ABSTRACT Few studies have explored the informed consent process among research participants in developing countries. This study aimed to evaluate the informed consent process, therapeutic misconception and motivation for participation among Egyptians participating in clinical trials. In a cross-sectional qualitative pilot study 103 participants in 10 clinical trials responded to a questionnaire. Over 90% agreed they had time to ask questions and received adequate information about the risks prior to consenting. All participants thought the research and the drug would improve their condition; only 46.1% were aware of receiving a non-approved experimental drug and 21.3% of being randomized. Reasons for participation included: better treatment (100%), to benefit society & advance science (85.4%), to receive free drugs (42.6%) and medical care (43.6%), to get hospitalized (15.8%) and to receive money or
Gifts (4.9%). Investigators need to emphasize the distinction between research and clinical care to address the high rate of therapeutic misconception.

**Introduction**

The principle of autonomy has guided important aspects of research enrolment and participation, particularly the process of informed consent. International research ethics...
guidelines have specified the essential requirements for a valid informed consent: disclosure of sufficient information; adequate decision-making capacity; and voluntary acceptance to participate by the potential research participant (1).

In the last decade, local and international health research, including pharmaceutical company-sponsored clinical trials, have increased exponentially in the developing world, including the World Health Organization Eastern Mediterranean Region (EMR) (2–4). Yet there are many challenges to obtaining a valid, informed consent in this Region. For example, the high rates of illiteracy make understanding of research concepts challenging; the superior societal status of physicians can deter patients from questioning their doctors; poor access to medical services increases the likelihood of coercion; patients may be suspicious of signing anything other than vital documents such as a marriage license or property transactions; and physicians may be unaware of the procedural details of obtaining informed consent (5). While research participants’ views of the informed consent process have been investigated elsewhere (6,7), little is known about the views of research participants in the EMR. A detailed understanding of the impediments to obtaining a valid informed consent can aid researchers in improving the consent process.

Informed consent may also be jeopardized by the phenomenon of the therapeutic misconception, i.e. participants’ inability to distinguish between research and standard clinical care, and this presents additional challenges to informed consent (8). Essentially, if research participants believe they are receiving the usual medical care, and have incorrect beliefs that their treatment will be tailored to their needs and be beneficial to them, they might not appreciate the risk associated with clinical trials, thus further undermining the validity of their informed consent (9). While the prevalence and factors associated with therapeutic misconception in the developed world have been explored (10,11), only a few studies have explored the extent to which it exists in the developing world, including the EMR (12). A better understanding of the prevalence and the underlying factors associated with therapeutic misconception would allow investigators to address these issues prior to initiating their research.

Few studies have explored the motivations of participants in developing countries. Most studies done in the developed world reveal that reasons for enrolment include: a desire to support scientific research and to help future patients (13); the opportunity for enhanced access to medical treatment (14); altruism (13); and a concern that they may disappoint their health-care provider or that they may receive suboptimal care in their medical settings if they refused to participate in the research (15). Additional tangible motivations include financial or other material incentives (16) with their potential for coercion or undue inducement. By identifying the motivations of participants to join a research project, researchers will be better informed on how to best approach each individual in a culturally appropriate manner.
Accordingly, the goal of our survey was to evaluate Egyptian research participants’ perspectives regarding the informed consent process, therapeutic misconception and motivation for participating in research.

Methods

Study design

This was an observational, analytical, cross-sectional, qualitative pilot study that was conducted at the Clinical Research Centre, Faculty of Medicine, University of Alexandria, Egypt from October 2011 to July 2012.

Participants

We recruited individuals who were already participating in 10 different therapeutic clinical trials being conducted at the Centre (Table 1). This was a convenience sample of subjects with an inclusion criterion of being already actively enrolled in an ongoing clinical trial at the Centre and willing to participate in this study. The only exclusion criterion was refusing to consent to participate in this study.

The conditions being studied were: cancer (3 studies); infectious diseases (2 studies); diabetes (1 study); rheumatoid arthritis (1 study); acute coronary syndrome (1 study); schizophrenia (1 study); and uveitis (1 study). The clinical trials included phase II/III (2 studies), phase III (6 studies) and post-marketing phase IV studies (2 studies). Only 1 study was non-randomized, and all studies had a control arm (6 comparator and 4 placebo arms). Five of the randomized studies were double-blind and 4 of those were placebo-controlled trials (Table 1). All 10 trials required that blood be withdrawn for testing.

Study tool

A questionnaire to determine participants’ perspectives regarding several aspects of research was developed by the research team after reviewing prior published and validated questionnaires (17–19). The questionnaire was in Arabic, the native language of the participants, and included the following domains: demographic data; views regarding the informed consent process; evidence of therapeutic misconceptions; and motivation for participation. Participants responded to questions on a 5-point Likert scale (strongly agree; agree; uncertain; disagree; and strongly disagree). The questionnaire was administered by the same investigator (N.S.) after the subject had signed the consent form. Literate subjects were encouraged to read the questionnaire and ask questions, and for illiterate subjects the questionnaire was read to them by the same investigator in the presence of a literate relative.
and an impartial witness. The Arabic questionnaire and the English translation are available on request from the authors.

**Ethics**

All participants provided written informed consent, and the ethics committees at the University of Alexandria Faculty of Medicine and the University of Maryland School of Medicine institutional review board approved this study prior to the enrolment of any subjects.

**Statistical analysis**

We analysed the findings in 3 groups: age (55 years); education (illiterate, high school or less and higher education); and employment status (professional, manual labourer and unemployed). To improve clarity and arrive at meaningful conclusions, we collapsed participants’ responses into 2 variables: agree (total of strongly agree and agree) and disagree (total of uncertain, disagree and strongly disagree). To identify responses associated with participants’ characteristics, we used descriptive and bivariate analyses. Statistical differences within the age, education and occupation subgroups were determined using the Fisher exact test. A P-value of

**Results**

**Demographic characteristics**

Of the 103 individuals approached to participate in this study, all of them agreed to be enrolled. Table 2 shows their demographic data; similar numbers of men and women were enrolled, with a majority being married (83.5%), employed (62.1%) and high school or university educated (82.5%).

**Informed consent process**

Figure 1 shows the participants’ responses regarding the informed consent process. A majority (> 90%) acknowledged that the information they received was adequate to make a decision, that they had received a copy of the informed consent form with information about the study, including its duration and risks, and agreed that it was easy to understand. They felt that the person who obtained the consent was knowledgeable and respectful, the consent process was performed in a private place, and all of their questions were addressed. They felt comfortable signing it and that they had ample time to make an informed decision as to whether to participate or not, and they believed that their access to medical care would not be denied if they had refused enrolment and that there would not be any penalty if they withdrew from the study.
Individuals with higher education (78.8%) were significantly less likely to agree that they would receive their regular medical care if they refused enrolment compared with those who were illiterate (100%) or had a high school or less education (96.2%) ($P = 0.015$). Similarly, professionals (75.0%) were significantly less likely to agree with this statement regarding access to medical care compared with manual labourers (97.7%) and the unemployed (92.3%) ($P = 0.015$). In response to the question “I was made fully aware that some extra blood was taken from me that will be stored for future studies”, those with higher education (30.3%) were significantly less likely to agree with this statement compared with the other educational groups [illiterate (58.8%) and high school or less (69.2%)] ($P = 0.002$).

Therapeutic misconception

All participants

Figure 2 shows the participants’ responses related to therapeutic misconceptions. All participants (100%) thought that their doctor asked them to participate in the research because it would certainly improve their illness and that they would get the drug that was designed to improve their condition. Only 29.1% were aware that some research procedures might have no
Among the 89 participants enrolled in the 9 randomized trials, only 46.1% were aware that they might receive the experimental drug instead of the approved drug. Regarding randomization, only 21.3% were aware that they would be randomized (even though it was stated in the informed consent that they would be randomized by a computer program). Those with higher education level were significantly less likely to think they would receive the experimental drug (26.9%) compared with those who were educated only up to high school (57.4%) or who were illiterate (46.7%) (P = 0.045). Individuals aged 55 years respectively) (P = 0.037).

Participants enrolled in double-blinded trials

In the subset of 55 participants enrolled in the 5 randomized double-blinded trials, a larger proportion of participants (72.7%) were aware that they might receive the experimental drug (not
shown in Figure 2). The higher educated (50.0%) were significantly less likely to be aware compared with those who were educated only up to high school (87.1%) or who were illiterate (58.3%) (P = 0.028).

Only 30.9% were aware that they were randomized by a computer program, with the younger individuals more likely to be aware (53.3% of those 55 years) (P = 0.038). However, despite being informed that they and their physician were blinded to the treatment and that they were randomized by a computer, participants unanimously (100%) believed that participation in the study would improve their condition and that they would get the drug that improves their condition, while 98.2% believed that they would get the specific dose that was best for them. Only 16.4% knew that the procedures performed on them may have no benefit to them, 21.8% knew that they were taking a fixed dose and that their doctor cannot alter the dose according to their needs and 41.8% were aware that their doctor did not know which drug they were receiving. These perceptions were similar across all age, educational and occupational groups, with no significant difference between them (all P > 0.05).

**Motivation for participating**

Figure 3 shows the 103 participants’ reasons for participating in the clinical trials. All participants agreed that they enrolled in the study to get a chance to receive better treatment. About 90% of the respondents stated that they joined the study because their treating doctor thought it was a good idea and more than 70% participated to try a new drug that might be better for them. More than 85% wanted to benefit other patients and to support the advancement of science, and less than half participated to receive free drugs or to receive free medical care (42.6% and 43.6%, respectively). Only 4.9% participated to get money or gifts. About 15.8% said they participated as the study was the only way to get care from the hospital (35.3% of them were illiterate, 15.4% had a high school or less education and 6.3% had higher education) (P = 0.036). Only 2.0% said they joined because they were afraid that their treating doctor would be angry; and only 4.0% said that their family had pushed them to participate.
Discussion

In this cross-sectional survey of Egyptian patients who were already enrolled in clinical trials, we evaluated their perceptions of the informed consent process, therapeutic misconceptions and reasons for participation. Regarding the informed consent process, the participants seemed well informed and were given ample time to make an informed decision, and did not feel pressured or coerced by either their doctor or family members to enrol. Also, most believed they would still receive their usual medical care if they refused participation and all were certain they would receive the same level of medical service even if they left the study.

Only a small minority of patients felt they did not receive adequate information about the risks of the study and/or were not aware that other agencies such as the Ministry of Health or the sponsoring drug company might review their medical records. In general, we did not detect variable responses within the different groups regarding the informed consent process, except for those with a higher level of education and those with a professional occupation who were significantly less likely to believe that they would receive their regular medical care if they refused enrolment. This was an unexpected finding and may be a reflection of the study investigators’ incorrect assumption that those with a higher socioeconomic status did not need detailed explanations and would read the informed consent on their own; and/or a hesitation by these participants to question the investigator(s) about the study for fear of being perceived as unsophisticated or uneducated. Patients with a higher level of education were almost always from a higher socioeconomic class and were frequently referred from their private practitioner.
who gave them a general overview of the study, and the patients may have assumed that this was a better form of therapy since their private doctor recommended that they participate. Many times, even after having the consent form clearly explained to them, they still assumed that this was an opportunity for a better type of therapy, illustrating the greater likelihood of misconceptions about the therapeutic benefits of participation by this group. Furthermore, it is also possible that the investigators enrolling them into the clinical trial expended less effort in clarifying the study and its details when the subject were referred from their doctor and already fully willing to sign the consent form.

Conversely, patients who were illiterate and/or from a lower socioeconomic level may have been more suspicious of the medical establishment and once they became aware that a research study was being conducted they may have asked more questions and consulted several persons to read the consent and advise them, especially regarding the risks and adverse events. Hence they became better aware of the contents of the consent form before they signed it.

In a study by Joffre et al. of the quality of informed consent among cancer trial participants 74% of 287 subjects had major deficiencies in their comprehension of their study intervention, the risks of their participation and the unproven nature of their treatment; 29% did not realize the possible lack of any direct benefit to their participation (14). A study by Khalil et al. noted that research participants in Egyptian medical research were comfortable with studies involving surveys and blood sampling, but viewed drug trials as too risky. All participants valued the concept of informed consent, and felt that it was paramount to secure their permission before enrolling them in a research study (5).

Our results showed a high degree of therapeutic misconception among the research participants. These results are similar to an interview study that was performed involving Egyptians in an outpatient setting, whereby a majority of participants (80%) either expressed inaccurate beliefs regarding the degree with which individualized care would be maintained in the research setting or an unreasonable belief in the likelihood of benefits to be obtained from a research study (19). The authors concluded that the phenomenon of therapeutic misconception is not uncommon among Egyptian patients. These findings are similar to our study where participants in double-blind trials believed that they would receive the drug that would improve their condition, and that the drug dose would be adjusted to their condition. Only 16.4% were aware that research procedures would have no direct benefit to them, and 100% believed that they would get the drug that was designed to improve their condition. Given that participants unanimously stated that the information they received was adequate to make a decision, and that all their questions were answered by a knowledgeable and respectful person, these findings uncover a deeper level of misunderstanding, possibly related to the concepts of equipoise and randomization in clinical trials (11,20). In addition, although the information
appeared to be appropriately conveyed to and properly understood by the participants, it is possible that retention of information was short-lived or diluted by the quantity of information provided to them at the time of consent (21,22).

These findings are also consistent with many other studies involving participants in developed countries (10,11,22). For example, in a study specifically designed to identify therapeutic misconception, 225 subjects who were enrolled in 44 varied, mostly non-psychiatric clinical protocols were interviewed and 31% of the participants expressed inaccurate beliefs regarding the degree of individualization of their treatment, whereas 51% manifested an unreasonable belief in the nature or likelihood of the benefits gained from the study in which they were enrolled. A total of 62% of the participants were judged to manifest therapeutic misconception (9). In general, older age, lower education and worse self-described health were risk factors for having therapeutic misconception. In another study involving early-phase gene transfer trials, participants with cancer or vascular diseases had lower therapeutic misconception scores compared with those with inherited or infectious diseases (23). In our study, therapeutic misconceptions were highly prevalent in all categories of education level, profession and age group.

Investigators have explored the frequency and the factors (both participant- and study-related) that might underlie the existence of the therapeutic misconception in clinical research (9,23). The identification of such factors, as well as attempts to prevent or mitigate therapeutic misconception might have limited applicability to individuals in resource-limited countries, due to the existence of extreme poverty and lack of access to health care, high illiteracy rates, language and cultural barriers, gender inequality and patients’ unquestioning trust of their physicians compared with that in more developed countries (24).

Our findings regarding participants’ motivation to enrol in research are similar to other studies; specifically, the most frequent reason for participation in the research trial was the desire to advance medical science (13). Less than half of our study subjects participated to receive free drugs or free medical care, and this did not seem to be their main motivation for participation in the research, regardless of age, occupation or education, a finding which is similar to observations by other studies (15).

We would like to mention several limitations of our study. First, we recognize that we enrolled a biased sample, as we did not elicit the views of individuals who were not enrolled in a research studies and who might hold different perspectives regarding the informed consent process. Furthermore, we acknowledge that the sample size was not sufficiently large to be able to draw definitive analytical conclusions for individual associations. We also recognize that the sample
for this pilot study was a convenience sample of subjects from different types of clinical trials. Given that the objective of this study was to determine the research participants’ perceptions of the informed consent process, therapeutic benefit and reasons for participation it was not necessary to select a homogenous population. It is more likely that selecting subjects from different studies would make the results more generalizable to Egyptian research participants, regardless of the type of study. We further acknowledge that since we were not investigators on the original 10 clinical trials, we could not collect detailed information about the original enrolment or selection of participants in those studies. However, since the objective of this study was to understand the participants’ perceptions about their participation in a clinical trial, regardless of the aims or type of the original trial, then we do not believe that lack of information related to the parent clinical trials would have interfered with the objectives of our current study.

The fact that all 103 individuals approached for this study agreed to participate is unusual. However, these were highly motivated individuals who were already participating in high-risk interventional clinical trials, and hence more likely to agree to participate in this low-risk one-hour survey administered by a health-care worker in a research centre they already trusted. Our study had a higher proportion of educated participants compared with the country as a whole, with only 16.5% being illiterate compared with a national adult illiteracy rate of 26.1% (25). Furthermore, although employment status can be a proxy for income, we did not directly explore the association of income with participants’ responses in our study. Responses regarding motivations for participation might be associated with income status, as individuals from the lower income classes might be more motivated to enrol in studies by the prospect of monetary incentives, free drugs or free medical care. A study of 136 healthy subjects volunteering in phase I trials in Portugal identified financial reward as the most important motivation by subjects with a lower monthly income (26). In another study of participants in a smoking cessation trial in the United States, participants were more likely to be single, have a lower income, be more nicotine-dependent and have higher levels of depressed mood and stress (27). In our study, those with a higher education were less likely to agree that they were fully aware that some extra blood was taken for future studies. However, while all 10 trials required that blood be drawn, we could not ascertain whether the informed consent in all the studies included a statement to that effect, or that subjects were made aware of such a possibility. If some studies did not include such a statement then it would be expected that those with a higher education would be significantly less likely to agree with that statement. Finally, participants in our study were enrolled in research in an established clinical trial centre in a major university in Egypt and hence our results, especially those regarding the informed consent process, might not be generalizable to less established clinical sites in Egypt.

Our pilot study demonstrated that participants in clinical trials at this research centre were willing to share information freely about their participation, and that information collected through this study was meaningful and strongly suggestive of the presence of therapeutic misconception. Our study demonstrated that enrolled research participants had a favourable perspective of the informed consent process in a well-established clinical site in a developing country. Our study
also demonstrated that similar to developed countries, there was high degree of therapeutic misconception among the patients and hence there needs to be enhanced educational efforts for potential participants as well as for investigators to minimize such misconception. This study has revealed the importance of conducting more detailed interviews in Egypt using a standardized and/or validated questionnaire to measure and understand the reasons for therapeutic misconception among clinical trial participants. Furthermore, it would be important to enrol a large enough sample size to allow for the enrolment of multiple patients from each clinical trial to facilitate comparisons within, and between, clinical trials. In general, and based on the preliminary findings from this study, we recommend a focus on identifying participants or protocols (e.g. higher-risk studies) where therapeutic misconception is more likely to occur and develop educational interventions to mitigate it. Suggestions for countering therapeutic misconception have focused on being more explicit about procedures unique to research (e.g., random assignment or placebos) (28) particularly because many people have little understanding of these terms (29). It has also been suggested that highlighting that payments or other compensation is often given for participation in research may serve to alert participants that they are participating in a research study and help reduce therapeutic misconception, although empirical evidence for this is lacking (30).

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**References**

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