing public awareness about the benefits of clinical trials and conduction process helps to alleviate the concerns of the Saudi people and to increase their likelihood of enrollment.

Introduction

First-in-human (FIH) clinical trials constitute the phase in which humans are initially exposed to the investigational new drug (IND) to test its safety and mechanism of action in human subjects. They are always implemented with a relatively small sample size, ranging from 20 to 80 individuals [1]. Safety measures are also taken to eliminate the risks in accordance with the regulations of the regulatory bodies in each country, namely food and drug authorities. These regulations aim to protect the rights, safety, and welfare of subjects involved in a clinical trial. In addition, the regulations dic-

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[*] Corresponding author at: King Abdullah International Medical Research Center, King Saud bin Abdulaziz University for Health Sciences, Ministry of National Guard Health Affairs, 22490, Riyadh, 11426, Saudi Arabia

E-mail addresses: almutairiAd1@ngha.med.sa (A.F. Almutairi), almutairiba1@ngha.med.sa (B.M. Almutairi), alturkiab@ngha.med.sa (A.S. Alturki), adlana@ngha.med.sa (A.A. Adlan), salamma@ngha.med.sa (M. Salam), JeraisyM@ngha.med.sa (M.I. Al-Jeraisy), balkhyH@ngha.med.sa (H.H. Balkhy).

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tate the responsibilities of study team members and emphasize compliance with the approved study protocol, the goal of which is to eventually end up with a product that is reasonably safe and effective [2,3].

Human history has recorded a number of such clinical trials, the first, which was known as a legumes trial, having taken place in 500 BC according to a biblical account [4]. The practice continued in a similar fashion until the early 20th century, when the first randomized controlled trial for streptomycin occurred in 1946 [4]. However, there are many scientific and ethical challenges associated with the old practice, and there are many historical examples of violations of human rights. For instance, in the past, vulnerable populations were the go-to subjects for clinical trials, sometimes even without their knowledge. During World War II, for example, Nazi physicians conducted painful and brutal experiments on prisoners in concentration camps. One experiment was the freezing trial in which the Nazis were trying to find a treatment for hypothermia [5–7].

Generally, when one thinks of medical experimentation that represented a major violation of human rights, the Nazi often come to mind; however, there are many other examples from the early 1900s. The Tuskegee Syphilis Study on African Americans in the US and Shiro Ishii Experiments in Japan both resulted in serious tragedies that changed the ethical regulations related to medical research forever [5]. In the US, biomedical experiments were largely performed on prisoners: 85% of new drugs were tested on them in 42 prisons during the early 1950s. Investigational products ranged from soap and cosmetics to dioxin, psychological warfare agents, and radioactive isotopes. As result, prisoners suffered a great deal of adverse events and serious abuse [8].

Generally, those who were economically disadvantaged, prisoners, and people who were easily manipulated and misled have suffered a great deal throughout the history of clinical trials, which raised a number of ethical concerns in the field of research. These concerns eventually led to regulatory authorities restricting and eliminating certain types of unethical and predatory practices. Today, while the criteria for choosing human subjects have changed, the stigma associated with historical violations still makes it hard for modern investigators to find subjects. They now rely on healthy young and middle-aged adults who are paid to participate in FIH trials as their participant population of choice [9]. People nowadays have more awareness than in the past of their rights as potential subjects, with all the ethical guidelines supporting their willingness to choose whether to participate or not. This freedom of choice has led us to ask the following important question: What motives would lead anyone to want to participate in an FIH clinical trial?

To answer this question, a thorough literature review was conducted. Some previous research suggested that people take part in clinical trials mostly for altruistic reasons, and that deriving personal benefit is a secondary consideration [10,11]. However, these reasons were not consistent in other studies, in which volunteers disclosed that financial gain and therapeutic alternatives were the most frequent reasons to participate, and that altruism was not a common motive [12,13]. Another qualitative study with 42 men and women showed that the reasons for taking part were complex and a wide variety of personal considerations were evident. Gaining some personal benefit emerged as an important primary motivation in this group of respondents, whereas altruistic considerations appeared to be largely subsidiary. People who decided not to take part were also mainly concerned about the balance of personal risk and benefit [14].

In Saudi Arabia, where FIH studies have never been conducted, it is unclear whether or not the Saudi population would be willing to participate in such studies. The US National Library of Medicine has more than 400 clinical trial studies from Saudi Arabia registered in their database; however, most of these clinical trials are phase-III and phase-IV, or they have no classifications [15]. The reasons behind this lag in conducting FIH studies could be related to religious, ethical, or cultural constraints that all should be explored prior the implementation of these trials. Thus, this study aims to investigate the public perception of FIH clinical trials as well as people's willingness and preferences for participating in these kinds of trials. Given the fact that the first phase-I clinical trial facility in the country will be launched next year (2019) under the umbrella of King Abdullah International Medical Research Center (KAIMRC) and that the final rules and regulations for conducting phase-I clinical trial have not yet been released by Saudi Food and Drug Authority (SFDA), this study's findings are particularly relevant and important.

Method

Population and sampling

This cross-sectional study was conducted in February 2018 on a sample of the general public in Saudi Arabia to examine their understanding of the concept of FIH clinical trials and their willingness to participate in this kind of study. Saudi Arabia is over 2 million square kilometer in space, with a census exceeding 33 million, characterised by a high gross domestic product (GDP) per capita ($55,859) and a young population (more than half <25 years old). The potential participants were selected from the community using social media. In particular, convenience sampling was employed by distributing the questionnaires electronically to the public. This strategy is cost-effective and efficient as it helped in obtaining the views of a wide variety of people of different genders, ages, and educational levels from all regions of Saudi Arabia. The sample was augmented by inviting visitors to the annual festival for cultural and heritage in Riyadh, a major event that attracts people from all over the country. The sample size was calculated using the following parameters: If we assume 15% as the average proportion of participation in clinical trial research, a 3% margin of error, and 95% confidence limits, the required sample size is 545. In order to obtain the required completed questionnaires, the research team oversampled by 50%.

Data collection

An introductory letter explained the objectives of the study and highlighted its operational definitions, such as the definition of first in human clinical trials, as well as its presumed benefits and potential risks. The team of data collectors (who were previously trained) carefully responded to any query raised by the study participants and clarified any ambiguous terms. To overcome any cultural influence bias, the team of data collectors comprised of both male and female research coordinators. The data was collected using an electronic questionnaire, which was developed by the research team based on previous studies [16–19]. The questionnaire was divided into two main parts: (1) socio-demographic data, including age, gender, educational level, marital status, occupation, and perception of health status; and (2) items that measure public attitudes, concerns and willingness to participate. Each of the attitudes and concerns scales consisted of nine statements, rated on a five-point Likert scale, ranging from strongly disagree to strongly agree. A thorough literature review was undertaken to identify the factors that should be included in the questionnaire. Experts in social and health sciences were consulted to review the questionnaire from all perspectives, including clarity, appropriateness of the words to the community, comprehensibility, and relevance of the items to the research topic under investigation. As a result, few variables were refined or added. The questionnaire was then piloted with 10 participants from the public to ensure accuracy and readability. As their comments were positive, no changes were made. Cronbach's alpha was calculated for the attitudes and concerns scales, which resulted with 0.85 and 0.73 respectively.

Data analysis

The collected data were entered, stored, managed, and analyzed with the Statistical Package for the Social Sciences (Version 25, SPSS Inc., Chicago, IL, USA). The participants' demographic data and knowledge were analyzed using descriptive statistics. Bivariate analysis was undertaken to examine the difference between groups in terms of willingness and preferences to participate in FIH studies based on a number of demographic variables, including age, gender, and educational level. Outliers were dropped out. A number of linear and Logistic regressions were employed to identify the factors associated with attitudes, concerns and willingness to participate in FIH studies. Statistical significance was originally set at P-value <0.05, yet it was corrected using the Holm–Bonferroni method which made it to be $P < 0.02$.

Ethical considerations

Before conducting this study, ethical clearance and approval was obtained from the Institutional Review Board of Bioethics at the Ministry of National Guard-Health Affairs. Participants' confidentiality and anonymity were maintained by refraining from collecting any personal identifiers and disclosing the data to anyone outside the research team.

Results

Participants' profile

The sample of this study was composed of 657 Saudi participants. There were insignificant gender differences; females comprised 335 (51%) and males made up 322 (49%). Participants fell into two age categories (30.7 ± 9.6), with 334 (50.8%) under 30, and 323 (49.2%) were 30 years of age or more. The majority of the sample had a university level of education —540 (82.2%), of which 363 (55.3%) were employed. There were 202 (58.1%) who were healthcare employees. Single participants (n = 378, 57.5%) formed the majority, and married numbered 279 (42.5%). Only 93 (14.2%) reported their financial status as uncomfortable. Regarding chronic diseases, only 104 (15.8%) who reported having different types of chronic diseases such as diabetes, asthma, hypertension and dyslipidemia. Interestingly, participants had different perceptions of the quality of healthcare services in Saudi Arabia, where 115 (17.5%) rated services as excellent, 313 (47.6%) as good, 180 (27.4%) as fair, and 49 (7.5%) as weak.

Attitudes, concerns, and motives for participation

The overall percentage means score (PMS) and standard deviation (SD) of the nine statements that measures participants' attitudes toward participation in clinical trial phase I was 70.1 ± 16.4. The statements that obtained the highest percentage mean scores were 'participation helps in advancing in medical knowledge' (PMS = 80.9 ± 16.7), 'participation will benefit society' (PMS = 77.4 ± 22.0), and 'participation increases the survival or quality of life of my child/family' (75.4 ± 22.3). Whereas, the statements that were least rated by participants were 'participation provides financial compensation for me' (PMS = 53.5 ± 27.7), and 'participation gives me off-days at work' (PMS = 50.6.0 ± 30.3). Regarding concerns of participation, the overall PMS and SD were 58.3 ± 15.3, which is more than average. 'Fear of the unknown when participating in clinical trials phase I' was a highly rated statement with PMS (71.2 ± 26.3). Participants also rated the factors that would make them decline participation in clinical trial phase I including social reasons (PMS = 57.2 ± 23.1), religious reasons (PMS = 55.4 ± 28.2), and moral reasons (PMS = 54.1 ± 30.1). Some participants indicated that they would also decline participation as they perceive that in clinical trials, human beings are treated like animals (PMS = 41.9 ± 31.7).

Bivariate analysis showed that those who were singles (PMS = 71.4 ± 16.0) had a better attitude towards participation in clinical trial phase I compared to the married respondents (P = 0.021). Those who were working in healthcare fields (71.6 ± 15.7), and those who perceived healthcare services as good/excellent (72.5 ± 15.5), had significantly better attitudes than their counterparts (P = 0.006 and $P < 0.001$, respectively). Participants who had higher concerns scores (62.3 ± 14.8) would not enroll in a clinical trial phase I study even if advised by their physician, compared to those with less concerns ($P < 0.001$). Table 1 shows participants' attitudes and concerns regarding participation across the sample characteristics.

Out of 653 respondents, 470 (71.5%) reported their interest in accepting enrollment in a future clinical trial phase I. It was also found that 366 (81.7%) would accept the enrollment if it was advised by their physician. Younger people (n = 253, 75.7%) were more willing to accept enrollment in future clinical trials, compared to older ones ($\geq$30), P = 0.015. It was also found that single people (n = 284, 75.1%) are more likely to accept enrollment than married people, P = 0.017. People with a school level education (n = 94, 80.3%), and healthcare employees (n = 147, 72.8%) are more accepting of enrollment in future clinical trials phase I compared to others, respectively (Table 1). The participants' attitudes and concerns in relation to their willingness to participate in future clinical trial phase I is illustrated in Fig. 1.

Two linear regression models were constructed, which showed factors that were significantly associated with higher attitude scores included those who perceived healthcare services as good/excellent ($\beta = 0.179$, adj. $P < 0.001$) compared to weak, and those who had less concerns ($\beta = -0.108$, adj. P = 0.005) compared to high concerns scores, as indicated in Table 2. This inverse relationship between positive attitude and concerns was indicated by using Pearson correlation tests, which revealed a significant negative relationship between these two variables, P = 0.003 ($y = 65.91 - 0.11 \times x$). A binary logistic regression model showed three factors significantly associated with the people's interest in accepting enrollment in a future clinical trial. Study participants with school level of education were 1.75 [95%CI = 1.04–2.93] more likely to enroll in prospective clinical trials compared to their counter group, adj.P = 0.035. For every one unit increase in the attitudinal score, study participants were 1.03 [95%CI = 1.02–1.04] more likely to enroll in future trials, adj.$P < 0.001$. In contrary, for every one unit decrease in concern scores, the odds of enrollment decreased among study participants by 0.98 [95%CI = 0.97–0.99], adj.P = 0.017, Table 3.

Preferences of Saudi participants

The majority of participants (n = 255, 54.2%) expressed a preference to enroll in clinical studies conducted in a government hospital, compared to private or outside the country. There were almost identical scores for interest regarding enrolling in studies that are locally initiated (n = 250, 54.0%) compared to others (n = 224, 46.0%). The preferred duration for participation was indicated to be 1–3 days (n = 268, 57%), and only 24.5% reported their willingness to enroll in a study for a one week or more. Regarding the types of interventional studies, participants indicated their

Table 1
Attitude and concerns towards clinical trials phase I across sample characteristics.

	Attitude domain PMS ± SD 70.1 ± 16.4	Concern domain PMS ± SD 58.3 ± 15.3	Enrollment in clinical trials n (%) 470 (71.5%)
Gender			
Female	70.4 ± 16.1	58.9 ± 14.0	235 (70.1%)
Male	69.8 ± 16.8	57.6 ± 16.6	235 (73.0%)
	t = 0.526, P = 0.599	t = 1.140, P = 0.255	χ2 = 0.647, P = 0.421
Age category (years)			
<30	70.9 ± 16.0	58.3 ± 15.5	253 (75.7%)
≥30	69.3 ± 16.8	58.3 ± 15.2	217 (67.2%)
	t = 1.282, P = 0.200	t = 0.051, P = 0.960	χ2 = 5.917, P = 0.015*
Marital status			
Single/separated	71.4 ± 16.0	58.3 ± 15.2	284 (75.1%)
Married	68.4 ± 16.8	58.3 ± 15.6	186 (66.7%)
	t = 2.370, P = 0.021	t = 0.005, P = 0.996	χ2 = 5.650, P = 0.017*
Level of education			
School	70.9 ± 18.4	58.7 ± 15.0	94 (80.3%)
University	69.9 ± 16.0	58.2 ± 15.5	376 (69.6%)
	t = 0.563, P = 0.574	t = 0.364, P = 0.716	χ2 = 5.420, P = 0.020
Employment status			
Unemployed/retired	70.5 ± 16.6	58.2 ± 14.6	220 (74.8%)
Employed	69.8 ± 16.3	58.4 ± 16.0	250 (68.9%)
	t = 0.488, P = 0.626	t = −0.202, P = 0.840	χ2 = 2.833, P = 0.092
Healthcare employee			
No	66.8 ± 16.6	59.6 ± 15.6	94 (61.8%)
Yes	71.6 ± 15.7	57.8 ± 16.3	147 (72.8%)
	t = −2.750, P = 0.006*	t = 1.098, P = 0.273	χ2 = 4.768, P = 0.029
Financial status			
Uncomfortable	70.1 ± 16.5	57.7 ± 16.9	64 (68.8%)
Comfortable	70.1 ± 16.4	58.4 ± 15.1	406 (72.0%)
	t = −0.010, P = 0.992	t = −0.381, P = 0.704	χ2 = 0.394, P = 0.530
Evaluate healthcare services			
Weak/fair	65.7 ± 17.3	59.3 ± 15.5	164 (71.6%)
Good/excellent	72.5 ± 15.5	57.7 ± 15.2	306 (71.5%)
	t = −4.914, P < 0.001*	t = 1.253, P = 0.211	χ2 = 0.001, P = 0.974
Would you enroll if advised by your physician?			
No	61.4 ± 19.1	62.3 ± 14.8	103 (50.2%)
Yes	74.1 ± 13.3	56.4 ± 15.2	366 (81.7%)
	t = −9.819, P < 0.001*	t = 4.708, P < 0.001*	χ2 = 68.749, P < 0.001*

Note: PMS: percentage mean score; SD: standard deviation; n: frequency, %: percentage, t: student t-test, χ2: Pearson Chi-square test.

* Holm Bonferroni corrected P-value statistically significant at <0.02.

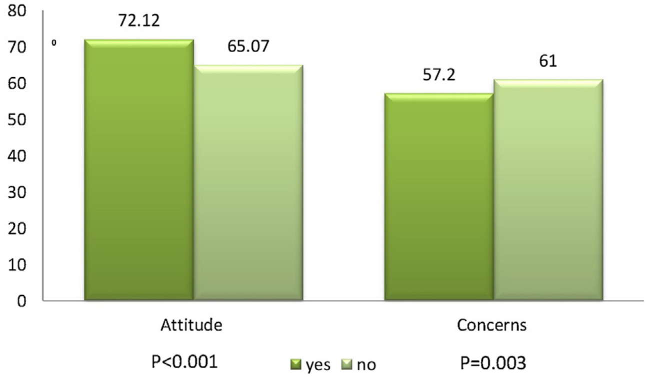

Fig. 1. Participants' attitudes and concerns in relation to their willingness to participate in future clinical trial phase I.

preferences as follows: (a) vaccines (n = 209, 44.5%), (b) treatment drugs (n = 232, 49.4%), and c) medical devices (n = 310, 66.0%). Table 4 provides comparisons of participants' preferences based on the sample characteristics.

As shown in Table 5, older people (≥30) (n = 136, 62.7%) prefer the duration of clinical trial to be from 1 to 3 days comparatively, whereas young people (n = 121, 47.8%) prefer a trial duration of more than 3 days (P = 0.022). Single participants prefer (n = 135, 47.5%) to enroll in clinical studies lasting more than three days, compared to married ones (n = 67, 36.0%), P = 0.014.

Discussion

Lack of knowledge about the public's attitudes, concerns, and preferences may hinder the conduction of FIH clinical trials in Saudi Arabia, which have never been done before in the country. Therefore, this study offers important knowledge that can help researchers, organizations, and other stakeholders understand Saudi people's fears, attitudes, preferences, and motives for participation so they may better target them. The current study revealed that the overall attitude (70.1%) of public toward participation is positive, which indicates the people's trust in the Saudi Arabian healthcare system, yet people's concerns toward participation remains above average (58.3%). Comparing these findings with those in the literature revealed that people in different countries had varying attitudes, ranging from 39.3% to 63.9%, toward participation in clinical trial research [16,18,20,21].

For instance, in western communities, the individualist life is the norm, in a sense that nobody communicates with the other unless it is deemed necessary, which is rare or uncommon. This might encourage pharmaceutical companies or sponsors of clinical trials to ask the members of the western public community to participate in new drug testing. In Middle Eastern communities, things are very different as the cultural relationships or bonds are very strong and no barriers are built in between the populations. In Saudi, the culture supersedes any other factors, and therefore, any issue about studies will be met with severe resistance from the society and this could be escalated by social media. The findings of these studies also revealed that people's concerns or worries determine the direction

Table 2
Factors significantly associated with higher attitude and concern scores.

	Attitude			Concern		
	β (S.E.)	t	Adj.P-value	β (S.E.)	t	Adj.P-value
Sex (male vs. female)	−0.01 (1.3)	−0.074	0.941	−0.06	−1.367	0.172
Age (years)	−0.05 (0.09)	−0.920	0.358	−0.01	−0.107	0.915
Education level (University vs. School)	−0.03 (1.68)	−0.695	0.487	−0.03	−0.644	0.520
Marital Status (married vs. single)	−0.06 (1.63)	−1.259	0.208	0.001	0.021	0.984
Occupation (unemployed vs. employed)	0.04 (1.41)	0.821	0.412	0.03	0.558	0.577
Financial status (comfortable vs. not)	−0.01 (1.83)	−0.258	0.796	0.013	0.321	0.748
Self-evaluation healthcare services (good vs. weak)	0.79 (1.34)	4.611	<0.001[*]	−0.05	−1.383	0.167
Concern (PMS)	−0.11 (0.04)	−2.827	0.005[*]	–	–	–
Constant	(4.18)	18.359	<0.001[*]	(3.24)	18.705	<0.001[*]

β: coefficient of determination, S.E.: standard error, t: students t-test, adj.: adjusted, PMS: percentage mean score.

[*] P-value statistically significant at <0.05.

Table 3
Factors significantly associated with enrollment in clinical trials.

	Enrollment in clinical trials		
	β (S.E.)	Adj.P-value	Adj.OR [95%CI]
Sex (female vs. male)	0.19 (0.19)	0.311	1.21 [0.83–1.76]
Age (years)	0.003 (0.12)	0.774	1.00 [0.98–1.03]
Education level (School vs. University)	0.56 (0.26)	0.035	1.75 [1.04–2.93]
Marital status (married vs. single)	0.37 (0.23)	0.104	1.45 [0.93–2.28]
Occupation (unemployed vs. employed)	0.19 (0.20)	0.344	1.21 [0.82–1.79]
Financial status (comfortable vs. not)	0.21 (0.26)	0.407	1.24 [0.75–2.03]
Self-evaluation healthcare services (weak vs. good)	0.21 (0.19)	0.281	1.23 [0.84–1.80]
Attitude (PMS)	0.03(0.01)	<0.001[*]	1.03 [1.02–1.04]
Concern (PMS)	−0.02(0.01)	0.017[*]	0.98 [0.97–0.99]
Constant	−0.81 (0.79)	0.305	

β: coefficient of determination, S.E.: standard error, adj.: adjusted, OR: odds ratio, CI: confidence interval.

[*] Holm Bonferroni corrected P-value statistically significant at <0.05.

Table 4
Participants' preferences in regard of the types of interventional studies across the sample characteristics.

	Vaccines n (%)	Treatment drugs n (%)	Medical devices n (%)
Gender			
Female	98 (41.7 %)	105 (44.7%)	149 (63.4%)
Male	111 (47.2%)	127 (54.0%)	161 (68.5%)
	$\chi 2 = 1.456$, P = 0.228	$\chi 2 = 4.120$, P = 0.042	$\chi 2 = 1.365$, P = 0.243
Age category (years)			
<30	122 (48.2%)	119 (47%)	167 (66%)
≥30	87 (40.1%)	113 (52.1%)	143 (65.9%)
	$\chi 2 = 3.126$, P = 0.077	$\chi 2 = 1.186$, P = 0.276	$\chi 2 = 0.001$, P = 0.980
Marital status			
Single/separated	133 (46.8%)	136 (47.9%)	189 (66.5%)
Married	76 (40.9%)	96 (51.6%)	121 (65.1%)
	$\chi 2 = 1.623$, P = 0.203	$\chi 2 = 0.624$, P = 0.430	$\chi 2 = 0.112$, P = 0.738
Level of education			
School	48 (51.1%)	43 (45.7%)	62 (66%)
University	161 (42.8%)	189 (50.3%)	248 (66%)
	$\chi 2 = 2.070$, P = 0.150	$\chi 2 = 6.15$, P = 0.433	$\chi 2 = 0.001$, P = 1.000
Employment status			
Unemployed/retired	104 (47.3%)	95 (43.2%)	140 (63.6%)
Employed	105 (42%)	137 (54.8%)	170 (68%)
	$\chi 2 = 1.317$, P = 0.251	$\chi 2 = 6.319$, P = 0.012[*]	$\chi 2 = 0.992$, P = 0.319
Healthcare employee			
No	34 (36.2%)	45 (47.9%)	59 (62.8%)
Yes	66 (44.9%)	86 (58.5%)	103 (70.1%)
	$\chi 2 = 1.799$, P = 0.180	$\chi 2 = 2.612$, P = 0.106	$\chi 2 = 1.387$, P = 0.239
Financial status			
Uncomfortable	27 (42.2%)	31 (48.4%)	42 (65.6%)
Comfortable	182 (44.8%)	201 (49.5%)	268 (66.0%)
	$\chi 2 = 0.156$, P = 0.693	$\chi 2 = 0.025$, P = 0.874	$\chi 2 = 0.004$, P = 0.952
Evaluate healthcare services			
Weak/fair	70 (42.7%)	79 (48.2%)	106 (64.6%)
Good/excellent	139 (45.4%)	153 (50%)	204 (66.7%)
	$\chi 2 = 0.325$, P = 0.569	$\chi 2 = 0.143$, P = 0.705	$\chi 2 = 0.196$, P = 0.658

n: frequency, %: percentage, $\chi 2$: Pearson Chi-square test, P: P-value.

[*] Holm Bonferroni corrected P-value statistically significant at <0.02.

Table 5
Preferences of Saudi participants willing enroll in FIH clinical trials across the sample characteristics.

	Duration of enrollment		Setting of enrollment		Type of trial	
	1–3 days	>3 days	Inside kingdom	Outside kingdom	Local initiated	External initiated
Gender						
Female	131 (48.9%)	104 (51.1%)	165 (70.2%)	70 (28.8%)	58 (65.2%)	31 (34.8%)
Male	137 (51.1%)	98 (48.9%)	154 (65.5%)	81 (34.5%)	44 (51.8%)	41 (48.2%)
	$\chi2 = 0.313$, P = 0.576		$\chi2 = 1.181$, P = 0.277		$\chi2 = 3.220$, P = 0.073	
Age category (years)						
<30	132 (52.2%)	121 (47.8%)	171 (67.6%)	82 (32.4%)	62 (63.3%)	36 (36.7%)
≥30	136 (62.7%)	81 (37.3%)	148 (68.2%)	69 (31.8%)	40 (52.6%)	36 (47.4%)
	df = 3, $\chi2 = 5.254$, P = 0.022*		$\chi2 = 0.020$, P = 0.887		$\chi2 = 1.995$, P = 0.158	
Marital status						
Single/separated	149 (52.5%)	135 (47.5%)	188 (66.2%)	96 (33.8%)	64 (57.1%)	48 (42.9%)
Married	119 (64.0%)	67 (36.0%)	131 (70.4%)	55 (29.6%)	38 (61.3%)	24 (38.7%)
	$\chi2 = 6.080$, P = 0.014*		$\chi2 = 0.924$, P = 0.337		$\chi2 = 0.283$, P = 0.595	
Level of education						
School	56 (59.6%)	38 (40.4%)	65 (69.1%)	29 (30.9%)	29 (65.9%)	15 (34.1%)
University	212 (56.4%)	164 (43.6%)	254 (67.6%)	122 (32.4%)	73 (56.2%)	57 (43.8%)
	$\chi2 = 0.313$, P = 0.576		$\chi2 = 0.088$, P = 0.767		$\chi2 = 1.290$, P = 0.256	
Employment status						
Unemployed/retired	120 (54.5%)	100 (45.5%)	154 (70.0%)	66 (30.0%)	56 (65.1%)	30 (34.9%)
Employed	148 (59.2%)	102 (40.8%)	165 (66.0%)	85 (34.0%)	46 (52.3%)	42 (47.7%)
	$\chi2 = 1.034$, P = 0.309		$\chi2 = 0.859$, P = 0.354		$\chi2 = 2.958$, P = 0.085	
Healthcare employee						
No	62 (66.0%)	32 (34.0%)	65 (69.1%)	29 (30.9%)	17 (54.8%)	14 (45.2%)
Yes	80 (54.4%)	67 (45.6%)	95 (64.6%)	52 (35.4%)	28 (52.8%)	25 (47.2%)
	$\chi2 = 1.943$, P = 0.081		$\chi2 = 0.525$, P = 0.468		$\chi2 = 0.03$, P = 0.858	
Financial status						
Uncomfortable	32 (50.0%)	32 (50.0%)	44 (68.8%)	20 (31.1%)	10 (47.6%)	11 (52.4%)
Comfortable	236 (58.1%)	170 (41.9%)	275 (67.7%)	131 (32.3%)	92 (60.1%)	61 (39.9%)
	$\chi2 = 1.490$, P = 0.222		$\chi2 = 0.026$, P = 0.871		$\chi2 = 1.192$, P = 0.275	

n: frequency, %: percentage, $\chi2$: Pearson Chi-square test, P: P-value.

* Holm Bonferroni corrected P-value statistically significant at <0.02.

of their attitudes. A Saudi Arabian study conducted in Riyadh with 232 Saudi patients and their families showed a positive attitude in which 75% out of patients who were invited to participate in clinical trials agreed to take part [22]. Yet the difference between the current study and theirs is that their study was about participation in clinical trials in general, whereas our study was about participation in FIH clinical trials.

This study also highlighted the most common driving factors for people to participate in FIH clinical trials: beliefs that CT will benefit society, will advance medical knowledge, and will lead to access for better treatment. These common reasons were also identified in studies from different countries, including South Korea, India, and Qatar [16,20,21]. Interestingly, the Korean study identified that altruism was a common reason for participation [16]. In contrary, the driving factors for people to decline participation were identified in our study as follows: fears, social reasons, religious reasons, moral reasons, and the concern over human beings being treated as animals or guinea pigs. Similar concerns were echoed in a number of studies [16,18,20]. A possible explanation is that some rumours were spread that hospitals were using human beings as lab rats without patients' knowledge, which is absolutely contrary to the reality. Clinical studies in Saudi Arabia are strictly governed by scientific and ethical regulations. Another possibility for declining is due to religious reasons and their viewing clinical studies as risky and as potentially causing harm to the body—the concern that made them apply the verse, in this context, stated in the holy Quran "do not throw [yourselves] with your [own] hands into destruction [by refraining]" [23]. Financial compensation was least rated by Saudi participants as a driver for participation, which was similarly perceived by people in another Gulf country, specifically Qatar [20].

The findings of this study also show that single people not only have a significantly better attitude but they are more likely to enroll in prospective FIH clinical trials in comparison to married ones. Most of the reviewed studies have not considered marital status as a factor that could influence people's participation decision, whereas the current study does [16,18,20]. Other studies have reported that family members mostly recommend against participating in clinical trials [24–26]. The current study corroborates this finding, as single people are more to take more risks because they do not have a spouse and children to be concerned about; their decision is mainly self-focussed. However, it is worth mentioning that being married is not an exclusion criterion for first in human clinical trials. Although some studies have found no significant difference between patients' age and their willingness to participate in clinical trials, the current study shows how this factor is important [18,20,22–24]: younger people are more willing to accept enrollment as compared to older ones (≥30). For instance, in a study undertaken in the Northeastern USA on patients' attitudes toward participation in clinical trials, the age cut-off point ≥65 years, and the mean age was 50 years; the current study, however, has a participant mean age of 30.7 ± 9.6. Interestingly, the trust between Saudi people and their physicians is very strong, and as the current study highlights, people are more likely to participate in FIH trials if they are advised to by their physician. Another study had similar findings about the strong relationship between Saudi patients and their physicians [27].

The level of commitment from the study participants should be maintained by accommodating their preferences and resolving their concerns. In this study, the authors noted that more than half of the participants preferred clinical trial phase I studies conducted in governmental hospitals, whereas a minority preferred enrollment in trials at private hospitals or hospitals located outside the country. A reason for this could be the fact that the governmental healthcare sector in Saudi Arabia follows the directory of the Ministry of Health, which ensures that the highest level of care and accreditation are implemented. Another possible reason is that the governmental healthcare settings are widely distributed across various geographical regions in the country; their outreach, follow-ups, and monitoring are much more extensive. The financial capacity of governmental settings is more sustainable than private hospitals; developing and operating clinical trial units at their facilities are done to the highest standards.

Previous studies reported that the governmental health sector should be responsible for establishing policy frameworks for the clinical trial industry and for creating a regulatory environment capable of ensuring their conduct without violating ethical and social norms [28]. In countries with no nationalized healthcare system, unlike Saudi Arabia, clinical research may take place in various sites [29]. All these factors may have enhanced the level of trust of study participants who favoured enrollment in clinical trial phase I studies in governmental healthcare facilities. The study findings revealed that there was a discrepancy among study participants concerning their enrollment in locally initiated clinical trials phase I or enrollment in externally initiated trials. In Saudi Arabia, clinical trials follow strict rules and regulations as per the International Conference on Harmonisation-Good Clinical Practice ICH-GCP, Saudi Food and Drug Authority FDA and other regulatory authorities, so the dispute can be resolved by clarifying this matter to prospective enrollees [29].

The type of intervention can be accounted as one of the main preferences for prospective enrollees and a significant highlight to principal investigators of clinical trials. Almost two thirds of the current study participants preferred enrolling in trials of new medical devices, probably because they perceived it as a safe noninvasive intervention. Trials based on newly developed drugs and vaccines were preferred by 44%–49.4% of the participants. In Saudi Arabia, almost 80% of trials phase II and beyond were related to testing new drugs, followed by medical devices (6.3%) and procedures (5.1%). Drug-related clinical trials phases in Saudi Arabia were mainly related to cancer, cardiac, neurological, diabetic, and endocrine diseases [30].

The preference of enrollment duration in clinical trials is a vital factor, as this indicates the amount of time prospective study enrollees are willing to give. Almost 24.5% reported their willingness to enroll for a one week or more. Enrollment projections are a key component of clinical trial planning. For instance, some cancer drug-related phase I trials may require at least one week of observations post intervention at the clinical trial unit [31], whereas others may be longer. Either way, participants' preferences should be in line with the principal investigators' expectations.

A few limitations have been observed in this study. There is a concern about that fact that study participants were eager to participate in prospective phase I trials at the time of survey, but there is no guarantee that all of them will be committed to the required conditions that may require reallocation, time off from work, and full and clear medical checkup. In addition, there might be a certain degree of cultural influence bias among the younger group of participants since the whole perspectives of first in human clinical trials might have been shared and discussed rigorously among the youth through the social media. Findings in this study act as a preliminary feasibility assessment of the Saudi Arabian setting for conducting clinical trial phase I studies, yet principal investigators and/or research sponsors may need to inquire on further details that have not been investigated in this study. Another limitation is that the types of drugs, medical devices, and vaccines have not been questioned in this study in terms of indications being tested. This could have been another factor that either encouraged or discouraged prospective participants to enroll in clinical trial phase I studies.

Conclusion and recommendations

The Saudi public community showed a high level of enthusiasm for participation in some of prospective FIH clinical trials, yet they had some reservations, including fears of the unknown, potential risks, work obligations, and physical exhaustion. Increasing public awareness about the benefits of clinical trials and conduction process helps to alleviate the concerns of the Saudi people and to increase their likelihood of enrollment. Since the preferences of prospective phase I clinical trial participants are of great interest to healthcare sectors and researchers, this study offers important knowledge about Saudi people's preferences in terms of duration of the CT, type, setting, and nature of interventions. Accommodating the enrollment conditions of people will enhance their active participation and commitment.

This study was based on a survey of public community members to determine their general attitude, concerns, and preferences toward clinical trials phase I. Since this type of trial has not been previously conducted in Saudi Arabia, these findings will aid prospective principal investigators and certified research sites and centers in determining the ideal candidates, settings, and conditions pertinent to achieving higher rates of enrollment in future clinical trials phase I. Study participants reported their concerns over these trials, yet these concerns are actually opportunities to resolve them and remove them. The level of trust in governmental health sectors, as a sponsor for prospective trials, entails that establishing clinical trial units should be a priority for the Saudi Ministry of Health. A huge responsibility lies on the shoulders of media, since it is capable of disseminating further awareness on clinical trials phase I among the general public.

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Ethical approval

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