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RESEARCH

Profiles and voices of participants in clinical research in Brazil

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Abstract

This case study aimed to trace the socioeconomic profile of participants in clinical research at a Brazilian research center, analyzing their decisions, motivations, experiences, knowledge of risks, benefits and health care provided, and the consent process. The data of 327 participants were collected, and semi-structured interviews conducted with 19 of them. In the research carried out at the center studied there was a greater participation of men and of people with few years of formal education and low income. Most are retired and have no private health plan, tend not to notice the effects of the investigation, or to overestimate its direct medical benefits. The search for medical treatment was the main factor influencing their decisions/participation, and signing the informed consent form did not guarantee the expression of autonomy. We concluded that the participants' profile and speeches content are sensitive indicators of vulnerability and social inequality.

Keywords: Researcher-subject relations. Clinical trials as topic. Social vulnerability. Health equity. Socioeconomic factors. Ethics in research. Bioethics.

Resumo

Perfil e vozes de participantes de pesquisas clínicas no Brasil

Este estudo de caso buscou traçar o perfil socioeconômico de participantes de ensaios clínicos em centro de pesquisa brasileiro, analisando suas decisões, motivações e experiências, seu conhecimento sobre riscos, benefícios e cuidados dispensados e o processo de consentimento. Dados de 327 participantes foram coletados, realizando-se entrevistas semiestruturadas com 19 deles. Nas pesquisas executadas no centro estudado houve maior participação de homens, de pessoas com poucos anos de estudo formal e de baixa renda. A maioria é aposentada, não tem assistência privada à saúde e tende a não perceber os efeitos da investigação ou superestimar os benefícios médicos diretos. A busca pelo tratamento médico foi o principal fator que influenciou suas decisões/participação, e a assinatura do termo de consentimento livre e esclarecido não garantiu a expressão da autonomia. Conclui-se que o perfil e o conteúdo dos discursos dos participantes são sensíveis indicadores de vulnerabilidade e desigualdade social.

Palavras-chave: Relações pesquisador-sujeito. Ensaios clínicos como assunto. Vulnerabilidade social. Equidade em saúde. Fatores socioeconômicos. Ética em pesquisa. Bioética.

Resumen

Perfil y voces de los participantes de investigaciones clínicas en Brasil

Este estudio de caso trató de esbozar el perfil socioeconómico de participantes de ensayos clínicos en un centro de investigación brasileño, analizando sus decisiones, motivaciones y experiencias, su conocimiento sobre los riesgos, beneficios y cuidados prestados y el proceso de consentimiento. Se recopilaron datos de 327 participantes y se realizaron entrevistas semiestructuradas con 19 de ellos. En las investigaciones realizadas en el centro estudiado hubo una mayor participación de hombres, de personas con pocos años de educación formal y con bajos ingresos. La mayoría es jubilada y no tiene asistencia sanitaria privada, tiende a no percibir los efectos de la investigación o a sobrestimar los beneficios médicos directos. La búsqueda de tratamiento médico fue el factor principal que influyó en sus decisiones/participación, y la firma del término de consentimiento libre e informado no garantizó la expresión de la autonomía. Se concluye que el perfil y el contenido de los discursos de los participantes son sensibles indicadores de vulnerabilidad y desigualdad social.

Palabras clave: Relaciones investigador-sujeto. Ensayos clínicos como asunto. Vulnerabilidad social. Equidad en salud. Factores socioeconómicos. Ética en investigación. Bioética.

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As a result of university and industry becoming closer, scientific activity in the health area – especially clinical trials [1] – ceased to be an amateur practice, becoming in the twentieth century a scientific-industrial-technological complex [2]. The several national and international documents that regulate the matter are not fully capable of guaranteeing the respect for the integrity of research participants, and even today conflicts and abuses are common.

As an example, studies carried out in peripheral countries on vertical transmission of HIV in pregnant women via placebo-controlled groups stand out [3]. These cases lead to the conclusion that, in contexts of high social inequality, people without access to primary healthcare become more vulnerable and may be subject to unjust and suffering situations. It is imperative to reflect on the dignity of human beings and their autonomy, including the informed consent form (ICF), whose mere signature, without proper understanding, raises complex issues in contexts of socioeconomic vulnerability and illiteracy.

The reason why subjects accept to participate in clinical research is another essential issue for the debate on public health and research ethics. Such studies are scarce [4-6], requiring reflection and updating of the guidelines related to research involving human beings. Little is known about research participants, little attention is paid to them, and little is said about them. In this sense, this article involved participants in cardiology clinical trials conducted at a research center in Northeast Brazil. To know who these people are, their socioeconomic profile was traced, and we analyzed questions related to their motivations, decisions and experiences in clinical trials, in addition to their knowledge of risks and benefits involved, care provided during and after the study, and the informed consent process.

Method

This study was conducted in a private clinical research center, connected to the Unified Health System (SUS), located in the city of Natal, Rio Grande do Norte, Brazil. We analyzed documents of 327 patients who participated or were participating in cardiology clinical trials at the research center, of which 19 were also interviewed.

This is an observational case study, with an exploratory and descriptive nature and a two-stage qualitative and quantitative approach. The latter aimed to establish the socioeconomic profile (age, gender, education level, family income, place of residence, access to private health care, etc.) of the 528 participants in the 26 clinical trials developed at the center studied. The purpose of this step was to carry out a census, but data from 201 people were unavailable, leading to a total sample of 327 patients. This data was collected from medical records and research protocols between October 2012 and July 2013. Absolute frequencies, percentages and distributions of this information were recorded and analyzed with SPSS for Windows.

In the qualitative stage, semi-structured interviews were conducted with 19 participants, identified by the letter "S" followed by a number and selected for convenience – that is, subjects who could be invited to the research center were interviewed. The number of respondents was determined by saturation, i.e., the sample did not follow numerical criteria, but was concluded when the repetition of meanings in the speeches made it unlikely to deepen the understanding of the topic [7].

The inclusion criteria in the second phase were to have participated or be participating in a clinical trial; be over 18 years old, and not to have any alteration, disorder, disability or mental illness that would impair or impede understanding at the time of the interview. We sought to search in the testimonies for information about the motivations, decisions and experience of participating in clinical trials, as well as about the consent process, the knowledge of risks and benefits and care provided to the subjects during and after the research.

The interviews followed a semi-structured script, were recorded and transcribed in full. The content analysis method was used according to the steps described by Bardin [8], and NVivo software was used as an auxiliary tool to organize the material and objectively establish the frequency of what was verbalized.

Qualitative data were treated in three stages. In the first stage, or pre-analysis, the material was organized, starting with a fast and repeated reading of the transcriptions, aiming at a general meaning, and posterior identification of convergent, representative and significant points. In the second stage, the

empirical material was explored, coded and decomposed, with seven categories of analysis defined, whose units of meaning were grouped, classified, categorized, and investigated. In the third and final stage, the results and interpretations converted the collected content into qualitative data and reflective analyzes. Thus, summaries, inferences and articulations were carried out between the information obtained and the theoretical contribution of the research.

Results

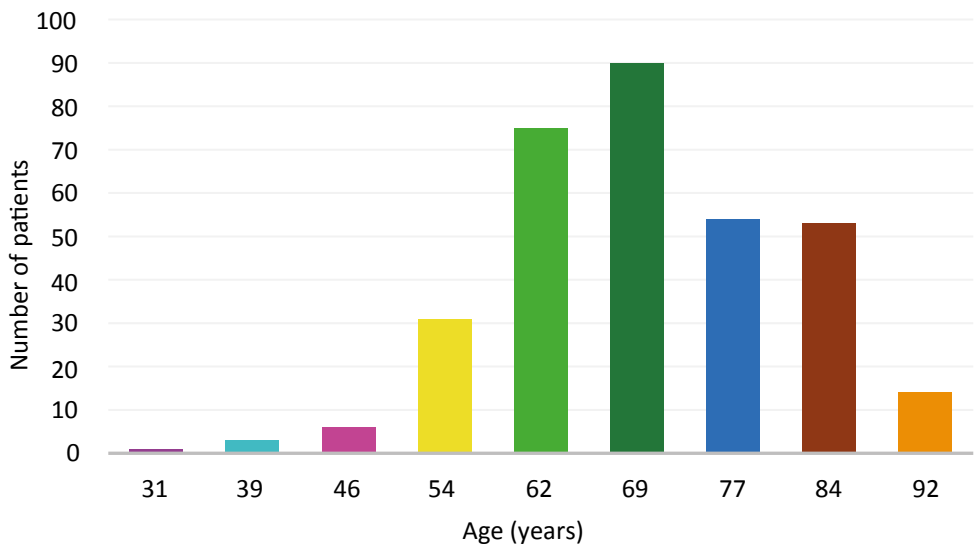
To favor the presentation and understanding of the results, the quantitative data (related to the information of the 327 participants registered at the research center) and qualitative data (based on the interviews) were used together, when possible, and by categories of analysis of the study, in a complementary manner.

The analysis of the 327 documents included in the first stage of this research indicated that 80.4% of the patients participated in clinical trials in phase III, 14.1% in phase II, and 5.5% in phase IV. In the trials already completed, only 10 patients did not participate until the conclusion: five died, two had aggravated health conditions, two left the study with no record of motivation, and one asked to leave.

Who were the participants?

Based on the records of 327 patients, 66.7% were men and 33.3% were women, with ages distributed according to Graph 1. Only 107 (32.7%) documents indicated the patient's education level, of which 55 (51.4%) had only elementary education, 25 (23.4%) were illiterate, 19 (17.8%) had attended high school, and only eight (7.5%) had completed tertiary education. Regarding the patient's profession, most (33.6%) were retired, and 23.5% of the records did not have this information. Only one medical record informed the patient's family income, who received up to one minimum wage. Among the 19 interviewees, eight had this same income, nine received up to 2 minimum wages, one received three minimum wages, and one received four minimum wages.

Graph 1. Age distribution of clinical trial participants at the research center



The participants' place of residence did not appear in 5.5% of the forms, but the others showed that 49.2% lived in Natal, and 45.3% lived in other cities in the state. Regarding those who lived in the capital, most lived in the west of the city (15.9% of the total investigated, and 32.3% analyzing only data from Natal), its poorest region. Most patients (79.5%) did not have a private health plan – including the 19 interviewees –, and 3.4% of the documents did not present these data.

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How did they find out about the research and why did they decide to participate?

Most respondents reported that they learned about the research after having a heart attack or a severe heart condition. Fifteen came from public hospitals and were invited to participate in the research by a doctor or nurse after performing some procedure at the institution where the research center is located.

In summary, they decided to accept the invitation because they suffered a serious, life-threatening condition, and wanted to heal and receive good care. At that time, they judged it to be the best option, given the guarantee of regular and frequent medical examinations and follow-up, something with a deficit in public service. The following statements are emblematic:

"[I decided to participate] *because I thought it was better, I was going to be more frequently assisted*" (S1).

"*Firstly, because I don't have a health plan, and I couldn't afford it* (…) *because I have to be examined every three months, I have to do tests, because I'm diabetic, you know? I am hypertensive, I have to be followed-up, right?*" (S3).

"*The reason is my well-being, my health. I've already had a heart attack, I got a pacemaker, so it's something I need, I don't have a health plan; these health centers, nobody can count on them, right?*" (S6).

Some patients considered the research a health plan or treatment, as it can be observed in the following statements:

"*They asked if I would like to participate in this research, in this treatment. I got sort of… I didn't know, country people don't know anything, right? Then the nurse said: it is very good for your health; accept it, your problem is serious. And then I accepted it*" (S17).

"*I had a heart attack, right? About two years ago. Then, when I left, the doctor who made the surgery called me over to his office and asked if I would like to be part of a plan, because it was very important for me*"(S12).

"*I have been followed-up by Dr. Y, making a lot of sacrifice to pay for private consultations, then one day she told me about this research: I will include you in this plan, because I see that you make great effort to pay for this consultation and the research follow-up is a very good thing for you*" (S4).

How was the consent process?

All respondents confirmed having signed the ICF, but most confessed to having asked for help to understand it, while others stated that they had difficulties, and some even revealed that they had not read it. Although four patients reported having understood the ICF easily, none of them knew how to answer more profound questions – about, for example, the risks present in the study – in the interview. The participants were unaware of the methodological procedures and their adverse effects, and associated the research objectives with their cardiological treatment, believing that the protocol was based on their needs and interests. The following statements shows the consent process:

"*Well* (…) *I could have read it, or not. I have not. She said, 'you have to sign it in this way,' I signed, but I haven't read it*" (S1).

"*No. It was a little difficult, I was in doubt about something, right? Because they are words which I don't understand, and I got sort of… but that's okay*" (S12).

"*Actually, I haven't read it completely, no. More or less. The girl who made this medication plan explained it to me more or less, and I signed the terms without reading it in full*" (S14).

The participants in clinical trials do not understand what "placebo" means, since only two of the 19 patients interviewed addressed this issue, and only one of them used that term. The following report exposes this serious ethical issue, as it shows that, although S12 has been in the research for almost two years, the participant only came to know the topic in the last consultation:

"*The last time I have been here, the girl made a survey on me and said: this medication that we're giving to patients, we don't know it, it comes from the United States and we give it to the patient, despite everything. It may be good for you, it may be useful for something, and it may be useless. That's what she told me. I said okay, then she said: do you want to continue or not?*" (S12).

The following statement reveals how the occasion for recruitment demands attention

and reflection in favor of a respectful and true consent process:

"*I left the ICU, went to the infirmary, then I was already discharged from the hospital and had to leave the bed to another patient. I signed to stay in this study. She said it was for my well-being, because I needed it, because I've had a heart attack, I needed to take this medication, it was for free. I was so nervous! Such a distress*" (S10).

Were the participants aware of the risks and benefits to which they were exposed?

No interviewee spoke with any conviction about the risks. Eleven said they did not know them, and eight said they did, but did not remember what they were:

"*Risks? What do you mean? No*" (S2).

"*More or less. I'm not getting it right. I have the complete paper at home, I've sort of read it very quickly. If it's not bad for me, it's good*" (S14).

"*I don't remember. I was so bad that day*"(S17).

This last report reinforces the care needed when recruiting people to participate in health research, safeguarding their dignity and autonomy. Interviewees associated the benefits with the quality treatment they had been receiving.

What is the care research subjects are provided with during and after the study?

No interviewee knew how to talk about post-study care. Fifteen participants stated that nothing was said about it, and the other four did not remember what it was about. Many also showed great concern at the time of the interview, expressing sadness and insecurity regarding the continuity of their treatment once the study was finished. Such aspects are confirmed in the following statements:

"*No, I don't remember if it was promised, but I don't think so. Then, no*" (S1).

"*No, not so far. After the research, I don't know what will happen, because I don't have money to pay a cardiologist, and here I thought it was good because I had a cardiologist without paying. Nobody can count on public health centers"* (S6).

"*If it's on the paper that was signed, I don't understand, I didn't understand. I don't know what it will be after the research finishes*" (S14).

Particularly, the following statement reveals the participant's total vulnerability, need and alienation levels and, at the same time, denounces the serious social context involved in the discussion about clinical trials:

"*Nobody told me, I don't remember. When it finishes, I don't know. I even said: lady, when it finishes, don't take me out of it, put me here in any case.*" (S19).

How do they evaluate the experience of participating in clinical research?

The results presented so far already allow outlining the answer to this question. In general, the interviewees evaluated the participation in the research as good, very good, and excellent. They spoke of good assistance, access to medication and the guarantee of regular monitoring. In short, they are satisfied with the assistance they have received or are receiving:

"*It's an examination, it's the doctor, if you need to undergo surgery tomorrow or later, it will be right away. Now by SUS, right? By SUS! I don't have anything to complain about, neither about the doctor nor about the hospital, everything is very good. I got very good assistance here. Amazing!*" (S11).

Spontaneous reflections

In this last category, the statements that the interviewees gave spontaneously at the end of the interview will be explored. Only three patients declined to add comments. Regarding the others, four expressed concern and sadness about the end of the research and the desire to remain at the center; one had doubts about the symptoms felt, whether they were the effect of the studied medication or of the other drugs taken; eight commented how much they liked the professionals, the assistance and care received; and nine thanked the excellence and quality of this care.

It is worth mentioning S12's unique reflections, which reveal issues that go beyond the eminently technical view, also contemplating political, social and ethical aspects involved in clinical research:

"*Why don't we have access to the examinations? I believe it is our right as patients, right? Even if I don't understand anything, seeing the examinations makes me feel good* (...). *I was really shaken when I felt I was being treated like a guinea pig, because in reality that medicine may be nothing* (...). *And, certainly, there are these people from the countryside who have the same doubts, but we, who have more information, understand* (...). *But all that happens is that our system is very precarious. If we had a good health plan, if the government paid for everyone to have a good health plan* (...). *The person often enters into something like that, searching for* a *service that does not exist, there is no service at all, and thinking that there will be something for their own benefit. And we know that, in fact, this research that will benefit, all right, in the future, but nobody knows when. It will benefit the researchers because they will earn a lot on the medication patent, the laboratory will benefit because it will sell the medication, and the persons who will receive the medication, okay, it will be good for them, because they will buy it and be benefited, but the government, and not us, should pay for that and everything, for this medication that is researched now and a lot of people is being used as a guinea pig*" (S12).

Discussion

The data shows that participation in clinical research was seen by the subjects as alternative medical treatment, possibly indicating the precariousness of the health services available to the population – a common occurrence in several communities around the world [4-6,9-13]. By showing that some patients consider research to be a health plan or guaranteed treatment, it is evident that they do not understand what this participation means. It points to the need to establish a more critical view of the ICF, the consent process and the respect for autonomy, especially in contexts of vulnerability.

The situation becomes more complex when associating the accounts listed with the double image of a doctor-researcher. The speeches collected during the interviews show that patients tend not to question the physician [14], due to the relationship of trust created and the authority of this professional [15,16]. We should question this double role, as well as the contradictions between research and treatment [10,17].

The informed consent should confirm the participant's understanding of the difference between proven therapy and experimental drug [18]. In this context, the term "therapeutic research" should be avoided as it is potentially misleading [19] and induces confusion. This fact was evidenced in this study and described in the results, showing that, in addition to ignoring fundamental aspects of the research – as objective, methodological procedures and adverse effects of substances [10,20] –, patients believed they were receiving individualized treatment, specific to their health needs.

These mistakes reveal failure in the consent process, and may result in a relationship based on an uninformed decision, feeding expectations based on incorrect criteria and also compromising the assessment of risks and benefits by patients [10]. Most participants in clinical trials do not understand the meaning of "placebo," that is, that there is a 50% chance of not receiving any medication [21]. This situation was observed in this study, in which only two participants addressed the topic, and only one used the appropriate word.

The consent of clinical research participants has to be seen as an educational process to respect their autonomy, being more than a signature on a paper, as shown in this study. Low socioeconomic and educational levels are associated with less ability to question and less confidence when obtaining the ICF [10,22]. The research center studied is located in Northeast Brazil, which concentrates the largest number of illiterates in the country (54.2%) [23]. This situation is aggravated when considering functional illiterates, represented mainly by older people [23] – age group of most of the participants in this case.

Since clinical research of new drugs implies more potential risks for the subjects, they should have more discernment and be more aware and informed to accept participating; however, the educational level has been neglected when addressing this topic [10]. The ICF format in clinical research is another issue: they are usually long documents and sometimes have complex terms and medical and technical language that even those with a high educational level may find difficult to understand [10,24].

In practice, consent is limited to giving information and signing the form, far from informed and conscious decisions, especially in cases involving social vulnerabilities [10].

This condition can be considered critical, and is generally incorporated in a vertical manner [25].

The relationship between clinical trials and social vulnerability is often unaddressed. In this study, we found that data related to the patients' socioeconomic profile is absent from most of the documents analyzed. Discussing this profile is extremely important and deserves special attention in view of the current market logic that permeates clinical research, especially in social inequality scenarios [10]. Conflicts of interest and adverse effects of the growing relationship between researchers, universities and health services with the pharmaceutical industry have been also evidenced [26].

All these issues need to be explained to patients, especially when they have low educational level and lack knowledge on the nature of clinical research and its distinction from medical care. Economic and social vulnerability is evident in contexts of difficult access to basic health services and medicines, and this scenario may stimulate the proliferation of research with questionable ethical standards [10].

By neglecting this aspect, the scientific community somehow contributes to this practice. The few studies that seek to analyze the profile of clinical trial subjects indicate that poorer people, without access to healthcare, usually participate [27]. Another study, which aimed to analyze strategies to improve recruitment for clinical trials among Latin American patients, found that almost all people with lower wages and poor healthcare agreed to participate [28].

As shown in the results of our research, all respondents had recently suffered a serious and life-threatening episode. Their accounts show that consent was sometimes given in a context of pressure and vulnerability, in which they would only have access to assistance if they accepted to participate in the study proposed. In such situations, the patient feels compelled to participate and remain in the research [29]. The interviewees were extremely vulnerable and dependent on the doctor, a situation reflected and aggravated by the lack of knowledge on the issues involved and related to their participation in the research protocol [10,30].

Moreover, in this case the ICF proved to be insufficient to express a truly autonomous decision. Other studies [10,31-33] present the same conclusion, although the findings by Lacativa and collaborators [34] are inconsistent. Clarifying the risks and benefits to which participants are or will be exposed in clinical research is a basic ethical need, but volunteers often consent to participate with little [35,36] or no knowledge of important information [10]. The interviews in our research reveal that none of them knew how to talk about the risks.

The guarantee of post-study care also does not seem to have been clearly addressed, giving rise to the hypothesis of not being routine in the studies at the researched center, which is a serious ethical issue [10]. In view of the observed, there is a real need for effective healthcare and critical analysis followed by a debate about the identification and responsibilities of each institution directly and indirectly involved in clinical trials. This study verified that 8.9% of the forms did not indicate the institution proposing the trial, and that 84.7% of the patients participated in studies proposed by pharmaceutical laboratories, 5.5% in those proposed by public universities, and 0.9% in research proposed by a private hospital.

When analyzing the countries proposing studies carried out at the center, we found that 1.5% of the forms did not present this information, 77.4% of the patients participated in trials conducted by North American institutions, 9.5% in trials by French institutions, 6.7% by Brazilian institutions, and 4.9% by Canadian institutions. Considering this, it is imperative that the critical discourse on outsourcing clinical trials should not only emphasize the dangers of this practice, but also address more general issues of equity and justice that determine access to healthcare in developing countries [37].

Final considerations

Even with the increase in the number of clinical studies carried out in the last decades, there is little debate about its participants. Although this research was developed in only one research center located in the Northeast of the country and with a limited number of participants, and thus not representing the general scenario in Brazil, it is possible to focus on people, identify who they are and pay attention to their speeches

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and interpretations. The primary intention, in this context, is not to generalize the situation, but to contribute with reflections on the topic.

There is a direct relationship between a greater participation in clinical research and a condition of greater socioeconomic vulnerability, and evidence indicates that research priorities may be taking precedence over the patient's individual needs. Research participants tend not to notice the effects of the investigation or to overestimate the direct medical benefits of their involvement in the studies, even though the search for "medical treatment" offered by the clinical trial is the main reason for their agreement to participate.

In practice, signing the ICF has not guaranteed the expression of autonomy. Documents are signed, but the essential information for the autonomous decision – such as objectives, benefits and risks and the right to continue the treatment in case of leaving the study – is little known. In this sense, science favors such questionable practice by not analyzing and discussing these aspects.

We conclude that the participants' profile in this study and the content of their speeches are sensitive indicators of vulnerability and social inequality. The expectation is that these results can encourage interdisciplinary and critical exercise and dialogue between the different actors and institutions involved in the area of research with human beings, as to prevent situations of disrespect, inequality, vulnerability, and moral suffering.

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Participation of the authors

Karla Patrícia Cardoso Amorim participated in all stages of the study, conceiving it together with Volnei Garrafa. Alana Dantas de Melo, Andressa Vellasco Brito Costa, Gabriella Caldas Leonardo Oliveira, Heitor Giovanni Lopes, Eduardo Judene da Silva Pereira and Francisco Ademar Fernandes Júnior collected the data. All authors analyzed the data and wrote and revised the manuscript.

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