Readability of the terms of consent in clinical research

Lucas Lobato [1], Beatriz Santana Caçador [2], Maria Flávia Gazzinelli [3]

Abstract

The aim of this study is to analyze the readability of two Informed Consent Forms (ICF) used for the participation in a clinical trial and the correlation of the degree of difficulty with the education level of the participants. The two ICF were analyzed using the Flesch Reading Ease (FRE) and the Flesch-Kincaid (FLK) readability tests. Through analysis by the Flesch score the ICF for selection of volunteers and participation in a clinical trial had, respectively, a value of 61 and 56, while the FLK values were 6.59 and 8.4 respectively. The ICF for selection and participation in the clinical trial was inadequate for 49% and 72% of these participants. Those two ICF used for participation in clinical trials were not suitable for the education of the majority of its participants.
Key words: Bioethics. Ethics, research. Clinical trial.

Resumo

Legibilidade dos termos de consentimento livre e esclarecido em ensaios clínicos

O estudo objetiva analisar a legibilidade de dois termos de consentimento livre e esclarecido (TCLE) utilizados para participação em ensaio clínico e correlacionar o grau de dificuldade dos documentos com o nível de escolaridade dos participantes. Sendo um TCLE para a elegibilidade no estudo e outro para a participação. Os TCLE foram analisados mediante utilização do índice de facilidade de leitura de Flesch (IFLF) e índice de legibilidade de Flesch-Kincaid (ILFK). Por meio da análise pelo IFLF, os TCLE para a seleção dos voluntários e participação no ensaio clínico obtiveram, respectivamente, o valor de 61 e 56, enquanto pelo IFLK os valores foram 6,59 e 8,4, respectivamente. O TCLE para elegibilidade de voluntários e para a participação no ensaio clínico foi inadequado para 49% e 72% desses participantes. Os dois TCLE utilizados para a participação em ensaios clínicos não foram adequados para a escolaridade da maioria de seus participantes.
Palavras-chave: Bioética. Ética em pesquisa. Ensaio clínico.

Resumen

La legibilidad del consentimiento en la investigación clínica

El objetivo de este estudio es analizar la legibilidad de dos términos de consentimiento libre y aclarado (TCLA) utilizados para participar en un ensayo clínico y correlacionar el grado de dificultad de los documentos con el nivel educativo de los participantes. Siendo un TCLA para la elegibilidad en el estudio y otro para la participación.Los TCLA fueron analizados mediante utilización del índice de facilidad de lectura de Flesch Reading Ease (IFLF) Index y el Flesch-Kincaid (ILFK). A través del análisis por el IFRE, los TCLA para la selección de los voluntarios y participación en el ensayo clínico obtuvieron respectivamente, el valor de 61 y 56, mientras por el IFLK los valores fueron 6,59 y 8,4, respectivamente. El TCLA para la selección de voluntarios y para la participación en el ensayo clínico fue insuficiente para el 49% y el 72% de esos participantes. Los dos TCLA utilizados para la participación en los ensayos clínicos no eran adecuados para la escolaridad de la mayoría de sus participantes.
Palabras-clave: Bioética. Ética en investigación. Ensayo clínico.

Aprovação CEP UFMG Protocolo n° 01743412.3.0000.5149

1. Master lucaslobato87@gmail.com **2. Master** biacacador@gmail.com **3**. **Doctor** flaviagazzinelli@yahoo.com.br – School of Nursing, Federal University of Minas Gerais, Belo Horizonte/MG, Brazil.

Correspondence
Lucas Lobato – School of Nursing, Federal University of Minas Gerais. Av. Alfredo Balena, 190, sala 508 CEP 30130-100. Belo Horizonte/MG, Brazil.

The authors declare no conflict of interest.

Research article

Regulations and international guidelines for conducting research with human subjects require that researchers must obtain the participants' informed consent (IC) [1]. In some countries, like in Brazil, the IC is a legal requirement and must be embodied in a formal document called the term of free and informed consent (TFIC).

TFIC is the document describing the research and explaining the voluntariness in participating and the retention in the study, which shall provide, clearly, all the information needed to enable a decision as to the subject's participation. This document's indispensable information aims at giving the research's volunteers all prerogatives to the full exercise of their human dignity, with respect to their participation in research involving human beings, through the protection and promotion of the principle of autonomy [2].

The Resolution 196/96 of the National Health Council (NHC, CNS in Brazil) defines that this document shall include the following aspects: justification of the research, alternative methods, risks, assistance to the research subject; assurance of information related to the patient's possible concerns during the study; freedom to withdraw at any stage of the research, confidentiality of data collected and reimbursement of expenses or damages. There is a consensus that the understanding of study information and the rights of the research participant can be guaranteed by providing a valid FIC [3]. In order to obtain a valid FIC, it is essential that the information shall be passed on to the subject in an accessible language to all potential study participants [4].

Currently, much has been discussed regarding the sufficiency of the TFIC for the clarification and effective understanding of the research participants. The literature reveals that many participants, even after signing the consent form, have little knowledge of the information contained in the document [5-9]. The education level of the participants of a research plays a fundamental role in explaining the little knowledge of the information contained in the TFIC, since several studies have shown a negative association between the level of education and the document information's knowledge [10-15]. Similarly, the TFIC might be often considered difficult to understand for a large portion of research participants [15-19].

When dealing with the analysis of the TFIC's level of understanding, it deserves highlighting a topic that is rarely studied in Brazil: a review of the readability of those documents' texts which are used in clinical trials. The assessment of the TFIC used in Brazil is important in order to consider the educational profile of most part of the population that largely considers a great number of Brazilians classified as functional illiterate or with low formal education [15,19]. Understanding the information of the TFIC has become even more important in the context of clinical research for various reasons, such as the complexity of the information contained in the TFIC on clinical investigations and risks associated with the subject's participation.

The complexity of the TFIC used in clinical research elapses from the very nature of these investigations, requiring a detailed explanation of their methodological procedures. Therefore, the inclusion of such information may affect the understanding of documents, given that the methodology of clinical research is often unknown to the research participants [6,19-21]. We know that clinical trials are experimental investigations in humans, involving them inevitably in prominent risks. Thus, a proper understanding of the information is essential, whereas the risk associated with a decision must be proportional to the necessary autonomy for its effectiveness [22].

The above mentioned impasse engendered by the need for the research participant to understand the TFIC, and the difficulty in understanding this document, which has traditionally been a characteristic of it, make clinical trials a field of interest for the development of research able to profile the reality and contribute to the TFIC's planning and obtainment process, validating their application. Based on the foregoing, this research aims to analyze the readability of the consent forms used in clinical trials and to correlate the documents' degree of difficulty with the education profile of the participants. The study also aims to verify the information requirements to be included in these documents, according to Resolution CNS 196/96.

We emphasize that this article was based on the recommendations for obtaining the informed consent for research participants, which were proposed by Resolution CNS 196/96, considering the relevance of its validity during the course of this study. This resolution, however, was repealed and

replaced by Resolution CNS 466/12, published in the Official Gazette only on June 13, 2013. This new resolution addresses in a didactic way the process of free and informed consent, demanding the research's participants to be informed the same information contained in the previous resolution.

Method

This is a cross-sectional and descriptive study on the quality and readability of two TFIC which should be signed if the volunteers wished to participate in a clinical trial of intestinal helminthes. The first TFIC (TFIC 1) was related to an eligibility study, preliminary the clinical trial, which aimed at recruiting potential participants for the clinical research. So that volunteers could be triaged for the trial, they should participate in this first study.

The second TFIC (TFIC 2) was referent to the consent on participating in a clinical research named "Double-blind, randomized, controlled study of the tolerability of regular consumption of a mixture of oils, in adults living in an endemic area for helminthes (ABS-00- 02)" – whose objective was to evaluate the tolerability of functional food with anthelmintic qualities in adults living in areas endemic for helminthes. So that the volunteer could integrate the clinical trial, he should necessarily participate in the eligibility study and subsequently sign the clinical study's TFIC. Thus, it was necessary to sign two documents so that volunteers could enroll in the clinical trial ABS-00-02.

The research was carried out from August 2009 to February 2012 in Americaninhas, a Municipality District of Novo Oriente de Minas, located in the middle region of the Mucuri Valley, northeast of Minas Gerais/Brazil. The inclusion criterion was the participation in the clinical trial ABS-00-02, i.e., the signature of the two TFIC; while the exclusion criterion was the participant being illiterate, as it was considered they could not read the document. It is noteworthy that these participants' TFIC were obtained through the reading of these documents by the researcher, before a witness. On that occasion, all the participants' doubts were clarified. With regards to family income, age, race and gender, no statistically significant difference between the illiterate participants and those who had schooling was observed.

Participants in these studies were men and women aged between 18 and 45 years. The education profile of the trial participants was assessed by a structured questionnaire administered one week after signing the informed consent of the clinical trial ABS-00-02. In the questionnaire, the participant was asked about his formal education and age. The responses were recorded and tabulated in the software SPSS *(Statistical Package for Social Sciences)* version 17.0 for Windows. The number of years of education was categorized according to their year of formal schooling. Data on participants' age and their education were presented and analyzed using descriptive statistics.

The TFIC were analyzed using the Flesch Reading Ease (FRE) and the Flesch-Kincaid (FLK) readability tests, both methods validated for the Portuguese language [16]. Such readability indices are mathematical models that assess the structure of a text as to their sentences, paragraphs, and number of syllables of words (size). The identification of the elements required for the calculation of these indices was operationalized by Microsoft Word 2010 software.

The Flesch Reading Ease index rates text on a scale of 100 points and the result classifies text according to the difficulty of reading (Table 1). The FRE index was calculated by the following formula: FRE = 206.835 – [(1.015 x average sentence length) + 84.6 x (average number of syllables)].

Table 1. Flesch scale distributed according to the level of education

Flesch Scale	Level of readability
0-29	Very difficult
30-49	Difficult
50-59	Somewhat difficult
60-69	Standard
70-79	Fairly easy
80-89	Easy
90-100	Very easy

The Flesch-Kincaid readability index has been the most widely used to assess the readability of a text and its result estimates the years of education needed for proper understanding [23] (Table 2). The FLK most effective values are the ones requiring 6-10 years of schooling [16]. The following formula was used to calculate the index: FLK = [(0.39 x average words per sentence) + (11.8 x average syllables per word)] - 15.59.

Table 2. Index scores of Flesch-Kincaid readability according to the years of schooling

Years of schooling	School Equivalency
Uneducated and less than 1 year	Never attended school or did not complete the 5th grade of elementary school
1 a 3	Completion of 1st, 2nd or 3rd year of elementary school
4 a 7	Completion of 4, 5, 6 or 7 years of primary education
8 a 10	Completion of 8 or 9 years of elementary school or the first year of high school
11 a 14	Completion of the 2nd and 3rd grades of high school or incomplete higher education
15 or more	Tertiary education or master's and doctoral studies

The quality analysis of the TFIC was made by checking the information required by the Resolution CNS 196/96 as well as the presence of this information in both documents. In this sense, the quality of TFIC refers to meeting the research information required by that resolution, which shall be present in these documents. In order to perform this analysis, we used a script to assess these documents [18], in which the items indicated as required by the Resolution CNS 196/96 were assessed according to the following topics: absence of the item; quotes the item without explaining it; quotes and explains the item.

This study was approved by the Research Ethics Committee of the George Washington University (Washington/USA) and the René Rachou Research Center (Minas Gerais/Brazil), as well as the clinical trial ABS-00-02 and the study ABS-00-1, all approved by the National Committee for Research Ethics.

Results

A total of 148 volunteers participated in the clinical trial ABS-00-02, who had first signed the TFIC 1 of the eligibility study and, later, the TFIC 2 for participation in the clinical trial. Of this total, 23 volunteers did not participate in the study because they were illiterate. Thus, 125 individuals participated in the study with a mean age of 34.2 years, and minimum and maximum of 18 and 45 years, respectively. Most participants were female (65.2%), married or in a stable union (77.7%). Regarding the participant's education, 49% and 29% had completed the 1st to the 3rd grades and the 4th to the 7th grades of primary school, respectively; while 13% had attended between the 8th grade of primary school and 1st year of high school. The other participants had attended the 2nd or 3rd year of high school or incomplete/complete higher education (9%).

It was observed by the FRE index applied to the TFIC 2 of the clinical trial ABS-00-02 that the degree of readability was 56, a result that is fairly difficult as the structure of the document. By the FLK index it was obtained the value 8.4, which corresponds to the need for at least eight years of schooling for proper understanding. In terms of school equivalency, if necessary, it means to make the completion of at least the 8th grade of primary school. Considering that a minority of participants (22%) had education above the 8th grade, this document was considered inappropriate for the other 78% of participants whose education was lower to eight years of schooling.

Regarding the eligibility study's TFIC 1, by assessing the FRE index the ease of reading was 61, meaning that the document's level of readability was considered "standard". By the FLK index it was obtained the value 6.59, which corresponds to the need for at least six years of schooling to adequately understand the document. In terms of school equivalence, it means that the person must have completed at least the 4th grade of elementary school. Whereas 51% of participants had education above the 4th grade, this document was considered inappropriate for the other 49% of participants who had lower education.

Regarding the quality assessment of the TFIC studied according to the scale used in this study, it can be observed that these documents are well prepared technically, considering that they contained all the elements described in the Resolutions CNS 466/12 and 196/96 (Table 3). The analysis of Table 3 shows that in both observed papers the form of reimbursement or indemnification of expenses or damage incurred by the study was just cited, without a proper explanation of these themes.

Table 3. Items of Resolution 466/12 which must be present in the term of free and informed consent and the presence of these items in the TFIC of the studies ABS-00-01 and ABS-00-02

Item	ABS-00-01			ABS-00-02		
	A	P	P + E	A	P	P + E
Rationale			X			X
Objectives			X			X
Procedures			X			X
Discomforts and risks			X			X
Alternative methods		X				X
Form of responsible monitoring and care			X			X
Subject's freedom to refuse participating in the research			X			X
Guarantee of confidentiality			X			X
Forms of reimbursement		X			X	
Forms of indemnification		X			X	
On the methodology			X			X
Expected benefits			X			X

Note: A - Absent, P - Present, P + E = Present and explanation.

Discussion

The TFIC used to participate in the eligibility study and in the clinical trial ABS-00-02, which were analyzed through the FRE and FLK indexes, were considered unsuitable for a large proportion of trial participants, the first being inappropriate for volunteers with formal schooling above the 4th grade of primary school and the second, for participants who did not complete the 8th grade of elementary school. Given this reality it stands out, however, that these documents have better readability than the TFIC used in clinical multicenter studies conducted in São Paulo, where the coefficients of readability FRE ranged 32-44 (arithmetic mean: 38.5) and medium FLK of 18 years [18].

The concern with the results of this study lies especially in the inadequacy of the two TFIC used for participation in the clinical trial ABS-00-02 to the education of the majority of its participants profile. The discrepancy between the education required to understand the TFIC and the sample profile in which this document was applied was also perceived in a study conducted in Porto Alegre, in which it was observed that for the understanding of 91.7% of the TFIC used in 1998 and 1999 eleven or more years of schooling were needed, but only 16.6% of the population had met this profile [23]. Similar results were also found in other studies conducted in Brazil and France [24,25].

This problem becomes enhanced when we consider that the education profile of the participants in the clinical trial ABS-00-02 is similar to that observed in other clinical trials in Brazil. It was observed that the sample profile of studies with participants from clinical trials conducted in [17] public hospitals in Brazil and in specialized centers in clinical research [26] has a similar percentage of participants who had only completed elementary school. Considering that in this study only 40% of respondents presented adequate schooling for the understanding of the document, the others shall probably have encountered difficulties in understanding the information contained in the TFIC, a fact that allows us to consider it as "inappropriate", preventing thus the effectiveness of the consent. It is known that a misunderstood text can result in impairment regarding the information clarification, the voluntariness, and the consent itself [18].

Besides the ethical implications on the validity of the free and informed consent of the participants in the clinical trial ABS-00-02, this discussion shall be extended to other contexts in Brazil. It is noteworthy

that the situation observed in this study reflects the educational debt of the country, where 28% of the population between 15 and 64 years old is considered absolute or rudimentary illiterate. Among those who attend or attended the 6th to the 9th grade of elementary school, 24% are still in the rudimentary level, i.e., the can only read and understand short, simple sentences, such as news headlines, for example. Among the people who attended any grade or completed high school, only 41% achieve full literacy level [19].

Not far from this situation, in Minas Gerais, within the population group of 18-24 years, 44.5% of the population has less than eight years of education, and among them 3.3% are illiterate. More alarming situation occurs in the adult population (aged 25 or older), in which these rates rise to 67.9% and 14.8%, respectively [27]. This situation worsens in a micro-regional analysis, since in the municipality of Novo Oriente de Minas, among the population aged 18-24 years, the percentage of people with less than eight years of education reaches 75.4%, with 19.3% of illiterates. By extending the discussion to the adult population (aged above 25 years), these values rise to 93.2% and 57.1%, respectively. Indeed, this age group, on average, has two years of study [27].

Faced with this alarming reality, it is important to reflect on the impact of that situation in conducting clinical research in Brazil, as many participants may not be able to read and understand the term of free and informed consent. This document, according to Resolution CNS 196/96, shall be applied to the research subject and it is advisable to ask its perusal as well as its verbal explanation [4]. The discrepancy between the educational profile of Brazil, in almost all its regions, and the appropriate level of education that is necessary for understanding a TFIC bring up the need to promote discussions and reflections among the scientific community, universities and civil society, in order to intervene on this overview and build transformation pathways of this disturbing reality.

It is thus put under discussion the authenticity of the consent of participants who may not have understood the research and the procedures that are involved in it, although they express permission of their participation by signing the document. Legally, there is consistency with the requirements of Resolution CNS 196/96, but we question the ethical dimension which involves the autonomy to consent without understanding what the research proposes.

Given the fragility of the educational process in Brazil, revealed by the significant number of illiterates in the country, associated with the complexity of the terms used in the TFIC, especially in clinical research, we come across the outlines of situations that reinforce the logic of domination exerted by health professionals and researchers on the population. Before the social determinants and the inequalities to what much of the Brazilian population is routinely exposed, we question the ethical implications of a practice that, legitimately and in accordance with statutory and legal requirements, has put people in a position of subservience, harming the ethical principle of autonomy. Thus, it reinforces the logic of empowerment from knowledge, a technical knowledge that is inaccessible and beyond the possibility of comprehension of a given population group. As they do not understand, there are no questions, reflections and critiques, causing the subjects to submit their lives to the researchers' interests and the determinations of health professionals.

This reflection resonates with Foucault's perspective of *biopower.* According to the author, biopower refers to a logical assignment of life from its application in biological fields, backed by scientific knowledge and technical knowhow that establishes knowledge-power, which, in turn, creates control and domination mechanisms on the subjects [28]. It settles thus an asymmetrical power relationship between the researcher and the research participant. In this respect, the researcher who detains the research's technical language transposes this language to the TFIC, making the understanding of participants inaccessible. And before this limited understanding that participants have of the research in which they consent to take part, their freedom of choice and decision making is almost nonexistent. Thus a major contradiction is settled because while the TFIC is intended to protect the autonomy and informed decision-making of individuals, it can also be transformed into an instrument that legitimates the domination strategies over vulnerable populations, bringing ethical implications of major proportions.

It shall be noted that despite the implications of the inadequacy of this document to the education profile of the participants, this reason shall not be solely appointed as a barrier in understanding the TFIC's information. This conclusion is supported by a study conducted in France, noting that improving the TFIC's quality and attempting to adapt this document to the education profile of the participants had not improve the understanding of the information contained in the document [29]. Another structural element assessed in this study relates to

the provision of required information for a valid free and informed consent. It was observed that the TFIC had evaluated all the information described in Resolution CNS 196/96 as indispensable to a valid FIC, as well as in Resolution 466/12 [30]. However, even the disposition of all this information is not able to explain the inadequacy of this document to the sample profile of clinical trials, since studies conducted in Brazil and in developed countries have pointed to the possibility that the TFIC is complete and at the same time, easy to read [31-33].

Final Considerations

Before the results of this study, it is concluded that the TFIC for participating in clinical trials may be, for a large portion of its participants, a barrier to the research information knowledge. Accordingly, this document may not achieve its role of promoting the autonomy of participants in the studies, revealing a major contradiction that can even put its reason to exist under discussion, considering the way it is structured.

The development of a TFIC at different levels of readability, according to the respective formal schooling required for their proper understanding, can be considered a possibility to circumvent these barriers. The development of educational interventions related to the FIC also emerges as a possibility to circumvent the TFIC's failure in disclosing information. This strategy has proven effective for participants to understand the survey information, such as its objectives, nature and the rights of the research participant [5]. Resolution CNS 466/12 has also introduced the research's term of consent as a process of consent, and not just as a bureaucratic process of signing.

We emphasize that the results of this study remain current even with the repeal of Resolution CNS 196/96, given that the Resolution CNS 466/12 recommends that the research's participant shall be informed about the same aspects of the previous resolution. Similarly, the results of this study imply the need to consider the novelty brought by the new resolution on research ethics, in which, to be free and informed, the consent cannot be restricted to the bureaucratic signing of a document, but to a process of mutual trust between researcher and volunteer.

The results suggest the need to further enhance the debate on the purpose of the TFIC. This document does not, therefore, correspond to a mere formal requirement which makes it feasible to conduct research with human subjects. Instead, it answers to the broader ethical perspective whose commitment lies in building citizenship and the respect for the participants' autonomy.

Thus, the TFIC structured as inaccessible to the participants understanding can be considered a device [34] to strengthen the strategies of *biopower* through which it produces and perpetuates a controlling relationship between the researcher, holder of the knowledge and technical language contained in, and the research's subject that has his/her autonomy and otherness kidnapped by consenting to participate in a research whose purpose he/she could not understand – which suggests questioning the authenticity of their decision making.

Given the existent gap between the language of the TFIC and the social reality of the majority of the Brazilian population, it necessary emerges a discussion on bioethics of protection and the vulnerables' issue. The social organization of Brazil and most countries in Latin America is marked by strong inequalities, besides the restricted access to formal education, both in regard to the years of education as to the quality of the education that is provided. This reality determines that the subjects who are part of this context may experience adverse situations, for which they have no coping skills, creating social determinations that put vast portion of the population in a condition of vulnerability. Vulnerability is a concept related to a specific condition of existence of particular population groups exposed to adversity regardless of their wills, for which they have no needed coping means. In this paper, we have considered the few years of study as a situation of vulnerability, which makes them unable to understand not only the TFIC, but other issues related to the everyday life, as well as their choice's possibilities and autonomous decision making [35].

This study also highlights that the provision of all information described by the resolutions on research ethics does not necessarily imply a greater difficulty readability of the TFIC. Therefore, it is emphasized that all this information must be presented in these documents, but considering strategies that can facilitate its understanding. As a strategy potentially able to enable more effective understanding of the TFIC, we may cite as an example the implementation of educational interventions related to the process of obtaining free and informed consent, as a pedagogical resource capable of promoting awareness regarding the information in a clinical trial [10],

what has even been carried out with effectiveness in the region of this study [5,36].

The importance of these interventions is also imperative when considering the need of including the illiterates in research, who should also have access to the research information. Educational interventions associated to the process of obtaining free and informed consent shall create conditions for overcoming individuals' domination and heteronomy situations [37], enabling them to participate in research actually autonomous.

Special thanks

We thank the volunteers in the clinical trial ABS-00-02 who were willing to participate in this study and all fellow researchers who directly or indirectly contributed to its realization.

References

1. Council for International Organizations of Medical Sciences. International ethical guidelines for biomedical research involving human subjects. WHO, colaborador. Genebra: Cioms/OMS; 1993.
2. Junges JR. Exigências éticas do consentimento livre e esclarecido. Rev. bioét. (Impr.). 2007;15(1):77-82.
3. Beauchamp TL, Childress JF. Princípios de ética biomédica. 4ª ed. São Paulo: Loyola; 2013.
4. Brasil. Conselho Nacional de Saúde. Resolução nº 196, de 10 de outubro de 1996. Aprova diretrizes e normas regulamentadoras de pesquisas envolvendo seres humanos. [Internet]. 1996 (acesso 20 set. 2004). Disponível: http://conselho.saude.gov.br/docs/Reso196.do
5. Gazzinelli MF, Lobato L, Matoso L, Avila R, Marques RC, et al. Health education through analogies: preparation of a community for clinical trials of a vaccine against hookworm in an endemic area of Brazil. PLoS Negl Trop Dis. 2010;4(7):749-62.
6. Mandava A, Pace C, Campbell B, Emanuel E, Grady C. The quality of informed consent: mapping the landscape. A review of empirical data from developing and developed countries. J Med Ethics. 2012;38(6):356-65.
7. Kaewpoonsri N, Okanurak K, Kitayaporn D, Kaewkungwa J, Vijaykadg S, et al. Factors related to volunteer comprehension of informed consent for a clinical trial. Southeast Asian J Trop Med Public Health. 2006;37(5):996-1.004.
8. Minnies D, Hawkridge T, Hanekon W, Ehrlich R, London L, Hussey G. Evaluation of the quality of informed consent in a vaccine field trial in a developing country setting. BMC Med Ethics. 2008;9(15):1-9.
9. Chaisson LH, Kass NE, Chegeta B, Mathebula U, Samandari T. Repeated assessments of informed consent comprehension among hiv-infected participants of a three-year clinical trial in Botswana. PLoS One. 2011;6(10):e791.
10. Flory J, Emanuel E. Interventions to improve research participants' understanding in informed consent for research. Jama. 2004;292(13):1.593-601.
11. Hill Z, Tawiah-Agyemang C, Odei-Danso S, Kirkwood B. Informed consent in Ghana: what do participants really understand? J Med Ethics. 2008;34(1):48-53.
12. Moodley K, Parker M, Myer L. Informed consent and participants perceptions of influenza vaccine trials in South Africa. J Med Ethics. 2005;31(12):727-32.
13. Marshall PA. Adebamowo CA, Adeyemo AA, Ogundiran TO, Vekich M, et al. Voluntary participation and informed consent to international genetic research. Am J Public Health. 2006;96(11):1.989-95.
14. Araujo DVP, Zoboli ELCP, Massad E. Como tornar os termos de consentimento mais fáceis de ler? Rev Assoc Med Bras. 2010; 56(2):151-6.
15. Lorenzo C. O consentimento livre e esclarecido e a realidade do analfabetismo funcional no Brasil: uma abordagem para a norma e para além da norma. Rev. bioét. (Impr.). 2007;15(2):268-82.
16. Goldim, JR. Consentimento e informação: a importância da qualidade do texto utilizado. Rev HCPA. 2006;26(3)117-22.
17. Meneguin S, Zoboli ELCP, Domingues, RZL, Nobre MR, Cesar LAM. Entendimento do termo de consentimento por pacientes partícipes em pesquisas com fármaco na cardiologia. Arq Bras Cardiol. 2010; 94(1):4-9.
18. Miranda VC, Fêde ABS, Lera AT, Ueda A, Antomangelo DV, et al. Como consentir sem entender? Rev Assoc Med Bras. 2009;55(3):328-34.
19. Instituto Paulo Montenegro. Indicador de alfabetismo funcional: principais resultados – Inaf Brasil 2009. [Internet]. São Paulo; 2007. (acesso 12 jan. 2012). Disponível: http://www. ibope. com.br/ipm/relatorios/relatorio_inaf_2009.pdf
20. Khalil SS, Silverman HJ, Raafat M, El-Kamary S, El-Setouhy M. Attitudes, understanding, and concerns regarding medical research amongst Egyptians: a qualitative pilot study. BMC Med Ethics. 2007;8(9):131-40.

21. Pace C, Emanuel EJ, Chuenyam T, Duncombe C, Bebchuk JD, et al. The quality of informed consent in a clinical research study in Thailand. IRB. 2005;27(1):9-17.
22. Jansen LA. Two concepts of therapeutic optimism. J Med Ethics. 2011;37(9):563-6.
23. Schmitz EF, Cunha DID, Goldim JR. Índices de legibilidade em termos de consentimento livre e esclarecido de projetos de pesquisa do Hospital de Clínicas de Porto Alegre. III Congresso Brasileiro de Bioética e I Congresso de Bioética do Cone Sul. [anais]. Porto Alegre: UFRGS; 2000.
24. Francisconi CF, Benincasa C, Teixeira R, Bulla MC, Clotet J, Goldim JR. Termos de consentimento livre e esclarecido em uso nas áreas assistenciais do HCPA. III Congresso Brasileiro de Bioética e I Congresso de Bioética do Cone Sul. [anais]. Porto Alegre: Universidade Federal do Rio Grande do Sul; 2000.
25. Ménoni V, Lucas N, Leforestier JF, Dimet J, Doz F, et al. The readability of information and consent forms in clinical research in France. PLoS One. 2010;5(5):10.576.
26. Lacativa PGS, Szrajbman M, Silva DASM, Melazzi ACC, Gregório LH, et al. Perfil de sujeitos de pesquisa clínica em um centro ambulatorial independente. Cinc. Saúde Coletiva. 2008;13(3):1.023-32.
27. Programa das Nações Unidas para o Desenvolvimento. Atlas de desenvolvimento humano - IDH/2003. [Internet]. (acesso 12 dez. 2012). Disponível: http://www.pnud.org.br
28. Foucault M. Microfísica do poder. In: Machado R, organizador. Rio de Janeiro: Graal; 1979.
29. Paris A, Brandt C, Cornu C, Maison P, Thalamas C, Cracowski JL. Informed consent document improvement does not increase patients' comprehension in biomedical research. Br J Clin Pharmacol. 2010;69(3):231-7.
30. Brasil. Conselho Nacional de Saúde. Resolução nº 466, de 12 de dezembro de 2012. Aprova diretrizes e normas regulamentadoras de pesquisa envolvendo seres humanos. [Internet]. 2012 (acesso 10 jul. 2013). Disponível: http://conselho.saude.gov.br/resolucoes/2012/Reso466.pdf
31. Joffe S, Cook EF, Cleary PD, Clark JW, Weeks JC. Quality of informed consent in cancer clinical trials: a cross-sectional survey. Lancet. 2001;358(9.295):1.772-7
32. Doak CC, Doak LG, Friedell GH, Meade CD. Improving comprehension for cancer patients with low literacy skills: strategies for clinicians. CA Cancer J Clin. 1998;48(3):151-62.
33. Coyne CA, Xu R, Raich P, Plomer K, Dignan M, et al. Randomized controlled trial of an easy-to-read informed consent statement for clinical trial participation: a study of the Eastern Cooperative Oncology Group. J Clin Oncol. 2003;21(5):836-42.
34. Foucault M. História da sexualidade I: a vontade de saber. In: Albuquerque MTC, Albuquerque JAG, tradutores. 13ª ed. Rio de Janeiro: Graal; 1999.
35. Boy R, Schramm FR. Bioética da proteção e tratamento de doenças genéticas raras no Brasil: o caso das doenças de depósito lisossomal. Cad. Saúde Pública. 2009;25(6):1.276-84.
36. Lobato L, Souza V, Caçador B, Soares NA, Wingester ELC, Gazzinelli MF. Efeitos de intervenção educativa na qualidade ética do consentimento livre e esclarecido. Rev. bioét. (Impr.). 2012;20(3):479-89.
37. Freire P. Pedagogia da autonomia: saberes necessários à prática educativa. 25. ed. São Paulo: Paz e Terra; 1997.

Participation of the authors
All authors performed the following steps: fieldwork, conception and design of the study, statistical analysis and interpretation of data, writing the article, critical revision of the important intellectual content of the manuscript, final approval of the version to be published.

Received: Jan 7, 2013
Revised: Jul 16, 2013
Approved: Aug 12, 2013

Research article