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Informed consent process in clinical trials: development of a patient-reported questionnaire

Desarrollo de un cuestionario dirigido a conocer el proceso de consentimiento informado en investigación clínica desde la perspectiva del paciente

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Abstract

Objective: To develop a Spanish-language questionnaire aimed at evaluating patients' perception of the way they are briefed and their consent is obtained prior to participating in clinical trials. The tool was conceived to evaluate the following aspects: patients' personal experience, the way the informed consent process was implemented in practice, patients' level of satisfaction with the process, and their level of understanding of the study itself.

Method: This study looked into the development, adaptation and validation of a self-administered questionnaire intended to evaluate the informed consent process on the basis of information provided by respondents. The steps followed included: literature review, generation of an items pool, drawing up of the questionnaire, expert review, piloting, and reading ease optimization and analysis. A commonly-used English-language questionnaire was evaluated, translated into Spanish and adapted so as to determine the extent to which subjects understood the information conveyed to them.

KEYWORDS

Informed consent; Clinical trials as topic; Patient satisfaction; Comprehension; Decision making; Surveys and questionnaires; Validation study.

Resumen

Objetivo: Desarrollar un cuestionario en español dirigido a evaluar el proceso de información y obtención del consentimiento informado en investigación clínica desde la perspectiva del paciente. Con esta herramienta se pretende analizar en los pacientes que participan en un ensayo clínico los siguientes aspectos: la experiencia y desarrollo práctico del proceso de consentimiento informado, su nivel de satisfacción con dicho proceso y su nivel de comprensión del estudio.

Método: Estudio de desarrollo, adaptación y validación de un cuestionario autocumplimentable para evaluar el proceso de consentimiento informado a través de la información obtenida de los pacientes. Los pasos seguidos fueron: revisión bibliográfica, generación de un *pool* de *ítems*, redacción del cuestionario, revisión por expertos, pilotaje, optimización y análisis de legibilidad. También se realizó una evaluación, selección, traducción y adaptación al español de una herramienta disponible en lengua inglesa que permitiese valorar la comprensión del paciente de la información.

PALABRAS CLAVE

Consentimiento informado; Ensayos clínicos como asunto; Satisfacción del paciente; Comprensión; Toma de decisiones; Encuestas y cuestionarios; Estudios de validación.

Results: In its final version, the questionnaire came to comprise four sections intended to evaluate: 1) socio-demographic data; 2) practical aspects related with the development of the informed consent process; 3) patients' perception of the process (satisfaction, expectations and motivations); and 4) their level of understanding. Understanding was gaged using the QuIC questionnaire, translated by three bilingual translators. Additional questions were included to evaluate the understanding of concepts related with blinding and therapeutic misconception. The validity of the contents was evaluated by consulting with an expert panel. The reading ease analysis yielded an IFSZ score of 64.34, equivalent to an "average difficulty" grade on the Inflesz scale. In the pilot study, interviews were held with 32 patients, who did not appear to have any difficulties in understanding the questions asked of them or in using Likert-type scales to respond. Mean completion time was 16.6 minutes.

Conclusions: The tool developed as part of this study has shown itself capable of providing an understanding and an assessment of the informed consent process from the perspective of a patient who is invited to participate in a clinical trial. Implementation of the questionnaire could help investigators ascertain that the process has been correctly executed and identify specific aspects that may require to be changed or optimized.

Resultados: El cuestionario quedó conformado por cuatro apartados que permiten evaluar: 1) datos sociodemográficos, 2) aspectos prácticos relacionados con el desarrollo del proceso de consentimiento informado, 3) valoración del paciente del proceso (satisfacción, expectativas y motivaciones), 4) grado de comprensión. Para valorar la comprensión se seleccionó el cuestionario *Quality of Informed Consent questionnaire*, que fue traducido por tres traductores bilingües. Se incluyeron tres preguntas adicionales para evaluar la comprensión de conceptos relacionados con el equívoco terapéutico y el enmascaramiento de los tratamientos. La validez de contenido fue evaluada mediante consulta con un panel de expertos. En el análisis de legibilidad se obtuvo un valor de Índice de Flesch-Szigriszt de 64,34 equivalente a un grado de dificultad "normal" en la escala Inflesz. En el estudio piloto se entrevistó a 32 pacientes que mostraron no tener dificultades para comprender las preguntas ni problemas a la hora de utilizar las escalas de respuesta. El tiempo medio de cumplimentación del cuestionario fue de 16,6 minutos.

Conclusiones: La herramienta desarrollada es útil a la hora de conocer y valorar el proceso de consentimiento informado desde la perspectiva del paciente al que se le invita a participar en un estudio. Su aplicación podría resultar de ayuda a los investigadores para verificar que se ha seguido un adecuado proceso y para identificar aspectos concretos que son susceptibles de ser modificados y optimizados.

Introduction

The last few years have witnessed a growing interest in gaining a greater understanding and coming up with more efficient ways to manage the informed consent (IC) process in subjects participating in clinical trials[1,2]. The principle of IC is derived from the legal and ethical obligation of investigators to ensure that subjects to a research project freely and voluntarily consent to participating in such a project[3].

IC is a lengthy, complex and dynamic process that requires a high degree of engagement, respect and rigor from healthcare providers, investigators and evaluating agencies. Only patients who have received comprehensive information and are capable of understanding the basic aspects of the trial and of giving their consent in an autonomous way should be allowed to participate in a clinical trial[4].

The literature on the nature of the IC process is vast and includes numerous guidelines and documents laying out how IC should be managed[5-9]. Nonetheless, authors have in the most part focused on theoretical aspects, ignoring many of the difficulties that typically arise in clinical practice. In this respect, a series of problems and limitations have been documented, which could affect the quality of the process and even question its validity[4]. Bureaucratization of IC and its virtual reduction to a legal act, the difficulties arising from patient information sheets, comprehension problems and therapeutic misconception are just some of the difficulties reported in the literature[10-16]. As a result, daily practice of IC tends to be far removed from the theoretical ideal and the goals originally proposed.

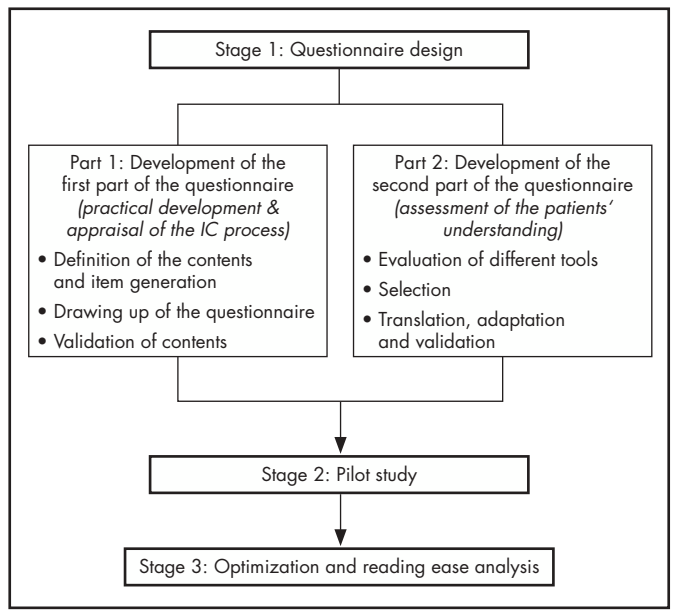
Spanish IC data tend to be scarce, most of them coming from studies that analyze the IC process from the point of view of ordinary clinical practice rather than that of research[17,18]. However, the very nature of experimental work entails a higher degree of therapeutic uncertainty, which is not always easy to convey or understand.

The purpose of this study is to develop and validate a Spanish-language questionnaire that can be used to analyze the IC process from the point of view of a patient participating in a drug-based clinical trial. More specifically, this article sets out to design a tool that may provide an insight into how the IC process came about, how patients feel about the process and what their level of understanding is about the clinical trial they are asked to participate in.

Methods

The authors set about developing, adapting and validating a self-administered Spanish-language questionnaire aimed at gaining an accurate understanding of patients' perception of the IC process. The research was conducted in three stages, following the pattern shown in figure 1.

Figure 1. *General research scheme.*



Stage 1. Questionnaire design

Part 1. Development of the 1st part of the questionnaire

The first part of the questionnaire was conceived to understand patients' experience of the IC process, gathering information about the practicalities of the process and about the patients' subjective perception of it.

The steps followed included:

1. Definition of the questionnaire contents and wording of the different items. A literature search was carried out for aspects such as the regulation in force concerning research projects[19,20], ethical recommendations relative to IC[5-7], expert work[8,9], and tools available to evaluate the IC process[21-23]. An analysis was also performed of the references of the articles reviewed so as to identify additional studies. A team of bioethics and research methodology experts used this material to define the domains under which the essential components of the IC process could be grouped and defined the items that were best suited to the purpose of our questionnaire.

2. Drafting of the questionnaire. Once the items had been selected, they were organized in a logical sequence and the questions were formulated.
3. Validation of the questionnaire contents. The questionnaire was evaluated by an expert panel made up of members of the La Paz Hospital Drug Research Ethics Committee (CEIm), members of the hospital pharmacy and clinical pharmacology departments, and a research methodology expert. A determination was made of the degree of agreement between experts when evaluating the adequacy, relevance and clarity of each one of the proposed items.

Part 2. Development of the 2nd part of the questionnaire

A second part was added to the questionnaire, intended to evaluate the degree to which patients understood the information given to them during the IC process. To this end, a series of validated English-language tools was selected and subsequently adapted.

The steps followed included:

1. Tools identification and evaluation.

   A literature search was carried out in Pubmed (Medline), IBECS, MEDES and COCHRANE for studies that used standardized tools to evaluate the subjects' understanding of instructions received. Tools specifically designed for patients with impaired capacity to consent and those for which no validation data were provided were excluded.

   The next step was to evaluate the tools' quality and applicability on the basis of the following criteria: construct, evaluated areas, item generation, evaluation method, administration time, items, scoring and validation.
2. Tool selection.

   The following selection criteria were established: use of objective criteria to measure understanding, adherence to the requirements and the regulations, and implementation feasibility. To qualify for selection, questionnaires had to be amenable to self-administration and should not require answers to be coded.
3. Translation and adaptation to Spanish.

   The translation work was done by a team of a specialist hospital pharmacist, an investigator working in the area of healthcare quality and a linguist, each of them working separately. All three had experience of doing research and were native speakers of Spanish yet bilingual in English and Spanish.

The validity of the contents was evaluated by recourse to the same panel of experts as in part 1.

Stage 2. Pilot study

After bringing together both parts, the full questionnaire was administered to a patient sample in order to evaluate its appropriateness and feasibility in the real world.

The sample included adult patients participating in one of the drug-based clinical trials our hospital is involved in and for which they had been asked to fill in an IC form in the previous 30 days. Patients who could not read or write and those on non-therapeutic or phase IV trials were excluded. The sample size was set at 30 patients as this amount was considered appropriate for an initial exploratory analysis. The pilot study lasted two months, with subjects being selected using convenience sampling. Completion time was duly recoded, and the clarity of the questions and the appropriateness of the format were evaluated by in the course of a personal interview with the patients. Patients' comments and suggestions were also recorded.

All patients were provided with oral and written information about the project and asked to sign an IC form. The study was approved by the La Paz Hospital's Drug Research Ethics Committee.

Stage 3. Reading ease: optimization and analysis

The definitive questionnaire was drawn up based on the results of the pilot study. Reading ease was assessed using the Flesch-Szigriszt reading ease score (IFSZ), considered to be a standard for determining the syntactic difficulty of Spanish-language texts[24].

IFSZ = 206.835 – 62.3 x (syllables/words – words/sentences)

The Inflesz computer software was used to determine the reading ease of the text based on the ISFZ score. An IFSZ score ≥ 55 indicates acceptable reading ease.

Results

Questionnaire design

First part of the questionnaire

After reviewing and evaluating the information obtained, a group of items was developed related to the practical development of the IC process, together with another group of items related to the patients' perception of the process. Table 1 shows the domains and the items included in the questionnaire as well as the number of questions under each.

Table 1 was used as a basis to put together 27 closed-ended questions aimed at gaining an understanding of the patients' perception of the overall IC process. Most questions offered respondents the possibility to choose from a 5-point Likert scale going from "I completely disagree" to "I totally agree". Some items had to be answered on a Visual Numeric Scale going from 0 to 10. Other types of questions (dichotomous or polytomous) were used in cases where neither of the two scales could be used.

Given that following the validation process experts reached a level of agreement above 70% for all the items, it was decided to keep them

Table 1. Questionnaire design: evaluated items and domains

Questionnaire (part 1)			
Purpose	**Items**	**Domains**	**Questions**
Practical development of the IC process	Staff member who administered the questionnaire	Experience	1, 2, 3
	Discussion of the study was part of the briefing process	Experience	4
	Duration of the briefing session	Experience	5
	Location of the briefing session	Experience	6
	Use of multimedia resources	Experience	7
	Presence of friends or family members	Experience	8
	Mode: inpatient/ outpatient	Experience	9
	Information sources reviewed	Experience	10
	Persons consulted from patient's family/social circle	Experience	11
	Reading of PIS	Experience	12
	Time elapsed between inviting the patient to participate and their eventual signing of consent form	Experience	13
	Delivery of signed copy of consent form	Experience	14

Table 1 *(cont.).* Questionnaire design: evaluated items and domains

Questionnaire (part 1)			
Purpose	**Items**	**Domains**	**Questions**
Patients' assessment and perception of the IC process	**1. Motivations to participate**	Motivations-Expectations	15, 16
	2. Appraisal of the briefing process		21
	2.1 Characteristics of the information provided: clarity and complexity of the PIS, relevance of the PIS, equivalence between oral and written information, total amount of information, comprehensibility of the information	Satisfaction-expectations	18, 19
	2.2 Nature of the clinical environment where the IC process took place: time and place, respect of intimacy and privacy	Satisfaction-expectations	19
	2.3 Professionality and humaneness of the treatment offered. Clarity and comprehensibility of information. Clarification of doubts. Closeness and empathy	Satisfaction-expectations	19
	3. Appraisal of the decision-making process		17
	Perceived pressure	Autonomy	20
	Consequences of declining to participate	Autonomy	20
	Time to make a decision	Autonomy	20
	Other factors influencing the decision	Autonomy	20
	4. Expectations from the study		
	Risk	Consequences	24
	Benefit	Consequences	25, 26
	Importance of the study	Consequences	27
Questionnaire (part 2)			
Assessment of patients' understanding	**1. Experimental nature of the study**		
	The fact that it is an investigational study	Purpose	A1, B1
	Identification of experimental treatments and procedures	Purpose	A4, B5
	2. Process		
	Expected duration of the subject's participation	Consequences	A3, B3
	For studies involving more than a minimum risk, availability of insurance. Economic compensation and treatment in case of injury or damage	Consequences	A17, B11
	Persons responsible for informing the subject, clarifying their doubts and answering their questions	Expectations	A18, B12
	3. Benefits		
	Potential benefits subjects may derive from the study	Consequences	A9, A13, B7
	Potential benefits other parties may derive from the study	Consequences	A14, B8
	Goals of each phase of the study	Purpose	A2, A5, A6, A7, A8, B2
	4. Risks and inconveniences		
	Potential side effects, risks and inconveniences derived from the study	Consequences	A12, B6
	5. Procedures used		B4
	Randomization	Consequences	A11
	Dose escalation	Consequences	A10
	Blinding	Consequences	A22, A23
	6. Alternatives		
	Alternative treatments and procedures available	Consequences	A16, B9
	7. Confidentiality		
	Aspects relative to confidentiality and data access	Consequences	A15, B10
	8. Voluntariness		
	Voluntary nature of participation	Autonomy	A19, B13
	Freedom to withdraw at any time without loss of routine care or prejudice to future medical treatment	Autonomy	A20
	9. Aspects related to therapeutic misconception	Lack of individualization	A4, A21, B5

IC: informed consent PIS: patient information sheet.

unchanged. Experts nevertheless did decide to remove the intermediate option on the 5-point Likert scale to prevent answers from erring towards the option involving the least commitment. Items related with the patient information sheet were all grouped together.

When asked to review the final version, experts agreed that the questions tackled all the essential aspects of the IC process, that the potential answers were properly categorized, and that the questions were suitably presented.

Second part of the questionnaire

Based on the established criteria, the following instruments were selected to evaluate the subjects' level understanding: the Deaconess Informed Consent Comprehension Test (DICCT)[25], the Quality of Informed Consent questionnaire (QuIC)[26], the Brief Informed Consent Evaluation Protocol (BICEP)[22], the Index of Clinical Trial Understanding (ICTU)[27], the Questionnaire-Patient Understanding of Research (Q-PUR)[28], and the Modular Informed Consent Comprehension Assessment (MICCA)[29]. A comparison of the results obtained is shown in table 2.

After a thorough analysis, S. Joffe *et al.*'s QuIC questionnaire was selected as it m*et al.*l the predefined criteria. The questionnaire is divided into two sections. Section A seeks to determine the subject's real (objective) understanding through 20 closed-ended questions with three possible answers each: *I agree*, *I disagree* or *I don't know*. Section B seeks to determine the patient's (subjective) understanding of the knowledge through 14 Likert-type questions where they are asked to state their perceived understanding of the different aspects of the study. Response options range from 1 ("I understood nothing") to 5 ("I fully understood").

In section A, 100 points were assigned for each correct response, 0 points for each incorrect response and 50 points if the response was *I am not sure*. The overall score was calculated by estimating the average score. In section B a calculation was made of the mean scores of the 14 questions included. The resulting mean score (range: 1-5) was transformed into a 0-100 score. For both sections it was considered that the higher the score, the higher the level of understanding.

The Spanish translation tried to preserve the semantic and conceptual equivalence of the English version, as well as its original structure. As hardly any discrepancies were found between the versions prepared by each translator, it was decided to combine all translations into one single document.

After evaluating the Spanish version for sufficiency, clarity, coherence and relevance, the experts concluded that the questionnaire allowed an evaluation of the essential aspects of a study which, according to the GCP principles and the existing regulations, must be disclosed to any patient participating in a clinical trial.

A decision was made to include four additional questions to determine the patients' understanding of aspects related to blinding and therapeutic misconception (questions 21, 22, 23 of section A). The responses to these questions were considered separately when analyzing the results.

Table 1 shows the items included and the IC domains evaluated in the second part of the questionnaire.

Pilot study

The study comprised 32 patients, 50% of whom were male (n = 16) with a mean age of 59.2 years (± 17.3). Of them, 19 (59.4%) were participating in phase III clinical trials, 12 (37.5%) in phase II trials, and 1 (3.1%) in a phase I trial. The most widely represented medical specialties were oncology (9 patients; 28.1%), rheumatology (8 patients; 25%), internal medicine (6 patients; 18.8%) and GI (5 patients; 15.6%).

Table 3 shows the most common responses obtained in the first part of the questionnaire, where the aim was to understand the patients' perception and appraisal of the overall IC process.

The second part of the questionnaire, which was geared toward evaluating patients' level of understanding, produced a mean overall score of 69.5 (SD = 10) for objective comprehension and 77.4 (interquartile range [IQR] = 67.3-85.3) for subjective comprehension. Responses to questions 21, 22 and 23 in section A were analyzed separately and produced a mean score of 69.4, 66.1 y 68.8 respectively.

Mean completion time was 16.6 minutes (range: 14-20). As regards acceptability, all respondents were positive about the clarity of the questions and the appropriateness of the questionnaire's format. Further to patient feedback, it was decided to modify question 19.4, replacing the term "confidentiality" by "intimacy and privacy". A decision was also made to highlight some words phrases in the questions to prevent respondents from following an automatic repetitive pattern in their answers. Finally, a question about the amount of information provided was removed as there was a similar question elsewhere in the questionnaire.

Reading ease: optimization and analysis

Once the pilot was over, the definitive questionnaire was designed (Appendix 1), which was made up of the following sections: general details, practical development of the IC process, appraisal of the IC process, and evaluation of patients' level of understanding.

The reading ease analysis provided an IFSZ score of 64.34, which corresponds to an "average difficulty" grade on the INFLESZ scale.

The questionnaire was approved by La Paz hospital's Innovation Committee and was notarized by Miguel García Gil, member of the Notarial College of Madrid on 29 November 2019. It was assigned protocol nr 2145[30].

Discussion

Several tools have been designed in the last few years to evaluate the IC process in the context of clinical research[21,22,25-29]. Although implementation of such tools undoubtedly constitutes a major development, none of them is fully aligned with the goals of this study, as they are more often than not intended to analyze specific aspects of the process such as the contents of the information provided, the understanding of such information, therapeutic misconception, or the reasons why patients agree to participate in a study. Moreover, most of the tools were developed abroad, which makes them difficult to implement without a previous adaptation process that takes into account potential differences concerning language, culture and social and healthcare conditions.

Our tool was developed to gain a better understanding of the overall IC process from the patient's standpoint, with a view to identifying and analyzing the strengths and weaknesses they perceive during the briefing and decision-making processes.

The questionnaire designed under this study is meant to be self-administered, which provides access to a greater number of patients and precludes the risk of interviewer bias. Unlike other similar questionnaires[23,25], the survey presented here does not include open-ended questions as these pose difficulties concerning response coding and standardization, and are more burdensome for both patients and investigators.

Our questionnaire includes the translated and adapted version of the QuIC survey, which is a simple and practical way of appraising patients' understanding of the IC process. The QuIC tool was developed specifically for oncologic studies, which may at first sight be considered to limit its application to trials related to other medical specialties. Nonetheless, as none of the questions make specific reference to cancer research, it was possible to adapt and validate the instrument for use in other kinds of trials. In this regard, all the questions included in the QuIC refer to the basic general aspects that any patient participating in a clinical trial should be aware of, regardless of the condition or medications investigated. In spite of that, we believe complementary studies should be conducted to confirm our findings and evaluate the psychometric properties of the translated and adapted version of the QuIC tool.

Our work presents a series of limitations that must be taken into account when interpreting the results obtained. Firstly, the questionnaire is exclusively aimed at evaluating the IC process in patients participating in clinical research studies. It is not meant for patients who, after being briefed and invited to participate in a study, are not finally included in it either because they decline to participate or because they do not meet some of the inclusion criteria. In addition, given that the information is based on patients' memories, variations may appear in the results because of discrepancies with respect to what really happened.

Table 2. Comparison of the different tools evaluated

Tool	Construct	Domain	Item generation	Evaluation method	Time	Items	Question time	Score	Validation
Deaconess Informed Consent Comprehension Test (DICCT) Miller C, *et al.*, 1996	Comprehension	Experimental nature Process Benefits Risks and inconveniences Alternatives Voluntariness Confidentiality	United States IC regulations	Structured interview	< 10 min	14 items	Open-ended questions on: - General research-related aspects - Specific research-related aspects	Comprehension (0-28 points)	Inter-observer concordance (r = 0.84) Score correlation with: - WAIS-R test (r = 0.44) - WRAT-R test (r = 0.38)
Quality of Informed Consent (QuIC) Joffe S, *et al.*, 2001	Objective comprehension (real) Subjective comprehension (as perceived by the patient)	Experimental nature Process Benefits Risks and inconveniences Randomization Confidentiality Alternatives Voluntariness Therapeutic misconception	United States regulations Work by the author Appelbaum's work on therapeutic misconception Recommendations of the NCI work group	Self-administered questionnaire	< 10 min	34 items	Questions on the general aspects of a clinical trial - Part A: 20 statements with 3 possible answers (I agree, I disagree, I am not sure) - Part B: 14 Likert-scale questions	Objective comprehension (0-100 points) Subjective comprehension (1-5 points) Overall score (0-100 points)	Test-retest: - Part A: ICC = 0.66 - Part B: ICC = 0.77
Brief Informed Consent Evaluation Protocol (BICEP) Sugarman J, *et al.*, 2005	Quality of IC: - Autonomy of the decision made - Comprehension	Process Voluntariness Benefits Satisfaction Risks Therapeutic misconception Experimental nature	Literature review Consultation with experts	Structured interview	< 10 min	15 items	Open-ended questions on general aspects	TMAS score (0-5 points) ICAS score (0-10 points)	Inter-observer concordance (ICC = 0.75)
Questionnaire-Patient Understanding of Research (Q-PUR) Hutchison C, *et al.*, 2007	Understanding of concepts related with: - Standard of care - Randomization - Placebo - Which treatment is best	Experimental nature Benefits Uncertainty Process Voluntariness Randomization Placebo	Literature review Consultation with experts Consultation with patients	Self-administered questionnaire	< 11 min	13 items	Multiple-choice questions on the general aspects of clinical trials Four possible answers, always including the *I am not sure option*	Comprehension: the percentage of correct answers is calculated	Internal consistency (α = 0.77)
Modular Informed Consent Comprehension Assessment (MICCA) Buccini LD, 2009	Understanding of the information provided as part of the IC process	Experimental nature Voluntariness Process Confidentiality Risk/benefit Randomization Alternatives Therapeutic misconception	United States, Australian and Canadian regulations. Best practice standards Work by other authors	Self-administered web-based questionnaire	< 10 min	25 items	Closed-ended questions on general research-related aspects and on the specifics of each study - 14 true-false type - 11 multiple choice	General comprehension Specific comprehension of the study Overall comprehension	Validity of the contents determined by consultations with experts Internal consistenc (α = 0.89-0.93)
Index of Clinical Trial Understanding (ICTU) Miller J, *et al.*, 2011	Understanding of: - Control group - Randomization - Standard of care - Placebo - Nature of the study	Randomization process Experimental nature	Not specified	Self-administered questionnaire (not explicitly described)	< 10 min	7 items	Questions on the general aspects of clinical trials: - Open-ended (item 1) - Multiple choice (items 2,3,4 and 5) - Likert-scale (items 6 and 7)	Comprehension (0-9 points)	Construct validity Predictive validity

IC: Informed consent; ICC: intraclass correlation coefficient; NCI: National Cancer Institute; WAIS-R: Wechsler Adult Intelligent Scale-revised; WRAT-R: Wide-Range Achievement Test-revised.

Table 3. Pilot study: responses to part 1 of the questionnaire

Implementation of the informed consent process	***n* (%)**
Manner in which the information was presented	
Orally and in writing	32 (100.0%)
Staff member in charge of the briefing session	
Had you been seen previously to by the same staff member?	20 (62.5%)
Were you seen to by that staff member after signing the IC form?	24 (75.0%)
Presence of a nurse in the briefing session	10 (31.3%)
Duration of the briefing session	
– Less than 15 min.	8 (25.0%)
– Between 15 and 30 min.	17 (53.1%)
– Between 30 min and 1 hr.	7 (21.9%)
Where did the briefing session take place?	
– Office/surgery	25 (78.1%)
– Hospital room	5 (15.6%)
– Other	2 (6.3%)
Use of multimedia resources	1 (3.1%)
Review of other information sources	10 (31.3%)
– Internet	5 (12.5%)
– Other doctors	6 (18.8%)
Consultation with people in your family/social circle	23 (71.9%)
Reading of the PIS prior to signing the IC form	25 (78.1%)
IC form was signed on the same day you were invited to participate	16 (50.0%)
You were given a copy of the signed PIS	32 (100.0%)
Appraisal and perception of the informed consent process	
Main reason to participate	***n* (%)**
– Finding a cure for my disease	10 (31.3%)
– Better monitoring and control of my disease	6 (18.8%)
– Recommendation by the medical team	7 (21.9%)
– Help other patients	3 (9.4%)
– Contribute to furthering the understanding of the disease	3 (9.4%)
– Other	3 (9.4%)
Assessment of the IC process*	***n* (%)**
– I am satisfied with the IC process	30 (93.8%)
– The PIS is too complex	19 (59.4%)
– The PIS is too long	18 (56.3%)
– I received enough information	25 (78.1%)
– The duration of the briefing process was adequate	28 (87.5%)
– I was given the opportunity to seek clarification of all my doubts	31 (96.9%)
Appraisal of the decision-making process*	***n* (%)**
– I felt under pressure to make a decision	1 (3.1%)
– I felt I was going to receive poorer treatment if I declined to participate	2 (6.3%)
– I had enough time to make my decision	25 (78.1%)
Expectations about the study	**Media ± DE**
– Patient risk score	2.9 ± 2.6
– Patient benefit score	7.1 ± 2.6
– Benefit score for future patients	8.1 ± 1.7

IC: informed consent; PIS: patient information sheet. *Patients who responded agree or fully agree.

Our tool helps understand and evaluate the IC process from the standpoint of patients invited to participate in a clinical trial. Investigators will surely find it useful both to ensure that the IC process has been correctly followed, and to identify specific clinical aspects requiring improvement.

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Conflict of interests

No conflict of interests.

Contribution to the scientific literature

Informed consent is one of the main pillars of research. It is not only an indispensable legal requirement to carry out any clinical trial but also an ethical imperative for healthcare professionals. The literature shows that in spite of the theoretical and regulatory efforts made to improve the briefing and consent-taking processes, a number of barriers and difficulties still exist that create a gulf between daily practice and the theoretical ideal.

The present study provides researchers with a new tool to come to grips with the realities of the informed consent process and evaluate how it works in everyday practice. Implementation of the tool presented here may be useful for designing new strategies conducive to improving the quality of the process and ensuring that consent has been obtained in accordance with the relevant ethical and legal requirements.

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APPENDIX 1

SELF-COMPLETION QUESTIONNAIRE TO ASSESS STUDY PARTICIPANTS' UNDERSTANDING OF THE INFORMED CONSENT PROCESS

Thank you for giving your consent to participate in the clinical trial. We would now like to ask you for your opinion on adequacy of the information provided to you before the trial and on the way your consent was obtained. We would also like to gage your level of understanding of different aspects related to the study. The information you share with us will help us improve some aspects of the research conducted in this hospital.

This is an anonymous questionnaire to be used for statistical and research purposes. Estimated completion time is 16 minutes.

The questionnaire is voluntary so you may choose not to complete it or discontinue your participation at any time without prejudice.

Please tick the appropriate box or fill in your answer in the space provided:

GENERAL DETAILS

Date of completion of this questionnaire**:** _____

Sex: ☐ Male ☐ Female

Age: _____

What is the highest level of education you completed?

☐ None ☐ Primary ☐ Secondary ☐ University or equivalent

Current occupational status:

☐ Student ☐ Trainee/ doing an internship ☐ Wage earner or self-employed ☐ Unemployed

☐ Retired/old age pensioner ☐ Other: _____

Mother tongue: ☐ Spanish ☐ Other: _____

If Spanish is NOT your mother tongue, has the language factor interfered with your understanding of the study?

☐ Yes ☐ No ☐ I am not sure

Have you participated in other clinical trials? Yes ☐ No ☐ ☐ I am not sure

If your answer was YES: What was your level of satisfaction with the study?

☐ Satisfied ☐ Neutral ☐ Dissatisfied

PART 1. THE INFORMED CONSENT PROCESS

A) Practical development of the informed consent process

1. How was the i**nformation** about the clinical trial given to you?
☐ Orally ☐ In writing ☐ Both

2. Had you been seen to by the **staff member who briefed you** on some previous occasion?
☐ Yes ☐ No, it was the first time ☐ I am not sure

3. Were you seen to by that staff member after signing the informed consent form?
☐ Yes ☐ No ☐ I am not sure

4. How long did the briefing process **last**?
☐ Less than 15 min ☐ 15-30 min ☐ 30 min-1 hr. ☐ Over 1 hr.

5. Where did it take place?
☐ In an office/surgery ☐ In a hospital room ☐ Other. Where?_____

6. Were **multimedia resources** (video, audio, etc.) used to illustrate the explanations?
☐ Yes. Which? _____ ☐ No ☐ I am not sure

7. Was a **nurse** present during in the briefing session?
☐ Yes ☐ No ☐ I am not sure

8. Were you accompanied by some **friend or family member**?
☐ Yes. Who? _____ ☐ No ☐ I am not sure

9. Were you offered to participate in the clinical trial while you were hospitalized?
☐ Yes ☐ No ☐ I am not sure

10. Did you review **other sources of information** before you agreed to participate?
☐ Yes ☐ No ☐ I am not sure

If you ticked the YES box, please state which sources you used:
☐ Internet ☐ Books or magazines ☐ Other doctors ☐ Other patients

11. Did you consult your decision with **other people in your family or social circle**?
☐ Yes ☐ No ☐ I am not sure

If you ticked the YES box, please tell us who you consulted:
☐ Spouse ☐ Children ☐ Other family members ☐ Friends ☐ Other

12. **Did you read the patient information sheet** before signing the informed consent form?
☐ Yes ☐ No ☐ I am not sure

13. **How many days elapsed** between the moment you were asked to participate in the trial and the time you signed the informed consent form? *(if you don't remember the exact number of days please provide a ballpark figure)*

☐ I signed the form the same day I was invited to participate ☐ _____ days elapsed

14. **Were you given a copy** of the informed consent form once you had signed it?
☐ Yes ☐ No ☐ I am not sure

B) Appraisal of the informed consent process

Please tick the appropriate box or fill in your answer in the space provided:

15. What was your **main reason** for participating in the trial? (indicate just one)

☐ Finding a cure for my disease
☐ Better monitoring and control of my disease
☐ Recommendation by my medical team
☐ Access to new drugs
☐ Help future patients
☐ Contribute to the furthering of knowledge
☐ Other: _____

16. Apart from the main reason stated above, which of the **other reasons** above was/were important for you? *(you may indicate one or more):*

☐ Finding a cure for my disease
☐ Better monitoring and control of my disease
☐ Recommendation by my medical team
☐ Access to new drugs
☐ Help future patients
☐ Contribute to the furthering of knowledge
☐ Other: _____

17. Who played the **main role in making the decision that you should participate** in the trial?

☐ You ☐ Family members ☐ The medical team

18. **Did you read the patient information sheet**?

☐ Yes ☐ No ☐ I wasn't given a patient information sheet

*If you ticked the **NO** or the **I WASN'T GIVEN A ...** box, please proceed to question 6.*

If you ticked the YES box, tell us whether you agree with the following statements:

18.1 You read the patient information sheet **carefully**.

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

18.2 The patient information sheet was **too complex.**

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

18.3 The patient information sheet was **too long.**

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

18.4 The information in the patient information sheet was **the same as** the information provided to me orally in the briefing session.

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

18.5 The patient information sheet **was important for making the decision.**

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

19. Please state the extent to which you would agree with the following statements concerning the **briefing process**. Please read them carefully.

19.1 I received **enough information** about the trial.

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

19.2 I **correctly understood** the information given to me about the trial

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

19.3 The **duration** of the briefing process was **adequate**.

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

19.4 I felt that my **privacy and intimacy** were respected throughout the briefing process.

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

19.5 I was given the opportunity to **seek clarification** of **all my doubts**.

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

19.6 The staff answered by questions in manner that was **clear and easy to understand**.

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

19.7 The person in charge of the briefing treated me **humanely and empathetically**.

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

20. Please state the extent to which you would agree with the following statements concerning the **decision-making process.** Please read them carefully.

20.1 I **felt under pressure** to make a decision.

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

20.2 I felt **I was going to receive poorer treatment** if I declined to participate.

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

20.3 I had **enough time** to make my decision.

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

20.4 I believe it was necessary to start the treatment under the study **as soon as possible.**

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

20.5 I believe that if I participate in this trial I will receive **better healthcare** than if I don't participate.

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

20.6 When making the final decision, my confidence in the medical team **outweighed the information received about the trial**.

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

20.7 I think I have a **positive attitude towards medical research.**

☐ I fully agree ☐ I agree ☐ I disagree ☐ I totally disagree

Please rate the following aspects by circling the appropriate score:

21. Your **degree of satisfaction with the briefing process and your discussion** with the healthcare staff.

0 1 2 3 4 5 6 7 8 9 10
Completely dissatisfied — Fully satisfied

22. The **difficulty you experienced in making the decision** to participate in the trial.

0 1 2 3 4 5 6 7 8 9 10
Not difficult at all — Extremely difficult

23. The **level of anxiety** you experienced when making the decision to participate

0 1 2 3 4 5 6 7 8 9 10
No anxiety at all — Maximum anxiety

24. How much **risk** do you think the trial entails for you?

0 1 2 3 4 5 6 7 8 9 10
No risk at all — Maximum risk

25. How much **benefit** do you think you can get from the trial?

0 1 2 3 4 5 6 7 8 9 10
No benefit — Extremely beneficial

26. How much **benefit** do you think future patients may get from the trial?

0 1 2 3 4 5 6 7 8 9 10
No benefit — Extremely beneficial

27. How **important** do you think the trial is?

0 1 2 3 4 5 6 7 8 9 10
Not important at all — Extremely important

PART 2. LEVEL OF UNDERSTANDING (adapted from the QuIC questionnaire)

Section A: *Below you will find several statements about clinical trials (otherwise known as research studies). Thinking about your clinical trial, please read each statement carefully. Then tell us whether you agree with the statement, you disagree with the statement, or you are unsure about the statement by circling the appropriate response. Please respond to each statement as best as you can. We are interested in your opinions.*

A1. When I signed the consent form for my current therapy, I knew that I was agreeing to participate in a clinical trial.

☐ Disagree ☐ Unsure ☐ Agree

A2. The main reason clinical trials are done is to improve the treatment of future patients.

☐ Disagree ☐ Unsure ☐ Agree

A3. I have been informed how long my participation in this clinical trial is likely to last.

☐ Disagree ☐ Unsure ☐ Agree

A4. All the treatments and procedures in my clinical trial are standard for my disease.

☐ Disagree ☐ Unsure ☐ Agree

A5. In my clinical trial, one of the researchers' major purposes is to compare the effects (good and bad) of two or more different ways of treating patients with the same disease or condition, in order to see which is better.

☐ Disagree ☐ Unsure ☐ Agree

A6. In my clinical trial, one of the researchers' major purposes is to test the safety of a new drug or treatment.

☐ Disagree ☐ Unsure ☐ Agree

A7. In my clinical trial, one of the researchers` major purposes is to find the highest dose of a new drug or treatment that can be given without causing severe side effects.

☐ Disagree ☐ Unsure ☐ Agree

A8. In my clinical trial, one of the researchers` major purposes is to find out what effects (good and bad) a new treatment has on me.

☐ Disagree ☐ Unsure ☐ Agree

A9. The treatment being researched in my clinical trial has been proven to be the best treatment for my conditition.

☐ Disagree ☐ Unsure ☐ Agree

A10. In my clinical trial, each group of patients receives a higher dose of the treatment than the group before, until some patients have serious side effects.

☐ Disagree ☐ Unsure ☐ Agree

A11. After I agreed to participate in my clinical trial, my treatment was chosen randomly (by chance) from two or more possibilities.

☐ Disagree ☐ Unsure ☐ Agree

A12. Compared with standard treatments for disease, my clinical trial does not carry any additional risks or discomforts.

☐ Disagree ☐ Unsure ☐ Agree

A13. There may NOT be direct medical benefit to me from my participation in this clinical trial.

☐ Disagree ☐ Unsure ☐ Agree

A14. By participating in this clinical trial, I am helping the researchers learn information that may benefit future patients.

☐ Disagree ☐ Unsure ☐ Agree

A15. Because I am participating in a clinical trial, it is possible that the study sponsor, various government agencies, or others who are not directly involved in my care could review my medical records.

☐ Disagree ☐ Unsure ☐ Agree

A16. My doctor did not offer me any alternatives besides treatment in this clinical trial.

☐ Disagree ☐ Unsure ☐ Agree

A17. The consent form I signed describes who will pay for treatment if I am injured or become ill as a result of participation in this clinical trial.

☐ Disagree ☐ Unsure ☐ Agree

A18. The consent form I signed lists the name of the person (or persons) whom I should contact if I have any questions or concerns about the clinical trial.

☐ Disagree ☐ Unsure ☐ Agree

A19. If I had not wanted to participate in this clinical trial, I could have declined to sigh the consent form.

☐ Disagree ☐ Unsure ☐ Agree

A20. I will have to remain in the clinical trial even if I decide someday that I want to withdraw.

☐ Disagree ☐ Unsure ☐ Agree

A21. At any point during the trial, my doctor may decide to change my medication according to my individual needs.

☐ Disagree ☐ Unsure ☐ Agree

A22. There is a possibility that given the characteristics of the trial my doctor may NOT be aware of exactly what treatment I am being administered.

☐ Disagree ☐ Unsure ☐ Agree

A23. There is a possibility that given the characteristics of the trial I may NOT be aware of the treatment I am being administered.

☐ Disagree ☐ Unsure ☐ Agree

Section B: *How well did you understand the following aspects or items of the clinical trial when you were asked to sign the informed consent form? Please circle a number from 1 to 5 to state your level of understanding of each item: 1 indicates a complete lack of understanding, whereas 5 indicates full understanding.*

	I Didn't Understand This at All (1)				**I Understood it VERY WELL (5)**
B1. The fact that your treatment involves research	1	2	3	4	5
B2. What the researchers are trying to find out in the clinical trial	1	2	3	4	5
B3. How long will be in the clinical trial	1	2	3	4	5
B4. The treatments and procedures you will undergo	1	2	3	4	5
B5. Which of these treatments and procedures are experimental	1	2	3	4	5
B6. The possible risks and discomforts of participating in the clinical trial	1	2	3	4	5
B7. The possible benefits to you of participating in the clinical trial	1	2	3	4	5
B8. How your participation in this clinical trial may benefit future patients	1	2	3	4	5
B9. The alternatives to participation in the clinical trial	1	2	3	4	5
B10. The effect of the clinical trial on the confidentiality of your medical records	1	2	3	4	5
B11. Who will pay for treatment if you are injured or become ill because of participation in this clinical trial	1	2	3	4	5
B12. Whom you should contact if you have questions or concerns about the clinical trial	1	2	3	4	5
B13. The fact that participation in the clinical trial is voluntary	1	2	3	4	5
B14. Overall, how well did you understand your clinical trial when you signed the consent form?	1	2	3	4	5

REMARKS AND SUGGESTIONS

THANK YOU VERY MUCH FOR YOUR COOPERATION

INVESTIGATOR'S APPENDIX

Answer key for Part 2, section A (adapted from the QuIC questionnaire*)*

Question	Correct answer	Remarks
A1	Agree	
A2	Agree	
A3	Agree	
A4	Disagree	
A5	Agree[1]	[1]Only considered in phase III clinical trials
A6	Agree[2]	[2]Only considered in phase I clinical trials
A7	Agree[3]	[3]Only considered in phase I clinical trials
A8	Agree[4]	[4]Only considered in phase II clinical trials
A9	Disagree	
A10	Disagree[5] Agree[6]	[5]Correct response in trials without dose escalation [6]Correct response in dose escalation studies
A11	Disagree[7] Agree[8]	[7]Correct response in non-randomized clinical trials [8]Correct response in randomized clinical trials
A12	Disagree	
A13	Agree	
A14	Agree	
A15	Agree	
A16	Disagree	
A17	Agree	
A18	Agree	
A19	Agree	
A20	Disagree	
A21	Disagree	
A22	Disagree[9] Agree[10]	[9]Correct response in open-ended or single-blind trials [10]Correct response in double-blind clinical trials
A23	Disagree[11] Agree[12]	[11]Correct response in open-ended clinical trials [12]Correct response in single- or double-blind trials