BMJ Open

Knowledge and Attitudes toward Clinical Trials in Saudi Arabia: Cross-sectional study.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-031305
Article Type:	Original research
Date Submitted by the Author:	27-Apr-2019
Complete List of Authors:	Al Rawashdeh, Nedal Damsees, Rana Al-Jeraisy, Majed Al Qasim, Eman Deeb, Ahmad; King Abdullah International Medical Research Center,
Keywords:	Knowledge, Attitudes, Clinical trials < THERAPEUTICS

Knowledge and Attitudes toward Clinical Trials in Saudi Arabia: Cross-sectional study

Nedal Al Rawashdeh[1,2], Rana Damsees[1,2], Majed Al Jeraisy[1], Eman Al Qasim[1] and Ahmad M. Deeb[1]*

1. Research office, King Abdullah International Medical Research Center, Riyadh, Saudi Arabia; King Saud bin Abdulaziz University for Health Sciences, Riyadh Saudi Arabia; Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia.
2. The Office of Scientific Affairs and Research, King Hussein Cancer Center, Amman, Jordan

Nedal Al Rawashdeh: rawashdehne@gmail.com

Rana Damsees: rdamsees@gmail.com

Majed Al Jeraisy: JeraisyM@NGHA.MED.SA

Eman Al Qasim: alqasimem@NGHA.MED.SA

Ahmad M. Deeb: rn_a_deeb@hotmail.com

* **Corresponding Author**

Ahmad M. Deeb, RN, MSN, CCRC®

Senior Clinical Research Coordinator
Research Office
King Abdullah International Medical Research Center
King Saud Bin Abdulaziz University for Health Sciences
King Abdulaziz Medical City
Ministry of National Guard - Health Affairs
PO Box 22490, Mail Code 1515
Riyadh 11426, Kingdom of Saudi Arabia
Tel. No: +966118011111 ext. 18950
Monile: +966547883491
rn_a_deeb@hotmail.com

Short title: Knowledge & Attitude toward Clinical Trials

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board (IRB) at King Abdul-Aziz Medical City – Riyadh, KSA.

Consent for publication

Not applicable

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was supported by research grant RC16/010/R by King Abdullah International Medical Research Center. The study sponsor doesn't have any role in the study design, management, analysis, interpretation of the data, or in writing the manuscript.

Author contributions statement

Ahmad Deeb and Nedal Al Rawashdeh: Conception and design, data acquisition, data collection, analytical plan, drafting of the manuscript. Rana Damsees: Conception and

design and data acquisition. Majed Al Jeraisy: Conception and design, data acquisition and supervision. Eman Al Qasim: Conception and design and data collection. All authors critically revised the manuscript for important intellectual content, and approved of the final version to be published and agreed to be accountable for all aspects of the work.

Acknowledgements

Not applicable

Abstract

Objectives: Clinical trials (CTs) considered one of the important methods for devolving new treatments and provide access to new potential effective drugs that are still under investigation. Measuring public knowledge and attitudes toward CTs is important to assess the public readiness and acceptance for testing drugs on human subjects, which wasn't assessed before in the Kingdom Saudi Arabia (KSA). The objective of this study is to assess the status of Saudi public knowledge and attitudes toward CTs and toward participation to test new or approved drugs.

Design: Cross-sectional.

Setting: AlJenadriyah cultural/heritage festival in Riyadh/KSA.

Participants: A structured questionnaire was developed and distributed during the 2016 AlJenadriyah cultural/heritage festival. A convenience sampling approach was used. Participating booths/exhibition halls and visitors in the festival were approached to participate in the study. The responses were converted to percentage mean scores out of 100 for each knowledge and attitudes.

Primary and secondary outcome Measures: knowledge and attitudes toward CTs

Results: Total participants were of 938. The total knowledge score was 56.8 (24.8) and 61.5 (28.0) for attitudes. Although most of participants supported testing approved/off-label and new drugs on adult and pediatric patients, only (30.5%) agreed that new drugs can be tested on healthy volunteers. Study results showed that gender, educational-level, income, medical background, age-group and health insurance were independent

predictors for Knowledge of CTs. While gender, educational-level and medical background were independent predictor for attitudes toward CTs.

Conclusion: The Saudi public has low level of knowledge and moderate level of attitudes toward CTs and there is a moderate positive correlation between these two factors. Our results suggest conduction and investment of CTs in KSA; however, public educational campaigns about CTs are needed in specific the importance of testing new drugs on healthy volunteers.

Strength and limitation of the study

- Studies that have measured knowledge and attitudes of the Saudi public in general toward CTs are lacking.
- This is the first study to solicit public opinions on the way different phases of CTs are conducted in adult and pediatric populations.
- The main limitation is related to the possible selection bias as a result of convenience sampling.

Introduction

The clinical trial (CT) is a superior research tool for advancing medical knowledge and practice, and CT results are considered to provide the highest levels of evidence for medical practice and decision-making.[1] Subject recruitment is at the core of a successful CT. The acquisition of an adequate number of study subjects is crucial in being able to achieve the study objectives of testing the hypothesis and answering the research questions, and failure to recruit an adequate number of participants can result in wasted time, money, and effort.[2] Additionally, it can lead to a delay in the acceptance of the trial results and, thus, in the completion of the drug development process.

Knowledge and attitudes toward CTs are considered to be major challenges for subject recruitment.[3-6] Several studies have revealed that knowledge of CTs and attitudes toward participation are interrelated.[7-11] as increased knowledge likely promotes positive attitudes toward CT participation. Accordingly, low recruitment rates for CTs may be improved by increasing the public's knowledge about CTs [6,9,11] and by emphasizing the social responsibility perspective of how participation can contribute to the improvement of CTs.[12,13] Thus, improving the knowledge level of the public toward CTs represents an initial important step in being able to improve CT recruitment efforts in the future.[9,12,14]

In the Kingdom of Saudi Arabia (KSA), the clinical research domain has developed during the last few decades.[15] KSA researchers have contributed to the medical literature by conducting different types of research, including investigator-initiated CTs and international multicenter-sponsored CTs.[15] Measuring the knowledge and attitudes of the

Saudi public toward CTs will be crucial to assess their readiness and acceptance of CTs conduction in Saudi Arabi; and then to improve the CT recruitment and decision-making processes. Additionally, it will provide reliable information to researchers and healthcare leaders for proper strategic planning of public engagement in CT awareness campaigns. In return, these efforts may provide public benefits by increasing knowledge and awareness of CTs, enriching medical knowledge through updates of CT results, and the sharing of public preferences for future CTs.

Several studies have reported patient (or family) knowledge and attitude toward CTs at health care settings in Saudi Arabia [16-20]; however, studies that have measured knowledge and attitudes of the Saudi public in general toward CTs are lacking.

The purpose of this study was to assess the status of Saudi public knowledge and attitudes toward CTs in general and more specific the attitudes toward participation in CTs to test drugs.

The study addressed the following questions: What does the Saudi public know about CTs? What is the attitude of individuals in Saudi Arabia toward CTs and toward participation in CTs? Is there a correlation between the level of public knowledge and the attitudes of individuals in Saudi Arabia toward CTs? What factors can be predictive of the levels of public knowledge and the attitudes toward CTs in the Saudi population?

Materials and Methods

Setting

This cross-sectional study was conducted between February 2 and February 19, 2016 at the Al Jenadriyah Cultural and Heritage Festival, which takes place in Riyadh city

and hosts millions of residents and visitors from different regions of the country. We selected this event since it provided us with a unique chance to interview a representative cross-section from all regions of the KSA. This study was approved by the Institutional Review Board (IRB) at King Abdul-Aziz Medical City – Riyadh, KSA.

Study subjects

This study included adults of both genders who were willing to participate. A convenience sampling approach was used. Participating booths/exhibition halls in the festival were approached and festival visitors were invited to participate in the study. All of the participants provided a one-page informed consent by checking the YES box in order to accept filling the questionnaire which was administered by three investigators. Participants didn't receive any compensation for agreeing to fill out the questionnaire.

Patient and public involvement

Public were not included in the development of the research questions or design of the study. However, the questionnaire was piloted on public before use.

Sample size

The population of the KSA is approximately 31,742,308 (as per the Central Department of Statistics and Information), including 11,677,338 expatriates (Non-Saudi).[21] On the basis of this population estimate, a 0.05 margin of error, a 95% confidence level, and a response rate of 50%, we calculated that a minimum sample size of 385 subjects was needed; however, we increased the sample size to 1,000 to ensure that all regions of the KSA will be adequately represented in the sample.

Data collection

A structured questionnaire was developed in Arabic for this study. It was composed of questions that were divided into three sections: demographics, knowledge and attitude.

Data for the following variables were collected in the demographics section: gender, age, educational level, monthly income, nationality, residential area, employment status, marital status, health insurance, chronic diseases, medical background (working in a healthcare facility or having health-related education), and previous participation in medical research.

The knowledge section was composed of 12 questions, and participant answers were scored as correct (score = 1) or incorrect/not sure (score = 0). The total knowledge score was converted to the percentage mean score with a possible maximum value of 100, where a score of 100 indicates the perfect knowledge of CTs.

The attitude section was composed of nine direct questions, and participant answers were scored as positive (score = 1) or negative/not sure (score = 0). The total attitude score was converted to the percentage mean score with a possible maximum value of 100, where a score of 100 indicates the best positive attitudes toward CTs.

Based on previous studies, overall knowledge and attitude was classified into three levels following blooms cut-off point criteria as following: Above 80% (High level), 60-79% (Moderate level), less than 59% (Low level). [22-24]

We made an effort to present the questions in a language that was simple enough to enable the participants to understand and answer the questions, even if they were not

aware of CTs. The questionnaire was validated using content validity where each question is given to a panel of expert analysts, and they rate it and give their opinion about whether the question is essential, useful or irrelevant for measuring the knowledge and attitudes. It was piloted on a group of 28 participants, and complex scientific terms were simplified. Reliability was tested using Cronbach's alpha for the pilot sample for both knowledge and attitude sections (21 items) and it was 0.81. During the analysis, we verified the reliability using the Cronbach's alpha for questions in the knowledge section (12 items) was 0.771 and for those in the attitude section (9 items) was 0.782.

Data analysis

Data for categorical variables were represented as frequencies and percentages. Data for continuous variables were represented as mean ± standard deviation (s.d.). Normality was tested by the skewness coefficient, which indicated that knowledge and attitude data were normally distributed. The Student's *t*-test and one-way analysis of variance (ANOVA) were used as tests of significance. The Pearson correlation coefficient was used to determine the correlation between knowledge and attitude scores. A generalized linear model was used to determine the independent predictors of knowledge and attitudes toward CTs. All calculations were performed using the Statistical Package for the Social Sciences (version 23; SPSS Inc., Chicago, IL, USA).

Results

Subject characteristics

A total of 1,084 subjects were approached for participation in this study. In total, 938 (86.5%) agreed to complete the study questionnaire with one missing value in gender

and Nationality variables. Of the 938 participants, male individuals were predominant (61.6%). The age groups with the greatest representation among the participants were 18–30 (54.2%) and 31–40 (27.6%) of participants. In all, (60.1%) of participants reported holding a University, college degree or more , whereas (75.7%) reported monthly incomes of less than 10,000 SAR (Saudi Arabian Riyal) which is equivalent to around 2,700 USD (United States Dollar). Approximately half of the participants were single (48.7%), and (22.2%) of participants had chronic diseases. Participants with medical background (working in a healthcare facility or having health-related education) were (27.7%). In all, (15.9%) of participants declared that they had participated in medical research, and (26.5%) of participants knew someone who had participated in medical research (**Table 1**).

Knowledge about clinical trials in Saudi Arabia

The overall percentage mean score (SD) for knowledge regarding CTs was 56.8 (24.8) out of 100 score. Although study subjects were not aware of the term 'clinical trial', (43.7%) of could define the concept correctly. Most of the participants (71.8%) agreed that CTs are subject to ethical guidelines, but only (26.8%) were aware of the concept of an institutional review board (**table 2)**. In all, (81.1%) of participants were aware of the Saudi Food and Drug Authority (SFDA), and (66.4%) were aware of their role in the regulation of CTs. Most of the participants (72.1%) agreed that CTs benefit the community, and (46.5%) correctly answered the question regarding the benefits of CTs for their study subjects. Subjects' answers for questions regarding the time that investigators can start CTs and the rights of CT participants to withdraw from studies were

correct on average, with (56.0%) and (47.6%) of correct responses, respectively. Other findings from the knowledge portion of the questionnaire are listed in **table 2**.

Attitudes toward clinical trials in Saudi Arabia

The overall percentage mean score ±SD for Saudi attitudes toward CTs was 61.5 (28.0) out of 100 score. Most of the participants (59.5%) had positive attitudes toward testing new drugs on adult patients in Saudi Arabia, and (63.2%) showed positive attitudes toward testing approved/off-label drugs (approved and marketed drug for other indication) on patients. However, only (30.5%) of participants have positive attitudes regarding the conduct of CTs on healthy volunteers (phase I). The attitudes were similar regarding pediatric CTs, as (48.2%) and (56.4%) agreed with testing new drugs or approved/off-label drugs on pediatric patients, respectively. Majority of the participants (72.7%) expressed agreement that CTs were important for drug development, and (69.1%) affirmed the possibility of participation in CTs if the opportunity were offered to them or to a close family member. Most of the subjects (86.8%) showed a willingness to learn more about CTs. Other findings from the attitude portion of the questionnaire are listed in **table 3**.

Factors associated with increased knowledge and better attitudes toward clinical trials

The univariate analysis revealed that females had a higher level of knowledge about CTs than males, and subjects 31–40 years old had a higher level of knowledge than those in the other age categories (**Table 1**). Clinical trials knowledge increased with

an increased level of education (*P*= 0.001) and with increased monthly income (*P*= 0.001). Subjects from the central region of KSA showed a higher level of CT knowledge than subjects from other regions (*P*= 0.001) (**Table 1**). Undergraduate students and governmental employees showed a higher level of knowledge than subjects from other employment categories (*P*= 0.001) (**Table 1**). Having governmental or private health insurance (*P*= 0.001) was associated with a higher level of CT knowledge. Subjects with no chronic diseases had a higher level of knowledge than those with chronic diseases (*P*= 0.017). Previous participation in medical research or the knowledge of someone who participated in medical research was associated with better CT knowledge (*P*= 0.001) (table 1).

After adjusting for the possible confounders, males beta coefficients (B= –14.1; *P*= 0.001), non-educated participants (B= –19.6; *P*= 0.001), subjects with no income (B= –9.7; *P*= 0.011), and subjects with no medical background (B= –4.7; *P* = 0.015) had significantly worse knowledge scores regarding CTs. By contrast, people with age group between 41 to 60 (B = 12.1; *P* = 0.036) and those with health insurance (B= 12.9; *P*= 0.003) seemed to have more knowledge of CTs (**Table 4**).

Females had more positive attitudes toward CTs (*P*= 0.001) than males. The 31–40 and 41–60 age groups had more positive attitudes than the other age categories (*P*= 0.007), and higher education was associated with better attitudes (*P*= 0.001) (**Table 1**). As with the knowledge portion of the study, both undergraduate students and governmental employees showed more positive attitudes toward CTs (*P*= 0.028) than people in other employment categories (**Table 1**). Having governmental health insurance or private health insurance (*P*= 0.001) was associated with more positive attitudes as

well. Subjects with medical backgrounds or who had previously participated in medical research tended to have more positive attitudes (*P*= 0.001) than Subjects with no medical backgrounds or never participated in medical research before (**Table 1**).

After adjusting for the possible confounders, being male (B= –9.2; *P*= 0.001) or uneducated (B= –18.4, *P*= 0.004), or not having a medical background (B= –5.0; *P*= 0.039), were all associated with more negative attitudes toward CTs (**Table 4**).

Correlation between Saudi public knowledge and attitudes toward clinical trials

Our results showed a moderately positive relationship between Saudi public knowledge and attitudes toward CTs (Pearson's *r*= 0.564, *P*= 0.0001). Therefore, we predict that as knowledge of CTs increases, the Saudi public will show more positive attitudes toward them.

Discussion

This public survey revealed an overall relative lack of knowledge regarding CTs. Most of the participants could not identify or correctly define the term 'clinical trials'. Although most of the Saudi public is aware of their right to voluntarily participate in CTs, they were not aware of the rights of subjects to withdraw from CTs. The lack of knowledge about CTs has been observed in studies that were conducted in healthcare settings (with patients and/or their families) within Saudi Arabia.[17-20] The reason underlying this lack of knowledge can be interpreted by the lack of institutional and national campaigns that promote CTs. [5,25]

Although most of the participants believed that CTs are controlled by ethical principles, they were not aware of an IRB and its role in protecting human subjects. In the healthcare setting, Sheblaq et al. reported that the majority of patients with cancer were not aware of the role of the IRB.[17] The public tends to trust the authorities with the belief that the authorities protect the public even when there is a lack of knowledge about who is responsible for playing this role. We observed this phenomenon clearly when subjects answered positively to questions regarding their trust in the study team and in their compliance with regulatory guidelines when initiating a trial or recruiting subjects. The Saudi public successfully recognized the SFDA and its role in CTs, most likely because of their well-known food and drug related regulatory activities in Saudi Arabia.

The overall level of attitudes among Saudi public were Moderate toward participation in CTs. The Saudi public believes that CTs might provide benefits for society as a whole and for the subjects in the CTs. Additionally, trust in the study team may explain the favorable attitudes toward participation in CTs. It could be argued that the participants' answers might change in real-life situations such as in healthcare settings. Nevertheless, our results were consistent with other studies conducted in the health care settings in Saudi Arabia that investigated patients'/families' opinions regarding participation in CTs.[16-18]

Similarly, but to a lesser degree, the Saudi public agreed with the idea of conducting pediatric CTs for approved/off-label drugs. However, only 48% of the survey participants found that it was acceptable to test new drugs in pediatric subjects. Objection to the use of new drugs or vaccines was one of the factors underlying the opposition to pediatric CTs [26]. Although the study didn't assess the reasons behind

motivation to participate in CTs, we believe that the fear of adverse events, as well as safety concerns, may explain this objection.[25,27]

Phase I CTs, which involve testing of new drugs in healthy volunteers, are important in the process of drug development. However, several ethical dilemmas affect the ability of these studies to be conducted on healthy volunteers and patients.[28] In our study, the Saudi public showed negative opinions toward testing new drugs on healthy volunteers. Only 30.5% of participants agreed with the idea of conducting CTs on healthy volunteers in Saudi Arabia. This sentiment may be related to the lack of knowledge regarding the purpose of testing new drugs on healthy volunteers. Conduction of educational campaigns for public about CTs in Saudi Arabia is crucial to improve their knowledge and awareness about CTs.

Consistent with other studies [9,11], our results revealed that participant attitudes toward CTs were markedly dependent on their knowledge of CTs. We predict that as knowledge about CTs increases, the Saudi public will show more positive attitudes toward them. A low level of knowledge regarding CTs may indicate misunderstandings or confusion regarding the purposes of the different phases of CTs. In turn, participants' answers may have been affected by insufficient knowledge. We believe that many respondents used their common sense to answer some survey questions and may have begun to recognize the meaning of CTs while answering further questions. These observations suggest for the need for public educational campaigns about CTs, particularly when the majority of respondents were interested to have more information about CTs.

Male gender, less education, lack of a medical background, less monthly income, a lower age group, and lack of health insurance were independent predictors of a low

level of knowledge regarding CTs among the Saudi public. Male gender, less education and lack of a medical background were independent predictors of negative attitudes toward CTs. Our results were consistent with a United States household survey conducted to assess levels of public participation in and awareness of clinical and translational research, in which higher levels of income and education were associated with better participation and awareness.[29] In a study on patients with cancer in a healthcare setting, lower amounts of education and income were associated with decreased awareness toward CTs, as were race and ethnicity [9]. Similarly, lower incomes and education, were associated with reduced willingness to participate in CTs in African-American patients with cancer [30]. A study of patients with cancer in Saudi Arabia found that higher education was the only significant predictor of trial participation.[17]

Unlike other studies on the public or in healthcare settings [5,9,25,31-33], gender was an independent predictor of knowledge and attitudes. Males were associated with a lower level of knowledge and with more negative attitudes toward CTs. The underlying rationale has not been clearly discussed in the literature. However, we believe that gender differences regarding knowledge and attitudes toward CTs should be considered for future studies.

While previous studies have looked at knowledge and attitudes toward CTs in Saudi Arabia, they were much smaller and mainly involved surveying patients and/or their families in healthcare settings.[17,18] To our knowledge, this is the first study of Saudi public knowledge and attitudes toward CTs outside of a healthcare setting. Furthermore, it is the first study to solicit public opinions on the way different phases of CTs are conducted in adult and pediatric populations.

Conclusion

The Saudi public has a low level of knowledge and moderate level attitudes toward CTs. Increasing Saudi public knowledge regarding CTs may contribute to positive attitudes toward participation in and support of CTs. Accordingly, we suggest the use of educational campaigns to increase awareness and knowledge of CTs among the Saudi public. These campaigns should be targeted preferentially to the less knowledgeable populations identified in this study and focusing on the importance of testing new drugs on healthy volunteers (phase I clinical trials). In addition, our results support the conduction and investment of CTs in KSA. Conducting similar studies in the future, taking the limitations of this study into consideration, may be helpful for measuring the improvement of knowledge over time. We also recommend in-depth qualitative and focus-group-based studies for a better understanding of participant responses.

Study limitations

The main limitation in this study is related to the possible selection bias as a result of using of convenience sampling; however we believe that this limitation can be partial due to the large number and the diversity of the visitors.

Abbreviations

ANOVA: Analysis of variance

CTs: Clinical Trials

IRB: Institutional review board

KSA: Kingdom of Saudi Arabia

SAR: Saudi Arabian Riyal

S.D: Standard Deviation

SFDA: Saudi Food and Drug Authority

USD: United States Dollar

References

1. Oxford Centre for Evidence-based Medicine – Levels of Evidence. 2009. 2017, at http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/.)
2. Wyse RK. Accelerating patient recruitment in clinical trials: in-depth report from the SMi 2nd annual conference In: Ross C, editor. The SMi 2nd annual conference 2006; London: NetworkPharma Ltd.
3. Verheggen FW, Nieman FH, Reerink E, Kok GJ. Patient satisfaction with clinical trial participation. Int J Qual Health Care 1998;10:319-30.
4. Public Engagement and Clinical Trials: New Models and Disruptive Technologies: Workshop Summary. Washington (DC)2012.
5. Leiter A, Diefenbach MA, Doucette J, Oh WK, Galsky MD. Clinical trial awareness: Changes over time and sociodemographic disparities. Clin Trials 2015;12:215-23.
6. The Need for Awareness of Clinical Research. National Institute of Health, 2016. 2017, at https://www.nih.gov/health-information/nih-clinical-research-trials-you/need-awareness-clinical-research.)
7. Kim SH, Tanner A, Friedman DB, Foster C, Bergeron C. Barriers to Clinical Trial Participation: Comparing Perceptions and Knowledge of African American and White South Carolinians. J Health Commun 2015;20:816-26.
8. Kim SH, Tanner A, Friedman DB, Foster C, Bergeron CD. Barriers to clinical trial participation: a comparison of rural and urban communities in South Carolina. J Community Health 2014;39:562-71.
9. Lara PN, Jr., Paterniti DA, Chiechi C, et al. Evaluation of factors affecting awareness of and willingness to participate in cancer clinical trials. J Clin Oncol 2005;23:9282-9.
10. Joshi V, Kulkarni AA. Public awareness of clinical trials: A qualitative pilot study in Pune. Perspect Clin Res 2012;3:125-32.
11. Miller S, Hudson S, Egleston B, et al. The relationships among knowledge, self-efficacy, preparedness, decisional conflict and decisions to participate in a cancer clinical trial. Psychooncology 2013;22: 481–9.
12. Denicoff AM, McCaskill-Stevens W, Grubbs SS, et al. The National Cancer Institute-American Society of Clinical Oncology Cancer Trial Accrual Symposium: summary and recommendations. J Oncol Pract 2013;9:267-76.
13. Trantham LC, Carpenter WR, DiMartino LD, et al. Perceptions of Cancer Clinical Research Among African American Men in North Carolina. J Natl Med Assoc 2015;107:33-41.
14. Featherstone K, Donovan JL. "Why don't they just tell me straight, why allocate it?" The struggle to make sense of participating in a randomised controlled trial. Soc Sci Med 2002;55:709-19.
15. Jamjoom AB, Jamjoom AM, Samman AM, Gahtani AY. Fate of registered clinical trials performed in Saudi Arabia. Saudi Med J 2015;36:1245-8.

16. Bazarbashi S, Hassan A, Eldin AM, Soudy H, Hussain F. Awareness and Perceptions of Clinical Trials in Cancer Patients and Their Families in Saudi Arabia. J Cancer Educ 2015;30:655-9.
17. Sheblaq NR, Traifi S, Sakiani MA, Gasmelseed A, Abolfotouh MA, Jazieh AR. Awareness and attitude of cancer patients about participation in clinical research (CR) in Saudi Arabia. J Clin Oncol 2013;(suppl; abstr e17528).
18. Al-Tannir MA, El-Bakri N, Abu-Shaheen AK. Knowledge, Attitudes and Perceptions of Saudis towards Participating in Clinical Trials. PLoS One 2016;11:e0143893.
19. Al-Dakhil LO, Alanazy R, Al-Hamed RE, Al-Mandeel H, Alobaid A. Attitudes of Patients in Developing Countries Toward Participating in Clinical Trials: A Survey of Saudi Patients Attending Primary Health Care Services. Oman Med J 2016;31:284-9.
20. Almutairi KM, Alonazi WB, Alodhayani AA, et al. Barriers to Cancer Clinical Trial Participation Among Saudi Nationals: A Cross-Sectional Study. J Relig Health 2017;56:623-34.
21. The Central Department of Statistics and Information 2016. (Accessed 24/04/2017, 2017, at https://www.stats.gov.sa/sites/default/files/en-demographic-research-2016_4.pdf.)
22. Abdullahi A, Hassan A, Kadarman N, Saleh A, Baraya YuSa, Lua PL. Food safety knowledge, attitude, and practice toward compliance with abattoir laws among the abattoir workers in Malaysia. International journal of general medicine 2016;9:79-87.
23. Nur Ain M, Azfar M, Omarulharis S, et al. Knowledge, Attitude And Practice Of Dengue Prevention Among Sub Urban Community In Sepang, Selangor. International Journal of Public Health and Clinical Sciences 2017;4:73-83.
24. Malhotra V, Kaura S, Sharma H. Knowledge, attitude and practices about hepatitis B and Infection Control Measures among dental students in Patiala. Journal of Dental and Allied Sciences 2017;6:65-9.
25. Choi YJ, Beck SH, Kang WY, et al. Knowledge and Perception about Clinical Research Shapes Behavior: Face to Face Survey in Korean General Public. J Korean Med Sci 2016;31:674-81.
26. Nasef N, Shabaan A, Mohammed S, et al. Factors influencing parental consent for participation in clinical research involving their children in Egypt. East Mediterr Health J 2014;20:162-8.
27. Nabulsi M, Khalil Y, Makhoul J. Parental attitudes towards and perceptions of their children's participation in clinical research: a developing-country perspective. J Med Ethics 2011;37:420-3.
28. Elliott C, Abadie R. Exploiting a research underclass in phase 1 clinical trials. N Engl J Med 2008;358:2316-7.
29. Davis MM, Clark SJ, Butchart AT, Singer DC, Shanley TP, Gipson DS. Public participation in, and awareness about, medical research opportunities in the era of clinical and translational research. Clin Transl Sci 2013;6:88-93.
30. Advani AS, Atkeson B, Brown CL, et al. Barriers to the participation of African-American patients with cancer in clinical trials: a pilot study. Cancer 2003;97:1499-506.
31. Comis RL, Miller JD, Aldige CR, Krebs L, Stoval E. Public attitudes toward participation in cancer clinical trials. J Clin Oncol 2003;21:830-5.
32. Joshi VD, Oka GA, Kulkarni AA, Bivalkar VV. Public awareness and perception of clinical trials: Quantitative study in Pune. Perspect Clin Res 2013;4:169-74.
33. Ohmann C, Deimling A. Attitude towards clinical trials: results of a survey of persons interested in research. Inflamm Res 2004;53 Suppl 2:S142-7.

Table 1. Characteristics of the study participants and the unadjusted prectors for knowledge and attitudes

		Overall *N* = 938		Knowledge Overall mean = 56.8 ± 24.8			Attitudes Overall mean = 61.5 ± 28.0		
Characteristics	*Group*	*N*	%	Mean	s.d.	*P*	Mean	s.d.	*P*
Gender	*Male*	577	61.6	51.37	24.4		57.40	28.0	
	Female	360	38.4	65.62	22.9	0.001*	67.90	26.8	0.001*
Age	*18–30*	508	54.2	55.45	26.0		59.36	28.2	
	31– 40	259	27.6	60.07	23.2		63.28	27.8	
	41–60	153	16.3	58.17	22.0		66.67	26.0	
	61+	18	1.9	37.50	22.7	0.001*	50.62	34.1	0.007*
Education	*Not educated*	27	2.9	35.19	18.0		46.09	29.8	
	High school or less	347	37.0	48.37	22.7		57.25	28.0	
	University, college or more	563	60.1	63.06	24.2	0.001*	64.81	27.3	0.001*
Monthly income	• *No income*	195	20.8	49.62	22.7		57.78	28.5	
	• *Less than 5,000 SAR* • *Less than 1,300 USD*	280	29.9	56.13	26.1		62.02	27.2	
	• *5,001 to 10,000 SAR* • *1,301 to 2,700 USD*	234	25.0	56.73	23.0		60.64	28.2	
	• *SAR 10,001 to 15,000* • *USD 2,701 to 4,000*	148	15.8	61.43	24.2		63.74	28.0	
	• *More than 15,000 SAR* • *More than 4,000 USD*	79	8.5	68.88	25.3	0.001*	67.37	27.9	0.084
Nationality	*Saudi*	817	87.3	57.27	24.6		62.10	27.7	
	Non-Saudi	119	12.7	53.71	25.8	0.143	57.52	29.4	0.095
Residency	*Central region*	707	75.4	59.21	24.4		62.93	28.5	
	Western region	86	9.2	52.52	27.6		59.04	28.3	
	Northern region	59	6.3	46.19	25.0		53.48	25.1	
	Southern region	60	6.4	49.31	20.7		57.04	22.5	
	Eastern region	26	2.8	47.76	21.3	0.001*	58.12	26.9	0.055
Marital Status	*Single*	455	48.7	56.06	26.7		60.59	28.3	
	Married	444	47.5	57.04	22.8		61.61	27.5	
	Other	35	3.8	60.48	22.1	0.549	70.48	28.8	0.130
Employment	*Student in school*	78	8.3	47.54	24.0		56.13	27.4	
	Undergraduate student/ university or college	166	17.8	63.15	26.0		65.66	25.6	
	Government sector	235	25.0	61.70	24.1		64.68	28.1	
	Private sector	208	22.2	56.29	25.4		59.56	28.0	
	Military	54	5.7	52.16	23.2		55.76	30.6	
	Private work/ owener	61	6.8	50.68	22.5		56.65	31.1	
	Retired	26	2.7	51.92	21.9		65.38	31.5	
	Not working	62	6.6	44.49	21.7		57.17	26.3	
	Housewife	47	4.9	59.22	18.9	0.001*	64.30	26.2	0.028*
Health insurance	*Governmental*	560	59.7	58.23	25.2		64.09	27.4	
	Private	116	12.4	58.41	25.0		58.43	30.1	
	Other	226	24.1	55.20	22.5		58.46	27.4	
	No insurance	36	3.8	40.05	24.9	0.001*	49.38	28.8	0.001*
Chronic disease	*Yes*	208	22.2	53.21	23.7		59.19	27.7	
	No	730	77.8	57.85	25.0		62.12	28.0	0.183
Medical background	*Yes*	259	27.7	65.99	26.6	0.017*	67.35	27.5	
	No	677	72.3	53.37	23.1	0.001*	59.23	27.9	0.001*
Previous medical research participation	*Yes*	149	15.9	65.83	25.8		66.44	27.6	
	Was requested, but didn't participate	11	1.1	50.00	22.4		63.64	27.3	
	No	737	78.6	55.54	24.3		60.65	28.1	
	Not sure	41	4.4	48.98	22.3	0.001*	57.45	26.0	0.001*
Do you know somebody who has participated in medical research?	*Yes*	248	26.5	60.42	24.6		62.23	27.6	
	No	596	63.6	57.30	24.6		62.99	27.8	
	Not sure	93	9.9	44.18	23.1	0.001*	49.46	27.7	0.100

* Significant at α = 0.05.

Table 2. Participants' responses to the knowledge questions

Variables	*N* (% of participants)
Have you heard about clinical trials before?	
Yes	289 (30.8)
No/not sure	648 (69.1)
What is the definition of a clinical trial?	
Studies in clinics to survey patients opinion about health care topics	139 (14.8)
Experiments on animals	119 (12.7)
Studies to test new drugs or procedure on humans	410 (43.7)
Graduation projects for medical students	62 (6.6)
Not sure	208 (22.2)
Have you heard about an IRB before?	
Yes	251 (26.8)
No	685 (73.1)
Have you heard of the SFDA before?	
Yes	761 (81.1)
No	177 (18.9)
Does the SFDA have a role in regulating clinical trials?	
Yes	622 (66.4)
No	315 (33.6)
Is there an ethical guidelines to regulate the conduction of clinical trials?	
Yes	673 (71.8)
No	265 (28.3)
Are there a direct benefits for participants to conduct Clinical Trials?	
Definitely	313 (33.4)
Definitely not	35 (3.7)
No benefit or harm	19 (2.0)
Possible benefit or harm	436 (46.5)
Not sure	135 (14.4)
Are there a direct benefits for community to conduct Clinical Trials?	
Yes	676 (72.1)
No	262 (27.9)
When can an investigator start clinical trials?	
Any time they want	42 (4.5)
Only with participant agreement	135 (14.4)
After obtaining manager approval	41 (4.4)
They should obtain approvals from responsible authorities	525 (56.0)
Not sure	195 (20.8)
Can an investigator recruit patients without their approval?	
Yes	250 (26.7)
No	687 (73.3)
Can participants freely withdraw from clinical trials anytime?	
Yes	446 (47.6)
No	492 (52.5)
May published articles include confidential patient information (e.g., names)?	
Yes	318 (33.9)
No	620 (66.1)
Knowledge score out of 100 (12 questions)	**56.8 ± 24.8**

IRB: Institutional Review Board; SFDA: Saudi Food Drug Authority

Table 3. Participants' responses to the attitudes questions

Variables	*n* (%)
Do you agree with testing new drugs in patients?	
Yes	558 (59.5)
No/not sure	380 (40.5)
Do you agree with testing approved drugs in patients?	
Yes	593 (63.2)
No/not sure	345 (36.8)
Do you agree with testing new drugs in healthy volunteers?	
Yes	286 (30.5)
No/not sure	651(69.5)
Do you agree with testing new drugs in pediatric patients?	
Yes	452 (48.2)
No/not sure	485 (51.8)
Do you agree with testing approved drugs in pediatric patients?	
Yes	528 (56.4)
No/not sure	409 (43.7)
Do you agree with participating/having a family member participate in clinical trials?	
Yes	252 (26.9)
Possibly	395 (42.2)
No/not sure	290 (31.0)
What is your perception regarding clinical trials?	
Not important	41(4.4)
Very important for drug development	682 (72.7)
Important only for pharmaceutical companies to earn money	54 (5.8)
Not sure	161(17.2)
Are you willing to learn about clinical trials?	
Yes	814 (86.8)
No	124 (13.2)
Do you trust research teams?	
Yes	629 (67.1)
No/not sure	309 (32.9)
Attitude score out of 100 (9 questions)	**61.5 ± 28.0**

Table 4. Independent predictors of the Saudi public knowledge and attitudes toward clinical trials

		Knowledge				Attitudes		
		95% Wald CI				95% Wald CI		
Characteristics	B	Lower	Upper	*P*	B	Lower	Upper	*P*
(Intercept)	48.2	26.83	69.48	0.001*	57.4	30.72	84.01	0.001*
Gender (reference: female)								
Male	–14.1	–17.49	–10.65	0.001*	–9.2	–13.42	–4.88	0.001*
Age (reference: 61+)								
18–30	9.2	–2.86	21.31	0.135	–0.8	–15.87	14.33	0.920
31–40	11.2	–0.56	22.92	0.062	3.7	–10.98	18.34	0.623
41–60	12.1	0.80	23.44	0.036*	10.6	–3.55	24.73	0.142
Education (reference: University, college or more)								
Not educated	–19.6	–29.64	–9.66	0.001*	–18.4	–30.88	–5.92	0.004*
High school or less	–8.2	–12.10	–4.37	0.001*	–5.1	–9.94	–0.29	0.038*
Monthly income (reference: SR 15,000 or more)								
No income	–9.7	–17.17	–2.19	0.011*	–1.0	–10.38	8.34	0.831
SR 5,000 or less	–9.1	–15.48	–2.79	0.005*	0.4	–7.50	8.35	0.916
SR 6,000 to SR 10,000	–6.9	–12.71	–1.00	0.022*	0.0	–7.36	7.28	0.992
SR 11,000 to SR 15,000	–3.6	–9.65	2.38	0.236	1.2	–6.28	8.73	0.749
Nationality (reference: non-Saudi)								
Saudi	–1.6	–6.80	3.63	0.552	1.0	–5.52	7.51	0.764
Residency (reference: Eastern region)								
Central region	3.6	–4.94	12.05	0.412	–0.5	–11.14	10.08	0.922
Western region	1.9	–7.60	11.39	0.696	–0.9	–12.73	11.00	0.886
Northern region	–10.8	–20.77	–0.76	0.035*	–12.7	–25.19	–0.20	0.046*
Southern region	–1.1	–10.89	8.76	0.832	–5.3	–17.61	6.93	0.393
Marital Status (reference: other)								
Single	1.4	–6.94	9.81	0.736	–3.1	–13.55	7.37	0.563
Married	0.9	–6.80	8.67	0.813	–4.5	–14.17	5.15	0.360
Employment (reference: housewife)								
Student	–5.1	–14.08	3.97	0.272	2.1	–9.21	13.34	0.719
Undergraduate student	0.2	–8.60	8.99	0.965	3.7	–7.26	14.71	0.506
Government sector	–3.0	–11.56	5.55	0.491	1.0	–9.70	11.67	0.857
Private sector	–5.1	–13.65	3.51	0.247	–1.0	–11.75	9.69	0.850
Military	–10.3	–20.56	–0.03	0.049*	–0.9	–13.75	11.89	0.887
Private work	–6.4	–15.54	2.72	0.169	–2.8	–14.18	8.64	0.634
Retired	–0.3	–11.73	11.19	0.963	8.5	–5.86	22.76	0.247
Not working	–5.2	–14.01	3.53	0.241	3.5	–7.45	14.45	0.531
Health insurance (reference: no insurance)								
Governmental	12.9	4.48	21.33	0.003*	10.1	–0.45	20.60	0.061
Private	16.5	7.06	25.95	0.001*	4.4	–7.42	16.18	0.467
Other	12.8	4.49	21.08	0.003*	7.9	–2.50	18.22	0.137
Chronic diseases (reference: yes)								
No	–2.2	–5.75	1.27	0.211	–3.5	–7.91	0.87	0.116
Medical background (reference: yes)								
No	–4.7	–8.47	–0.90	0.015*	–5.0	–9.70	–0.24	0.039*
Participated in medical research (reference: no)								
Yes	6.0	–1.78	13.77	0.131	1.7	–8.04	11.38	0.736
Knows somebody who participated in medical research (reference: no)								

Yes	12.3	7.07	17.55	0.001*	10.4	3.88	16.97	0.002*

*Significant at α = 0.05. CI, confidence interval.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*9*
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	10
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11

		(*b*) Report category boundaries when continuous variables were categorized	11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	2

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Knowledge of and Attitudes toward Clinical Trials in Saudi Arabia: A Cross-sectional study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-031305.R1
Article Type:	Original research
Date Submitted by the Author:	29-Jul-2019
Complete List of Authors:	Al Rawashdeh, Nedal ; King Abdullah International Medical Research Center, Research Office; King Hussein Cancer Center, The Office of Scientific Affairs and Research Damsees, Rana ; King Abdullah International Medical Research Center, Research Office; King Hussein Cancer Center, The Office of Scientific Affairs and Research Al-Jeraisy, Majed ; King Abdullah International Medical Research Center, Research Office; King Saud bin Abdulaziz University for Health Sciences Al Qasim, Eman ; King Abdullah International Medical Research Center, Research Office; King Saud bin Abdulaziz University for Health Sciences Deeb, Ahmad; King Abdullah International Medical Research Center, Research Office; King Saud bin Abdulaziz University for Health Sciences
Primary Subject Heading:	Public health
Secondary Subject Heading:	Public health, Research methods
Keywords:	Knowledge, Attitudes, Clinical trials < THERAPEUTICS

Knowledge of and Attitudes toward Clinical Trials in Saudi Arabia: A Cross-sectional study

Nedal Al-Rawashdeh[1,2], Rana Damsees[1,2], Majed Al Jeraisy[1], Eman Al Qasim[1], Ahmad M. Deeb[1]*

1. Research Office, King Abdullah International Medical Research Center, Riyadh, Saudi Arabia; King Saud bin Abdulaziz University for Health Sciences, Riyadh Saudi Arabia; Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia.
2. The Office of Scientific Affairs and Research, King Hussein Cancer Center, Amman, Jordan

Nedal Al-Rawashdeh: rawashdehne@gmail.com

Rana Damsees: rdamsees@gmail.com

Majed Al Jeraisy: JeraisyM@NGHA.MED.SA

Eman Al Qasim: alqasimem@NGHA.MED.SA

Ahmad M. Deeb: rn_a_deeb@hotmail.com

* **Corresponding Author**

Ahmad M. Deeb, RN, MSN, CCRC®

Senior Clinical Research Coordinator
Research Office
King Abdullah International Medical Research Center
King Saud Bin Abdulaziz University for Health Sciences
King Abdulaziz Medical City
Ministry of National Guard - Health Affairs
PO Box 22490, Mail Code 1515
Riyadh 11426, Kingdom of Saudi Arabia
Tel. No: +966118011111 ext. 18950
Monile: +966547883491
rn_a_deeb@hotmail.com

Short title: Knowledge & Attitude toward Clinical Trials

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board (IRB) at King Abdulaziz Medical City, Riyadh, KSA.

Consent for publication

Not applicable

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests.

Funding

This study was supported by research grant RC16/010/R by King Abdullah International Medical Research Center. The study sponsor does not have any role in the study design, management, analysis, interpretation of the data, or in writing the manuscript.

Author contributions statement

Ahmad Deeb and Nedal Al Rawashdeh: Conception and design, data acquisition, data collection, analytical plan, drafting of the manuscript. Rana Damsees: Conception and design and data acquisition. Majed Al Jeraisy: Conception and design, data acquisition and supervision. Eman Al Qasim: Conception and design and data collection. All authors critically revised the manuscript for important intellectual content, and approved of the final version to be published and agreed to be accountable for all aspects of the work.

Acknowledgements

Not applicable

Abstract

Objectives: Clinical trials (CTs) are considered one of the important methods for developing new treatments and providing access to new potentially effective drugs that are still under investigation. Measuring the public's knowledge of and attitudes toward CTs is important to assessing the public's readiness and acceptance of testing drugs on human participants, which hasn't previously been assessed in the Kingdom of Saudi Arabia (KSA). The objective of this study is to explore the Saudi public's knowledge of and attitudes toward CTs as well as participation in trials to test new or approved drugs.

Design: Cross-sectional.

Setting: Al Jenadriyah cultural/heritage festival in Riyadh/KSA.

Participants: A structured questionnaire was developed and distributed during the 2016 Al Jenadriyah cultural/heritage festival, using a convenience sampling approach. Participating booths, exhibition halls and visitors in the festival were approached to participate in the study. The responses were converted to a percentage mean score (out of 100) for each knowledge related response and attitude.

Primary and secondary outcome measures: Knowledge and attitudes toward CTs.

Results: The sample realized as 938 (n=938). The total mean knowledge score was 56.8 ±24.8 and the attitude related score was 61.5±28.0. Although most of the participants supported testing approved or off-label and new drugs on adult and pediatric patients, only a third 30.5% agreed that new drugs could be tested on healthy volunteers. The results indicated that gender,

educational-level, income, medical background, age-group and health insurance were independent predictors of the level of Knowledge of CTs. In terms of attitudes toward CTs, the independent predictors were gender, educational-level and medical background.

Conclusion: The Saudi public has a low level of knowledge and a moderately positive attitude toward CTs. There is a moderate positive correlation between the two factors as knowledge of CTs increases, the Saudi public will become more positive toward CTs.

Strength and limitations of the study

- The knowledge and attitudes of the Saudi public toward CTs are under-researched.
- This is the first study to explore the Saudi public's knowledge and attitudes in terms of the different phases of CTs in adult and pediatric populations.
- The main limitation is possible selection bias due to employing a convenience sampling method.

Introduction

A clinical trial (CT) is a superior research tool for advancing medical knowledge and practice, as the results are considered to provide the highest level of evidence for medical practice and decision-making.[1] Volunteer participation is at the core of a successful CT. The participation of an adequate number of study participants is crucial in achieving the study's objectives, namely testing the hypothesis and answering the research questions. Failure to recruit an adequate number of participants could result in wasted time, money, and effort.[2] It may also delay the acceptance of the trial results as well as the completion of the drug development process.

Knowledge of and attitudes toward CTs are considered as major challenges for participant recruitment.[3-6] Several studies reported that knowledge of CTs and attitudes toward participation are interrelated [7-11] as increased knowledge promotes a positive attitude toward CT participation. Low recruitment rates for CTs may be improved through increasing the public's knowledge about CTs [6,9,11] and by highlighting the social responsibility perspective of how participation can contribute to the improvement of CTs.[12,13] Improving the public's knowledge of CTs represents an important initial step in improving CT recruitment in the future.[9,12,14]

In the Kingdom of Saudi Arabia (KSA), clinical research has advanced during the last few decades.[15] KSA researchers have contributed to medical literature in conducting different types of research, including investigator-initiated CTs and international multicenter-sponsored CTs.[15] Measuring the knowledge and attitudes of the Saudi public toward CTs is crucial to assess their readiness and acceptance of CTs in Saudi Arabia and to provide an evidence-base to improve CT

recruitment and decision-making processes. In addition, it will provide reliable information for researchers and healthcare leaders for strategic planning of public engagement in CT awareness campaigns. From the public's perspective, these efforts may be beneficial through increasing their knowledge and awareness of CTs, improved medical knowledge through updates of CT results, and sharing of public preferences for future CTs.

Several studies have reported the knowledge and attitudes of patients, or families, toward CTs in health care settings in Saudi Arabia [16-20]; however, studies measuring the knowledge and attitudes of the Saudi public in general are lacking. The purpose of this study was to assess the Saudi public's knowledge of and attitudes toward CTs in general and more specifically, the attitudes toward participation in CTs for drug development.

The study addressed the following four questions: What does the Saudi public know about CTs? What is the attitude of individuals in Saudi Arabia toward CTs and toward participation in CTs? Is there a correlation between the level of public knowledge and the attitudes of individuals in Saudi Arabia toward CTs? What factors can be predictive of the levels of public knowledge and attitudes toward CTs in the Saudi population?

Materials and Methods

Setting

This cross-sectional study was conducted between February 2 and February 19, 2016 at the Al Jenadriyah Cultural and Heritage Festival. The festival takes place in Riyadh and hosts millions of residents and visitors from the different regions in the country. We selected this event as it provided us with a unique chance to interview a representative cross-section from all regions

of KSA. The study was approved by the Institutional Review Board (IRB) at King Abdulaziz Medical City, Riyadh, KSA.

Study participants

The study included adults of both genders who were willing to participate. A convenience sampling approach was used. Participating booths and exhibition halls in the festival were approached and festival visitors were invited to participate in the study. All of the participants gave informed consent by checking the YES box indicating their willingness to complete the questionnaire. Participants did not receive any compensation for participation in the study.

Patient and public involvement

The public was not included in the development of the research questions or the design of the study. However, the questionnaire was pre-tested with a different sample of the general public before implementation.

Sample size

The population of KSA is approximately 31,742,308 (Central Department of Statistics and Information), including 11,677,338 expatriates (Non-Saudi).[21] On the basis of this population estimate, a 0.05 margin of error, a 95% confidence level, and a response rate of 50%, the minimum sample size calculated for this study was 385. We increased our sample to 1000 to reduce the sampling errors and variability between the characteristics of the sample and the Saudi general population.

.

Data collection

A structured questionnaire was developed in Arabic. The questionnaire was divided in three sections: demographic information, knowledge and attitude.

The following variables were included in the demographic information section: gender, age, educational level, monthly income, nationality, residential area, employment status, marital status, health insurance, chronic diseases, medical background (working in a healthcare facility or having health-related education), and previous participation in medical research.

The knowledge section was composed of 12 questions, and the participant's responses were scored as correct (score = 1) or incorrect/not sure (score = 0). The total knowledge score was converted to a percentage mean score with a possible maximum value of 100, a score of 100 indicates perfect knowledge of CTs.

The attitude section was composed of nine direct questions, and participant answers were scored as positive (score = 1) or negative/not sure (score = 0). The total attitude score was converted to a percentage mean score with a possible maximum value of 100, a score of 100 indicates a positive attitude toward CTs.

Based on previous studies, the overall level of knowledge and attitude was classified in three levels following Bloom's cut-off point criteria: above 80% (High level), 60-79% (Moderate level), less than 60% (Low level). [22-24]

We ensured that the language used for the questions was clear and understandable to enable the participants to answer the questions, even if they were not aware of CTs. The

questionnaire was validated using content validity. A panel of expert analysts was used to evaluate the questions and they rated each question as essential, useful or irrelevant in the context of measuring knowledge and attitudes. It was pre-tested using a sample of 28 participants. The result of the pre-test was that complex scientific terms were simplified. Reliability was tested by calculating the Cronbach alpha for the pre-test sample for both the knowledge and attitude sections (21 items). The Cronbach alpha score was 0.81.

Data analysis

The categorical variables are represented as frequency and percentage and the continuous variables as mean ± standard deviation (s.d.). Normality was tested by the skewness coefficient, which indicated that the knowledge and attitude data were normally distributed. The Student's *t*-test and one-way analysis of variance (ANOVA) were used as tests of significance. The Pearson correlation coefficient was used to calculate the correlation between the knowledge and attitude scores. A generalized linear model was used to determine the independent predictors of knowledge and attitudes toward CTs. In this models, we controlled for gender, age, education, monthly income, nationality, residency, marital status, employment, health insurance, chronic disease, medical background, previous medical research participation and medical research participation of someone close. All calculations were performed using the Statistical Package for the Social Sciences (version 23; SPSS Inc., Chicago, IL, USA).

Results

Participant characteristics

A total of 1,084 members of the public were approached to participate in the study. In total, 938 (86.5%) agreed to complete the questionnaire with one missing value in the gender and nationality variables. Of the 938 participants, males were predominant (61.6%). The age groups with the highest representation were the 18-30 years (54.2%) and 31-40 years (27.6%). The majority of the participants (60.1%) reported achieving a tertiary educational level and 75.7% reported a monthly income of less than 10,000 SAR (Saudi Arabian Riyal) which is equivalent to approximately 2,700 USD (United States Dollar). Approximately half of the participants were single (48.7%), and 22.2% indicated being diagnosed with a chronic disease. Just more than a quarter (27.7%) of the sample had a medical background (working in a healthcare facility or having health-related education). A small group (15.9%) declared that they already participated in medical research, and 26.5% knew someone who participated in medical research in the past (**Table 1**).

Knowledge about clinical trials in Saudi Arabia

The overall percentage mean score ±SD for knowledge regarding CTs was 56.8 ±24.8. Although some participants were not aware of the term 'clinical trial', almost half (43.7%) could define the concept correctly. Most of the participants (71.8%) agreed that CTs are subject to ethical guidelines, but only 26.8% were aware of the concept of an institutional review board (**Table 2)**. The majority (81.1%) was aware of the Saudi Food and Drug Authority (SFDA), and 66.4% were aware of their role in the regulation of CTs. Most of the participants (72.1%) agreed

that CTs benefit the community, and 46.5% responded correctly regarding the benefits of CTs for the study participants. Approximately half of the sample knew the time that investigators can initiate a CT (56.0%) as well as the right of CT participants to withdraw from (47.6%) from a study. Other findings from the knowledge section of the questionnaire are listed in **Table 2**.

Attitudes toward clinical trials in Saudi Arabia

The overall percentage mean score ±SD for Saudi attitudes toward CTs was 61.5 ±28.0 out of a 100 score. Most of the participants (59.5%) had a positive attitude toward testing new drugs with adult patients in Saudi Arabia, and 63.2% were positive about testing approved/off-label drugs (approved and marketed drug for other indication) using patients. However, only 30.5% of the participants were positive about conducting CTs using healthy volunteers (Phase I). The attitudes were similar for pediatric CTs, as 48.2% and 56.4% agreed with testing new drugs or approved/off-label drugs on pediatric patients, respectively. The majority of the participants (72.7%) agreed that CTs were important in terms of drug development, and 69.1% confirmed the possibility of participating in a CT should the opportunity arise to them or a close family member. The majority of the participants (86.8%) indicated a willingness to learn more about CTs. Other findings from the attitude section of the questionnaire are listed in **Table 3**.

Factors associated with increased knowledge and more positive attitudes toward clinical trials

The univariate analysis revealed that females had a higher level of knowledge about CTs than males. In addition, the 31-40 years age group had the highest level of knowledge compared to other age categories (**Table 1**). Clinical trial related knowledge increased with an increased

level of education (*P*=0.001) as well as an increased monthly income (*P*=0.001). Participants from the Central Region of KSA had a higher level knowledge compared to other regions (*P*=0.001) (**Table 1**). Undergraduate students and governmental employees had a higher level of knowledge compared to other employment categories (*P*=0.001) (**Table 1**). Having governmental or private health insurance (*P*=0.001) was associated with a higher level of CT related knowledge. Noteworthy is that participants without chronic diseases had a higher level of knowledge than those with chronic diseases (*P*=0.017). Previous participation in medical research or knowing someone who participated in the past was associated with better CT related knowledge (*P*=0.001) (**Table 1**).

After adjusting for possible confounders, males beta coefficients (B= –14.1; *P*=0.001), non-educated participants (B= –19.6; *P*=0.001), participants with no income (B= –9.7; *P*=0.011), and no medical background (B= –4.7; *P*=0.015) had significantly lower knowledge scores. By contrast, participants in the 41-60 years age (B = 12.1; *P*=0.036) and having health insurance (B= 12.9; *P*=0.003) were more knowledgeable regarding CTs (**Table 4**).

In terms of attitudes, females were more positive toward CTs (*P*= 0.001) than males. The 31-40 years and 41-60 years age groups were more positive compared to other age categories (*P*=0.007), having a higher educational level is also associated with a more positive attitude (*P*=0.001) (**Table 1**). As with the knowledge section, undergraduate students and governmental employees were more positive toward CTs (*P*= 0.028) than participants in other employment categories (**Table 1**) as well as having governmental or private health insurance (*P*=0.001). Participants with a medical background or who had previously participated in medical research

tended to be more positive (*P*=0.001) compared to participants with no medical background or who had never participated in medical research (**Table 1**).

After adjusting for the possible confounders, being male (B= –9.2; *P*=0.001), uneducated (B= –18.4, *P*=0.004), or not having a medical background (B= –5.0; *P*=0.039), were associated with more a negative attitudes toward CTs (**Table 4**).

Correlation between Saudi public's knowledge and attitudes toward clinical trials

Our results indicated a moderately positive relationship between the Saudi public's knowledge and attitudes toward CTs (Pearson's *r*= 0.564, *P*=0.0001). Therefore, we predict that as knowledge of CTs increases, the Saudi public will become more positive toward CTs.

Discussion

This public survey revealed a general lack of knowledge regarding CTs. Most of the participants could not identify or correctly define the term 'clinical trial'. Although most of the Saudi public is aware of their right to voluntarily participate in CTs, they were not aware of their right to withdraw from CTs. The current study is supported with similar findings in studies conducted in healthcare settings (with patients and/or their families) within Saudi Arabia.[17-20] The reason may possibly be interpreted as the lack of institutional and national campaigns promoting CTs. [5,25]

Although most of the participants agreed that CTs are controlled by ethical principles, they were not aware of an IRB and its role in protecting human participants. In a study done in a healthcare setting, Sheblaq et al. reported that the majority of the patients diagnosed with cancer was not aware of the role of the IRB.[17] The public tends to trust authorities to protect them even though they do not know who are responsible for playing this role. We observed this phenomenon repeatedly when participants answered positively to questions regarding their trust in the study team and in their compliance with regulatory guidelines when initiating a trial or recruiting participants. The Saudi public recognized the SFDA and its role in CTs, most likely due to their well-known food and drug related regulatory activities in Saudi Arabia.

The overall level of attitude of the Saudi public toward participation in CTs was Moderately Positive. The Saudi public agrees that CTs may provide benefits for society as a whole and the participants. In addition, trust in the study team may explain the favorable attitude toward participation in CTs. It could be argued that participant responses may change in real-life situations such as in healthcare settings. However, our results were consistent with other studies conducted in health care settings in Saudi Arabia investigating the opinions of patients and families regarding participation in CTs.[16-18]

Similarly, but to a lesser degree, the Saudi public agreed with the idea of conducting pediatric CTs for approved/off-label drugs. However, only 48% of the participants indicated that it was acceptable to test new drugs in pediatric participants. Objection to the use of new drugs or vaccines was one of the factors underlying the opposition to pediatric CTs [26]. Although the study did not explore the reasons underpinning the motivation to participate in CTs, we believe that the fear of adverse events, as well as safety concerns, may explain this objection.[25,27]

Phase I CTs, which involve testing new drugs in healthy volunteers, are important in the process of drug development. However, several ethical dilemmas influence conducting such studies with healthy volunteers and patients.[28] In our study, the Saudi public was negative regarding testing new drugs on healthy volunteers. Only 30.5% of the participants agreed with the idea of conducting CTs on healthy volunteers in Saudi Arabia. This sentiment may be related to the lack of knowledge regarding the purpose of testing new drugs on healthy volunteers. Conducting public educational campaigns about CTs in Saudi Arabia is pivotal to improve their knowledge and awareness about CTs.

Consistent with other studies [9,11], participants' attitudes toward CTs were markedly dependent on their knowledge of CTs. We predict that as knowledge about CTs increases, the Saudi public will become more positive. A low level of knowledge regarding CTs may indicate misunderstanding or confusion regarding the purposes of the different phases of CTs. In turn, participants' answers may have been affected by insufficient knowledge. We believe that many participants used their common sense to answer some survey questions and may have begun to recognize the meaning of CTs while answering further questions. These observations support the need for CT related public educational campaigns, since the majority of the participants were interested to learn more about CTs.

Male gender, lower education, lack of a medical background, lower monthly income, a lower age group, and lack of health insurance were independent predictors of a low level of knowledge regarding CTs among the Saudi public. Male gender, less education and lack of a medical background were independent predictors of a negative attitude toward CTs. Our results are consistent with a United States household survey conducted to assess the level of

public participation in and awareness of clinical and translational research, higher levels of income and education were associated with better participation and awareness.[29] In a study conducted with patients diagnosed with cancer in a healthcare setting, a lower level of education and income, as well as race and ethnicity, were associated with decreased awareness of CTs [9]. Similarly, lower income and education were associated with a reduced willingness to participate in CTs in African-American patients diagnosed with cancer [30]. A study of patients with cancer in Saudi Arabia found that higher education was the only significant predictor of trial participation.[17]

Unlike other studies with the public or in healthcare settings [5,9,25,31-33], gender was an independent predictor of knowledge and attitudes. Males were associated with a lower level of knowledge and with a more negative attitude toward CTs. The underlying rationale has not been clearly discussed in literature. Gender differences regarding knowledge and attitudes toward CTs should be considered for future studies.

In the previous studies investigating knowledge and attitudes toward CTs in Saudi Arabia, the sample size was much smaller and mainly involved patients and/or their families in healthcare settings.[17,18] To our knowledge, this is the first study exploring the Saudi public's knowledge and attitudes toward CTs, external of a healthcare setting. Furthermore, it is the first study to solicit public perspectives regarding the different phases of CTs conducted in adult and pediatric populations.

Conclusion

The Saudi public has a low level of knowledge and moderately positive attitudes toward CTs. Increasing the Saudi public's knowledge may contribute to positive attitudes toward

participation in and support of CTs; supporting our proposition of educational campaigns to increase awareness and knowledge of CTs. These campaigns should target the less knowledgeable sub-groups identified in the study and focus on the importance of evaluating new drugs on healthy volunteers (Phase I clinical trials). In addition, our results support conducting and investing in CTs in KSA. Conducting similar studies in the future, taking the limitations of this study in consideration, may facilitate measuring the improvement of knowledge over time. We also recommend in-depth qualitative and focus-group-based studies for a deeper understanding of participant perspectives.

Study limitations

The main limitation in this study is related to possible selection bias due to using a convenient sampling method; however the effect of the limitation may have been minimized by the large sample size and the diversity of the visitors. For example, in our sample the distribution of male gender 61.6% was slightly larger than in general population while in the age group 31 to 40 it was 27.6% which is slightly lower.

Abbreviations

ANOVA: Analysis of variance

CTs: Clinical Trials

IRB: Institutional review board

KSA: Kingdom of Saudi Arabia

SAR: Saudi Arabian Riyal

S.D: Standard Deviation

SFDA: Saudi Food and Drug Authority

USD: United States Dollar

References

1. Oxford Centre for Evidence-based Medicine – Levels of Evidence. 2009. 2017, at http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/.)
2. Wyse RK. Accelerating patient recruitment in clinical trials: in-depth report from the SMi 2nd annual conference In: Ross C, editor. The SMi 2nd annual conference 2006; London: NetworkPharma Ltd.
3. Verheggen FW, Nieman FH, Reerink E, Kok GJ. Patient satisfaction with clinical trial participation. Int J Qual Health Care 1998;10:319-30.
4. Public Engagement and Clinical Trials: New Models and Disruptive Technologies: Workshop Summary. Washington (DC)2012.
5. Leiter A, Diefenbach MA, Doucette J, Oh WK, Galsky MD. Clinical trial awareness: Changes over time and sociodemographic disparities. Clin Trials 2015;12:215-23.
6. The Need for Awareness of Clinical Research. National Institute of Health, 2016. 2017, at https://www.nih.gov/health-information/nih-clinical-research-trials-you/need-awareness-clinical-research.)
7. Kim SH, Tanner A, Friedman DB, Foster C, Bergeron C. Barriers to Clinical Trial Participation: Comparing Perceptions and Knowledge of African American and White South Carolinians. J Health Commun 2015;20:816-26.
8. Kim SH, Tanner A, Friedman DB, Foster C, Bergeron CD. Barriers to clinical trial participation: a comparison of rural and urban communities in South Carolina. J Community Health 2014;39:562-71.
9. Lara PN, Jr., Paterniti DA, Chiechi C, et al. Evaluation of factors affecting awareness of and willingness to participate in cancer clinical trials. J Clin Oncol 2005;23:9282-9.
10. Joshi V, Kulkarni AA. Public awareness of clinical trials: A qualitative pilot study in Pune. Perspect Clin Res 2012;3:125-32.
11. Miller S, Hudson S, Egleston B, et al. The relationships among knowledge, self-efficacy, preparedness, decisional conflict and decisions to participate in a cancer clinical trial. Psychooncology 2013;22: 481–9.
12. Denicoff AM, McCaskill-Stevens W, Grubbs SS, et al. The National Cancer Institute-American Society of Clinical Oncology Cancer Trial Accrual Symposium: summary and recommendations. J Oncol Pract 2013;9:267-76.
13. Trantham LC, Carpenter WR, DiMartino LD, et al. Perceptions of Cancer Clinical Research Among African American Men in North Carolina. J Natl Med Assoc 2015;107:33-41.
14. Featherstone K, Donovan JL. "Why don't they just tell me straight, why allocate it?" The struggle to make sense of participating in a randomised controlled trial. Soc Sci Med 2002;55:709-19.
15. Jamjoom AB, Jamjoom AM, Samman AM, Gahtani AY. Fate of registered clinical trials performed in Saudi Arabia. Saudi Med J 2015;36:1245-8.
16. Bazarbashi S, Hassan A, Eldin AM, Soudy H, Hussain F. Awareness and Perceptions of Clinical Trials in Cancer Patients and Their Families in Saudi Arabia. J Cancer Educ 2015;30:655-9.
17. Sheblaq NR, Traifi S, Sakiani MA, Gasmelseed A, Abolfotouh MA, Jazieh AR. Awareness and attitude of cancer patients about participation in clinical research (CR) in Saudi Arabia. J Clin Oncol 2013;(suppl; abstr e17528).
18. Al-Tannir MA, El-Bakri N, Abu-Shaheen AK. Knowledge, Attitudes and Perceptions of Saudis towards Participating in Clinical Trials. PLoS One 2016;11:e0143893.
19. Al-Dakhil LO, Alanazy R, Al-Hamed RE, Al-Mandeel H, Alobaid A. Attitudes of Patients in Developing Countries Toward Participating in Clinical Trials: A Survey of Saudi Patients Attending Primary Health Care Services. Oman Med J 2016;31:284-9.

20. Almutairi KM, Alonazi WB, Alodhayani AA, et al. Barriers to Cancer Clinical Trial Participation Among Saudi Nationals: A Cross-Sectional Study. J Relig Health 2017;56:623-34.
21. The Central Department of Statistics and Information 2016. (Accessed 24/04/2017, 2017, at https://www.stats.gov.sa/sites/default/files/en-demographic-research-2016_4.pdf.)
22. Abdullahi A, Hassan A, Kadarman N, Saleh A, Baraya YuSa, Lua PL. Food safety knowledge, attitude, and practice toward compliance with abattoir laws among the abattoir workers in Malaysia. International journal of general medicine 2016;9:79-87.
23. Nur Ain M, Azfar M, Omarulharis S, et al. Knowledge, Attitude And Practice Of Dengue Prevention Among Sub Urban Community In Sepang, Selangor. International Journal of Public Health and Clinical Sciences 2017;4:73-83.
24. Malhotra V, Kaura S, Sharma H. Knowledge, attitude and practices about hepatitis B and Infection Control Measures among dental students in Patiala. Journal of Dental and Allied Sciences 2017;6:65-9.
25. Choi YJ, Beck SH, Kang WY, et al. Knowledge and Perception about Clinical Research Shapes Behavior: Face to Face Survey in Korean General Public. J Korean Med Sci 2016;31:674-81.
26. Nasef N, Shabaan A, Mohammed S, et al. Factors influencing parental consent for participation in clinical research involving their children in Egypt. East Mediterr Health J 2014;20:162-8.
27. Nabulsi M, Khalil Y, Makhoul J. Parental attitudes towards and perceptions of their children's participation in clinical research: a developing-country perspective. J Med Ethics 2011;37:420-3.
28. Elliott C, Abadie R. Exploiting a research underclass in phase 1 clinical trials. N Engl J Med 2008;358:2316-7.
29. Davis MM, Clark SJ, Butchart AT, Singer DC, Shanley TP, Gipson DS. Public participation in, and awareness about, medical research opportunities in the era of clinical and translational research. Clin Transl Sci 2013;6:88-93.
30. Advani AS, Atkeson B, Brown CL, et al. Barriers to the participation of African-American patients with cancer in clinical trials: a pilot study. Cancer 2003;97:1499-506.
31. Comis RL, Miller JD, Aldige CR, Krebs L, Stoval E. Public attitudes toward participation in cancer clinical trials. J Clin Oncol 2003;21:830-5.
32. Joshi VD, Oka GA, Kulkarni AA, Bivalkar VV. Public awareness and perception of clinical trials: Quantitative study in Pune. Perspect Clin Res 2013;4:169-74.
33. Ohmann C, Deimling A. Attitude towards clinical trials: results of a survey of persons interested in research. Inflamm Res 2004;53 Suppl 2:S142-7.

Table 1. Participant characteristics and the unadjusted prectors for knowledge and attitudes

		Overall *N* = 938		Knowledge Overall mean = 56.8 ± 24.8			Attitudes Overall mean = 61.5 ± 28.0		
Characteristics	*Group*	*N*	%	Mean	s.d.	*P*	Mean	s.d.	*P*
Gender	*Male*	577	61.6	51.37	24.4		57.40	28.0	
	Female	360	38.4	65.62	22.9	0.001*	67.90	26.8	0.001*
Age	*18–30*	508	54.2	55.45	26.0		59.36	28.2	
	31– 40	259	27.6	60.07	23.2		63.28	27.8	
	41–60	153	16.3	58.17	22.0		66.67	26.0	
	61+	18	1.9	37.50	22.7	0.001*	50.62	34.1	0.007*
Education	*Not educated*	27	2.9	35.19	18.0		46.09	29.8	
	High school or less	347	37.0	48.37	22.7		57.25	28.0	
	University, college or more	563	60.1	63.06	24.2	0.001*	64.81	27.3	0.001*
Monthly income	● *No income*	195	20.8	49.62	22.7		57.78	28.5	
	● *Less than 5,000 SAR* ● *Less than 1,300 USD*	280	29.9	56.13	26.1		62.02	27.2	
	● *5,001 to 10,000 SAR* ● *1,301 to 2,700 USD*	234	25.0	56.73	23.0		60.64	28.2	
	● *SAR 10,001 to 15,000* ● *USD 2,701 to 4,000*	148	15.8	61.43	24.2		63.74	28.0	
	● *More than 15,000 SAR* ● *More than 4,000 USD*	79	8.5	68.88	25.3	0.001*	67.37	27.9	0.084
Nationality	*Saudi*	817	87.3	57.27	24.6		62.10	27.7	
	Non-Saudi	119	12.7	53.71	25.8	0.143	57.52	29.4	0.095
Residency	*Central region*	707	75.4	59.21	24.4		62.93	28.5	
	Western region	86	9.2	52.52	27.6		59.04	28.3	
	Northern region	59	6.3	46.19	25.0		53.48	25.1	
	Southern region	60	6.4	49.31	20.7		57.04	22.5	
	Eastern region	26	2.8	47.76	21.3	0.001*	58.12	26.9	0.055
Marital Status	*Single*	455	48.7	56.06	26.7		60.59	28.3	
	Married	444	47.5	57.04	22.8		61.61	27.5	
	Other	35	3.8	60.48	22.1	0.549	70.48	28.8	0.130
Employment	*Student in school*	78	8.3	47.54	24.0		56.13	27.4	
	Undergraduate student/ university or college	166	17.8	63.15	26.0		65.66	25.6	
	Government sector	235	25.0	61.70	24.1		64.68	28.1	
	Private sector	208	22.2	56.29	25.4		59.56	28.0	
	Military	54	5.7	52.16	23.2		55.76	30.6	
	Private work/ owener	61	6.8	50.68	22.5		56.65	31.1	
	Retired	26	2.7	51.92	21.9		65.38	31.5	
	Not working	62	6.6	44.49	21.7		57.17	26.3	
	Housewife	47	4.9	59.22	18.9	0.001*	64.30	26.2	0.028*
Health insurance	*Governmental*	560	59.7	58.23	25.2		64.09	27.4	
	Private	116	12.4	58.41	25.0		58.43	30.1	
	Other	226	24.1	55.20	22.5		58.46	27.4	
	No insurance	36	3.8	40.05	24.9	0.001*	49.38	28.8	0.001*
Chronic disease	*Yes*	208	22.2	53.21	23.7		59.19	27.7	
	No	730	77.8	57.85	25.0	0.017*	62.12	28.0	0.183
Medical background	*Yes*	259	27.7	65.99	26.6		67.35	27.5	
	No	677	72.3	53.37	23.1	0.001*	59.23	27.9	0.001*
Previous medical research participation	*Yes*	149	15.9	65.83	25.8		66.44	27.6	
	Was requested, but didn't participate	11	1.1	50.00	22.4		63.64	27.3	
	No	737	78.6	55.54	24.3		60.65	28.1	
	Not sure	41	4.4	48.98	22.3	0.001*	57.45	26.0	0.001*
Do you know somebody who has participated in medical research?	*Yes*	248	26.5	60.42	24.6		62.23	27.6	
	No	596	63.6	57.30	24.6		62.99	27.8	
	Not sure	93	9.9	44.18	23.1	0.001*	49.46	27.7	0.100

* Significant at α = 0.05.

Table 2. Participant knowledge related responses

Variables	*N* (% of participants)
Have you heard about clinical trials before?	
Yes	289 (30.8)
No/not sure	648 (69.1)
What is the definition of a clinical trial?	
Studies in clinics to survey patients opinion about health care topics	139 (14.8)
Experiments on animals	119 (12.7)
Studies to test new drugs or procedure on humans	410 (43.7)
Graduation projects for medical students	62 (6.6)
Not sure	208 (22.2)
Have you heard about an IRB before?	
Yes	251 (26.8)
No	685 (73.1)
Have you heard of the SFDA before?	
Yes	761 (81.1)
No	177 (18.9)
Does the SFDA have a role in regulating clinical trials?	
Yes	622 (66.4)
No	315 (33.6)
Is there an ethical guidelines to regulate the conduction of clinical trials?	
Yes	673 (71.8)
No	265 (28.3)
Are there a direct benefits for participants to conduct Clinical Trials?	
Definitely	313 (33.4)
Definitely not	35 (3.7)
No benefit or harm	19 (2.0)
Possible benefit or harm	436 (46.5)
Not sure	135 (14.4)
Are there a direct benefits for community to conduct Clinical Trials?	
Yes	676 (72.1)
No	262 (27.9)
When can an investigator start clinical trials?	
Any time they want	42 (4.5)
Only with participant agreement	135 (14.4)
After obtaining manager approval	41 (4.4)
They should obtain approvals from responsible authorities	525 (56.0)
Not sure	195 (20.8)
Can an investigator recruit patients without their approval?	
Yes	250 (26.7)
No	687 (73.3)
Can participants freely withdraw from clinical trials anytime?	
Yes	446 (47.6)
No	492 (52.5)
May published articles include confidential patient information (e.g., names)?	
Yes	318 (33.9)
No	620 (66.1)
Knowledge score out of 100 (12 questions)	**56.8 ± 24.8**

IRB: Institutional Review Board; SFDA: Saudi Food Drug Authority

Table 3. Participants' attitude related responses

Variables	*n* (%)
Do you agree with testing new drugs in patients?	
Yes	558 (59.5)
No/not sure	380 (40.5)
Do you agree with testing approved drugs in patients?	
Yes	593 (63.2)
No/not sure	345 (36.8)
Do you agree with testing new drugs in healthy volunteers?	
Yes	286 (30.5)
No/not sure	651(69.5)
Do you agree with testing new drugs in pediatric patients?	
Yes	452 (48.2)
No/not sure	485 (51.8)
Do you agree with testing approved drugs in pediatric patients?	
Yes	528 (56.4)
No/not sure	409 (43.7)
Do you agree with participating/having a family member participate in clinical trials?	
Yes	252 (26.9)
Possibly	395 (42.2)
No/not sure	290 (31.0)
What is your perception regarding clinical trials?	
Not important	41(4.4)
Very important for drug development	682 (72.7)
Important only for pharmaceutical companies to earn money	54 (5.8)
Not sure	161(17.2)
Are you willing to learn about clinical trials?	
Yes	814 (86.8)
No	124 (13.2)
Do you trust research teams?	
Yes	629 (67.1)
No/not sure	309 (32.9)
Attitude score out of 100 (9 questions)	**61.5 ± 28.0**

Table 4. Independent predictors of the Saudi public's knowledge and attitudes toward clinical trials

		Knowledge				Attitudes		
		95% Wald CI				95% Wald CI		
Characteristics	B	Lower	Upper	*P*	B	Lower	Upper	*P*
(Intercept)	48.2	26.83	69.48	0.001*	57.4	30.72	84.01	0.001*
Gender (reference: female)								
Male	–14.1	–17.49	–10.65	0.001*	–9.2	–13.42	–4.88	0.001*
Age (reference: 61+)								
18–30	9.2	–2.86	21.31	0.135	–0.8	–15.87	14.33	0.920
31–40	11.2	–0.56	22.92	0.062	3.7	–10.98	18.34	0.623
41–60	12.1	0.80	23.44	0.036*	10.6	–3.55	24.73	0.142
Education (reference: University, college or more)								
Not educated	–19.6	–29.64	–9.66	0.001*	–18.4	–30.88	–5.92	0.004*
High school or less	–8.2	–12.10	–4.37	0.001*	–5.1	–9.94	–0.29	0.038*
Monthly income (reference: SR 15,000 or more)								
No income	–9.7	–17.17	–2.19	0.011*	–1.0	–10.38	8.34	0.831
SR 5,000 or less	–9.1	–15.48	–2.79	0.005*	0.4	–7.50	8.35	0.916
SR 6,000 to SR 10,000	–6.9	–12.71	–1.00	0.022*	0.0	–7.36	7.28	0.992
SR 11,000 to SR 15,000	–3.6	–9.65	2.38	0.236	1.2	–6.28	8.73	0.749
Nationality (reference: non-Saudi)								
Saudi	–1.6	–6.80	3.63	0.552	1.0	–5.52	7.51	0.764
Residency (reference: Eastern region)								
Central region	3.6	–4.94	12.05	0.412	–0.5	–11.14	10.08	0.922
Western region	1.9	–7.60	11.39	0.696	–0.9	–12.73	11.00	0.886
Northern region	–10.8	–20.77	–0.76	0.035*	–12.7	–25.19	–0.20	0.046*
Southern region	–1.1	–10.89	8.76	0.832	–5.3	–17.61	6.93	0.393
Marital Status (reference: other)								
Single	1.4	–6.94	9.81	0.736	–3.1	–13.55	7.37	0.563
Married	0.9	–6.80	8.67	0.813	–4.5	–14.17	5.15	0.360
Employment (reference: housewife)								
Student	–5.1	–14.08	3.97	0.272	2.1	–9.21	13.34	0.719
Undergraduate student	0.2	–8.60	8.99	0.965	3.7	–7.26	14.71	0.506
Government sector	–3.0	–11.56	5.55	0.491	1.0	–9.70	11.67	0.857
Private sector	–5.1	–13.65	3.51	0.247	–1.0	–11.75	9.69	0.850
Military	–10.3	–20.56	–0.03	0.049*	–0.9	–13.75	11.89	0.887
Private work	–6.4	–15.54	2.72	0.169	–2.8	–14.18	8.64	0.634
Retired	–0.3	–11.73	11.19	0.963	8.5	–5.86	22.76	0.247
Not working	–5.2	–14.01	3.53	0.241	3.5	–7.45	14.45	0.531
Health insurance (reference: no insurance)								
Governmental	12.9	4.48	21.33	0.003*	10.1	–0.45	20.60	0.061
Private	16.5	7.06	25.95	0.001*	4.4	–7.42	16.18	0.467
Other	12.8	4.49	21.08	0.003*	7.9	–2.50	18.22	0.137
Chronic diseases (reference: yes)								
No	–2.2	–5.75	1.27	0.211	–3.5	–7.91	0.87	0.116
Medical background (reference: yes)								
No	–4.7	–8.47	–0.90	0.015*	–5.0	–9.70	–0.24	0.039*
Participated in medical research (reference: no)								
Yes	6.0	–1.78	13.77	0.131	1.7	–8.04	11.38	0.736
Knows somebody who participated in medical research (reference: no)								
Yes	12.3	7.07	17.55	0.001*	10.4	3.88	16.97	0.002*

*Significant at α = 0.05. CI, confidence interval.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 4
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*9*
Bias	9	Describe any efforts to address potential sources of bias	8,9,10
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9,10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	11
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11, 22
		(b) Indicate number of participants with missing data for each variable of interest	

Outcome data	15*	Report numbers of outcome events or summary measures	11,12,22-25
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10, 11, 12, 22, 25
		(*b*) Report category boundaries when continuous variables were categorized	11, 22, 25
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	14
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	2

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Knowledge of and Attitudes toward Clinical Trials in Saudi Arabia: A Cross-sectional study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-031305.R2
Article Type:	Original research
Date Submitted by the Author:	22-Aug-2019
Complete List of Authors:	Al Rawashdeh, Nedal ; King Abdullah International Medical Research Center, Research Office; King Hussein Cancer Center, The Office of Scientific Affairs and Research Damsees, Rana ; King Abdullah International Medical Research Center, Research Office; King Hussein Cancer Center, The Office of Scientific Affairs and Research Al-Jeraisy, Majed ; King Abdullah International Medical Research Center, Research Office; King Saud bin Abdulaziz University for Health Sciences Al Qasim, Eman ; King Abdullah International Medical Research Center, Research Office; King Saud bin Abdulaziz University for Health Sciences Deeb, Ahmad; King Abdullah International Medical Research Center, Research Office; King Saud bin Abdulaziz University for Health Sciences
Primary Subject Heading:	Public health
Secondary Subject Heading:	Public health, Research methods
Keywords:	Knowledge, Attitudes, Clinical trials < THERAPEUTICS

Knowledge of and Attitudes toward Clinical Trials in Saudi Arabia: A Cross-sectional study

Nedal Al-Rawashdeh[1,2], Rana Damsees[1,2], Majed Al Jeraisy[1], Eman Al Qasim[1], Ahmad M. Deeb[1]*

1. Research Office, King Abdullah International Medical Research Center, Riyadh, Saudi Arabia; King Saud bin Abdulaziz University for Health Sciences, Riyadh Saudi Arabia; Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia.
2. The Office of Scientific Affairs and Research, King Hussein Cancer Center, Amman, Jordan

Nedal Al-Rawashdeh: rawashdehne@gmail.com

Rana Damsees: rdamsees@gmail.com

Majed Al Jeraisy: JeraisyM@NGHA.MED.SA

Eman Al Qasim: alqasimem@NGHA.MED.SA

Ahmad M. Deeb: rn_a_deeb@hotmail.com

* **Corresponding Author**

Ahmad M. Deeb, RN, MSN, CCRC®

Senior Clinical Research Coordinator
Research Office
King Abdullah International Medical Research Center
King Saud Bin Abdulaziz University for Health Sciences
King Abdulaziz Medical City
Ministry of National Guard - Health Affairs
PO Box 22490, Mail Code 1515
Riyadh 11426, Kingdom of Saudi Arabia
Tel. No: +966118011111 ext. 18950
Monile: +966547883491
rn_a_deeb@hotmail.com

Short title: Knowledge & Attitude toward Clinical Trials

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board (IRB) at King Abdulaziz Medical City, Riyadh, KSA.

Consent for publication

Not applicable

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests.

Funding

This study was supported by research grant RC16/010/R by King Abdullah International Medical Research Center. The study sponsor does not have any role in the study design, management, analysis, interpretation of the data, or in writing the manuscript.

Author contributions statement

Ahmad Deeb and Nedal Al Rawashdeh: Conception and design, data acquisition, data collection, analytical plan, drafting of the manuscript. Rana Damsees: Conception and design and data acquisition. Majed Al Jeraisy: Conception and design, data acquisition and supervision. Eman Al Qasim: Conception and design and data collection. All authors critically revised the manuscript for important intellectual content, and approved of the final version to be published and agreed to be accountable for all aspects of the work.

Acknowledgements

Not applicable

Abstract

Objectives: Clinical trials (CTs) are considered one of the important methods for developing new treatments and providing access to new potentially effective drugs that are still under investigation. Measuring the public's knowledge of and attitudes toward CTs is important to assessing the public's readiness and acceptance of testing drugs on human participants, which hasn't previously been assessed in the Kingdom of Saudi Arabia (KSA). The objective of this study is to explore the Saudi public's knowledge of and attitudes toward CTs as well as participation in trials to test new or approved drugs.

Design: Cross-sectional.

Setting: Al Jenadriyah cultural/heritage festival in Riyadh/KSA.

Participants: A structured questionnaire was developed and distributed during the 2016 Al Jenadriyah cultural/heritage festival, using a convenience sampling approach. Participating booths, exhibition halls and visitors in the festival were approached to participate in the study. The responses were converted to a percentage mean score (out of 100) for each knowledge related response and attitude.

Primary and secondary outcome measures: Knowledge and attitudes toward CTs.

Results: The sample realized as 938 (n=938). The total mean knowledge score was 56.8 ±24.8 and the attitude related score was 61.5±28.0. Although most of the participants supported testing approved or off-label and new drugs on adult and pediatric patients, only a third 30.5% agreed that new drugs could be tested on healthy volunteers. The results indicated that gender,

educational-level, income, medical background, age-group and health insurance were independent predictors of the level of Knowledge of CTs. In terms of attitudes toward CTs, the independent predictors were gender, educational-level and medical background.

Conclusion: The Saudi public has a low level of knowledge and a moderately positive attitude toward CTs. There is a moderate positive correlation between the two factors as knowledge of CTs increases, the Saudi public will become more positive toward CTs.

Strength and limitations of the study

- The knowledge and attitudes of the Saudi public toward CTs are under-researched.
- This is the first study to explore the Saudi public's knowledge and attitudes in terms of the different phases of CTs in adult and pediatric populations.
- The main limitation is possible selection bias due to employing a convenience sampling method.

Introduction

A clinical trial (CT) is a superior research tool for advancing medical knowledge and practice, as the results are considered to provide the highest level of evidence for medical practice and decision-making.[1] Volunteer participation is at the core of a successful CT. The participation of an adequate number of study participants is crucial in achieving the study's objectives, namely testing the hypothesis and answering the research questions. Failure to recruit an adequate number of participants could result in wasted time, money, and effort.[2] It may also delay the acceptance of the trial results as well as the completion of the drug development process.

Knowledge of and attitudes toward CTs are considered major challenges for participant recruitment.[3-6] Several studies reported that knowledge of CTs and attitudes toward participation are interrelated,[7-11] as increased knowledge promotes a positive attitude toward CT participation. Low recruitment rates for CTs may be improved through increasing the public's knowledge about CTs[6,9,11] and by highlighting the social responsibility perspective of how participation in CTs can contribute to the improvement of the public's health.[12,13] Improving the public's knowledge of CTs represents an important initial step in improving CT recruitment in the future.[9,12,14]

In the Kingdom of Saudi Arabia (KSA), clinical research has advanced during the last few decades.[15] KSA researchers have contributed to medical literature by conducting different types of research, including investigator-initiated CTs and international multicenter-sponsored CTs.[15] Measuring the knowledge and attitudes of the Saudi public toward CTs is crucial to assess their

readiness and acceptance of CTs in Saudi Arabia and to provide an evidence-base to improve CT recruitment and decision-making processes. In addition, it will provide reliable information for researchers and healthcare leaders for strategic planning of public engagement in CT awareness campaigns. From the public's perspective, these efforts may be beneficial through increasing their knowledge and awareness of CTs, improved medical knowledge through dissemination of CT results, and sharing of public preferences for future CTs.

Several studies have reported the knowledge and attitudes of patients, or families, toward CTs in health care settings in Saudi Arabia[16-20]; however, studies measuring the knowledge and attitudes of the Saudi public in general are lacking. The purpose of this study was to assess the Saudi public's knowledge of and attitudes toward CTs in general and more specifically, the attitudes toward participation in CTs for drug development.

The study addressed the following four questions: What does the Saudi public know about CTs? What is the attitude of individuals in Saudi Arabia toward CTs and toward participation in CTs? Is there a correlation between the level of public knowledge and the attitudes of individuals in Saudi Arabia toward CTs? What factors can be predictive of the levels of public knowledge and attitudes toward CTs in the Saudi population?

Materials and Methods

Setting

This cross-sectional study was conducted between February 2 and February 19, 2016 at the Al Jenadriyah Cultural and Heritage Festival. The festival takes place in Riyadh and hosts millions of residents and visitors from the different regions in the country. We selected this event

as it provided us with a unique chance to interview a representative cross-section from all regions of KSA. The study was approved by the Institutional Review Board (IRB) at King Abdulaziz Medical City, Riyadh, KSA.

Study participants

The study included adults of both genders who were willing to participate. A convenience sampling approach was used. Participating booths and exhibition halls in the festival were approached and festival visitors were invited to participate in the study. All of the participants gave informed consent by checking the YES box indicating their willingness to complete the questionnaire. Participants did not receive any compensation for participation in the study.

Patient and public involvement

The public was not included in the development of the research questions or the design of the study. However, the questionnaire was pre-tested with a different sample of the general public before implementation.

Sample size

The population of KSA is approximately 31,742,308 (Central Department of Statistics and Information), including 11,677,338 expatriates (Non-Saudi).[21] On the basis of this population estimate, a 0.05 margin of error, a 95% confidence level, and a response rate of 50%, the minimum sample size calculated for this study was 385. We increased our sample to 1000 to reduce the sampling errors and variability between the characteristics of the sample and the Saudi general population.

Data collection

A structured questionnaire was developed in Arabic. The questionnaire was divided in three sections: demographic information, knowledge and attitude.

The following variables were included in the demographic information section: gender, age, educational level, monthly income, nationality, residential area, employment status, marital status, health insurance, chronic diseases, medical background (working in a healthcare facility or having health-related education), and previous participation in medical research.

The knowledge section was composed of 12 questions, and the participant's responses were scored as correct (score = 1) or incorrect/not sure (score = 0). The total knowledge score was converted to a percentage mean score with a possible maximum value of 100, a score of 100 indicates perfect knowledge of CTs.

The attitude section was composed of nine direct questions, and participant answers were scored as positive (score = 1) or negative/not sure (score = 0). The total attitude score was converted to a percentage mean score with a possible maximum value of 100, a score of 100 indicates a positive attitude toward CTs.

Based on previous studies, the overall level of knowledge and attitude was classified in three levels following Bloom's cut-off point criteria: above 80% (High level), 60-79% (Moderate level), less than 60% (Low level).[22-24]

We ensured that the language used for the questions was clear and understandable to enable the participants to answer the questions, even if they were not aware of CTs. The questionnaire was validated using a content validation process. A panel of expert analysts was used to evaluate the questions and they rated each question as essential, useful or irrelevant in the context of measuring knowledge and attitudes. It was pre-tested using a sample of 28 participants. The result of the pre-test was that complex scientific terms were simplified. Reliability was tested by calculating the Cronbach alpha for the pre-test sample for both the knowledge and attitude sections (21 items). The Cronbach alpha score was 0.81.

Data analysis

The categorical variables are represented as frequency and percentage and the continuous variables as mean ± standard deviation (s.d.). Normality was tested by the skewness coefficient, which indicated that the knowledge and attitude data were normally distributed. The Student's *t*-test and one-way analysis of variance (ANOVA) were used as tests of significance. The Pearson correlation coefficient was used to calculate the correlation between the knowledge and attitude scores. A generalized linear model was used to determine the independent predictors of knowledge and attitudes toward CTs. In this models, we controlled for gender, age, education, monthly income, nationality, residency, marital status, employment, health insurance, chronic disease, medical background, previous medical research participation and medical research participation of someone close. All calculations were performed using the Statistical Package for the Social Sciences (version 23; SPSS Inc., Chicago, IL, USA).

Results

Participant characteristics

A total of 1,084 members of the public were approached to participate in the study. In total, 938 (86.5%) agreed to complete the questionnaire with one missing value in the gender and nationality variables. Of the 938 participants, males were predominant (61.6%). The age groups with the highest representation were the 18-30 years (54.2%) and 31-40 years (27.6%). The majority of the participants (60.1%) reported achieving a tertiary educational level and 75.7% reported a monthly income of less than 10,000 SAR (Saudi Arabian Riyal) which is equivalent to approximately 2,700 USD (United States Dollar). Approximately half of the participants were single (48.7%), and 22.2% indicated being diagnosed with a chronic disease. Just more than a quarter (27.7%) of the sample had a medical background (working in a healthcare facility or having health-related education). A small group (15.9%) declared that they already participated in medical research, and 26.5% knew someone who participated in medical research in the past (**Table 1**).

Knowledge about clinical trials in Saudi Arabia

The overall percentage mean score ±SD for knowledge regarding CTs was 56.8 ±24.8. Although some participants were not aware of the term 'clinical trial', almost half (43.7%) could define the concept correctly. Most of the participants (71.8%) agreed that CTs are subject to ethical guidelines, but only 26.8% were aware of the concept of an institutional review board

(**Table 2)**. The majority (81.1%) was aware of the Saudi Food and Drug Authority (SFDA), and 66.4% were aware of their role in the regulation of CTs. Most of the participants (72.1%) agreed that CTs benefit the community, and 46.5% responded correctly regarding the benefits of CTs for the study participants. Approximately half of the sample knew the time that investigators can initiate a CT (56.0%) as well as the right of CT participants to withdraw from (47.6%) from a study. Other findings from the knowledge section of the questionnaire are listed in **Table 2**.

Attitudes toward clinical trials in Saudi Arabia

The overall percentage mean score ±SD for Saudi attitudes toward CTs was 61.5 ±28.0 out of a 100 score. Most of the participants (59.5%) had a positive attitude toward testing new drugs with adult patients in Saudi Arabia, and 63.2% were positive about testing approved/off-label drugs (approved and marketed drug for other indication) using patients. However, only 30.5% of the participants were positive about conducting CTs using healthy volunteers (Phase I). The attitudes were similar for pediatric CTs, as 48.2% and 56.4% agreed with testing new drugs or approved/off-label drugs on pediatric patients, respectively. The majority of the participants (72.7%) agreed that CTs were important in terms of drug development, and 69.1% confirmed the possibility of participating in a CT should the opportunity arise to them or a close family member. The majority of the participants (86.8%) indicated a willingness to learn more about CTs. Other findings from the attitude section of the questionnaire are listed in **Table 3**.

Factors associated with increased knowledge and more positive attitudes toward clinical trials

The univariate analysis revealed that females had a higher level of knowledge about CTs than males. In addition, the 31-40 years age group had the highest level of knowledge compared to other age categories (**Table 1**). Clinical trial related knowledge increased with an increased level of education (*P*=0.001) as well as an increased monthly income (*P*=0.001). Participants from the Central Region of KSA had a higher level knowledge compared to other regions (*P*=0.001) (**Table 1**). Undergraduate students and governmental employees had a higher level of knowledge compared to other employment categories (*P*=0.001) (**Table 1**). Having governmental or private health insurance (*P*=0.001) was associated with a higher level of CT related knowledge. Noteworthy is that participants without chronic diseases had a higher level of knowledge than those with chronic diseases (*P*=0.017). Previous participation in medical research or knowing someone who participated in the past was associated with better CT related knowledge (*P*=0.001) (**Table 1**).

After adjusting for possible confounders, the beta coefficients for males (B= –14.1; *P*=0.001), non-educated participants (B= –19.6; *P*=0.001), participants with no income (B= –9.7; *P*=0.011), and no medical background (B= –4.7; *P*=0.015) had significantly lower knowledge scores. By contrast, participants in the 41-60 years age (B = 12.1; *P*=0.036) and those with health insurance (B= 12.9; *P*=0.003) were more knowledgeable regarding CTs (**Table 4**).

In terms of attitudes, females were more positive toward CTs (*P*= 0.001) than males. The 31-40 years and 41-60 years age groups were more positive compared to other age categories (*P*=0.007), and having a higher educational level was also associated with a more positive attitude (*P*=0.001) (**Table 1**). As with the knowledge section, undergraduate students and governmental

employees were more positive toward CTs (*P*= 0.028) than participants in other employment categories (**Table 1**) as well as having governmental or private health insurance (*P*=0.001). Participants with a medical background or who had previously participated in medical research tended to be more positive (*P*=0.001) compared to participants with no medical background or who had never participated in medical research (**Table 1**).

After adjusting for the possible confounders, being male (B= –9.2; *P*=0.001), uneducated (B= –18.4, *P*=0.004), or not having a medical background (B= –5.0; *P*=0.039), were associated with more a negative attitudes toward CTs (**Table 4**).

Correlation between Saudi public's knowledge and attitudes toward clinical trials

Our results indicated a moderately positive relationship between the Saudi public's knowledge and attitudes toward CTs (Pearson's *r*= 0.564, *P*=0.0001). Therefore, we predict that as knowledge of CTs increases, the Saudi public will become more positive toward CTs.

Discussion

This public survey revealed a general lack of knowledge regarding CTs. Most of the participants could not identify or correctly define the term 'clinical trial'. Although most of the Saudi public is aware of their right to voluntarily participate in CTs, they were not aware of their right to withdraw from CTs. The current study is supported with similar findings in studies conducted in healthcare settings (with patients and/or their families) within Saudi Arabia.[17-20]

The reason may possibly be interpreted as the lack of institutional and national campaigns promoting CTs. [5,25]

Although most of the participants agreed that CTs are governed by ethical principles, they were not aware of an IRB and its role in protecting human participants. In a study done in a healthcare setting, Sheblaq et al. reported that the majority of the patients diagnosed with cancer were not aware of the role of the IRB.[17] The public tends to trust authorities to protect them even though they do not know who are responsible for playing this role. We observed this phenomenon repeatedly when participants answered positively to questions regarding their trust in the study team and in their compliance with regulatory guidelines when initiating a trial or recruiting participants. The Saudi public recognized the SFDA and its role in CTs, most likely due to their well-known food and drug related regulatory activities in Saudi Arabia.

The overall level of attitude of the Saudi public toward participation in CTs was moderately positive. The Saudi public agrees that CTs may provide benefits for society as a whole and the participants. In addition, trust in the study team may explain the favorable attitude toward participation in CTs. It could be argued that participant responses may change in real-life situations such as in healthcare settings. However, our results were consistent with other studies conducted in health care settings in Saudi Arabia investigating the opinions of patients and families regarding participation in CTs.[16-18]

Similarly, but to a lesser degree, the Saudi public agreed with the idea of conducting pediatric CTs for approved/off-label drugs. However, only 48% of the participants indicated that it was acceptable to test new drugs in pediatric participants. Objection to the use of new drugs or vaccines was one of the factors underlying the opposition to pediatric CTs [26]. Although the

study did not explore the reasons underpinning the motivation to participate in CTs, we believe that the fear of adverse events, as well as safety concerns, may explain this objection.[25,27]

Phase I CTs, which often involve testing new drugs in healthy volunteers, are important in the process of drug development. However, several ethical dilemmas influence conducting such studies with healthy volunteers and patients.[28] In our study, the Saudi public was negative regarding testing new drugs on healthy volunteers. Only 30.5% of the participants agreed with the idea of conducting CTs on healthy volunteers in Saudi Arabia. This sentiment may be related to the lack of knowledge regarding the purpose of testing new drugs on healthy volunteers. Conducting public educational campaigns about CTs in Saudi Arabia is pivotal to improve their knowledge and awareness about CTs.

Consistent with other studies [9,11], participants' attitudes toward CTs were markedly dependent on their knowledge of CTs. We predict that as knowledge about CTs increases, the Saudi public will become more positive. A low level of knowledge regarding CTs may indicate misunderstanding or confusion regarding the purposes of the different phases of CTs. In turn, participants' answers may have been affected by insufficient knowledge. We believe that many participants used their common sense to answer some survey questions and may have begun to recognize the meaning of CTs while answering further questions. These observations support the need for CT related public educational campaigns, since the majority of the participants were interested to learn more about CTs.

Male gender, lower education, lack of a medical background, lower monthly income, a lower age group, and lack of health insurance were independent predictors of a low level of knowledge regarding CTs among the Saudi public. Male gender, less education and lack of a

medical background were independent predictors of a negative attitude toward CTs. Our results are consistent with a United States household survey conducted to assess the level of public participation in and awareness of clinical and translational research, higher levels of income and education were associated with better participation and awareness.[29] In a study conducted with patients diagnosed with cancer in a healthcare setting, a lower level of education and income, as well as race and ethnicity, were associated with decreased awareness of CTs [9]. Similarly, lower income and education were associated with a reduced willingness to participate in CTs in African-American patients diagnosed with cancer [30]. A study of patients with cancer in Saudi Arabia found that higher education was the only significant predictor of trial participation.[17]

Unlike other studies with the public or in healthcare settings [5,9,25,31-33], gender was an independent predictor of knowledge and attitudes. Males were associated with a lower level of knowledge and with a more negative attitude toward CTs. The underlying rationale has not been clearly discussed in literature. Gender differences regarding knowledge and attitudes toward CTs should be considered for future studies.

In the previous studies investigating knowledge and attitudes toward CTs in Saudi Arabia, the sample size was much smaller and mainly involved patients and/or their families in healthcare settings.[17,18] To our knowledge, this is the first study exploring the Saudi public's knowledge and attitudes toward CTs, external of a healthcare setting. Furthermore, it is the first study to solicit public perspectives regarding the different phases of CTs conducted in adult and pediatric populations.

Conclusion

The Saudi public has a low level of knowledge and moderately positive attitudes toward CTs. Increasing the Saudi public's knowledge may contribute to positive attitudes toward participation in and support of CTs; supporting our proposition of educational campaigns to increase awareness and knowledge of CTs. These campaigns should target the less knowledgeable sub-groups identified in the study and focus on the importance of evaluating new drugs on healthy volunteers (Phase I clinical trials). In addition, our results support conducting and investing in CTs in KSA. Conducting similar studies in the future, taking the limitations of this study in consideration, may facilitate measuring the improvement of knowledge over time. We also recommend in-depth qualitative and focus-group-based studies for a deeper understanding of participant perspectives.

Study limitations

The main limitation in this study is related to possible selection bias due to using a convenient sampling method; however the effect of the limitation may have been minimized by the large sample size and the diversity of the visitors. For example, in our sample the distribution of male gender 61.6% was slightly larger than in general population while in the age group 31 to 40 it was 27.6% which is slightly lower.

Abbreviations

ANOVA: Analysis of variance

CTs: Clinical Trials

IRB: Institutional review board

KSA: Kingdom of Saudi Arabia

SAR: Saudi Arabian Riyal

S.D: Standard Deviation

SFDA: Saudi Food and Drug Authority

USD: United States Dollar

References

1. Oxford Centre for Evidence-based Medicine – Levels of Evidence. 2009. 2017, at http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/.)
2. Wyse RK. Accelerating patient recruitment in clinical trials: in-depth report from the SMi 2nd annual conference In: Ross C, editor. The SMi 2nd annual conference 2006; London: NetworkPharma Ltd.
3. Verheggen FW, Nieman FH, Reerink E, Kok GJ. Patient satisfaction with clinical trial participation. Int J Qual Health Care 1998;10:319-30.
4. Public Engagement and Clinical Trials: New Models and Disruptive Technologies: Workshop Summary. Washington (DC)2012.
5. Leiter A, Diefenbach MA, Doucette J, Oh WK, Galsky MD. Clinical trial awareness: Changes over time and sociodemographic disparities. Clin Trials 2015;12:215-23.
6. The Need for Awareness of Clinical Research. National Institute of Health, 2016. 2017, at https://www.nih.gov/health-information/nih-clinical-research-trials-you/need-awareness-clinical-research.)
7. Kim SH, Tanner A, Friedman DB, Foster C, Bergeron C. Barriers to Clinical Trial Participation: Comparing Perceptions and Knowledge of African American and White South Carolinians. J Health Commun 2015;20:816-26.
8. Kim SH, Tanner A, Friedman DB, Foster C, Bergeron CD. Barriers to clinical trial participation: a comparison of rural and urban communities in South Carolina. J Community Health 2014;39:562-71.
9. Lara PN, Jr., Paterniti DA, Chiechi C, et al. Evaluation of factors affecting awareness of and willingness to participate in cancer clinical trials. J Clin Oncol 2005;23:9282-9.
10. Joshi V, Kulkarni AA. Public awareness of clinical trials: A qualitative pilot study in Pune. Perspect Clin Res 2012;3:125-32.
11. Miller S, Hudson S, Egleston B, et al. The relationships among knowledge, self-efficacy, preparedness, decisional conflict and decisions to participate in a cancer clinical trial. Psychooncology 2013;22: 481–9.
12. Denicoff AM, McCaskill-Stevens W, Grubbs SS, et al. The National Cancer Institute-American Society of Clinical Oncology Cancer Trial Accrual Symposium: summary and recommendations. J Oncol Pract 2013;9:267-76.
13. Trantham LC, Carpenter WR, DiMartino LD, et al. Perceptions of Cancer Clinical Research Among African American Men in North Carolina. J Natl Med Assoc 2015;107:33-41.
14. Featherstone K, Donovan JL. "Why don't they just tell me straight, why allocate it?" The struggle to make sense of participating in a randomised controlled trial. Soc Sci Med 2002;55:709-19.
15. Jamjoom AB, Jamjoom AM, Samman AM, Gahtani AY. Fate of registered clinical trials performed in Saudi Arabia. Saudi Med J 2015;36:1245-8.
16. Bazarbashi S, Hassan A, Eldin AM, Soudy H, Hussain F. Awareness and Perceptions of Clinical Trials in Cancer Patients and Their Families in Saudi Arabia. J Cancer Educ 2015;30:655-9.
17. Sheblaq NR, Traifi S, Sakiani MA, Gasmelseed A, Abolfotouh MA, Jazieh AR. Awareness and attitude of cancer patients about participation in clinical research (CR) in Saudi Arabia. J Clin Oncol 2013;(suppl; abstr e17528).
18. Al-Tannir MA, El-Bakri N, Abu-Shaheen AK. Knowledge, Attitudes and Perceptions of Saudis towards Participating in Clinical Trials. PLoS One 2016;11:e0143893.
19. Al-Dakhil LO, Alanazy R, Al-Hamed RE, Al-Mandeel H, Alobaid A. Attitudes of Patients in Developing Countries Toward Participating in Clinical Trials: A Survey of Saudi Patients Attending Primary Health Care Services. Oman Med J 2016;31:284-9.

20. Almutairi KM, Alonazi WB, Alodhayani AA, et al. Barriers to Cancer Clinical Trial Participation Among Saudi Nationals: A Cross-Sectional Study. J Relig Health 2017;56:623-34.
21. The Central Department of Statistics and Information 2016. (Accessed 24/04/2017, 2017, at https://www.stats.gov.sa/sites/default/files/en-demographic-research-2016_4.pdf.)
22. Abdullahi A, Hassan A, Kadarman N, Saleh A, Baraya YuSa, Lua PL. Food safety knowledge, attitude, and practice toward compliance with abattoir laws among the abattoir workers in Malaysia. International journal of general medicine 2016;9:79-87.
23. Nur Ain M, Azfar M, Omarulharis S, et al. Knowledge, Attitude And Practice Of Dengue Prevention Among Sub Urban Community In Sepang, Selangor. International Journal of Public Health and Clinical Sciences 2017;4:73-83.
24. Malhotra V, Kaura S, Sharma H. Knowledge, attitude and practices about hepatitis B and Infection Control Measures among dental students in Patiala. Journal of Dental and Allied Sciences 2017;6:65-9.
25. Choi YJ, Beck SH, Kang WY, et al. Knowledge and Perception about Clinical Research Shapes Behavior: Face to Face Survey in Korean General Public. J Korean Med Sci 2016;31:674-81.
26. Nasef N, Shabaan A, Mohammed S, et al. Factors influencing parental consent for participation in clinical research involving their children in Egypt. East Mediterr Health J 2014;20:162-8.
27. Nabulsi M, Khalil Y, Makhoul J. Parental attitudes towards and perceptions of their children's participation in clinical research: a developing-country perspective. J Med Ethics 2011;37:420-3.
28. Elliott C, Abadie R. Exploiting a research underclass in phase 1 clinical trials. N Engl J Med 2008;358:2316-7.
29. Davis MM, Clark SJ, Butchart AT, Singer DC, Shanley TP, Gipson DS. Public participation in, and awareness about, medical research opportunities in the era of clinical and translational research. Clin Transl Sci 2013;6:88-93.
30. Advani AS, Atkeson B, Brown CL, et al. Barriers to the participation of African-American patients with cancer in clinical trials: a pilot study. Cancer 2003;97:1499-506.
31. Comis RL, Miller JD, Aldige CR, Krebs L, Stoval E. Public attitudes toward participation in cancer clinical trials. J Clin Oncol 2003;21:830-5.
32. Joshi VD, Oka GA, Kulkarni AA, Bivalkar VV. Public awareness and perception of clinical trials: Quantitative study in Pune. Perspect Clin Res 2013;4:169-74.
33. Ohmann C, Deimling A. Attitude towards clinical trials: results of a survey of persons interested in research. Inflamm Res 2004;53 Suppl 2:S142-7.

Table 1. Participant characteristics and the unadjusted prectors for knowledge and attitudes

		Overall *N* = 938		Knowledge Overall mean = 56.8 ± 24.8			Attitudes Overall mean = 61.5 ± 28.0		
Characteristics	*Group*	*N*	%	Mean	s.d.	*P*	Mean	s.d.	*P*
Gender	*Male*	577	61.6	51.37	24.4		57.40	28.0	
	Female	360	38.4	65.62	22.9	0.001*	67.90	26.8	0.001*
Age	*18–30*	508	54.2	55.45	26.0		59.36	28.2	
	31– 40	259	27.6	60.07	23.2		63.28	27.8	
	41–60	153	16.3	58.17	22.0		66.67	26.0	
	61+	18	1.9	37.50	22.7	0.001*	50.62	34.1	0.007*
Education	*Not educated*	27	2.9	35.19	18.0		46.09	29.8	
	High school or less	347	37.0	48.37	22.7		57.25	28.0	
	University, college or more	563	60.1	63.06	24.2	0.001*	64.81	27.3	0.001*
Monthly income	● *No income*	195	20.8	49.62	22.7		57.78	28.5	
	● *Less than 5,000 SAR* ● *Less than 1,300 USD*	280	29.9	56.13	26.1		62.02	27.2	
	● *5,001 to 10,000 SAR* ● *1,301 to 2,700 USD*	234	25.0	56.73	23.0		60.64	28.2	
	● *SAR 10,001 to 15,000* ● *USD 2,701 to 4,000*	148	15.8	61.43	24.2		63.74	28.0	
	● *More than 15,000 SAR* ● *More than 4,000 USD*	79	8.5	68.88	25.3	0.001*	67.37	27.9	0.084
Nationality	*Saudi*	817	87.3	57.27	24.6		62.10	27.7	
	Non-Saudi	119	12.7	53.71	25.8	0.143	57.52	29.4	0.095
Residency	*Central region*	707	75.4	59.21	24.4		62.93	28.5	
	Western region	86	9.2	52.52	27.6		59.04	28.3	
	Northern region	59	6.3	46.19	25.0		53.48	25.1	
	Southern region	60	6.4	49.31	20.7		57.04	22.5	
	Eastern region	26	2.8	47.76	21.3	0.001*	58.12	26.9	0.055
Marital Status	*Single*	455	48.7	56.06	26.7		60.59	28.3	
	Married	444	47.5	57.04	22.8		61.61	27.5	
	Other	35	3.8	60.48	22.1	0.549	70.48	28.8	0.130
Employment	*Student in school*	78	8.3	47.54	24.0		56.13	27.4	
	Undergraduate student/ university or college	166	17.8	63.15	26.0		65.66	25.6	
	Government sector	235	25.0	61.70	24.1		64.68	28.1	
	Private sector	208	22.2	56.29	25.4		59.56	28.0	
	Military	54	5.7	52.16	23.2		55.76	30.6	
	Private work/ owener	61	6.8	50.68	22.5		56.65	31.1	
	Retired	26	2.7	51.92	21.9		65.38	31.5	
	Not working	62	6.6	44.49	21.7		57.17	26.3	
	Housewife	47	4.9	59.22	18.9	0.001*	64.30	26.2	0.028*
Health insurance	*Governmental*	560	59.7	58.23	25.2		64.09	27.4	
	Private	116	12.4	58.41	25.0		58.43	30.1	
	Other	226	24.1	55.20	22.5		58.46	27.4	
	No insurance	36	3.8	40.05	24.9	0.001*	49.38	28.8	0.001*
Chronic disease	*Yes*	208	22.2	53.21	23.7		59.19	27.7	
	No	730	77.8	57.85	25.0	0.017*	62.12	28.0	0.183
Medical background	*Yes*	259	27.7	65.99	26.6		67.35	27.5	
	No	677	72.3	53.37	23.1	0.001*	59.23	27.9	0.001*
Previous medical research participation	*Yes*	149	15.9	65.83	25.8		66.44	27.6	
	Was requested, but didn't participate	11	1.1	50.00	22.4		63.64	27.3	
	No	737	78.6	55.54	24.3		60.65	28.1	
	Not sure	41	4.4	48.98	22.3	0.001*	57.45	26.0	0.001*
Do you know somebody who has participated in medical research?	*Yes*	248	26.5	60.42	24.6		62.23	27.6	
	No	596	63.6	57.30	24.6		62.99	27.8	
	Not sure	93	9.9	44.18	23.1	0.001*	49.46	27.7	0.100

* Significant at α = 0.05.

Table 2. Participant knowledge related responses

Variables	*N* (% of participants)
Have you heard about clinical trials before?	
Yes	289 (30.8)
No/not sure	648 (69.1)
What is the definition of a clinical trial?	
Studies in clinics to survey patients opinion about health care topics	139 (14.8)
Experiments on animals	119 (12.7)
Studies to test new drugs or procedure on humans	410 (43.7)
Graduation projects for medical students	62 (6.6)
Not sure	208 (22.2)
Have you heard about an IRB before?	
Yes	251 (26.8)
No	685 (73.1)
Have you heard of the SFDA before?	
Yes	761 (81.1)
No	177 (18.9)
Does the SFDA have a role in regulating clinical trials?	
Yes	622 (66.4)
No	315 (33.6)
Is there an ethical guidelines to regulate the conduction of clinical trials?	
Yes	673 (71.8)
No	265 (28.3)
Are there a direct benefits for participants to conduct Clinical Trials?	
Definitely	313 (33.4)
Definitely not	35 (3.7)
No benefit or harm	19 (2.0)
Possible benefit or harm	436 (46.5)
Not sure	135 (14.4)
Are there a direct benefits for community to conduct Clinical Trials?	
Yes	676 (72.1)
No	262 (27.9)
When can an investigator start clinical trials?	
Any time they want	42 (4.5)
Only with participant agreement	135 (14.4)
After obtaining manager approval	41 (4.4)
They should obtain approvals from responsible authorities	525 (56.0)
Not sure	195 (20.8)
Can an investigator recruit patients without their approval?	
Yes	250 (26.7)
No	687 (73.3)
Can participants freely withdraw from clinical trials anytime?	
Yes	446 (47.6)
No	492 (52.5)
May published articles include confidential patient information (e.g., names)?	
Yes	318 (33.9)
No	620 (66.1)
Knowledge score out of 100 (12 questions)	**56.8 ± 24.8**

IRB: Institutional Review Board; SFDA: Saudi Food Drug Authority

Table 3. Participants' attitude related responses

Variables	*n* (%)
Do you agree with testing new drugs in patients?	
Yes	558 (59.5)
No/not sure	380 (40.5)
Do you agree with testing approved drugs in patients?	
Yes	593 (63.2)
No/not sure	345 (36.8)
Do you agree with testing new drugs in healthy volunteers?	
Yes	286 (30.5)
No/not sure	651(69.5)
Do you agree with testing new drugs in pediatric patients?	
Yes	452 (48.2)
No/not sure	485 (51.8)
Do you agree with testing approved drugs in pediatric patients?	
Yes	528 (56.4)
No/not sure	409 (43.7)
Do you agree with participating/having a family member participate in clinical trials?	
Yes	252 (26.9)
Possibly	395 (42.2)
No/not sure	290 (31.0)
What is your perception regarding clinical trials?	
Not important	41(4.4)
Very important for drug development	682 (72.7)
Important only for pharmaceutical companies to earn money	54 (5.8)
Not sure	161(17.2)
Are you willing to learn about clinical trials?	
Yes	814 (86.8)
No	124 (13.2)
Do you trust research teams?	
Yes	629 (67.1)
No/not sure	309 (32.9)
Attitude score out of 100 (9 questions)	**61.5 ± 28.0**

Table 4. Independent predictors of the Saudi public's knowledge and attitudes toward clinical trials

		Knowledge				Attitudes		
		95% Wald CI				95% Wald CI		
Characteristics	B	Lower	Upper	*P*	B	Lower	Upper	*P*
(Intercept)	48.2	26.83	69.48	0.001*	57.4	30.72	84.01	0.001*
Gender (reference: female)								
Male	–14.1	–17.49	–10.65	0.001*	–9.2	–13.42	–4.88	0.001*
Age (reference: 61+)								
18–30	9.2	–2.86	21.31	0.135	–0.8	–15.87	14.33	0.920
31–40	11.2	–0.56	22.92	0.062	3.7	–10.98	18.34	0.623
41–60	12.1	0.80	23.44	0.036*	10.6	–3.55	24.73	0.142
Education (reference: University, college or more)								
Not educated	–19.6	–29.64	–9.66	0.001*	–18.4	–30.88	–5.92	0.004*
High school or less	–8.2	–12.10	–4.37	0.001*	–5.1	–9.94	–0.29	0.038*
Monthly income (reference: SR 15,000 or more)								
No income	–9.7	–17.17	–2.19	0.011*	–1.0	–10.38	8.34	0.831
SR 5,000 or less	–9.1	–15.48	–2.79	0.005*	0.4	–7.50	8.35	0.916
SR 6,000 to SR 10,000	–6.9	–12.71	–1.00	0.022*	0.0	–7.36	7.28	0.992
SR 11,000 to SR 15,000	–3.6	–9.65	2.38	0.236	1.2	–6.28	8.73	0.749
Nationality (reference: non-Saudi)								
Saudi	–1.6	–6.80	3.63	0.552	1.0	–5.52	7.51	0.764
Residency (reference: Eastern region)								
Central region	3.6	–4.94	12.05	0.412	–0.5	–11.14	10.08	0.922
Western region	1.9	–7.60	11.39	0.696	–0.9	–12.73	11.00	0.886
Northern region	–10.8	–20.77	–0.76	0.035*	–12.7	–25.19	–0.20	0.046*
Southern region	–1.1	–10.89	8.76	0.832	–5.3	–17.61	6.93	0.393
Marital Status (reference: other)								
Single	1.4	–6.94	9.81	0.736	–3.1	–13.55	7.37	0.563
Married	0.9	–6.80	8.67	0.813	–4.5	–14.17	5.15	0.360
Employment (reference: housewife)								
Student	–5.1	–14.08	3.97	0.272	2.1	–9.21	13.34	0.719
Undergraduate student	0.2	–8.60	8.99	0.965	3.7	–7.26	14.71	0.506
Government sector	–3.0	–11.56	5.55	0.491	1.0	–9.70	11.67	0.857
Private sector	–5.1	–13.65	3.51	0.247	–1.0	–11.75	9.69	0.850
Military	–10.3	–20.56	–0.03	0.049*	–0.9	–13.75	11.89	0.887
Private work	–6.4	–15.54	2.72	0.169	–2.8	–14.18	8.64	0.634
Retired	–0.3	–11.73	11.19	0.963	8.5	–5.86	22.76	0.247
Not working	–5.2	–14.01	3.53	0.241	3.5	–7.45	14.45	0.531
Health insurance (reference: no insurance)								
Governmental	12.9	4.48	21.33	0.003*	10.1	–0.45	20.60	0.061
Private	16.5	7.06	25.95	0.001*	4.4	–7.42	16.18	0.467
Other	12.8	4.49	21.08	0.003*	7.9	–2.50	18.22	0.137
Chronic diseases (reference: yes)								
No	–2.2	–5.75	1.27	0.211	–3.5	–7.91	0.87	0.116
Medical background (reference: yes)								
No	–4.7	–8.47	–0.90	0.015*	–5.0	–9.70	–0.24	0.039*
Participated in medical research (reference: no)								
Yes	6.0	–1.78	13.77	0.131	1.7	–8.04	11.38	0.736
Knows somebody who participated in medical research (reference: no)								
Yes	12.3	7.07	17.55	0.001*	10.4	3.88	16.97	0.002*

*Significant at α = 0.05. CI, confidence interval.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 4
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*9*
Bias	9	Describe any efforts to address potential sources of bias	8,9,10
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9,10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	11
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11, 22
		(b) Indicate number of participants with missing data for each variable of interest	

Outcome data	15*	Report numbers of outcome events or summary measures	11,12,22-25
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10, 11, 12, 22, 25
		(*b*) Report category boundaries when continuous variables were categorized	11, 22, 25
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	14
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	2

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Knowledge of and attitudes toward clinical trials in Saudi Arabia: a cross-sectional study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-031305.R3
Article Type:	Original research
Date Submitted by the Author:	10-Sep-2019
Complete List of Authors:	Al Rawashdeh, Nedal ; King Abdullah International Medical Research Center, Research Office; King Hussein Cancer Center, The Office of Scientific Affairs and Research Damsees, Rana ; King Abdullah International Medical Research Center, Research Office; King Hussein Cancer Center, The Office of Scientific Affairs and Research Al-Jeraisy, Majed ; King Abdullah International Medical Research Center, Research Office; King Saud bin Abdulaziz University for Health Sciences Al Qasim, Eman ; King Abdullah International Medical Research Center, Research Office; King Saud bin Abdulaziz University for Health Sciences Deeb, Ahmad; King Abdullah International Medical Research Center, Research Office; King Saud bin Abdulaziz University for Health Sciences
Primary Subject Heading:	Public health
Secondary Subject Heading:	Public health, Research methods
Keywords:	Knowledge, Attitudes, Clinical trials < THERAPEUTICS

Knowledge of and attitudes toward clinical trials in Saudi Arabia: a cross-sectional study

Nedal Al-Rawashdeh[1,2], Rana Damsees[1,2], Majed Al Jeraisy[1], Eman Al Qasim[1], Ahmad M. Deeb[1]*

1. Research Office, King Abdullah International Medical Research Center, Riyadh, Saudi Arabia; King Saud bin Abdulaziz University for Health Sciences, Riyadh Saudi Arabia; Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia.
2. The Office of Scientific Affairs and Research, King Hussein Cancer Center, Amman, Jordan.

* **Corresponding author**

Ahmad M. Deeb, RN, MSN, CCRC®

PO Box 22490, Mail Code 1515

Riyadh 11426, Kingdom of Saudi Arabia

Tel: +966118011111 ext. 18950

Email: rn_a_deeb@hotmail.com

Word count: 3255

ABSTRACT

Objectives: Clinical trials (CTs) are considered an important method for developing new treatments and providing access to potentially effective drugs that are still under investigation. Measuring the public's knowledge of and attitudes toward CTs is important for assessing their readiness for and acceptance of human drug testing, which has previously not been assessed in the Kingdom of Saudi Arabia (KSA). The objective of this study is to explore the Saudi public's knowledge of and attitudes toward CTs as well as participation in trials to test new or approved drugs.

Design: Cross-sectional.

Setting: The 2016 Al Jenadriyah cultural/heritage festival in Riyadh, KSA.

Participants: Participating booths and exhibition halls, as well as festival visitors, were approached to participate in the study.

Primary and secondary outcome measures: Knowledge of and attitudes toward CTs.

Results: The final number of participants was 938. The responses were converted to a percentage mean score (out of 100) for each knowledge-related response and attitude. The total mean knowledge score was 56.8 ± 24.8 and the attitude-related score was 61.5 ± 28.0. Although most of the participants supported testing approved or off-label and new drugs on adult and pediatric patients, only a third (30.5%) agreed that new drugs could be tested on healthy volunteers. The results indicated that gender, educational level, income, medical background, age, and health insurance were independently associated with the level of

knowledge of CTs. In terms of attitudes toward CTs, the factors that were independently associated were gender, educational level, and medical background.

Conclusions: The Saudi public has a low level of knowledge and a moderately positive attitude toward CTs. There is a moderate positive correlation between the two factors such that as knowledge of CTs increases, the Saudi public will hold more positive attitudes toward CTs.

Strengths and limitations of the study

- The Saudi public's knowledge of and attitudes toward CTs are under-researched.
- This is the first study to explore the Saudi public's knowledge and attitudes in terms of the different phases of CTs in adult and pediatric populations.
- The main limitation is possible selection bias due to convenience sampling.

INTRODUCTION

A clinical trial (CT) is a superior research tool for advancing medical knowledge and practice as the results are considered to provide the highest level of evidence for medical practice and decision-making.[1] Volunteer participation is at the core of a successful CT. The involvement of an adequate number of participants is crucial in achieving the study's objectives, namely testing the hypothesis and answering the research questions. Failure to recruit an adequate number of participants could result in wasted time, money, and effort.[2] It may also delay the acceptance of the trial results and the completion of the drug development process.

Knowledge of and attitudes toward CTs are considered major challenges in participant recruitment.[3-6] Several studies have reported that knowledge of CTs and attitudes toward participation are interrelated,[7-11] as increased knowledge promotes a positive attitude toward CT participation. Low recruitment rates for CTs may be improved by increasing the public's knowledge about CTs[6, 9, 11] and by highlighting how participation can contribute to the improvement of the public's health.[12, 13] Improving the public's knowledge of CTs represents an important initial step in improving CT recruitment in the future.[9, 12, 14]

Clinical research in the Kingdom of Saudi Arabia (KSA) has made advancements during the last few decades.[15] Saudi researchers have contributed to medical literature by conducting different types of research, including investigator-initiated CTs and international multicenter-sponsored CTs.[15] Measuring the Saudi public's knowledge of and attitudes toward CTs is crucial for assessing their acceptance of CTs and to provide an evidence base to

improve CT recruitment and decision-making. In addition, such an endeavor can provide reliable information that can aid researchers and healthcare leaders in strategic planning of public engagement in CT awareness campaigns. From the public's perspective, these efforts may be beneficial through increasing their knowledge and awareness of CTs, improving medical knowledge through dissemination of CT results, and sharing of public preferences for future CTs.

Several studies have reported the knowledge and attitudes of patients or families toward CTs in healthcare settings in the KSA;[16-20] however, studies measuring the knowledge and attitudes of the general Saudi public are lacking. The purpose of this study was to assess the Saudi public's general knowledge of and attitudes toward CTs and more specifically, their attitudes toward participation in CTs for drug development.

The study addressed the following four questions: What does the Saudi public know about CTs? What is the attitude of individuals in the KSA toward CTs and participation in CTs? Is there a correlation between the level of public knowledge and the attitudes of Saudi individuals toward CTs? What factors are associated with the levels of public knowledge and attitudes toward CTs in the Saudi population?

MATERIALS AND METHODS

Setting

This cross-sectional study was conducted between February 2 and 19, 2016 at the Al Jenadriyah Cultural and Heritage Festival. The festival takes place in Riyadh and hosts millions of residents and visitors from different regions in the country. We selected this event as it

provided us with a unique chance to interview a representative cross-section from all regions of the KSA. The study was approved by the Institutional Review Board of King Abdulaziz Medical City, Riyadh, KSA.

Study participants

The study included adults of both genders who were willing to participate. A convenience sampling approach was used. Participating booths and exhibition halls in the festival were approached and festival visitors were invited to participate in the study. All participants provided informed consent by checking the YES box indicating their willingness to complete the questionnaire. Respondents did not receive any compensation for participation in the study.

Patient and public involvement

The public was not included in the development of the research questions or the design of the study. However, the questionnaire was pre-tested with a different sample of the general public before implementation.

Sample size

The population of the KSA is approximately 31,742,308 (Central Department of Statistics and Information), including 11,677,338 expatriates (Non-Saudi).[21] On the basis of this population estimate, a 0.05 margin of error, a 95% confidence level, and a response rate of 50%, the minimum sample size calculated for this study was 385. We targeted a sample size of

1,000 to account for sampling errors and variability between the characteristics of our sample and the general Saudi population.

Data collection

A structured questionnaire, developed in Arabic, was divided into three sections: demographic information, knowledge, and attitudes.

The following variables were included in the demographic information section: gender, age, educational level, monthly income, nationality, residential area, employment status, marital status, health insurance, chronic diseases, medical background (working in a healthcare facility or having health-related education), and previous participation in medical research.

The knowledge section was composed of 12 questions, and the participants' responses were scored as correct (score = 1) or incorrect/not sure (score = 0). The total knowledge score was converted to a percentage mean score with a possible maximum value of 100, where a score of 100 indicates perfect knowledge of CTs.

The attitude section was composed of nine direct questions, and participant answers were scored as positive (score = 1) or negative/not sure (score = 0). The total attitude score was converted to a percentage mean score with a possible maximum value of 100, where a score of 100 indicates a positive attitude toward CTs.

Based on previous studies, the overall knowledge and attitude levels were classified into three categories following Bloom's cut-off point criteria: above 80% (high level), 60–79% (moderate level), and less than 60% (low level).[22-24]

We used simple language so as to enable the participants to answer the questions even if they were not aware of CTs. The questionnaire was validated using a content validation process. A panel of expert analysts evaluated the questions, rating each one as essential, useful, or irrelevant in the context of measuring knowledge and attitudes. The questionnaire was pre-tested using a sample of 28 participants. As a result of the pre-test, complex scientific terms were simplified. Reliability was tested by calculating the Cronbach's alpha for the pre-test sample for both the knowledge and attitude sections (21 items). The Cronbach's alpha was 0.81.

Data analysis

The categorical variables were represented as frequency and percentage and the continuous variables as mean ± standard deviation (SD). Normality was tested by the skewness coefficient, which indicated that the knowledge and attitude data were normally distributed. The Student's *t*-test and one-way analysis of variance were used as tests of significance. The Pearson's correlation coefficient was used to calculate the correlation between the knowledge and attitude scores. A generalized linear model was used to determine the factors independently associated with knowledge of and attitudes toward CTs. In this model, we controlled for gender, age, education, monthly income, nationality, residential area, marital status, employment, health insurance, chronic disease, medical background, previous medical

research participation, and medical research participation by someone close. All calculations were performed using SPSS version 23 (SPSS Inc., Chicago, IL, USA).

RESULTS

Participant characteristics

A total of 1,084 members of the public were approached to participate in the study. In total, 938 (86.5%) agreed to complete the questionnaire with one missing value in the gender and nationality variables. Of the 938 participants, most were males (61.6%). The age groups with the highest representation were 18–30 years (54.2%) and 31–40 years (27.6%). The majority of the participants (60.1%) reported achieving a tertiary educational level and 75.7% reported a monthly income of less than 10,000 Saudi Arabian riyal, which is equivalent to approximately 2,700 United States dollars. Approximately half of the participants were single (48.7%), and 22.2% indicated having been diagnosed with a chronic disease. Just more than a quarter (27.7%) of the sample had a medical background (working in a healthcare facility or having health-related education). A small group (15.9%) declared that they had previously participated in medical research, and 26.5% knew someone who had participated in medical research in the past (**Table 1**).

Table 1. Participant characteristics and unadjusted factors associated with knowledge and attitudes

		Overall *N* = 938		Knowledge Overall mean = 56.8 ± 24.8			Attitudes Overall mean = 61.5 ± 28.0		
Characteristics	*Group*	*N*	%	Mean	s.d.	*P*	Mean	s.d.	*P*
Gender	*Male*	57	61.	51.3	24.	0.00	57.4	28.	0.00

		7	6	7	4	1*	0	0	1*
	Female	360	38.4	65.62	22.9		67.90	26.8	
Age	*18–30*	508	54.2	55.45	26.0		59.36	28.2	
	31–40	259	27.6	60.07	23.2		63.28	27.8	
	41–60	153	16.3	58.17	22.0		66.67	26.0	
	61+	18	1.9	37.50	22.7	0.001*	50.62	34.1	0.007*
Education	*Not educated*	27	2.9	35.19	18.0		46.09	29.8	
	High school or lower	347	37.0	48.37	22.7		57.25	28.0	
	University, college or higher	563	60.1	63.06	24.2	0.001*	64.81	27.3	0.001*
Monthly income	●*No income*	195	20.8	49.62	22.7		57.78	28.5	
	●*Less than 5,000 SAR* ●*Less than 1,300 USD*	280	29.9	56.13	26.1		62.02	27.2	
	●*5,001 to 10,000 SAR* ●*1,301 to 2,700 USD*	234	25.0	56.73	23.0		60.64	28.2	
	●*10,001 to 15,000 SAR* ●*2,701 to 4,000 USD*	148	15.8	61.43	24.2		63.74	28.0	
	●*More than 15,000 SAR* ●*More than 4,000 USD*	79	8.5	68.88	25.3	0.001*	67.37	27.9	0.084
Nationality	*Saudi*	817	87.3	57.27	24.6		62.10	27.7	
	Non-Saudi	119	12.7	53.71	25.8	0.143	57.52	29.4	0.095
Residential area	*Central region*	707	75.4	59.21	24.4		62.93	28.5	
	Western region	86	9.2	52.52	27.6	0.001*	59.04	28.3	0.055
	Northern region	59	6.3	46.1	25.		53.4	25.	

				9	0		8	1	
	Southern region	60	6.4	49.31	20.7		57.04	22.5	
	Eastern region	26	2.8	47.76	21.3		58.12	26.9	
Marital status	*Single*	455	48.7	56.06	26.7		60.59	28.3	
	Married	444	47.5	57.04	22.8		61.61	27.5	
	Other	35	3.8	60.48	22.1	0.549	70.48	28.8	0.130
Employment	*Student in school*	78	8.3	47.54	24.0		56.13	27.4	
	Undergraduate student/university or college	166	17.8	63.15	26.0		65.66	25.6	
	Government sector	235	25.0	61.70	24.1		64.68	28.1	
	Private sector	208	22.2	56.29	25.4		59.56	28.0	
	Military	54	5.7	52.16	23.2		55.76	30.6	
	Private work/ owner	61	6.8	50.68	22.5		56.65	31.1	
	Retired	26	2.7	51.92	21.9		65.38	31.5	
	Not working	62	6.6	44.49	21.7		57.17	26.3	
	Housewife	47	4.9	59.22	18.9	0.001*	64.30	26.2	0.028*
Health insurance	*Governmental*	560	59.7	58.23	25.2		64.09	27.4	
	Private	116	12.4	58.41	25.0		58.43	30.1	
	Other	226	24.1	55.20	22.5		58.46	27.4	
	No insurance	36	3.8	40.05	24.9	0.001*	49.38	28.8	0.001*
Chronic disease	*Yes*	208	22.2	53.21	23.7		59.19	27.7	
	No	730	77.8	57.85	25.0	0.017*	62.12	28.0	0.183
Medical background	*Yes*	259	27.7	65.99	26.6	0.001*	67.35	27.5	0.001*

	No	677	72.3	53.37	23.1		59.23	27.9	
Previous medical research participation	*Yes*	149	15.9	65.83	25.8		66.44	27.6	
	Was requested, but didn't participate	11	1.1	50.00	22.4		63.64	27.3	
	No	737	78.6	55.54	24.3		60.65	28.1	
	Not sure	41	4.4	48.98	22.3	0.001*	57.45	26.0	0.001*
Do you know somebody who has participated in medical research?	*Yes*	248	26.5	60.42	24.6		62.23	27.6	
	No	596	63.6	57.30	24.6		62.99	27.8	
	Not sure	93	9.9	44.18	23.1	0.001*	49.46	27.7	0.100

* Significant at α = 0.05. SAR = Saudi Arabian riyal; USD = United States dollar

Knowledge about clinical trials in the KSA

The overall percentage mean score ± SD for knowledge regarding CTs was 56.8 ± 24.8. Although some participants were not aware of the term, almost half (43.7%) could define the concept correctly. Most of the participants (71.8%) agreed that CTs are subject to ethical guidelines, but only 26.8% were aware of the concept of an institutional review board (**Table 2)**. The majority (81.1%) was aware of the Saudi Food and Drug Authority (SFDA), and 66.4% were aware of the SFDA role in the regulation of CTs. Most of the participants (72.1%) agreed that CTs benefit the community, and 46.5% responded correctly regarding the benefits of CTs for the study participants. Approximately half of the sample was aware of the conditions governing the initiation of CTs (56.0%) as well as the right of CT participants to withdraw from a study at

any time (47.6%). Other findings from the knowledge section of the questionnaire are listed in **Table 2**.

Table 2. Participants' knowledge-related responses

Variables	*n* (% of participants)
Have you heard about clinical trials?	
Yes	289 (30.8)
No/not sure	648 (69.1)
What is the definition of a clinical trial?	
Studies in clinics to survey patients' opinions about healthcare topics	139 (14.8)
Experiments on animals	119 (12.7)
Studies to test new drugs or procedures on humans	410 (43.7)
Graduation projects for medical students	62 (6.6)
Not sure	208 (22.2)
Have you heard about an IRB?	
Yes	251 (26.8)
No	685 (73.1)
Have you heard of the SFDA?	
Yes	761 (81.1)
No	177 (18.9)
Does the SFDA play a role in regulating clinical trials?	
Yes	622 (66.4)
No	315 (33.6)
Are there ethical guidelines to regulate the conduct of clinical trials?	
Yes	673 (71.8)
No	265 (28.3)
Are there direct benefits for participants in clinical trials?	
Definitely	313 (33.4)
Definitely not	35 (3.7)
No benefit or harm	19 (2.0)
Possible benefit or harm	436 (46.5)
Not sure	135 (14.4)
Do clinical trials have direct benefits for the community?	
Yes	676 (72.1)
No	262 (27.9)
When can an investigator start clinical trials?	
Any time they want	42 (4.5)
Only with participant agreement	135 (14.4)
After obtaining manager approval	41 (4.4)

They should obtain approval from responsible authorities	525 (56.0)
Not sure	195 (20.8)
Can an investigator recruit patients without their approval?	
Yes	250 (26.7)
No	687 (73.3)
Can participants freely withdraw from clinical trials anytime?	
Yes	446 (47.6)
No	492 (52.5)
May published articles include confidential patient information (e.g., names)?	
Yes	318 (33.9)
No	620 (66.1)
Knowledge score out of 100 (12 questions)	**56.8 ± 24.8**

IRB: Institutional Review Board; SFDA: Saudi Food and Drug Authority

Attitudes toward CTs in the KSA

The overall percentage mean score ± SD for Saudi attitudes toward CTs was 61.5 ± 28.0 out of 100. Most of the participants (59.5%) had a positive attitude toward testing new drugs on adult patients in the KSA, and 63.2% were positive about testing approved/off-label drugs (approved and marketed drugs for other indications) on patients. However, only 30.5% of the participants were positive about conducting CTs using healthy volunteers (Phase I). The attitudes were similar for pediatric CTs, as 48.2% and 56.4% agreed with testing new drugs or approved/off-label drugs on pediatric patients, respectively. The majority of the participants (72.7%) agreed that CTs are important in terms of drug development, and 69.1% confirmed the possibility of participating in a CT should they or a close family member be presented with the opportunity. The majority of the participants (86.8%) indicated a willingness to learn more about CTs. Other findings from the attitude section of the questionnaire are listed in **Table 3**.

Table 3. Participants' attitude-related responses

Variables	*n* (%)
Do you agree with testing new drugs on patients?	
Yes	558 (59.5)
No/not sure	380 (40.5)
Do you agree with testing approved drugs on patients?	
Yes	593 (63.2)
No/not sure	345 (36.8)
Do you agree with testing new drugs on healthy volunteers?	
Yes	286 (30.5)
No/not sure	651(69.5)
Do you agree with testing new drugs on pediatric patients?	
Yes	452 (48.2)
No/not sure	485 (51.8)
Do you agree with testing approved drugs on pediatric patients?	
Yes	528 (56.4)
No/not sure	409 (43.7)
Do you agree with participating/having a family member participate in clinical trials?	
Yes	252 (26.9)
Possibly	395 (42.2)
No/not sure	290 (31.0)
What is your perception regarding clinical trials?	
Not important	41(4.4)
Very important for drug development	682 (72.7)
Important only for pharmaceutical companies to earn money	54 (5.8)
Not sure	161(17.2)
Are you willing to learn about clinical trials?	
Yes	814 (86.8)
No	124 (13.2)
Do you trust research teams?	
Yes	629 (67.1)
No/not sure	309 (32.9)
Attitude score out of 100 (9 questions)	**61.5 ± 28.0**

Factors associated with increased knowledge and more positive attitudes toward CTs

The univariate analysis revealed that females had a higher level of knowledge about CTs than males. In addition, participants in the 31–40 age group had the highest level of knowledge

(**Table 1**). CT-related knowledge increased with an increased level of education (*P* = 0.001) as well as an increased monthly income (*P* = 0.001). Participants from the Central region of the KSA had a higher level knowledge compared to those from other regions (*P* = 0.001) (**Table 1**). Undergraduate students and governmental employees had a higher level of knowledge compared to those from other employment categories (*P* = 0.001) (**Table 1**). Having governmental or private health insurance (*P* = 0.001) was associated with a higher level of CT-related knowledge. Noteworthy is that participants without chronic diseases had a higher level of knowledge than those with chronic diseases (*P* = 0.017). Previous participation in medical research or knowing someone who had participated was associated with better CT-related knowledge (*P* = 0.001) (**Table 1**).

After adjusting for possible confounders, the beta coefficients for participants who were male (B = –14.1; *P* = 0.001), uneducated (B = –19.6; *P* = 0.001), and unemployed (B = –9.7; *P* = 0.011) and who had no medical background (B = –4.7; *P* = 0.015) had significantly lower knowledge scores. By contrast, participants aged 41–60 years (B = 12.1; *P* = 0.036) and those with health insurance (B = 12.9; *P* = 0.003) were more knowledgeable regarding CTs (**Table 4**).

Table 4. Independent factors associated with the Saudi public's knowledge of and attitudes toward clinical trials

		Knowledge				Attitudes		
		95% Wald CI				95% Wald CI		
Characteristics	B	Lower	Upper	*P*	B	Lower	Upper	*P*
(Intercept)	48.2	26.83	69.48	0.001*	57.4	30.72	84.01	0.001*
Gender (reference: female)								
Male	–14.1	–17.49	–10.65	0.001*	–9.2	–13.42	–4.88	0.001*

Age (reference: 61+)								
18–30	9.2	–2.86	21.31	0.135	–0.8	–15.87	14.33	0.920
31–40	11.2	–0.56	22.92	0.062	3.7	–10.98	18.34	0.623
41–60	12.1	0.80	23.44	0.036*	10.6	–3.55	24.73	0.142
Education (reference: university, college or higher)								
Not educated	–19.6	–29.64	–9.66	0.001*	–18.4	–30.88	–5.92	0.004*
High school or lower	–8.2	–12.10	–4.37	0.001*	–5.1	–9.94	–0.29	0.038*
Monthly income (reference: 15,000 SAR or more)								
No income	–9.7	–17.17	–2.19	0.011*	–1.0	–10.38	8.34	0.831
5,000 SAR or less	–9.1	–15.48	–2.79	0.005*	0.4	–7.50	8.35	0.916
6,000 to 10,000 SAR	–6.9	–12.71	–1.00	0.022*	0.0	–7.36	7.28	0.992
11,000 to 15,000 SAR	–3.6	–9.65	2.38	0.236	1.2	–6.28	8.73	0.749
Nationality (reference: non-Saudi)								
Saudi	–1.6	–6.80	3.63	0.552	1.0	–5.52	7.51	0.764
Residential area (reference: Eastern region)								
Central region	3.6	–4.94	12.05	0.412	–0.5	–11.14	10.08	0.922
Western region	1.9	–7.60	11.39	0.696	–0.9	–12.73	11.00	0.886
Northern region	–10.8	–20.77	–0.76	0.035*	–12.7	–25.19	–0.20	0.046*
Southern region	–1.1	–10.89	8.76	0.832	–5.3	–17.61	6.93	0.393

Marital status (reference: other)								
Single	1.4	–6.94	9.81	0.736	–3.1	–13.55	7.37	0.563
Married	0.9	–6.80	8.67	0.813	–4.5	–14.17	5.15	0.360
Employment (reference: housewife)								
Student	–5.1	–14.08	3.97	0.272	2.1	–9.21	13.34	0.719
Undergraduate student	0.2	–8.60	8.99	0.965	3.7	–7.26	14.71	0.506
Government sector	–3.0	–11.56	5.55	0.491	1.0	–9.70	11.67	0.857
Private sector	–5.1	–13.65	3.51	0.247	–1.0	–11.75	9.69	0.850
Military	–10.3	–20.56	–0.03	0.049*	–0.9	–13.75	11.89	0.887
Private work	–6.4	–15.54	2.72	0.169	–2.8	–14.18	8.64	0.634
Retired	–0.3	–11.73	11.19	0.963	8.5	–5.86	22.76	0.247
Not working	–5.2	–14.01	3.53	0.241	3.5	–7.45	14.45	0.531
Health insurance (reference: no insurance)								
Governmental	12.9	4.48	21.33	0.003*	10.1	–0.45	20.60	0.061
Private	16.5	7.06	25.95	0.001*	4.4	–7.42	16.18	0.467
Other	12.8	4.49	21.08	0.003*	7.9	–2.50	18.22	0.137
Chronic diseases (reference: yes)								
No	–2.2	–5.75	1.27	0.211	–3.5	–7.91	0.87	0.116
Medical background (reference: yes)								
No	–4.7	–8.47	–0.90	0.015*	–5.0	–9.70	–0.24	0.039*

Participated in medical research (reference: no)								
Yes	6.0	–1.78	13.77	0.131	1.7	–8.04	11.38	0.736
Knew somebody who had participated in medical research (reference: no)								
Yes	12.3	7.07	17.55	0.001*	10.4	3.88	16.97	0.002*

*Significant at α = 0.05. CI, confidence interval, SAR = Saudi Arabian riyal.

In terms of attitudes, females were more positive toward CTs (*P* = 0.001) than males. The 31–40 and 41–60 age groups were more positive compared to other age categories (*P* = 0.007), and having a higher educational level was also associated with a more positive attitude (*P* = 0.001) (**Table 1**). As with the knowledge section, undergraduate students and governmental employees were more positive toward CTs (*P* = 0.028) than participants in other employment categories (**Table 1**), as were those with governmental or private health insurance (*P* = 0.001). Participants with a medical background or who had previously participated in medical research tended to be more positive (*P* = 0.001) compared to participants with no medical background or who had never participated in medical research (**Table 1**).

After adjusting for the possible confounders, participants who were male (B = –9.2; *P* = 0.001), uneducated (B= –18.4, *P* = 0.004), or did not have a medical background (B = –5.0; *P* = 0.039) were associated with more negative attitudes toward CTs (**Table 4**).

Correlation between Saudi public's knowledge of and attitudes toward clinical trials

Our results indicated a moderately positive relationship between the Saudi public's knowledge of and attitudes toward CTs (Pearson's *r* = 0.564, *P* = 0.0001). Therefore, we predict

that as the Saudi public's knowledge of CTs increases, they will become more positive toward CTs.

DISCUSSION

This public survey revealed a general lack of knowledge regarding CTs. Most of the participants could not identify or correctly define the term "CT." Although most of the participants were aware of the voluntary nature of participation in CTs, they were not aware of their right to withdraw from CTs. The current results are supported by similar findings in studies conducted in healthcare settings (with patients and/or their families) within the KSA.[17-20] The reason may be the lack of institutional and national campaigns promoting CTs.[5,25]

Although most of the participants agreed that CTs are governed by ethical principles, they were not aware of IRBs and their role in protecting human participants. In a study conducted in a healthcare setting, Sheblaq et al. reported that the majority of the patients diagnosed with cancer were not aware of the role of the IRB.[17] The public tends to expect the authorities to protect them, even though they are not aware of exactly who plays this role. We observed this phenomenon repeatedly when participants responded positively to questions regarding their trust in the study team and in their compliance with regulatory guidelines when initiating a trial or recruiting participants. The Saudi public recognized the SFDA and its role in CTs, most likely owing to their well-known food and drug-related regulatory activities in the KSA.

The Saudi public's overall attitude toward participation in CTs was moderately positive. The Saudi public agrees that CTs may be beneficial for both society as a whole and individual

participants. In addition, trust in the study team may explain the favorable attitude toward participation in CTs. It could be argued that participant responses may change in real-life situations such as in healthcare settings. However, our results are consistent with other studies investigating the opinions of patients and families regarding participation in CTs in the KSA. [16-18]

Similarly, but to a lesser degree, the Saudi public agreed with the idea of conducting pediatric CTs for approved/off-label drugs. However, only 48% of the participants indicated that it is acceptable to test new drugs on pediatric participants. Objection to the use of new drugs or vaccines was one of the factors underlying the opposition to pediatric CTs.[26] Although the study did not explore the reasons underpinning the objections to participating in CTs, we believe that the fear of adverse events, as well as safety concerns, may have been responsible.[25,27]

Phase I CTs, which often involve testing new drugs on healthy volunteers, are important in the process of drug development. However, several ethical dilemmas influence conducting such studies with healthy volunteers and patients.[28] In our study, the Saudi public displayed negative attitudes toward testing new drugs on healthy volunteers. Only 30.5% of the participants agreed with the idea of conducting CTs on healthy volunteers in the KSA. This sentiment may be related to the lack of knowledge regarding the purpose of testing new drugs on healthy volunteers. Conducting public educational campaigns about CTs is necessary for improving the Saudi public's knowledge and awareness about CTs.

Consistent with other studies[9,11], participants' attitudes toward CTs were markedly dependent on their knowledge of CTs. We predict that as their knowledge increases, the Saudi

public will become more positive regarding CTs. A low level of knowledge regarding CTs may indicate misunderstanding or confusion regarding the purposes of the different phases of CTs. In turn, participants' answers may have been affected by insufficient knowledge. We believe that many participants used their common sense to answer some survey questions and may have begun to recognize the meaning of CTs while answering further questions. These observations support the need for CT-related public educational campaigns, since the majority of the participants were interested in learning more about CTs.

Male gender, lower education, lack of a medical background, lower monthly income, a lower age group, and lack of health insurance were independently associated with a low level of knowledge regarding CTs among the Saudi public. Male gender, less education, and the lack of a medical background were independently associated with negative attitudes toward CTs. Our results are consistent with an American household survey conducted to assess the level of public participation in and awareness of clinical and translational research, where higher levels of income and education were associated with higher participation and awareness.[29] In a study conducted with patients diagnosed with cancer in a healthcare setting, lower educational and income levels, as well as race and ethnicity, were associated with decreased awareness of CTs.[9] Similarly, lower income and education were associated with a reduced willingness to participate in CTs in African American patients diagnosed with cancer.[30] A study of patients with cancer in the KSA found that higher education was the only significant predictor of trial participation.[17]

Unlike other studies with the public or in healthcare settings,[5,9,25,31-33] gender was independently associated with knowledge and attitudes. Males were associated with a lower

level of knowledge and with a more negative attitude toward CTs. The underlying rationale has not been clearly discussed in the literature. Gender differences regarding knowledge of and attitudes toward CTs should be considered in future studies.

In the previous studies investigating knowledge of and attitudes toward CTs in the KSA, sample sizes were much smaller than ours and mainly involved patients and/or their families in healthcare settings.[17,18] To our knowledge, this is the first Saudi study exploring the public's knowledge of and attitudes toward CTs outside of a healthcare setting. Furthermore, it is the first study to solicit public perspectives regarding the different phases of CTs conducted in adult and pediatric populations.

CONCLUSION

The Saudi public has a low level of knowledge and moderately positive attitudes toward CTs. Increasing the Saudi public's knowledge may contribute to positive attitudes toward participation in and support of CTs; this supports our proposition of educational campaigns to increase awareness and knowledge of CTs. These campaigns should target the less knowledgeable sub-groups identified in this study and focus on the importance of evaluating new drugs on healthy volunteers (Phase I clinical trials). In addition, our results support conducting and investing in CTs in the KSA. Conducting similar studies in the future, taking the limitations of this study into consideration, may facilitate measuring the improvement of knowledge over time. We also recommend in-depth qualitative and focus group-based studies for a deeper understanding of participant perspectives.

Study limitations

The main limitation in this study is related to possible selection bias due to the use of convenience sampling; however the effect of this limitation may have been minimized by the large sample size and the diversity of the visitors. For example, in our sample, the distribution of males (61.6%) was slightly higher than in the general population, while in the 31–40 age group, it was 27.6%, which is slightly lower than in the general population.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board at King Abdulaziz Medical City, Riyadh, KSA.

Consent for publication

Not applicable.

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests.

Funding

This study was supported by research grant RC16/010/R from the King Abdullah International Medical Research Center. The study sponsor did not have any role in the study design; management, analysis, and interpretation of the data; or in writing the manuscript.

Author contributions statement

Ahmad Deeb and Nedal Al Rawashdeh: Conception and design, data acquisition, data collection, analytical plan, and drafting of the manuscript. Rana Damsees: Conception and design and data acquisition. Majed Al Jeraisy: Conception and design, data acquisition, and supervision. Eman Al Qasim: Conception and design and data collection. All authors have critically revised the manuscript for important intellectual content, approve of the final version to be published, and agree to be accountable for all aspects of the work.

Acknowledgments

Not applicable.

REFERENCES

1. Oxford Centre for Evidence-based Medicine – Levels of Evidence. 2009. Accsesed 10/09/2019, at http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/.)

2. Wyse RK. Accelerating patient recruitment in clinical trials: in-depth report from the SMi 2nd annual conference In: Ross C, ed. The SMi 2nd Annual Conference. London: NetworkPharma Ltd 2006: 07-19.

3. Verheggen FW, Nieman FH, Reerink E, et al. Patient satisfaction with clinical trial participation. *Int J Qual Health Care* 1998;10:319–30.

4. Public Engagement and Clinical Trials: New Models and Disruptive Technologies: Workshop Summary. Washington, DC 2012.

5. Leiter A, Diefenbach MA, Doucette J, et al. Clinical trial awareness: changes over time and sociodemographic disparities. *Clin Trials* 2015;12:215–23.

6. The Need for Awareness of Clinical Research. National Institute of Health. 2016. Accsessed 10/09/2019, at https://www.nih.gov/health-information/nih-clinical-research-trials-you/need-awareness-clinical-research.)

7. Kim SH, Tanner A, Friedman DB, et al. Barriers to clinical trial participation: comparing perceptions and knowledge of African American and white South Carolinians. *J Health Commun* 2015;20:816–26.

8. Kim SH, Tanner A, Friedman DB, et al. Barriers to clinical trial participation: a comparison of rural and urban communities in South Carolina. *J Community Health* 2014;39:562–71.

9. Lara PN, Jr., Paterniti DA, Chiechi C, et al. Evaluation of factors affecting awareness of and willingness to participate in cancer clinical trials. *J Clin Oncol* 2005;23:9282–9.

10. Joshi V, Kulkarni AA. Public awareness of clinical trials: a qualitative pilot study in Pune. *Perspect Clin Res* 2012;3:125–32.

11. Miller S, Hudson S, Egleston B, et al. The relationships among knowledge, self-efficacy, preparedness, decisional conflict and decisions to participate in a cancer clinical trial. *Psychooncology* 2013;22:481–9.

12. Denicoff AM, McCaskill-Stevens W, Grubbs SS, et al. The National Cancer Institute-American Society of Clinical Oncology Cancer Trial Accrual Symposium: summary and recommendations. *J Oncol Pract* 2013;9:267–76.

13. Trantham LC, Carpenter WR, DiMartino LD, et al. Perceptions of cancer clinical research among African American men in North Carolina. *J Natl Med Assoc* 2015;107:33–41.

14. Featherstone K, Donovan JL. "Why don't they just tell me straight, why allocate it?" The struggle to make sense of participating in a randomised controlled trial. *Soc Sci Med* 2002;55:709–19.

15. Jamjoom AB, Jamjoom AM, Samman AM, et al. Fate of registered clinical trials performed in Saudi Arabia. *Saudi Med J* 2015;36:1245–8.

16. Bazarbashi S, Hassan A, Eldin AM, et al. Awareness and perceptions of clinical trials in cancer patients and their families in Saudi Arabia. *J Cancer Educ* 2015;30:655–9.

17. Sheblaq NR, Traifi S, Sakiani MA, et al. Awareness and attitude of cancer patients about participation in clinical research (CR) in Saudi Arabia [abstract]. *J Clin Oncol* 2013;(suppl; e17528).

18. Al-Tannir MA, El-Bakri N, Abu-Shaheen AK. Knowledge, attitudes and perceptions of Saudis towards participating in clinical trials. *PLoS One* 2016;11:e0143893.

19. Al-Dakhil LO, Alanazy R, Al-Hamed RE, et al. Attitudes of patients in developing countries toward participating in clinical trials: a survey of Saudi patients attending primary health care services. *Oman Med J* 2016;31:284–9.

20. Almutairi KM, Alonazi WB, Alodhayani AA, et al. Barriers to cancer clinical trial participation among Saudi nationals: a cross-sectional study. *J Relig Health* 2017;56:623–34.

21. The Central Department of Statistics and Information. 2016. (Accessed 24/04/2017, 2017, at https://www.stats.gov.sa/sites/default/files/en-demographic-research-2016_4.pdf.)

22. Abdullahi A, Hassan A, Kadarman N, et al. Food safety knowledge, attitude, and practice toward compliance with abattoir laws among the abattoir workers in Malaysia. *International Journal of General Medicine* 2016;9:79–87.

23. Nur Ain M, Azfar M, Omarulharis S, et al. Knowledge, attitude and practice of dengue prevention among sub urban community in Sepang, Selangor. *International Journal of Public Health and Clinical Sciences* 2017;4:73–83.

24. Malhotra V, Kaura S, Sharma H. Knowledge, attitude and practices about hepatitis B and infection control measures among dental students in Patiala. *Journal of Dental and Allied Sciences* 2017;6:65–9.

25. Choi YJ, Beck SH, Kang WY, et al. Knowledge and perception about clinical research shapes behavior: face to face survey in Korean general public. *J Korean Med Sci* 2016;31:674–81.

26. Nasef N, Shabaan A, Mohammed S, et al. Factors influencing parental consent for participation in clinical research involving their children in Egypt. *East Mediterr Health J* 2014;20:162–8.

27. Nabulsi M, Khalil Y, Makhoul J. Parental attitudes towards and perceptions of their children's participation in clinical research: a developing-country perspective. *J Med Ethics* 2011;37:420–3.

28. Elliott C, Abadie R. Exploiting a research underclass in phase 1 clinical trials. *N Engl J Med* 2008;358:2316–7.

29. Davis MM, Clark SJ, Butchart AT, et al. Public participation in, and awareness about, medical research opportunities in the era of clinical and translational research. *Clin Transl Sci* 2013;6:88–93.

30. Advani AS, Atkeson B, Brown CL, et al. Barriers to the participation of African-American patients with cancer in clinical trials: a pilot study. Cancer 2003;97:1499–506.

31. Comis RL, Miller JD, Aldige CR, et al. Public attitudes toward participation in cancer clinical trials. *J Clin Oncol* 2003;21:830–5.

32. Joshi VD, Oka GA, Kulkarni AA, et al. Public awareness and perception of clinical trials: quantitative study in Pune. *Perspect Clin Res* 2013;4:169–74.

33. Ohmann C, Deimling A. Attitude towards clinical trials: results of a survey of persons interested in research. *Inflamm Res* 2004;53(Suppl 2):S142–7.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1, 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6, 7*
Bias	9	Describe any efforts to address potential sources of bias	6,7,8
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9, 10
		(b) Indicate number of participants with missing data for each variable of interest	9
Outcome data	15*	Report numbers of outcome events or summary measures	9,12,22-25
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10, 12, 14, 15, 16

		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	19
Discussion			
Key results	18	Summarise key results with reference to study objectives	20
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	23, 24
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	20
Generalisability	21	Discuss the generalisability (external validity) of the study results	20, 23, 24
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	24

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.