# Understanding Barriers to Clinical Trial Participation Among Cancer Patients: Insights from a Brazilian Oncology Center

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## Abstract

**Introduction** Clinical trials are essential for advancing cancer care, yet patient participation remains low, particularly in regions with limited awareness such as Brazil.

**Materials and Methods** This cross-sectional survey was conducted between 2020 and 2022 at a single cancer center in São Paulo, Brazil. Adult cancer patients completed a structured questionnaire assessing awareness and barriers to clinical trial participation, categorized as patient-, protocol-, or physician-related.

**Results** Among the 206 oncologic patients enrolled in the study, 83.5% were female and 43.7% were treated in the public health system. The percentages of patients who self-identified as White and Brown/Black were 59.7 and 35.9%, respectively. Patient-related barriers included unfamiliarity with trial participants (84.6%), concerns about daily life disruptions (75.4%), and transportation difficulties (66.2%). Protocol-related barriers included fear of unknown side effects (62.3%), inability to choose treatment (47.6%), and potential assignment to the placebo group (46.8%). Physician-related barriers included communication issues, weak doctor-patient relationships (94.7%), and patient deference to doctors' decisions (55.4%). Patients with higher income (OR: 3.60; 95% CI: 1.18–10.9) and those treated in the public system (OR: 3.69; 95% CI: 1.58–8.63) were more likely to be aware of clinical research.

**Conclusion** This study highlights the multifactorial nature of barriers to clinical trial participation in Brazil, where access disparities persist. Increasing patients' educational level, enhancing doctor–patient communication, and addressing structural disparities are essential steps towards improving trial enrollment and promoting fair access to innovation in cancer care.

**Keywords**
- neoplasms
- patient participation
- health knowledge
- healthcare disparities
- Brazil

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## Introduction

Cancer is a leading cause of death worldwide, affecting nearly half of all men and one-third of women throughout their lives.[1] Clinical trials play a central role in evaluating the efficacy of new cancer treatments and are essential to advancing oncology care.[2] Their success depends on recruiting and retaining patients, yet fewer than 1 in 20 adult cancer patients participate in clinical trials, even though most patients in the United States view clinical trial participation favorably.[3]

This discrepancy between patient's willingness to participate in trials and their actual enrollment suggests the presence of barriers to trial participation, many of which might be removed.[3] Numerous studies have evaluated how cancer patients decide whether to participate in trials, often identifying structural and personal barriers, suggesting that the patients themselves are the primary limiting factor.[3,4] However, trial-related barriers such as restrictive eligibility criteria and logistical burdens significantly make access difficult and may highlight disparities. In response, initiatives like the US Food and Drug Administration (FDA)'s draft guidelines on decentralized clinical trials (DCTs) aim to reduce these limitations by enabling trial-related activities to occur outside traditional clinical settings, potentially increasing accessibility and cohort diversity.[5]

Brazil is internationally recognized for the technical capacity of its regulatory agency, the Agência Nacional de Vigilância Sanitária (ANVISA), and for its strong network of experienced clinical researchers.[6,7] Even so, clinical trial participation remains limited. The country ranks 20$^{th}$ globally in clinical research, with only 2.4% of studies.[8] Understanding the specific barriers faced by Brazilian patients is essential to guide the creation of new policies and to direct resources to improve trial participation.[3]

In an era that emphasizes shared decision-making and patient-centered care, ensuring that patients have the opportunity to consider trial participation is vital.[2,9] This study aims to evaluate the perspectives of cancer patients in Brazil regarding clinical trials, and to identify the key barriers to trial refusal.

## Materials and Methods

This was an observational, analytical, cross-sectional, single-center study with a quantitative approach, conducted to assess cancer patients' perceptions of clinical trials and the barriers associated with their refusal to participate, providing an overview of the current clinical oncology research scenario in Brazil. The study was carried out at Instituto Brasileiro de Controle do Câncer (IBCC), a cancer center located in São Paulo, Brazil, between May 2020 and December 2022.

Eligible patients were 18-years-old or older, with a current cancer diagnosis or a personal history of cancer. All participants were required to be lucid, oriented, and have any level of education. Recruitment was conducted consecutively among patients receiving care at IBCC, and the questionnaire was offered to all eligible patients attending the oncology clinic during the study period. All participants provided written informed consent prior to inclusion. The study was approved by the IBCC's Research Ethics Committee (CAAE: 26583019.6.0000.0062) and conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Data collection was done using a structured questionnaire (►**Appendix A**), developed based on a meta-analysis published in The Lancet in 2006, which aimed to identify barriers to participation in clinical trials across diverse patient groups.[1] This meta-analysis incorporated quantitative and qualitative analyses of studies that utilized structured questionnaires or frameworks to identify potential barriers. In alignment with this comprehensive review, our questionnaire was designed to categorize questions into three main blocks, including primary barriers related to the patient, protocol, and physician. The questionnaire included a guiding question: "Have you ever heard about clinical research?", designed to assess patients' baseline awareness and serve as a reference point for analyzing related barriers.

### Statistical Analysis

Descriptive statistics were used to represent the characteristics of the study participants. Categorical variables were reported as absolute and relative frequencies. Associations between questionnaire responses and patients' sociodemographic variables were analyzed using Pearson's chi-squared or Fisher's exact tests, as appropriate.

Multiple logistic regression was used to analyze factors associated with patients' awareness of clinical research. The dependent variable was previous knowledge of clinical research (yes, no), and the independent variables included education level, monthly income, health system (public or private), and race. Age and sex were included as potential confounders.

The internal validity of the questionnaire was assessed using Cronbach's alpha, considering the full set of questions and then stratified by the three barrier domains. A $p$-value $< 0.05$ was considered statistically significant. All analyses were conducted using the statistical software SPSS for Windows (IBM Corp.), version 25.0, and Stata (StataCorp LLC.), version 18.0.

## Results

A total of 206 cancer patients were interviewed between May 2020 and December 2022. The majority were female (83.5%), and under the age of 65 (72.3%), with a median age of 57 (range: 25–84) years. Most participants self-identified as white (59.7%), followed by brown or Black (35.9%). Approximately ⅓ (34.5%) had not completed higher education, and 20.1% had a monthly income between one and two minimum wages (MWs, between R$ 1,117.00 and 2,234.00, equivalent to US$ 224.00 and 448.00, respectively). Regarding health care coverage, 43.7% of the participants were treated in the Brazilian public health system (*Sistema Único de Saúde* [SUS]), while 56.3% had private health insurance. The main

primary tumors were breast and gynecological, representing 63.6% of the total (►**Supplementary Table S1**). Treatment intention (curative or palliative) was not assessed.

When asked the guiding question, "Have you ever heard about clinical research?" and whether they wanted to participate, 64.6% of patients reported having heard of clinical research, but only 14.4% knew someone who had previously participated in a trial. The majority expressed being open to joining a study in the absence of other treatment options (95.1%), and most of them believed they would have family support for this decision (90.7%). On the other hand, concerns such as fear of daily life disruption (75.4%), discomfort with being part of an experiment (31.5%), and transportation or work-related difficulties (66.2%) were reported. Patients with lower educational levels were less likely to be aware of clinical research ($p = 0.021$), and less willing to participate in longer and more complex trials ($p = 0.049$), as shown in ►**Supplementary Table S2**.

Regarding protocol-related barriers, most patients expressed concern about unknown side effects (62.3%), lack of choice of treatment arm (47.6%), and potential assignment to placebo (46.8%). On the other hand, 84.9% agreed to participate even if there was no direct benefit, for the sake of future patients, and 83.1% reported they would join knowing they could withdraw at any time (►**Supplementary Table S3**).

Nearly all participants indicated that the physician–patient relationship would be important for participation in the trial (94.7%), and 88.6% said they would join a study if invited by their physician. More than half believed that doctors should make all treatment decisions (55.4%) and 19.2% thought that physicians might have personal interests when inviting them to a study. The belief that physicians should make all treatment decisions was significantly associated with type of health care coverage ($p = 0.013$), as shown in ►**Supplementary Table S4**.

Multiple logistic regression analysis showed that both higher income and treatment in SUS were significantly associated with greater awareness of clinical trials. Patients earning more than three MWs were more likely to report prior knowledge (adjusted odds ratio [OR]: 3.60; 95% confidence interval [CI]: 1.18–10.9; $p = 0.024$), as did those treated in the public system (adjusted OR: 3.69; 95% CI: 1.58–8.63; $p = 0.003$). This information can be found in the ►**Supplementary Table S5**.

The internal consistency of the full questionnaire was moderate (Cronbach's alpha = 0.551). Among the three domains, physician-related barriers had the lowest internal consistency.

## Discussion

Clinical trials are a critical pathway for improving cancer treatment and shaping the future of patient care. Although many patients are open to participating, actual enrollment rates remain low.[10] Several barriers contribute to this gap. The decision to participate in a trial is complex, multifactorial, and deeply personal.[11]

This is, to our knowledge, the first study in Brazil to use a structured questionnaire to explore the perspectives of cancer patients on barriers to clinical trial participation across both public and private health systems. The main obstacles identified are consistent with the literature.[9,12–14] While earlier studies have addressed these issues, few have focused on Brazilian patients or included both health care systems.

Public system patients were more likely to report prior awareness of clinical trials. This may reflect the Brazilian scenario, where access to innovative treatments such as immunotherapy in SUS often depends on clinical trial participation or judicial action. Judicialization in health care is costly, not universally accessible and may exacerbate inequities, as few individuals can afford the legal process.[5,15] These findings contrast with those from developed countries, where lack of health insurance is a common barrier to research participation.[11] This highlights the need for region-specific data, particularly in low and middle-income countries.

Although our analysis did not find a statistically significant association between race and awareness of clinical trials, Black patients represented over ⅓ of the study population, and their inclusion remains critical. Historical mistrust in the health care system by this population persists and must be acknowledged.[16–18] Greater inclusion of racial minorities is essential for generalizing findings, understanding differential responses to treatment, and promoting fairness and equity in research.[19]

Higher-income patients were more likely to participate in longer protocols. While low-income patients are often discouraged by time and financial matters,[20] data may also be underreported due to social discomfort or the sense of intrusiveness.[21] Contrarily, participants from the private health system more often reported discomfort with experiencing side effects. While these statements have not been explicitly addressed in the literature, prior studies have shown that potential side effects of the treatment are a burden reported by the patients. Patients also report a general concern about the unknown future, including whether the study drug assigned would be beneficial.[22]

Physician-related barriers were also relevant. Nearly 89% of participants reported they would participate in a trial if invited by their treating physician, reinforcing their central role.[23] In Brazil, most oncologists report that less than 5% of their patients participate in trials, and ⅓ offer the opportunity to less than 1%.[24] Patients often rely on physicians to explain trial details and help with decision-making.[25] This shows the oncologist's importance in educating patients, as well as the effectiveness of patient-physician communication accrual in clinical trials. In this study, a proportion of participants also expressed the view that the physician should be the main decision-maker in their treatment, a finding relevant in the era of "shared decision-making" models.[26]

Education was another important factor. Patients with higher education levels, as well as those in longer and more complex trials, were more likely to report prior awareness of clinical trials. These findings are consistent with the literature, showing that improvements in education levels, clinical

trial methodology, and patients' safety could improve interest in and recruitment to clinical trials.[27,28] A prior Brazilian study has similarly reported that lack of information and education is a key barrier.[7] In developing countries, poverty, lack of education, and language barriers can further limit patients' participation.[7,29]

This study has strengths, including a relatively large and diverse sample of cancer patients treated in a specialized center. Both public and private health systems were represented, and patients of different racial, educational, and age backgrounds participated. However, it has limitations. Most participants were women, which may reflect both the IBCC's institutional profile, recognized as a reference center for breast and gynecological cancers, which together accounted for 63.6% of cases in our sample possibly reflecting a greater willingness among women to complete questionnaires in outpatient settings. This may introduce a selection bias and limit the generalizability of the findings, as barriers to clinical trial participation may differ between sexes. The questionnaire used was developed based on a meta-analysis from 2006 and has not been formally validated. Also, it was conducted at a single cancer center in São Paulo, Brazil's largest city. Our findings may not reflect the experiences in other regions or countries with different health care infrastructures.

## Conclusion

The study highlights the multifactorial nature of barriers to clinical trial participation among Brazilian cancer patients in a large oncology center. Education, particularly regarding patients' familiarity with research protocols, is a critical challenge.

Improving awareness and understanding of research protocols is essential to expanding access and promoting equity in cancer care. These findings offer valuable insight into the Brazilian clinical research landscape and can inform strategies to increase participation and continuity of care. By addressing these gaps, clinical research can become a more inclusive and impactful component of oncology treatment.

### Authors' Contributions

EBAA: conceptualization, methodology, visualization, writing – original draft, writing – review & editing, and project administration. ABNFP: conceptualization, data curation, and investigation. ALC, RMSP, and ACMBT: data curation, and investigation. EA: supervision, writing – review & editing, and validation. FJSMC: supervision, formal analysis, methodology, writing – review & editing, visualization, and resources. LARB: conceptualization, validation, supervision, writing – review & editing, project administration, and resources.

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### Conflict of Interests

The authors have no conflict of interests to declare.

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