Perceptions and attitudes toward participation in clinical research in the Eastern Mediterranean Region: A systematic review

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Abstract

Introduction: Successful recruitment of participants into clinical research has always been challenging and is affected by many factors. This systematic review aimed to explore the perceptions and attitudes as well as identify the factors affecting the participation in clinical research among the Eastern Mediterranean Regional Office countries’ population.

Methods: A systematic search of the literature was conducted to explore attitudes or perceptions of the general public or patients towards participation in clinical research. PubMed, Pro-Quest Central, World Health Organizations Index Medicus for the Eastern Mediterranean Region, and Google Scholar were searched. Studies were considered eligible for inclusion if they presented primary data and were conducted in one of the Eastern Mediterranean Regional Office countries. A data extraction sheet was used to record the following: year, country, aim, population, sample size, study design, data collection, and setting. The identified factors from the included studies were categorized into motivators and barriers.

Results: In total, 23 original research articles were identified that addressed perceptions or attitudes towards clinical research participation. Six main motivators and barriers of research participation among patients, the general public, and patient family members were identified. The most common cited motivators included personal benefits to the individual, altruism and the desire to help others, the research process, the influence of the physician, family encouragement, and religion. Concerns regarding safety, confidentiality, and other factors in addition to the research process, lack of trust in healthcare providers or healthcare system, lack of interest in research and no perceived personal benefit, religious concerns, and family/cultural concerns were the most cited barriers to participation.

Conclusion: The identified motivators and barriers are essential to tackle during clinical research planning among the population of Eastern Mediterranean Regional Office countries. Further research is needed to assess the attitudes and perceptions of individuals approached to participate in trials.

Abbreviations: CASP = Critical Appraisal Skills Programme, EMRO = Eastern Mediterranean Region Office, IMEMR = Index Medicus for the Eastern Mediterranean Region, MeSH = Medical Subject Headings, NOS = Newcastle-Ottawa Scale, PROSPERO = prospectively registered systematic reviews in health and social care, PubMed = Public/Publisher MEDLINE, WHO = World Health Organization.

Keywords: attitude, clinical research, EMRO, involvement, participation, perception
1. Introduction
Evidence-based medicine (EBM) is the practice that advocates the thorough examination of medical literature to extract the best available evidence when making clinical decisions. Such evidence is made available through the different types of research, including interventional and observational studies.\[1,2\]

Successful recruitment and retention of participants into clinical research have always presented as a challenge since the general public and patients might lack the awareness about the importance of clinical research for the advancement in healthcare and many other influencing factors.\[3,4\] This might result in failing to meet recruitment targets, and sometimes, failure or termination of trials. The literature shows that >50% of oncological trails were terminated prematurely due to a low recruitment rate.\[3,5\]

The World Health Organization (WHO) Eastern Mediterranean Region Office (EMRO) comprises a diverse population from 22 countries. This population shares numerous similar demographics, religious, and cultural characteristics, yet diverse socioeconomic, racial, and ethnic backgrounds. Additionally, this region is changing population size and health-related characteristics. Hence, the need for expanding clinical research is crucial to face the challenges relating to healthcare provision. However, participation in clinical research in the EMRO countries is yet underdeveloped. A study by Nair et al showed that the participants from the region countries accounts for <1% of the global research participants’ size and 0.5% of the total global sites of clinical trial.\[6,7\]

In order to improve participation in clinical research, there is a need to explore the perceptions and attitudes of the general public to tackle their concerns when intending to recruit them to clinical research. Hence, this systematic review aimed to explore the perceptions and attitudes and identify the factors affecting the participation in clinical research among the EMRO countries population.

2. Methods

2.1. Search strategy
This review is registered on PROSPERO International Prospective Register of Systematic Reviews (registration number CRD42020195763). A comprehensive systematic literature search was conducted and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.\[8\] The following databases were searched: PubMed, Pro-Quest Central, World Health Organizations Index Medicus for the Eastern Mediterranean Region (IMEMR), and Google Scholar. The databases were searched up to October 2021 using the following MeSH terms and keywords that were agreed upon by the authors: “research” AND “attitude” AND “involvement” OR “participation” AND the individual countries of the Eastern Mediterranean Region, a total of 22 countries (Afghanistan, Bahrain, Djibouti, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Pakistan, Palestine, Qatar, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, United Arab Emirates, and Yemen). As the search terms were broad, the search yielded many studies. Hence, we limited it to studies conducted in humans and published in English. Additionally, a manual search of the references list of the identified relevant articles was done to supplement the search.

2.2. Selection criteria

2.2.1. Inclusion criteria. Studies were included if they met the following criteria: presented original and primary research; explored attitudes or perceptions towards participation in clinical research among patients or the general public; conducted in one of the 22 countries of the EMRO region; and using a recognized method for data collections, such as questionnaire and structured interviews.

2.2.2. Exclusion criteria. Studies were excluded if they: did not meet all inclusion criteria or did not present original/primary research, such as reviews.

2.3. Data extraction and quality assessment
The titles of the articles retrieved by the initial search (Fig. 1) were independently screened by 2 authors. Those deemed relevant were further examined by reviewing the abstracts. After that, relevant abstracts were selected to be screened in full text. The full-text appraisal was independently performed by 2 authors using the following: The Newcastle-Ottawa Scale (NOS) for cross-sectional studies, adapted from the scale for cohort studies,\[9\] and Critical Appraisal Skills Programme (CASP) for qualitative studies,\[10\] aiming to ensure the quality of the included studies. In the case of disagreement, it was resolved through discussion among the authors. A coding template was developed to extract the data and categorize it into motivators and barriers to research participation among patients and the general public in the countries of the EMRO region.

3. Results
The systematic literature search across the databases yielded a total of 2041 studies, in addition to 9 articles that were identified through the supplemental search of the bibliographies of relevant articles (Fig. 1). Duplicates were subsequently removed, and 2033 studies were screened by title. The title screen yielded 44 studies that were to be assessed by abstract. Fourteen abstracts were excluded as they did not address the study question or were conducted among a population other than the targeted population. Thirty studies were assessed independently as full-text articles for meeting the inclusion criteria. At this stage, 7 articles were excluded for not exploring the perception/attitude toward participation and enrolling in research in the EMRO countries (n = 7). Twenty-three articles were agreed upon by the authors to be included in the review as they addressed the study question and met all the inclusion criteria. Table 1 presents all studies’ demographic and methodological characteristics included in the review.

3.1. Motivators
The included studies identified 6 main motivators of research participation among patients, general public, and patient family members as the most reported (Table 2). The belief that research participation might result in personal benefit was the most cited motivator by almost three quarters 17 (74%) of the studies. This might come in the shape of accessing hospital care or costly drugs that are more effective than the available treatments, drugs of fewer side effects or otherwise unavailable, as well as receiving better treatment or more attention from healthcare providers.\[15,17,21-23,27,28,30,31\] In addition to that, participation was motivated by having financial gains, expressing their opinions, sharing their complaints, or getting to learn about the scientific topic being researched.\[14,20,21,23,25,28,30,31,33\] Moreover, few of these studies showed that patients are often motivated to participate in research if they knew in advance that they would have access or receive feedback on their test results.\[12,16,27\] One study that aimed to assess participation in HIV/HCV cohort studies among people who inject drugs, few participants expressed that among the motivators to be enrolled in the protection from drug-related police interventions during the study period.\[39\] In 13 (57%) of the studies, clinical research in the EMRO region was motivated by the desire to help other patients and improve society and its healthcare system. This is driven by a
sense of duty and commitment to the country, community, and volunteerism. Furthermore, the desire to contribute to knowledge and scientific advancement was another driving factor.

The research process and design were the third common factors influencing the decision of participation in research, which was reported in 12 (52%) of the included studies. Participants were more likely to consent to participate in observational studies in which data are collected through an interview, survey or questionnaire; and in studies that include minimally invasive procedures such as blood sample collection. Additionally, participation in research was positively influenced by the adequacy of information provided to participants regarding the disease/condition being investigated, the importance of the research and its impact on patient’s health outcomes, the procedures being taken as part of the research, the benefits and potential hazards to expect, and the plan of monitoring the patients during their participation period. Additionally, participation in research was positively influenced by the adequacy of information provided to participants regarding the disease/condition being investigated, the importance of the research and its impact on patient’s health outcomes, the procedures being taken as part of the research, the benefits and potential hazards to expect, and the plan of monitoring the patients during their participation period.

Allowing the participants time to think before enrolling them in research motivated their participation and adequate explanation on their rights to sign an informed consent emphasizing that they will not be subjected to research without their approval and signature of a consent form. In addition to that, they preferred to learn that withdrawal from research is allowed and that the researchers have obtained the necessary governmental approvals. Informing participants about vital confidentiality and privacy measures throughout the study was an essential component in enrolling in research.

Interestingly, participants in 8 (35%) of the studies reported that they were more likely to enroll in research if this was recommended by their physician, if they had a chance to consult them, or if their physician approached them during the initial recruitment process. Others were motivated by the fear of jeopardizing the relationship with their physicians and healthcare providers or receiving suboptimal medical care if they refused research participation. Other factors played a role in motivating research participation, such as family encouragement, having a family member around during recruitment, religious permission of research participation, and knowing that God will reward them for this good deed.

3.2. Barriers

The main barriers to research participation include fear, the research process, trust, lack of interest or personal benefit, religious concerns, and family or cultural concerns (Table 3). In addition to fear of privacy or confidentiality breach, safety concerns were the most essential and commonly reported barrier in 20 (87%) studies. Participants also shared their fear of receiving suboptimal treatment if they decided to withdraw from research after an initial agreement to participate. Additionally, a misconception that research, especially trials of drugs or vaccines, should be conducted on animals but instead is being done on
### Table 1: Studies included in the systematic review.

| Study | Year | Country | Aim | Population | Sample size | Study design | Data collection | Setting |
|-------|------|---------|-----|------------|-------------|--------------|----------------|---------|
| Abou-Zeid et al.[11] | 2010 | Egypt | To determine the attitudes of patients regarding their participation in research and with the collection, storage and future use of blood samples for research purposes. | Adult patients | 600 | Cross-sectional survey | Interview questionnaire | Outpatient clinics |
| Aham et al.[12] | 2014 | Jordan | To assess factors influencing public participation in biobanking | Adult population | 3196 | Nationwide, cross-sectional survey | Interview survey | Household |
| Al-Amoud et al.[14] | 2020 | Jordan | To assess public knowledge of and willingness to participate in clinical trials and the associated sociodemographic characteristics. | Adult patients | 120 | Cross-sectional survey | Interview questionnaire | Household |
| Al-Dakhl et al.[15] | 2014 | Jordan | To evaluate and investigate the beliefs, and attitudes of patients in Saudi Arabia regarding participation and enrollment in the clinical trials. | Adult patients | 1081 | Self-administered questionnaire | Self-administered questionnaire | Dental clinics |
| Al-Jumah et al.[16] | 2011 | Saudi Arabia | To determine the attitude to research involving storage and use of human tissues in genetic research and biobanks. | Adult patients | 1051 | Cross-sectional survey | Interview questionnaire | Outpatient clinics |
| Al-Lawati et al.[17] | 2018 | Oman | To assess the knowledge and attitudes of patients and their relatives towards participating in clinical trials. | Adult patients and relatives | 100 | Cross-sectional survey | Self-administered questionnaire | Hospital and outpatient clinics |
| AL-Tannir et al.[18] | 2016 | Saudi Arabia | To assess the knowledge, attitudes, and perceptions of patients and their companions towards participating in clinical trials. | Patients and companions | 232 | Cross-sectional survey | Self-administered questionnaire | Outpatient clinics |
| Bazarbashi et al.[19] | 2015 | Saudi Arabia | To explore the perception, knowledge, and willingness of cancer patients to participate in oncology clinical trials. | Patients and family | 204 | Cross-sectional survey | Interview questionnaire | Outpatient clinics |
| B‘Idai et al.[20] | 2016 | United Arab Emirates | To explore participants general perceptions towards medical research. | Adult population | 42 | Qualitative study design | Focus groups | Academic institutions & blood bank |
| Gharaibeh et al.[21] | 2020 | Jordan | To assess the willingness of patients to participate in clinical trials, and patients' attitudes, perceptions to research. | Adult patients | 1201 | Cross-sectional survey | Interview questionnaire | Hospital |
| Hassona et al.[22] | 2016 | Jordan | To study the willingness of dental patients to donate biospecimens for research purpose and to examine decisions influencing factors. | Adult patients | 408 | Cross-sectional survey | Interview questionnaire | Hospital |
| Hifnawy et al.[23] | 2017 | Egypt, Lebanon, Saudi Arabia & Sudan | To determine patients' attitudes and perceptions toward research participation and perceptions of their rights. | Patients and family | 202 | Cross-sectional survey | Interview questionnaire | Outpatient clinics & hospital |
| Khalil et al.[24] | 2007 | Egypt | To examine the attitudes of Egyptian individuals toward medical research. | Adult patients | 15 | Qualitative study design | Semistructured interview | Outpatient clinics |
| Killawi et al.[25] | 2014 | Qatar | To describe procedures related to recruiting, obtaining informed consent, and compensating health research participants. | Adult patients | 84 | Qualitative study design | Field observations & interviews | Outpatient clinics |
| Lhoussni et al.[26] | 2020 | Morocco | To explore knowledge and attitude toward biobanks among patients and to evaluate their willingness to donate their own biological samples. | Adult patients | 1133 | Cross-sectional survey | Interview questionnaire | Health care centers |
| Makhlouf et al.[27] | 2019 | Jordan | To explore and understand population's perspectives, expectations, and concerns toward biobanks. | Adult Population | 500 | Cross-sectional survey | Self-administered questionnaire | Online survey |
| Mansour et al.[28] | 2015 | Egypt | To evaluate the informed consent process, misconceptions and motivations among clinical trials participants. | Clinical trials participants | 103 | Cross-sectional survey | Self-administered questionnaire | Online survey |
| Mirzaazadeh et al.[29] | 2020 | Iran | To understand the perceptions, concerns, barriers and motivators to participation and retention in HIV/AIDS cohort studies. | People who inject drugs | 30 | Qualitative study design | Qualitative study design | Urban setting |
| Nabulsi et al.[30] | 2011 | Lebanon | To explore the attitudes of parents from a developing country towards child participation in research trials. | Parents | 33 | Qualitative study design | In-depth interviews | Hospital |
| Nabulsi et al.[30] | 2011 | Lebanon | To explore the attitudes of parents from a developing country towards child participation in research trials. | Parents or guardians | 357 | Cross-sectional survey | Self-administered questionnaire | Hospital |
| Nasif et al.[31] | 2014 | Egypt | To explore the attitudes and beliefs influencing parents’ decision to involve their children in clinical research. | Patients or caregivers | 210 | Cross-sectional survey | Interview questionnaire | Outpatient clinics |
| Salem et al.[32] | 2019 | Lebanon | To explore the knowledge, attitudes, and perceptions of patients with cancer and their caregivers regarding participation in clinical trials. | Adults population | 2517 | Cross-sectional survey | Interview questionnaire | Major public events |
Barriers to participation in clinical research.

Table 3

| Barriers                  | Articles No. (%) | Observed examples                                                                                                                                 |
|---------------------------|------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| Fear/concerns             | 20 (87)          | - Withdrawal from research will result in receiving suboptimal medical care.                                                                      |
|                           |                  | - Safety concerns (i.e., fear of adverse effects, fear that new drugs/vaccines that have not been studied on humans are not safe, and misconception that all clinical trials are of new interventions with no established safety on humans). |
|                           |                  | - Privacy and confidentiality concerns and fear of information leakage.                                                                           |
|                           |                  | - Fear of the unknown (e.g., discovering they have a disease when they participate in the study).                                               |
|                           |                  | - Fear of pain with invasive procedures, and fear of acquiring infections.                                                                       |
| Research process          | 18 (78)          | - Study type and design (e.g., less likely to participate in drug clinical trials).                                                               |
|                           |                  | - Lack of awareness of research concepts and concerns regarding the consenting process and patients’ rights in research.                        |
|                           |                  | - Concerns regarding randomization, blinding, multiple visits, recontact by the research team, and the time and effort needed to participate in research. |
|                           |                  | - Concerns regarding the associated costs (e.g., transportation) and lack of monetary compensation.                                                 |
| Trust                     | 13 (57)          | - Mistrust in the healthcare systems and providers (e.g., belief that specimens collected for research purpose without patients’ consent).          |
|                           |                  | - Concerns regarding medical errors, lack of research supervision, indefinite storage of samples, and sample exploitation.                    |
|                           |                  | - Belief that research is only of interest to clinicians for selfish reasons (e.g., career advancement, monetary rewards).                   |
| Lack of benefits/interest | 8 (35)           | - Research participation has no direct benefit to participants (test results are not shared, no financial compensation).                          |
|                           |                  | - Lack of interest in participation due to stable health or dislike of hospitals and physicians.                                                 |
| Religious concerns        | 4 (17)           | - Religious concerns that research might be tampering with religion or that provided samples might be used for research prohibited by religion.    |
| Family, social, or cultural| 2 (9)            | - Social and cultural barriers (e.g., visits to medical/research center after working hours or family objects to participation).               |

In 13 (57%) studies, views reflecting lack of trust in the healthcare system and providers were observed. Some patients believed that their left-over specimens and samples (after routine surgery, for example) were collected for research purposes without their consent, which demotivated their participation. Others believed that the samples they provide for research might be exploited or stored indefinitely, and hence they prefer not to participate. Furthermore, some believed that research, especially research conducted in EMRO countries, lacks regulatory supervision, and they believed it is only of interest to clinicians as it is crucial for their career advancement. [12,15,17,19,23,26,28,30–33]
Additionally, a trend of lack of interest in research participation due to a stable health condition or lack of personal benefit was observed. Last, religious and cultural concerns had a role in discouraging research participation, as observed in a few of the included studies.

### 4. Discussion

In this review, we identified 6 main motivators and barriers to research participation among the population of the EMRO region. This population is unique in its diversity as it includes 22 countries with different ethnic and racial backgrounds and economic statuses. However, this complex population shares enormous similarities due to shared religious and cultural characteristics. Interestingly, some identified factors were interpreted as both motivators and barriers to research participation.

An essential factor that was perceived as a motivator and a barrier is the study design, including the method used for data collection. Participants were most likely to enroll in studies of observational nature, such as questionnaires, and in studies that include minimally invasive procedures. They were mainly resistant to participating in drug trials, including invasive procedures such as tissue biopsy.

This was opposed by study findings that reported a high proportion of patients considered participation in trials involving repeat biopsies. However, the study included patients with gastrointestinal malignancies or lymphoma only, and their views on biopsies may differ from other patients. Resistance to participate in such trials can be attributed to multiple factors: fear and safety concerns, lack of awareness on concepts of clinical research and its regulations, and mistrust in healthcare providers and in the system. This was confirmed by a global survey about attitudes and experiences of the public toward participation in clinical research. The study included more than twelve thousand individuals, representing 68 countries from North America, South America, Europe, Asia Pacific, and Africa. This study found that the top perceived risk to research participants included the fear of adverse drug events and risks to overall health. Additionally, while >80% of the respondents believed in the importance of research, only 30% were willing to participate.

The consenting process is another factor that was perceived as critical by many participants; however, some found the written informed consent complex enough to hinder the participation. Furthermore, we found that some participants believed that they were recruited into research without their knowledge and consent. This was consistent with the findings from a study conducted in Canada. The authors found that about 30% of their study participants were uncertain or believed that clinical research participants are rarely or never informed of their study participation. This creates a gap between the hypothesis and the real world. In Burns et al study, it was reported that only about 70% of participants were adequately informed about the risks and benefits of study.

Evaluating the factors influencing the perception and attitude towards participation in clinical research is crucial for the research in the region. Nevertheless, this could be challenging to be assessed precisely. In our review, there are several important strengths and limitations. This review comprehensively addressed the factors affecting participation in clinical research from studies conducted in the region. Among the limitations is the quality of the factors affecting participation in clinical research from studies conducted in the region. Among the limitations is the quality of data due to the observational cross-sectional design of the included studies.

Additionally, all the studies depended on self-reporting methods, which might bias the results depending on the participant's ability to recall or the desire to share what they believe they prefer to hear with the researchers. The majority of the included studies were based on approaching the participants giving a hypothetical scenario asking about their perceptions of participation in clinical research if they were contacted to be enrolled. This creates a gap between the hypothesis and the real world. However, these studies elucidate the factors that motivate or discourage participation in clinical research.

### 5. Conclusion

The included studies identified the motivators and barriers to clinical research participation among the patients and the general public in the EMRO countries. The identified factors are essential to consider when planning for future research. As they explain what motivates participation and explore some of the fears of the target population, these factors are important to address during the planning stage. There might be a gap between theory and practice due to the hypothetical design of most studies included in this review. Hence, future research to assess the perceptions and attitudes of patients who are actually enrolled in clinical research or those who are rejected to participate is further needed. Moreover, it is important to investigate the association of these factors and the likelihood of individuals participating in clinical research.
Author contributions
All authors of this review have participated to this article with different roles. M.A. provided the idea for the article and prepared the review proposal. B.I. provided supervision and guidance for the review concept, proposal, planning, and execution. I.A. and M.A. performed the literature search, data analysis, and initial draft. T.S. validated the review findings through a final assessment discussion with M.A. regarding the search strategy, selection criteria, data extraction and analysis, and quality assessment. M.I.B., I.A., and M.A. prepared the final manuscript version through critical review.

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