Review Article

Informed consent process: A step further towards making it meaningful!

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Abstract

Informed consent process is the cornerstone of ethics in clinical research. Obtaining informed consent from patients participating in clinical research is an important legal and ethical imperative for clinical trial researchers. Although informed consent is an important process in clinical research, its effectiveness and validity are always a concern. Issues related to understanding, comprehension, competence, and voluntariness of clinical trial participants may adversely affect the informed consent process. Communication of highly technical, complex, and specialized clinical trial information to participants with limited literacy, diverse sociocultural background, diminished autonomy, and debilitating diseases is a difficult task for clinical researchers. It is therefore essential to investigate and adopt innovative communication strategies to enhance understanding of clinical trial information among participants. This review article visits the challenges that affect the informed consent process and explores various innovative strategies to enhance the consent process.

Keywords: Clinical trials, comprehension, informed consent, strategies, understanding, competence

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INTRODUCTION

The dogma of informed consent is the cornerstone of ethics in clinical research. Informed consent process provides essential trial information to potential participants and empowers them to make a rational and informed decision about participation. However, advancements in medical research have generated complex medical protocols resulting in elaborate and complicated information to be conveyed during the informed consent process. The complexity of consent documents also stems from the fact that sponsors as well as investigators view it as a legal and symbolic document of participant's agreement to participate in the research study. This results in an informed consent process that is legally right but often inadequate in terms of simplicity and ease of understanding for the study participants.[1,2]

Although the importance of informed consent process in clinical research is emphasized and proven, its effectiveness and validity are always a concern. Issues related to competence, comprehension, and voluntariness of research participants are evident in international literature.[3] Challenges related to informed consent may have larger dimensions in developing countries with participants having issues related to study compliance, inability to assess clinical trial risks, fear of study procedures, and concern of decreased access to medical care. This may have an adverse impact on clinical research in developed countries battling with limited resources, infrastructure, and illiteracy

Access this article online	
Quick Response Code:	Website: www.picronline.org
	DOI: 10.4103/picr.PICR_147_16

How to cite this article: Kadam RA. Informed consent process: A step further towards making it meaningful!. Perspect Clin Res 2017;8:107-12.

and may require strategic interventions from researchers, sponsors as well as regulatory authorities.[4-6] This article intends to review the challenges affecting the informed consent process and highlights the potential strategies for enhancing it.

A "meaningful" informed consent

An "Informed" consent emphasizes a process where the clinical research participant must receive and comprehend information appropriately to make an autonomous decision. An informed consent process can be termed as complete, valid, and meaningful if all four criteria of information disclosure, competence, comprehension, and voluntariness are effectively satisfied [Figure 1]. It is essential to consider here that competence or capacity of an individual to make decision depends on his/her ability to understand relevant information, to appreciate the nature of situation along with its consequence, to reason the given information, and the ability to communicate choice.[7]

CHALLENGES IN THE INFORMED CONSENT PROCESS

As already stated, a meaningful and valid informed consent emphasizes on information disclosure, competence and comprehension, it is therefore essential to investigate the challenges affecting the validity of an informed consent process [Table 1].

Complex information

Informed consent is used as an information highway in clinical research to explain study procedures, risks, benefits and participant rights. The process thus extends beyond mere signing of consent form and encompasses a dynamic and continuing exchange of information between the research team and the participant.[8] An attempt to achieve regulatory compliance usually sees the consent document laden with complex scientific terminologies and technical jargon.[9] Readability is also an important factor that determines the effectiveness of informed consent document. Although recommendations have been put forth that the language of the informed consent form should be simplified to the 8th grade reading level, most of informed consent documents are written in significantly higher levels of readability.[10]

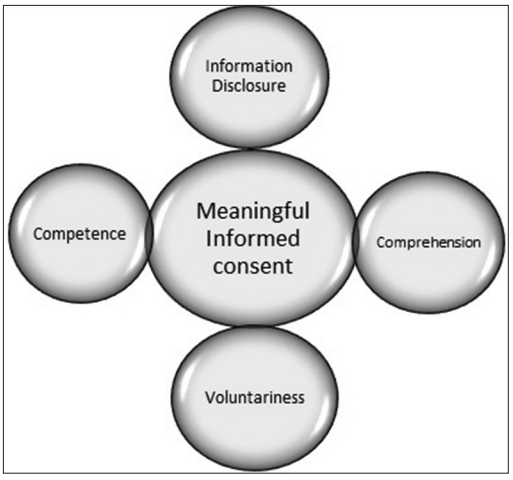

Figure 1: Components of a valid and meaningful informed consent

Poor understanding and comprehension of consent forms

Trial participant must be able to comprehend risks, benefits, and significance of participating in research to make an informed decision. In this process, it is presumed but not empirically documented that the prospective subject has grasped and digested relevant information to make a rational decision.[11] Studies conducted on informed consent process in the western world suggest that participants may not understand the study they are enrolled, neither their rights as participants despite having signed a consent form. Misunderstandings might be more frequent in less developed countries, where research participants are often poor, illiterate, unfamiliar with the conduct of medical research, and have different views on disease. Unfortunately, there are few practical guidelines on how best to inform research volunteers in less developed countries to ensure their understanding of the consent form.[12]

Patient competence

Another important aspect in ensuring the effectiveness of informed consent is the patient's capacity or competence to understand trial information. Factors such as age, disease severity, cognitive disability, especially in elderly patients, and those with mental disorders may affect a patient's decisional capacity. Patient's anxiety which could be due to the health condition or fear of a new procedure can affect comprehension ability. Poor patient understanding can be due to poor communication techniques by the investigator, due to lack of time on the part of research professionals, patient's anxiety, denial, and lack of reading comprehension.

Table 1: Challenges during the informed consent process

Research team
Poor communication technique
Lack of time for the consent process
Inability to detect lack of patient comprehension
Legal outlook toward consent process
Patients
Anxiety and fear of new procedures
Health status (terminal, debilitating diseases)
Cognitive impairment (neurological disorders, elderly)
Denial of disease state
Informed consent document
Complex language
Medical terminologies
Legal nature
Lengthy consent documents

Clinical trials in the area of terminal diseases where the difference between treatment and research is indistinct also present a conflicting scenario. Here, the investigator needs to explain the difference between "therapy" and "research" during the consent which may be difficult due to compromised patient competence.[13,14]

INFORMED CONSENT IN INDIA

Clinical research in India has flourished in the past few years with Indian regulatory authorities, investigators, and Ethics Committees striving toward conduct of quality, and ethical clinical trials with stringent regulations and updated guidelines. However, issues such as illiteracy, poverty, and prevailing socioeconomic conditions impose serious ethical questions in some areas of clinical trials with informed consent being the most crucial one.

Illiteracy or marginal literacy could be an important factor in patient comprehension and can adversely affect patient's decisional capacity. This was evident in an Indian study conducted by Kamath *et al*. in the second year medical students assessing their willingness to participate in clinical trials and understanding of the informed consent information. Study findings revealed that though medically qualified, students were unable to recall the study drug name and adverse effects mentioned in the consent form.[15] Sociocultural factors, diverse socioeconomic, and educational backgrounds also contribute to informed consent issues in Indian patients. A study by DeCosta *et al*. conducted in rural parts of north India reported that majority of study participants relied on discussion with other members of community for decisions to participate in clinical trials. This was also true for women participants who believed that they would be unable to decide for themselves. The study also reported a paternalistic relationship between doctor–patient, with patients having implicit trust in the medical system resulting in very limited participation in medical treatment decisions.[16]

Another study conducted by Bhansali *et al*. to evaluate the ability of clinical research participants in India to comprehend informed consent form reported that participants were able to comprehend more than 50% of informed consent content explained to them. The study highlighted that certain aspects of clinical trials such as blinding, randomization, and need for placebo were difficult to understand despite the language of the informed consent document kept simple. Another qualitative study conducted in south India using in-depth interviews conducted among patients and doctors working in a private hospital revealed that understanding of informed consent among study participants was moderate but inadequate for most part of the consent document. It also highlighted that poor patient understanding about the consent purpose, paternalistic attitude toward doctors, and fear of asking questions were deterrents to patient participation.[17,18]

The above studies investigating the informed consent process in Indian patients have thus highlighted the issues of diminished autonomy, influence of reference groups, paternalistic attitude toward doctors, and implicit trust in medical community as major challenges in consent process. These studies also put forth that adequate efforts taken in conducting informed consent may not necessarily translate into effective patient understanding of the consent document. All studies have recommended the need for participatory relationship between doctors and patients. It was suggested that an ideal environment for informed consent process should empower patients to freely air their concerns and doctors should recognize patient views. Till date, there have been limited studies investigating alternative consent procedures and innovative technologies to enhance and improve patient's understanding and comprehension of the consent process with very few studies conducted on patient population in developing world. A comparative study conducted by Davis *et al*. of standard versus simplified forms reported that simplifying informed consent material alone makes the forms easier and appealing to read but may not necessarily improve comprehension.[19] Studies have also shown that use of computers and multimedia in the consent process may help in improving patient's understanding and comprehension.[20] Hence, clinical research in developing countries needs to focus on enhancing informed consent guidelines keeping in perspective the diverse sociocultural environment of the country and implementing innovative strategies for conduct of informed consent process.

POTENTIAL STRATEGIES TO ENHANCE INFORMED CONSENT PROCESS IN INDIA

A meaningful and valid inform consent requires a patient to be given sufficient and understandable knowledge to make a valid decision. Communication of highly technical and specialized information to individuals with limited literacy, diverse sociocultural background, diminished autonomy, and debilitating diseases may be a difficult task. It is therefore essential to investigate and adopt innovative communication strategies to enhance understanding among study participants. Effective communication enables participants to receive clear information relevant to their specific learning needs and encourage informed decision making.[7,21] Following potential strategies [Table 2] have been recommended in for enhancing the consent procedure.

Simplification of consent documents

Consent forms must be brief, direct, and should aid understanding in trial participants. Use of simple language (eight standard reading level) for English language consent document as well as translation in local languages which is straight forward and easy to understand is recommended. It is documented that information written in plain language assists in decision making about medical treatments, increases positive feelings, and leads to perceived better control of information implementation.[22] Clinical trials have observed that simplified information appeals to patients and is associated with decreased anxiety and increased satisfaction with the consent document.[23] A strategic meeting convened by the Association of American Medical Colleges put forth strategies [Table 3] for facilitating greater understanding of the informed consent document by improving readability through the use of short, simple words, and keeping sentence length below 12 words and paragraph length below seven lines. It was recommended that concept of therapeutic misconception must be clearly explained in the consent document. It was also put forth that understanding and recall in trial participants may be improved if care is taken in reading the consent form, sufficient time is allocated for reading, length of consent form is reduced, and topics such as randomization and placebos are explained using simple language.[24]

Assessment of patient comprehension

Employing readability formulas such as Flesch–Kincaid scale may not give accurate reading level of a consent document.[25] Potential study participants may have diverse learning abilities and educational backgrounds. Hence, it is essential to assess participant's informed consent comprehension before signing the consent. Techniques such as "Teach back Method" wherein patients are asked to say in their own words what has been described can be employed. Various questionnaires using questions to test understanding such as "Yes/No," "disagree/agree/unsure," "short answer," "fill-in-the-blanks," and or "multiple choice" can be used. Tools to test comprehension such as Deaconess Informed Consent Comprehension Test or Brief Consent Evaluation Protocol and Quality of informed consent form which have been used in western population can be employed.[26-28] It is essential to develop and test tools and techniques which address issues related to comprehension relevant to the country's population.

Printed brochures and information sheets

Printed brochures and information sheets providing supplemental information about the clinical trial may also aid in improved patient's understanding as suggested in a comparative study of two study brochures conducted by Michielutte *et al.*[29] The study reported improved comprehension and patient satisfaction with the brochure that used illustrations and narrative text in cervical cancer patients as compared to the brochure which had simple bullet type format with no illustrations. The authors suggested that a more appealing format may engage the participant to read the entire message, and use of illustrations and text style may help patients with poor literacy skills to decode the meanings in print materials. Another study by Kass *et al.* reported a higher understanding in patients who were administered a bulleted fact sheet and question/answer session as compared to those who were administered the standard consent.[30] Printed brochures with pictorial depictions of a clinical trial translated in local languages (available from https://www.centerwatch.com/pdfs/informed-consent-brochure) may be helpful to Indian patients who are illiterate or have marginal literacy.[31]

Table 2: Potential strategies to enhance informed consent process

Simplification of informed consent documents
Assessment of patient comprehension
Use of printed brochure, information sheets
Use of multimedia and audio-video presentations
Extended discussions with patients
Use of decisional aids to help patients in decision making

Table 3: Strategies recommended by Association of American Medical Colleges for improving readability of informed consent documents

Simplify language using short, familiar, concrete, and simple words
Use adequate spacing and white space to make content inviting to read
Avoid crowding of words and letters
Use headings/subtitles. These reduce content density and serve as road signs
Use list rather than paragraphs when possible
Avoid medical terminology whenever possible. Explain medical terms (Edema-swelling, postoperative-after surgery, intradermal - under the skin, subcutaneous - under the skin)
Keep sentence length below 12 words
Keep paragraph length below 7 lines
Use clean, easy to read print type (e.g., fonts such as Times New Roman, Bookman old style)
Ensure each paragraph only conveys one idea. Use lists instead of paragraphs
Use active voice rather than passive. Write the way you talk
Use personal pronouns (you, we)
Avoid complex/unfamiliar words
Spell out abbreviated terms the first time you use them (e.g., Food and Drug Administration)
Focus on priority, "need to know" information. Omit nonessential information
Avoid research terms (instead of "randomize" use "lottery/tossing of coin")
Use acronyms, symbols ">," use commonly known measurements such as "teaspoon"
Consider using simple illustrations and diagrams

Audio-visual presentations

Audio-visual tools have been documented to be useful in conveying informed consent information. Audio-visual

tools enable immediate verbal reinforcement of written information, which aids in effective comprehension and recall. In a study conducted by Diabetes Control and Complications Trial (DCCT), audio-visual and written materials were used to inform prospective participants about the trial. The audio-visual tools involved a 25 min, trial specific video about the study design, treatment group procedures, risks, benefits, and screening procedures. This was supplemented by the 6th grade level detailed handbook and a 12-page dictionary of procedural terms and tests. Results of the multicomponent audio-visual educational program by DCCT revealed that participants had good trial knowledge and follow-up score (91%) attributed to repetition of content using the multiple communication modalities.[32] A study conducted by Wirshing *et al.* where a video intervention was used to enhance the informed consent process in psychiatric patients also reported larger gain in knowledge about informed consent.[33]

Another effective study conducted by Jimison *et al.* investigated the utility of multimedia tool to enhance the informed consent process. The interactive multimedia tool was designed based on inputs given by focus groups comprising of researchers, Ethics Committee members, and patients with serious diseases. The tool comprised trial specific and general knowledge audio-visual interactive modules. A videotaped presentation of researcher's consent discussion was also included. Study results reported participants had improved understanding of the video with better control over the rate and timing of information communicated during the informed consent process.[13] Another study conducted by Blake *et al.* have reported the use of mobile devices and internet for multimedia informed consent delivery. The intent of employing multimedia in the consent process was to translate complex study information into an understandable and visually appealing video format that is suitable for low-health-literacy participants and their family and may be very effective for illiterate or marginally literate potential trial participants.[34] In addition, an effective use of audio-visual tools and multimedia may help to save physician's time during the consent process and promote better understanding of complex trial information. The multiple modality approach of combining audio-visual presentations along with printed materials will enable trial participants to manage information overload through repetition and reinforcement and cater to diverse needs and learning abilities of trial participants.

Extended informed consent discussions

Another strategic approach toward enhancing informed consent process is to encourage extended discussions between the investigator's team and trial participants for better understanding and retention of trial information by study participant. These extended discussions can be conducted by investigators, nurses, clinical research coordinators, or medical social workers working with the study team after the actual consent process. Research teams can make use of flow charts, powerpoint presentations, models, and instructional videos to explain the concepts of research to study participant.

A study conducted on cancer patients who received subsequent telephonic discussion post standard informed consent process reported having increased understanding of several features of trial participation. It is recommended that discussions should focus on communicating trial information in a simple and clear manner with matters such as procedures, trial risks-benefits, costs, time implications, and voluntariness discussed with the trial participant. Support from family members and friends who can help the participant process trial information effectively can also be obtained. Overall sufficient time and an adequate opportunity of discussion must be provided to the trial participant to come to an informed decision.[35]

CONCLUSION

Informed consent must be viewed as a continuous dynamic process rather than an isolated event during the clinical study. Knowledge assimilated by the trial participant has a large impact on performance, compliance, and retention of the participant in a clinical study. It is important that informed consent process be viewed as a unique opportunity to build a communication channel with trial participants. Clinical trial researchers may face various challenges during consent process such as communication of complex trial-related aspects to trial participants who may have diverse needs of understanding and comprehension. The informed consent activity may be even more challenging for developing countries like India where illiteracy and diverse nature of local languages. It is therefore essential for all stakeholders in clinical research to have collaborative efforts and employ innovative strategies to promote and help researchers communicate information in an understandable manner to trial participants.[36] Conducting a valid, meaningful, and complete informed consent process with emphasis on patient understanding and comprehension will be an important step toward inculcating "Quality" in clinical research conducted in our country.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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