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Virtual consent and the use of electronic informed consent form in clinical research in Brazil

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SUMMARY

OBJECTIVE: In view of the need to apply term free and informed consent (IC) in clinical research involving humans, in accordance with the Brazilian ethical standards (CNS Resolution No. 466/2012), it is necessary to assess whether this practice is being effective and can be improved. The aim of this study was to evaluate the use of the IC in electronic format (e-IC), regarding its feasibility and suitability, as a complement to the written/physical consent form.

METHODS: Quantitative-qualitative research with a questionnaire instrument.

RESULTS: Greater retention of information and fewer wrong answers were observed after the application of the e-IC.

CONCLUSIONS: The use of e-IC is of great value to research participants in Brazil.

KEYWORDS: Clinical trials as topic. Informed consent. Ethics committees. Research.

INTRODUCTION

For the first time in world history, the need for research participants to voluntarily authorize their participation in clinical trials arose was in the Nuremberg code of ethics[1]. In this document, as a first principle, the consent of the volunteer was presented as being essential.

However, the nomenclature term *free and informed consent* (IC) had not yet been mentioned as a formal consent document. This term appears in 1964, with the Declaration of Helsinki. In this statement, it is stated that in any research with human subjects, each potential participant must be adequately informed about the objectives, methods, anticipated benefits, potential risks of the study, and the inconvenience that the study may entail. Participants must be informed that they are free to withdraw their consent at any time during the study[2].

The regulation in Brazil, which dealt for the first time on the mandatory nature of the IC, was in Resolution No. 196/1996. This resolution brought the competences of the Institutional Review Board (IRB), the National Research Ethics Commission — Conep, and the need for the IC in research in Brazil[3]. However, it cannot be said that this term did not exist in Brazil before that, considering that international research, which took place in centers in several countries, such as Brazil, already had this obligation.

Currently, in Brazil, the legislation that deals with the details regarding this issue is Resolution No. 466/2012. This resolution also brings all the information requirements that need to be clearly present in the IC. In addition, it also informs the situations in which it is not possible to apply the IC in the standard format for some populations, including children, adolescents, patients with psychological disabilities, and brain death. Considering these cases, another document needs to be applied, the Informed Consent Term[4].

The IC has ceased to be just a paper document for many years. The practice of free and informed consent is a process of continuous and effective communication[5]. Thus, it is necessary that the signing of the IC is not just an isolated fact, but it is the result of an awareness process so that the participant can be provided with all the information, clearly, and that they can make the decision accordingly, as autonomous and enlightened as possible.

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All research involving human beings needs the application of the IC; this research can be direct or indirect. Clinical research is considered direct, since the participant undergoes an intervention during the study, while the indirect occurs when the participant participates in the research through data collection, questionnaires, or forms, but does not receive any type of intervention that somehow alters its current state[6].

Even after all these precautions, it is debated whether this term is really understood by the research participants in a satisfactory way. Therefore, Souza et al.[7] carried out a study to assess the readability of ICs in Brazil with the aim of correlating the acceptance of the research participant with demographic status, social factors, risk-to-benefit ratio, and the level of education. It was observed that the ICs presented high degrees of difficulty in reading.

It is noteworthy that the research participant's consent needs to be performed in the best possible way and the patient needs to understand perfectly about the research or procedure in which they will be submitted. If the participant's autonomy is not respected and there is any assessment of medical misconduct, the responsible physician will respond civilly in the subjective and objective modalities[8-10].

Thus, even with all this concern expressed in Brazilian regulations, it is possible to observe that there are still problems with the application of these terms in the clinical practice.

In addition, the form of application of the IC needs to be improved and this became clear with the advent of the worldwide pandemic COVID-19, a highly contagious disease caused by the new coronavirus (SARS-CoV-2), which appeared for the first time in Wuhan, China, spreading rapidly around the world in just 2 months[11]. Along with the protective measures of quarantine and social distancing, the use of electronic IC (e-IC) form in Brazil can represent a gain for Brazilian clinical research.

For these reasons, this work aims to assess the applicability of an electronic consent form in Brazil, evaluating the viability and preference of volunteers, considering this new format. It is important to mention that this is not an exclusive study, the e-IC is not an instrument to replace the written informed consent, but rather, it will be used, as in other countries, in a complementary way. In this sense, the study aims to assess whether the use of the e-IC will be effective for greater understanding and retention of information, after the application of the written consent, in Brazil, and the feasibility of the completely virtual consent procedure.

METHODS

This study is a qualitative research, approved by the Ethics Committee of the University of Brasília (CAAE 26314719,1,0000,0030), with information collection through forms applied to volunteers who agreed to participate in this analysis. These volunteers were informed that they would be part of a simulation of participation in hypothetical clinical research and that they would help the research team with relevant information to improve this practice in Brazil.

The sample for this research was invited to participate by electronic means, such as cell phone messages or email. Recruitment was through email and telephone contacts, mainly through contacts via the University of Brasília. A total of 60 volunteers were included for this research. The profile chosen for the hypothetical research was phase 1, a study with a small number of participants, focusing on the safety of a new product, usually with healthy participants, since the volunteers for the hypothetical study would also be healthy. This number of participants was defined based on the median accepted for phase 1 clinical trials (20–100), that is, 60 research participants[12].

The inclusion criterion was >18 years old. The exclusion criteria were not having Brazilian Portuguese as a native language, presenting some type of cognitive deficiency that compromises the understanding of the material, and/or presenting complete or functional illiteracy.

All volunteers were informed that they would be participating in a survey to evaluate the e-IC instrument in a clinical research simulation; this IC was presented and should be signed by those interested in participating. In addition, these volunteers received a consent form simulating participation in the clinical research for a hypothetical new pain medication.

Regarding the hypothetical phase 1 study, all participants received the written consent form for reading this document. After reading, a questionnaire on their understanding of the study was applied and, after completing this form, an electronic consent form was also presented, in the form of a video lasting less than 5 minutes, containing all the information available in the consent form. After the end of the video, the same questionnaire was applied again to the group. This format was chosen to assess whether there would be greater retention of information about the study after the application of the e-IC. After the two questionnaires were answered, a third one was applied to assess preferences, suitability, and feasibility of applying this new tool in Brazil.

The video was recorded using an actor, for better performance in front of the cameras, who addressed all the points present in the written consent form, verbally, in the video.

The qualitative-quantitative interview guide, applied after reading the informed consent and after presenting the video, was developed based on a similar study carried out in the United States[13] and the knowledge of the research team on ethics, regulatory matters, and patient safety. Tables 1 and 2 list the questions that were asked during the interviews. The research and interviews in this study were purposely designed in brief to lessen the research burden on individuals.

Table 1. Questionnaire after reading the informed consent and post-e-informed consent.

Interview		
Questions	Answer option	Type of analysis and generated data
Sample identification		
Initials of your name	Open response	Sample identification
Date of birth	Date	Sample identification
Sociodemographic profile		
Sex	F; M; Not declared	Profile of research participants
Education	Education; Literacy; Elementary School; High school; University education; Postgraduate lato sensu; Master's degree; Doctorate degree; PhD	Profile of research participants
Do you have health insurance?	Yes; No	Profile of research participants
Do you have social networks?	Yes; No	Profile of research participants
Have you participated in previous clinical research?	Yes; No	Profile of research participants
Questionnaire about the IC after reading and after video		
What do you remember as relevant in relation to the research procedures presented in the Electronic Informed Consent Form?	Open response	Assess the amount of information retained for each participant
Can you say what the purpose of the survey was?	Open response	Assess the amount of information retained for each participant
Can you explain to me who should not participate in the study?	Open response	Assess the amount of information retained for each participant
Can you tell me what the risks are for this study?	Open response	Assess the amount of information retained for each participant
Can you tell me what the benefits of this study are?	Open response	Assess the amount of information retained for each participant
Can you tell me what assistance is offered at the end of the study?	Open response	Assess the amount of information retained for each participant

IC: Informed consent form.

Table 2. Objective questionnaire on feedback about the survey.

Interview		
Questions	Answer option	Type of analysis and generated data
Sample identification		
Was Electronic Informed Consent Form relevant for a better understanding of the research?	Yes; No	Objective
Do you think Informed Consent Form should be implemented in all surveys?	Yes; No	Objective
Do you think the Informed Consent Form is enough for the understanding of the research or the face-to-face care with the doctor is essential?	e-IC is sufficient; I still need face-to-face medical service	Objective
Do you think Informed Consent Form should be implemented in all surveys?	Yes; No	Objective
On a scale of 1 to 5, how important did you think the Informed Consent Form was for understanding the research? Being 1, not relevant, and 5, fundamental for understanding	1; 2; 3; 4 e 5	Objective

IC: Informed consent form.

RESULTS

The predicted number for this study was 60 volunteers and all were included. The profile of the population included in this study was evaluated, showing that the majority were females (55%) and had postgraduation *lato sensu* (43.31%). Notably, 73.3% of the participants had a health insurance plan, 96.7% had access to a social network, and 83.3% had never participated in a previous clinical research.

The results of this qualitative research were evaluated as follows. The answers after just reading the IC and the answers after reading and applying the video were, for all participants, read and classified as "correct," when they were in agreement with what was described in the text or in the video of the IC of the drug curadorzil, and as "wrong," when they did not correspond to what was presented. Correct answers for the same question were also compared in the postwritten consent and postelectronic consent questionnaires.

Considering the classification presented above, it was observed that the wrong answers decreased by 36% after the application of the e-TCLE and the more complete answers increased by 835% after the application of the term.

In addition to retaining and understanding the information presented in the IC and e-IC, the preference of the volunteers who participated in this study was quantitatively evaluated.

The first question asked was about the relevance of the presentation of the e-TCLE for the understanding of the research. Of the 60 volunteers who answered the questionnaire, 50 (83.3%) judged the e-IC as relevant for a better understanding of the research. Another question asked was in relation to the opinion of the volunteers if they thought that the e-IC should be implemented in all clinical trials. Notably, 49 (81.7%) thought that the e-IC should be part of all research in Brazil. As for the ease of understanding the research, 33 (55%) thought that the written consent form was easier to understand the content of the research. Regarding the question, "Do you think that the e-IC is sufficient for the understanding of the research or the face-to-face care with the doctor is essential?" 50 (83.3%) answered that the e-IC would be enough, while 10 participants answered that they would still need face-to-face medical care.

The volunteers were also asked to rate, on a scale of 1–5 (1=not relevant, 5=fundamental for understanding), how much they thought the e-IC was important for understanding the research. More than half of the volunteers, 32 (53.3%), marked the item referring to the maximum relevance of this instrument for the understanding of the research (item 5). The result is shown in Figure 1.

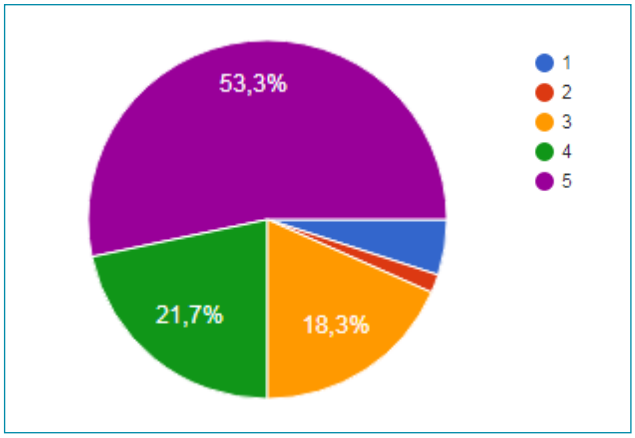

Figure 1. Ranking the relevance of adding e- informed consent in research in Brazil, with 1 indicating not relevant and 5 fundamental for understanding.

DISCUSSION

According to the results, it is possible to note that after the presentation of the e-IC, there was a more expressive number of correct and more complete answers than just the presentation of the IC in isolation. In addition, the number of responses considered "wrong" was lower after the volunteers watched the e-IC. Thus, it is possible to observe that, indeed, after the presentation of the e-IC, there was an increase in the understanding and retention of information about the study.

Considering the results previously presented, it was possible to verify, qualitatively and quantitatively, that the e-IC had a positive impact on the understanding of the hypothetical clinical research study.

Presenting a video, after having access to the written consent form, allowed a greater understanding of the research and greater retention of information, and, according to the opinion of the volunteers, the e-IC should be implemented in all trials. This format was intentionally chosen, as the presentation of the e-IC after the written consent is the methodology used internationally for the application of this instrument.

One result that stands out is related to the understanding that e-IC could replace face-to-face service. This is important considering that the implementation of this tool can help in critical moments of social distancing, such as the COVID-19 pandemic.

The constant updating of the IC is necessary, and recent efforts are being made in Brazil to cover patients with visual impairment in Brazil[14]. In this sense, this work has the benefit of extrapolating the understanding of the IC to different population groups.

A limitation of this study is that there was the small number of the sample and the recruitment hampered by the COVID-19 pandemic situation; thus, the population studied was the one with access to the Internet and with the highest level of education.

Furthermore, it is important to present experience with virtual consent, mainly as a strategy for clinical research in need of social distancing.

It is noteworthy that further studies are needed, including the analysis of the applicability of this tool in other phases of clinical research.

CONCLUSIONS

Given the above, the implementation of the e-IC in Brazilian research is characterized as a valuable procedure to increase the understanding and retention of information by volunteers, and, in cases of need for social distance, this resource can be used as a strategy in clinical research in Brazil.

AUTHORS' CONTRIBUTIONS

JCRAS: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **HCC:** Conceptualization, Writing – review & editing.

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