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Original Article

THE WRITTEN INFORMED CONSENT FORM (WICF): FACTORS THAT INTERFERE WITH ACCEPTANCE

Termo de consentimento livre e esclarecido (tcle): fatores que interferem na adesão

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ABSTRACT – *Background*: The written informed consent form (WICF) provides information that must be written in simple, easily understood language, highlighting voluntary participation safeguards, risks, possible benefits, and procedures. Currently, the possibility that research subjects do not fully understand the text of the WICF or their rights as participants, despite having signed the WICF and agreed to participate in the study, has been a point of discussion. ***Aim***: To evaluate the readability of the WICFs, as well as to correlate research subject acceptance of the WICF with demographic status, social factors, risk-benefit relationship, and education level. ***Methods***: The study involved 793 patients treated in public or private hospitals and asked to give informed consent for their inclusion. Were reviewed patient medical charts in order to obtain demographic and social data, and was used the Flesch Reading Ease and the Flesch-Kincaid Readability Indices to evaluate the reading level of the WICF texts. ***Results***: Acceptance was higher (99.7%) among patients treated in public health care facilities and among patients (99.73%) who participated in protocols involving lower risk. Although acceptance was not influenced by education level, 462 patients (58.26%) had eight or less years of schooling. The obtained readability index ranged from 9.9 to 12 on the Flesch-Kincaid test, and from 33.1 to 51.3 on the Flesch Reading Ease test. ***Conclusion***: The WICFs had high degree of reading difficulty. Although patient acceptance was not found to be related to demographic or social factors, it was found to be influenced by the risk-benefit relationship.

HEADINGS - Informed consent. Clinical trial. Research subjects.

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RESUMO – *Racional*: O Termo de Consentimento Livre e Esclarecido (TCLE) aborda informações que precisam estar descritas de forma clara e de fácil compreensão, destacando riscos, possíveis benefícios e procedimentos. Atualmente discute-se a possibilidade de sujeitos de pesquisa não entenderem totalmente o texto do TCLE nem seus direitos como participantes, mesmo tendo assinado o TCLE e aderido à pesquisa. ***Objetivos*:** Avaliar a legibilidade dos TCLE, bem como correlacionar a aceitação do sujeito da pesquisa com estado demográfico, fatores sociais, relação risco-benefício e nível de instrução. ***Métodos*** – Análise dos dados de 793 pacientes, que foram convidados a participar de diferentes protocolos de pesquisa clínica em hospitais privados e públicos. Foram revistos os dados dos prontuários médicos para obtenção dos dados demográficos e sociais. Foram usados os Índices de Legibilidade Flesch Reading Ease e Flesch-Kincaid para avaliar o nível de legibilidade dos textos dos TCLE. ***Resultados***: A adesão dos sujeitos de pesquisa aos protocolos propostos não teve influência dos fatores demográficos e sociais, no entanto, verificou-se maior adesão entre os pacientes de instituição de tratamento público (99,7%) em comparação com instituição de tratamento privada (93,7%). A adesão foi maior entre os pacientes que participaram de protocolos com menor risco (99,73%) em comparação com os que participaram de protocolos com maior risco (81,3%). Apesar da adesão não ter tido influência do nível de escolaridade, ele foi menor ou igual a oito anos de estudo para 462 pacientes (58,26%), entre os quais 444 (96,1%) eram de instituição de tratamento público. Os índices de legibilidade obtidos variaram de 9.9 a12 para o teste de Flesch-Kincaid e 33,1 a 51,3 para o teste de Flesch Reading Ease. ***Conclusões***: Os TCLE apresentaram altos graus de dificuldade para leitura. Apesar da aceitação pelo paciente não estar relacionada com fatores sociais ou demográficos, foi influenciado pela relação risco-benefício.

DESCRITORES - Consentimento informado. Estudos clínicos. Sujeitos de pesquisa..

INTRODUCTION

The written informed consent form (WICF) is an explanatory document in which all issues that might influence the decision of research subjects to enroll in a clinical study are addressed in order to ensure their voluntary participation. Willing participating in human research is based on the right to be informed of all aspects of the study, as well as to have one's questions answered clearly and in language that is easily understood[13]

By definition, voluntary participation does not involve pressure or coercion. In signing the WICF, research subjects acknowledge that they understand and accept all aspects of the study, including the potential risks and benefits.

The application of an appropriate WICF propitiates ethical behavior in the researcher-subject relationship and promotes respect for human rights, thereby resulting in its increasing use in recent years.

According to data from the Ethics in Research Committee of the Brazilian Ministry of Health National Council on Health, there has been an increase in the number of projects proposed in the country over the last years. An inappropriate WICF has been a major cause for rejection or approval with restrictions of those projects[2].

Data from the United States Food and Drug Administration (FDA) reveal that WICFs, despite their increasing use, present great inadequacies. Such inadequacies have constituted the leading cause of suspension of clinical studies by Ethics Committees over the last two years in that country. According to those data, the problems found include texts written in language that is difficult to understand, incomplete list of risks to which research subjects might be exposed over the course of the study, and failure to request the name of the person to contact in case of emergency.

In view of the increased use of the WICF reported in the literature, the discordant results regarding comprehension of the document by patients, as well as the need to evaluate its efficacy, it is appropriate to examine various aspects of its use.

This study had as objectives: 1) to evaluate the reading difficulty of the WICF; 2) to correlate research subject acceptance with demographic factors (race, gender, and age), social factors (place of birth, current dwelling, and type of health care facility), risk-benefit relationship, and education level; 3) evaluate, retrospectively, the critical attitude of research subjects regarding acceptance or non-acceptance of the WICF at the time of signing and level of formal education (years of scholarship).

METHODS

Were evaluated, retrospectively, the research protocols information related to 793 individuals invited to participate in scientific research. Before each protocol began, research subjects were presented with the corresponding WICF, which was to be read and signed after an oral explanation of the study objectives, methods and the members of the research team had given risks, as well as of the potential individual or collective benefits.

The present study evaluated five different WICFs applied to research subjects between October 17, 2000 and December 10, 2004. The participants were patients registered in the Hospital das Clínicas, University of São Paulo, School of Medicine (Department of Gastroenterology) or at one of two private facilities, both also located in the city of São Paulo: Angelita and Joaquim Gama Institute and Hospital Alemão Oswaldo Cruz. Were also reviewed the clinical charts and signed WICFs related to Clinical Genome Digestive Tract Cancer Project with control group and anti-inflammatory study to patients with polyp adenomatous - Project MK966.

In order to protect their privacy, the patients, as well as the members of the control group, were identified only by their initials. For all of the patients enrolled in the aforementioned studies, were collected information related to the following variables: gender; race; age; education level; current dwelling; place of birth; and type of health care facility.

Patients were classified by number of schooling years: group I (up to eight years), II (from nine to 11 years), and III (12 or more years). In order to determine current dwelling and place of birth, the cities were grouped into the five macro-regions of the country: Southeast, Northeast, Centralwest, North, and South. The foreign group comprises patients who were born in or live in another country.

The research subjects were also divided into two groups: WICF compliant and WICF non-compliant. For both groups, the WICFs were submitted to a linguistic analysis that determines the approximate length of time needed for the patient to study and understand the questionnaire. In an attempt to apply the readability tests typically used in North America, and not having found a similar instrument validated for the Portuguese language, there was WICFs for each group translated into English by a professional familiar with medical jargon, after which was applied the Flesch-Kincaid Grade Level and the Flesch Reading Ease tests.

The Flesch-Kincad test is defined as a grammar test that classify the text from 0 to 12, according to the American schools grades. A seven index means that one reader that is a seventh year student can understand the text. For average texts, the ideal index is around seven and eight.

The index is: (0.39 x ASL) + (11.8 x ASW) – 15,59. (ASL = average sentence lenght; ASW = average sentence words).

The Flesch Reading Ease is also a grammar test that classify the text in 100 points scale; higher index is

correlated with easier understanding. For the majority of texts, an ideal index is around 60 to 70.

The index is: 206.835 – (1.015 x ASL) – (84.6 x ASW)

It was also studied the correlations between WICF acceptance and data regarding demographic factors, social factors, and education level. The WICFs were classified as being associated with low or moderate risk according to the procedures involved in each study protocol, being low risk the Clinical Genome Digestive Tract Cancer Project and control group of the same project, and moderate risk the Project MK-966.

In order to evaluate, retrospectively, the attitude of research subjects regarding or non-acceptance of the WICF at the time of signing, was used a questionnaire, which was applied to the interviewers.

Statistical analysis

The results were evaluated using the chi-square test to determine associations among the variables, with the level of significance set at $p \leq 0.05$. The Spearman correlation coefficient was used to calculate the degree of association between the two readability tests applied to the WICFs. The SPSS software program for Windows, version 2000, was used (SPSS Inc., Philadelphia, PA, USA).

RESULTS

Seven hundred, ninety-three patients were evaluated. Four hundred, twenty-one (53%) were male. Age ranged from 17 to 96 years, with a mean of 58.2 ± 16 years. The ethnic groups distribution were: 614 caucasian (77.43%), 54 afro-brazilian (6,81), 91 mixed (11,5), 33 japanese descending (4,16), and 1 indian (0,13)

Table 1 shows the level of education of patients enrolled in this study. Most of them had lower than eight years of scholarship.

TABLE 1- Schooling level of the patients

Group	Year of scholarship	Level of education professed	N (%)
I	≤ 8	Illiterate Literate Did not finish Elementary school Finished Elementary school	56 (7.3) 27 (3.4) 234 (29.5) 43 (18)
II	9 - 11	Did not finish high school Finished high school Vocational school	33 (4.2) 124 (15.7) 16 (2.0)
II	≥ 12	Some college or college graduate	158 (19.9)

The current dwelling and place of birth were displayed in Table 2, showing the distribution among the five macro-regions of the country.

The results of the Flesch-Kincaid Grade Level and the Flesch Reading Ease tests among groups concerning the site of tumor and control group are described in Table 3. The reading index range from 9.9 to 12 and 33,1 to 51,3, respectively. The results showed a high level of understanding, what means a necessity of higher schooling level.

TABLE 2 – Regional distribution of the research subjects

Region	Place of birth (N)	Current dweling (N)
Abroad	50	1
Central-west	3	5
Northwest	188	19
North	8	8
Southeast	509	758
South	35	2

TABLE 3 – Readability indices

Index	WICF				
	Cto	Cr1	Eso1/Ca1	Ga1	Mk-966
Flesch Kincaid	12	11.4	10.7	9.7	9.9
Flesch Reading Ease	33.1	34.9	38.2	45.5	51.3

r = −0.91 WICF: written informed consent form; Clinical Genome Digestive Tract Cancer Project: Control Group; (Cto), Cr1: Esofagic Câncer Group; (Ca 1):Colon rectal Câncer Group; Eso 1: Cárdia Câncer Group;: Gastric Câncer Group; (Ga1), MK-966 Project: anti-inflamatory study to patients with polip adenomatous

There is no correlation between education level and acceptance of the written informed consent form (Figure 1).

There were no statistical correlational between WICF and demographic factors: age (p=0.81), gender (p=0.26), and ethnic groups (p=0.19).

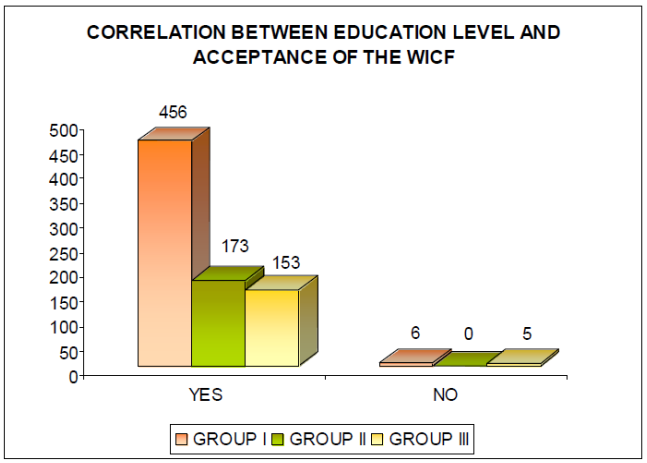
It was noticed a correlation between expected risk and acceptance of the WICF, with higher acceptance with low risk protocol (99.7% vs 81.2%; p<0.01). There is a correlation between education level and health care institution with higher level in private patients (Figure 2).

The correlation between health care facility and acceptance of the WICF showed lower acceptance in private hospitals (99.7% vs 69.2%; p<0.01). Was also analyzed the attitude of research subjects regarding the signing of the WICF (Table 4).

TABLE 4 – Attitude of research subjects regarding the signing of the WICF*

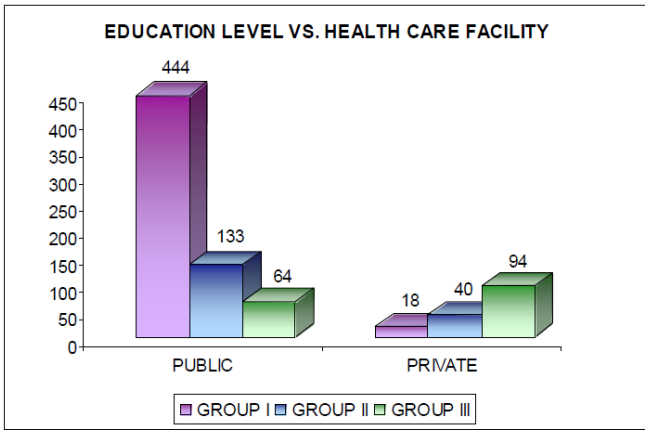
	Public Hospital (%)	Private Hospital (%)
Read WICF	10	60
Only given explanation	90	40

*Percentages estimated according to information provided retrospectively by the interviewers. WICF: written informed consent form



p = 0.19

FIGURE 1 – Correlation between education level and acceptance of the written informed consent form (WICF)



p < 0.001

FIGURE 2 – Correlation between education level and health care institution

DISCUSSION

Efforts to ensure the safety of patients as research subjects in clinical studies were initiated more than two centuries ago. Since then, discussions regarding the WICF have become more sophisticated. However, studies evaluating the process of obtaining informed consent and the factors related to its proper application in studies involving human beings, although increasingly more common, are a relatively recent advent in the international literature.

The application of the WICF preserves research subject autonomy. Autonomy is a term derived from the Greek words auto (relating to the self) and nomos (law, rule, norm). It refers to the capacity of human beings to decide what is "good" and what is in their best interest, according to values, an expectation, needs, priorities, and personal beliefs.

The education level of research subjects is one of the factors currently evaluated in the process of obtaining informed consent. Therefore, many researchers have discussed editing the text in order to ensure greater reading comprehension. Research has shown that people who have limited reading ability present equally limited listening ability. In 1988, Imel pointed out the difference between the traditional concept of reading instruction (academic) and the new concept of functional methods of teaching reading skills, the latter focusing on daily routines and especially on workplace activities[6].

Based on the relationship between functional illiteracy and limited schooling, Bruening proposed the following classification[1]: 1) functionally illiterate individuals: reading level equivalent to 0 to four years of schooling; 2) marginally literate: reading level equivalent to five to eight years of schooling; 3) functional literate: reading level equivalent to nine or more years of schooling; 4) functionally illiterate individuals (those having had less than four years of schooling) are not considered to have the reading, writing, or mathematical skills required to meet the needs of contemporary social and professional life. It is estimated that approximately 900 million people worldwide fit this profile.

In Latin America, the issue presents specific characteristics and greater complexity, although data based on extensive research is scarcer than in some other regions of the world. In relation to the countries evaluated, Brazil is at a disadvantage regarding measures taken to promote functional literacy. Following the recommendations made by UNESCO in the 1990s, the Brazilian Institute of Geography and Statistics also started making rates of functional illiteracy public, these rates being calculated based on the number of years of schooling and not on the self-evaluations of the respondents. According to the criteria adopted, people who have less than four years of schooling are functionally illiterate.

The results of studies evaluating the process of obtaining informed consent in the United States and Europe suggest that many participants might not fully understand the study in which they will participate and might not know their rights as participants, even after having read and signed the WICF[7,11].

Hopper et al., using a radiology-related WICF as the sole source of information provided to patients, demonstrated that the complexity of such documents puts them above the reading comprehension level of the average patient[5]. Researchers at the Pontifical Catholic University of Chile evaluated 44 research projects submitted to the Ethics Committee of that institution over the space of two consecutive years. The problem most frequently reported by the authors was the absence or inappropriateness of the informed consent process[8].

The results of a study carried out in Bangladesh suggest that a lack of reading comprehension may be

more frequently seen in less developed countries, where the volunteers are frequently poor and the educational level tends to be low[10].

The interest in editing WICFs in order to facilitate their comprehension has been growing in recent years. In 2000, Hochhauser reviewed 12 WICFs and concluded that the texts were difficult to understand, especially because they presented uncommon words and a high average number of words per sentence[4]. Zanecchia and Hochhauser both examined questions related to WICF readability and devised strategies to develop more understandable WICFs[3,14]. In general, such strategies focus on simplifying the text and using audiovisual resources as tools for facilitating their understanding.

In the present study, 40% of the research subjects had less than five years of schooling. Nevertheless, the education level of the research subjects was not found to be a crucial factor for acceptance of the WICF, in contrast to what had been expected at the study outset. In addition, no differences were found in the rate of acceptance in relation to demographic and social factors. However, the rate of acceptance in the public hospital was higher than that observed in the private health care facilities.

This result leads us to hypothesize that social factors are directly or indirectly related to education level and thereby influence the degree of acceptance. It is also of note that, in the private hospital evaluated, the schooling level was higher, 61.8% of the interviewees being college graduates or having some higher schooling, compared with 10% in the public hospital. Approximately 60% of the private hospital interviewees read the text of the WICF before deciding to sign it. In contrast, in the public hospital, only 10% of the interviewees read the text of the WICF, the others preferred that the interviewer read and explain the text. In view of these results, it is possible to speculate again on the reasons for the lower rate of WICF acceptance in the private facility.

Could the attitude of accepting and complying with the WICF be understood as a symbol of the spirit of cooperation? Could the latter be related to social and cultural factors, or even to psychological factors?

It is of note that the rate of WICF non-acceptance was higher in the population presenting the highest schooling level. The readability indices found showed that the texts are difficult to understand, demanding that subjects have a higher level of education.

The Flesch-Kincaid indices found for each WICF ranged from 9.7 to 12, 8.0 being the limit for easy understanding of the text. The Flesch Reading Ease indices ranged from 33.1 to 51.3, 60.0, being the minimum required for adequate understanding of the text.

Although the variation between the values found for each WICF was not significant, there was a correlation between the two indices: those WICFs that obtained the highest Flesch-Kincaid indices (12.0 and 11.4) were those that presented the lowest Flesch Reading Ease indices (33.1 and 34.9, respectively). These data suggest that two indices be validated, although they were applied to documents that had been translated into English.

The issue of risk inherent to, and possible benefits of, clinical studies, especially those carried out in underdeveloped or developing countries, has also generated discussion in the scientific world. One of the factors posing significant risk to the patient is the use of placebo groups in comparative studies of new drugs.

The risk perceived by the patient also needs to be evaluated. In a study on treatment risk carried out in England, patients overestimated surgical risk, which was actually 2%, to be as high as 65%[9]. This finding underscores the importance of adequately explaining the risks associated with experimental procedures. It is fundamental to determine to what extent the participants understand the information provided.

The fact that placebos are used to avoid false results and that their use is a fundamental component of clinical trials of new drugs needs to be made clear on the WICF so that research subjects can evaluate the risks of the treatment, whether they receive the placebo or the active drug.

In the present study, was chosen WICFs that presented two distinct situations regarding patient risk/discomfort. Therefore, it was also possible to evaluate the influence that the risk/discomfort factor may have on research subject decisions to participate in the scientific research project or not. In 1996, a resolution regulating the application of the WICF was approved by the Brazilian Ministry of Health. All of the guidelines put forth in this document should be followed.

Future research projects might arise from further reflection on these issues [12]. For example, such studies might involve the use of different WICFs for the various education levels, applied randomly to the research subjects. Another possibility would be to include audiovisual resources, such as educational videos, that would help the patient understand the study proposals.

In addition, a more appropriate system of determining the influence that cultural factors have on research subject acceptance of the WICF should be created. Nevertheless, it is essential to analyze the role played by reading comprehension, taking into consideration the adequate readability for all population groups to be recruited as research subjects in Brazil, as well as to promote the creation of WICF texts that use appropriate language to achieve their objectives.

Despite the high rates of acceptance, it is necessary to evaluate new methods of applying WICFs so that research subjects with less schooling might fully understand all of the proposals of the studies.

CONCLUSION

The WICFs had high degree of reading difficulty. Although patient acceptance was not found to be related to demographic or social factors, it was found to be influenced by the risk-benefit relationship.

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