

ARTICLE

Assessing decisional capacity for research participation in psychiatric patients and their relatives

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Abstract

A cross-sectional study among adult inpatients with non-organic psychiatric disorders, and among their key relatives, assessed their comprehension and recall of key information in consent forms. It also assessed their capacity to consent to participate in two hypothetical randomised controlled trials (RCTs) with different potential risks and burdens, using structured questionnaires and recorded interviews. Of the 24 participants (12 patient–key relative dyads), seven patients (58%) and three key relatives (25%) were clinically judged to lack the capacity to consent. Of the remaining 14 participants, less than half the patients (2/5; 40%) or relatives (3/9; 33%) accurately recalled 50% of the key information on both trials. Among the eight participants (3 patients, 5 relatives) independently assessed on the MacArthur Competence Assessment Tool for Clinical Research, the proportions judged competent for each trial varied with the criteria for defining competence. No one fulfilled the stringent competence criteria for both trials. Routine assessments of the capacity of psychiatric research participants, and of relatives providing proxy consent, appear to be warranted. However, neither suboptimal understanding of consent forms, nor incompetence determined by the use of formal assessment tools, necessarily denote an incapacity to consent to research if detailed clinical assessments indicate otherwise. Research into incorporating participants' health literacy and clinical status in formal assessments may help determine the optimal standards for defining competence.

Introduction

Ethical and regulatory requisites for informed consent to participate in randomised clinical trials (RCTs) obliges

researchers to provide, and research participants to understand, information on the scientific aims and methods of the study; the potential benefits, risks and discomforts; sources of funding; conflicts of interest; institutional affiliations and contact details of the researchers; post-study provisions; voluntary nature of participation; options of withdrawing from the study; and the results of the study (1). Information on aspects of care that are specifically research-related (1,2), provisions for confidentiality, remuneration for participation and compensation for study-related injury are also requisites (2,3). Unsurprisingly, this often results in long and complex consent forms. Key concepts (such as the aims of the study, the concept of equipoise, randomisation, chances of being allocated a placebo, risks and benefits, and the right to withdraw) are often poorly understood (4,5), even though participants' understanding can be improved by simplified and enhanced consent forms, and extended discussions (6).

The capacity to consent is integral to its validity. The assessment of competence (the capacity to consent) includes an evaluation of the person's ability to *understand* relevant information; *appreciate* the nature of the situation and the consequences; *manipulate* information rationally; and communicate choices regarding his/her participation in the research (7). Researchers are expected to evaluate these elements as part of consent procedures, but they usually become evident informally, and doubts are often raised about the validity of consent obtained from psychiatric patients and other vulnerable populations in the absence of formal competence assessments (8–10). For those judged to lack capacity to provide valid consent in India and in many other parts of the world, a responsible relative or a legally authorised person may provide proxy consent (1,2). Family members are often critical in decisions pertaining to consent (11–13). However, formal assessments of the understanding of information by the proxy decision-makers and their capacity to provide valid consent are rarely undertaken or documented.

In an exploratory study using quantitative and qualitative methods, we assessed the perspectives of inpatients with non-organic psychiatric disorders, and of their key relatives, to participation in RCTs. We also assessed their willingness to participate in two hypothetical RCTs that differed in their methods, and explored their reasons for or against participation. The results of these enquiries are reported elsewhere (14). In this report, we present the results of our evaluations of:

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1. The comprehension of inpatients with non-organic psychiatric disorders and of their key relatives of the information provided on the two hypothetical RCTs.
2. Their capacity to consent, based on clinical judgments during consent procedures, compared to that of a subset of consenting participants assessed using independent formal competence assessment, ie the MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR) (15).

Methods

Study setting, participants and study design

This study was conducted in the adult inpatient units of the department of psychiatry of a private, faith-based, not-for-profit, teaching, general and multi-specialty hospital in south India. Those who were eligible to participate were adults who spoke Tamil or English and had been admitted for at least one week on a voluntary or involuntary basis, according to the provisions of the Mental Health Act (16); and with a clinical diagnosis of a mental disorder, as described in the World Health Organisation's International Classification of Disorders (ICD-10), excluding organic psychiatric disorders, personality disorders and adjustment disorders (17). The disorder was required to be of at least moderate severity (scoring 4 or >) on the Clinical Global Impressions-Severity (CGI-S) scale (18). The patient should not have been in need of close supervision or restraints, or been judged to be at risk of self-harm or of harming others. The adult's treating clinician and key relatives should have had no objection to the patient's participation. One key relative of each eligible consenting patient, who spoke Tamil or English and did not have a current mental disorder, was also invited to participate.

We used the prospective preference assessment (PPA) method (19), which involves presenting hypothetical trial designs and using quantitative and qualitative measures to understand the preferences of potential participants, to evaluate and enhance the participants' understanding of the key concepts of trials, and to assess changes in their understanding following educational interventions (19–21).

Study instruments and procedures

Our earlier report provides the details of the information sheet and consent form for participation in the study, the sociodemographic and clinical data forms, the CGI-S scale, and the attitudes to the research questionnaire (14).

The instruments and procedures used in the study that are pertinent to this report were as follows:

1) To evaluate comprehension of the information provided during consent procedures

- a) *Information sheet for hypothetical RCT 1:* The information sheet invited participation in an eight-week RCT of a new hypothetical oral medicine developed overseas that, in previous uncontrolled studies, was reportedly effective in reducing stress-related symptoms among

people with psychiatric disorders. The RCT required the participants to be admitted for at least the first four weeks and undergo a wash-out period from their current medications before randomisation to the new drug or placebo. The information provided included the rationale for the wash-out period, and the randomised, blinded design that would allow neither the participant, nor the treating clinician to choose or know which medicine was allocated. It mentioned that the symptoms and adverse events would be assessed weekly, but no additional tests or investigations would be required. Trial medicines, sedatives and any other treatment needed for relief from symptoms or for managing adverse events (that were expected to be minor) would be provided to the participants free of cost. The inability to predict outcomes with either intervention was mentioned. Other standard elements required in consent forms for RCTs were also included and are detailed in our previous report (14).

- b) *Comprehension questionnaire for hypothetical RCT 1:* A questionnaire containing 10 statements, to be answered with "true/false/unsure/do not know", tested the patients' and key relatives' comprehension and recall of the information provided during the consent procedure. The 10 statements assessed their understanding of the key aspects of the trial. The answers were discussed with the participants on the completion of the questionnaire, and these discussions were audio recorded.
- c) *Assessing willingness to participate in RCT 1:* Open-ended questions were used to assess the patients' and key-relatives' willingness to participate in such a trial, and their perspectives on consenting or declining to participate. Our previous report details these results and the responses to supplementary probes evaluating the possible reasons for participation or non-participation (14).
- d) *Information sheet for hypothetical RCT 2:* This hypothetical RCT compared the same interventions as in the previous trial but differed in its methods, in that the participants were to continue with their current medication but be randomised to the new medicine or placebo for the eight-week duration of the trial. In addition, the patients were to undergo weekly blood tests for the first four weeks and at eight weeks (10 ml of blood each time, with unused blood discarded), and an EEG and ECG before and after the trial. The other aspects of the design were identical to that of the hypothetical RCT 1.
- e) *Comprehension questionnaire for hypothetical RCT 2:* A questionnaire consisting of five statements tested comprehension and the recall of key information provided for this RCT. The answers were discussed with the participants and the discussions audio recorded.

f) *Assessing willingness to participate in RCT 2*: The patients' willingness to participate in this trial and their reasons for consenting or declining to participate were explored as in the previous hypothetical RCT. The details are reported elsewhere (14).

2) **To assess competence (capacity) to provide valid consent to participate**

a) *Clinical assessment of capacity*: The primary assessment of the capacity of the patients and key relatives to consent to participate in the hypothetical trials was made by the first author during the clinical interviews. This included evaluations of the patients' mental state, degree of cooperation, ability to comprehend the information provided, and an overall assessment during the course of the interviews of how decisionally impaired the participants were. Participants deemed to lack capacity were re-assessed on two separate occasions, at weekly intervals.

b) *MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR)*: The second author, a consultant psychiatrist with prior experience in using the MacCAT-CR, independently interviewed a subset of consenting patients and key relatives. The MacCAT-CR is currently the most widely used scale for the formal assessment of competence to provide valid informed consent for participation in research (22). It assesses competence on four subscales: (i) *understanding information*, (ii) *appreciating the significance of the information*, (iii) *manipulating the information rationally*, and (iv) *expressing a choice*. Each question is scored on a scale of 0–2, and the scores on each component scale vary in range: *understanding* - 0–26; *reasoning* - 0–8; *appreciation* - 0–6; *expressing a choice* - 0–2. Higher scores indicate greater understanding, reasoning, appreciation of the significance of information, and expression of choice. The MacCAT-CR format can be individualised for research projects, and this tool was adapted to assess the information provided in the information sheets for the two hypothetical trials using open-ended questions, supplemented by additional probe questions. The MacCAT-CR has no established cut-score or algorithm for categorical determinations of capacity or incapacity; it is recommended that the scores be supplemented with other important information, such as mental status and the decision-making context (15). The scores on the MacCAT-CR have also not been validated in the Indian context.

We pilot tested the information sheets and informed consent forms. They were translated into Tamil and back-translated into English. We assessed the comprehension questionnaires for their cultural and linguistic appropriateness and pilot tested them. The information sheets used for consent procedures for the two hypothetical trials are provided in our previous report (14).

All written information was read out to the participants if they so wished, or if the first author deemed it necessary on the basis of the participants' literacy levels. Audio recordings of the relevant aspects of the interviews were transcribed verbatim (and translated into English, if necessary) by independent transcriptionists. All authors, or at least the first and third authors, independently reviewed the transcripts and the relevant sections of the audio recordings.

Ethical issues

The Institutional Review Board (Research and Ethics Committees) of the Christian Medical College, Vellore approved the study protocol, information sheets and consent forms. All participants provided written consent.

Data analysis

1. *Assessing comprehension*: We estimated the proportions of participants displaying adequate comprehension of the information pertaining to the two trials, using the audio recorded transcripts and field notes of the interviews assessing comprehension. We defined adequate comprehension in two ways: (i) answering 50% or > of the questions assessing comprehension and recall correctly, (ii) answering 75% or > of these questions correctly. We also assessed the proportions expressing a willingness to participate in these trials.

2. *Assessing competence (capacity)*: In the subset of participants assessed with the MacCAT-CR, we estimated the proportions of patients and relatives clinically assessed as competent to consent. Since competence assessments vary on the basis of the criteria used (23), standards of increasing stringency were employed to evaluate the competence of participants for whom the MacCAT-CR was used. We used the following standards to define competence: *least stringent*: (1a) scoring 50% or >, and (1b) scoring 75% or more of the maximum scores possible on the domains "expressing a choice" and "understanding"; *intermediate*: (2a) scoring 50% or >, and (2b) 75% or > of the maximum possible on the domains "expressing a choice", "understanding" and "appreciation"; *stringent*: (3a) scoring 50% or >, and *most stringent*: (3b) scoring 75% or > of the maximum possible on all four domains.

Results

Of the 40 eligible participants (20 patients, 20 key relatives) identified during the screening of consecutive admissions (July to October 2012), 24 (12 patient–key relative dyads) consented to participate in this study. The age of the 12 patients ranged from 18 to 38 years. Seven were female. Table 1 provides details of their education, diagnosis, ratings of clinical severity, and their age and relationship with their key relatives.

Of the 24, only 18 (8 patients; 10 relatives) could be interviewed on participating in the hypothetical RCT 1, and 17 (7 patients; 10 relatives) were assessed for their comprehension of the information. While 16 (7 patients; 9 relatives) were interviewed for the hypothetical RCT 2, only 15 (7 patients, 8 relatives) were

assessed for their comprehension of the information (Table 1). Of the remaining participants, two had exacerbations of clinical symptoms, which precluded their participation, while the remainder either declined further participation or could not be adequately assessed before discharge due to practical difficulties in scheduling interviews.

Comprehension and recall of information provided in the hypothetical RCTs

Patients

Individual patients' accuracy in recalling information related to the two hypothetical RCTs is detailed in Table 1.

Only 4/7 patients (57%) accurately answered 50% or more of the questions assessing comprehension of the information provided in the hypothetical RCT1 (Table 1). Overall, only 2/7 (40%) accurately recalled at least 50% of the key information on both RCTs (patients 2 and 12; Table 1). Only one (14%) managed 75% or > correct responses for RCT 1, and two (28%) for RCT 2. The three patients with suboptimal performance (<50% correct answers) in RCT 1 were being treated for schizophrenia of moderate severity on the CGI-S scale (patients 1, 5 and 8; Table 1). Two were graduates, while the third had studied up to class 12. One graduate's comprehension and recall of information improved from RCT 1 to RCT 2, while the other graduate's scores for comprehension and recall worsened.

Key relatives

Table 1 also shows the accuracy of the recall of information of individual key relatives for the two hypothetical RCTs. Six of the 10 key relatives (60%) correctly answered 50% or more of the 10 questions assessing the information on RCT 1. Only three of

them (30%) answered 75% or more of the questions correctly. Only 3/8 relatives (38%) assessed for the recall of information on RCT 2 answered 50% or more of the questions accurately; and only one (13%) scored above 75%. Overall, only 3/9 (33%) key relatives accurately recalled at least 50% of the information on both trials (Table 1).

Aspects of information recalled

Although on being asked, most participants replied that they had understood the contents of the information sheets, the discussions revealed otherwise.

Overall, the patients' performance was the poorest in the matter of comprehending the possible risks involved in RCT 1 and some details of the study interventions (Table 2). A poor understanding of the risks was also a problem with most relatives as far as RCT 1 was concerned. More patients than relatives understood that allocation to study drugs in RCT 1 would be randomised. Overall, the patients' understanding of the information given in RCT 2 was better than that of the relatives in many of the domains tested (Table 2).

Assessment of the capacity to consent

Clinical assessment of capacity to consent

Of the 24 consenting participants (12 patients, 12 key relatives), seven patients (58%) and three relatives (25%) were clinically considered to lack the capacity to provide consent (42% overall). Patient 10 was judged to lack this capacity immediately after recruitment, while in the other cases, the lack of capacity became clinically apparent during the discussions (patients 1,4,5 and 8) or due to a clear deterioration in their mental state (patients 6 and 9). Among the key relatives, three (of patients 4, 8 and 9) had difficulty understanding the

Table 1

Demographic and clinical details and accuracy of recall of information from the hypothetical trials in patients and key relatives

N	Age (years)	Sex	Education	Room type*	ICD-10**	CGI-S	Correct responses (%)		Age (years)	Relationship	Correct responses (%)	
							RCT 1	RCT 2			RCT 1	RCT 2
Patients						Key relatives						
1	38#	F	Graduate	2	1	Moderate	30	60	62	Mother	80	60
2	27	M	Graduate	2	1	Severe	50	60	56	Father	100	80
3	18	M	12th	2	1	Moderate	90	20	68	Grandfather	20	NA
4	27#	F	8th	3	5	Severe	NA	NA	55#	Mother	0	NA
5	26#	F	12th	1	1	Severe	10	80	36	Husband	90	40
6	23#	M	Graduate	1	3	Severe	50	40	54	Mother	50	40
7	21	M	Diploma	1	2	Moderate	NA	NA	45	Mother	NA	NA
8	23#	F	Graduate	3	1	Moderate	30	20	47#	Mother	20	20
9	18#	F	8th	3	4	Severe	NA	NA	41#	Mother	70	60
10	31#	M	12th	2	1	Severe	NA	NA	58	Father	0	40
11	26	F	Graduate	2	1	Moderate	NA	NA	55	Father	NA	NA
12	18	F	Graduate	1	6	Severe	70	100	40	Mother	50	40

N = Patient number; RCT = Randomised controlled trial; CGI-S = Clinical Global Impression - Severity; M = Male, F = Female; NA = Not assessed; * Room type: 1 = Private, 2 = Semi-private, 3 = General; **ICD 10 = International Classification of Diseases: 1 = Schizophrenia; 2 = Delusional disorder; 3 = Mania without psychotic symptoms; 4 = Mania with psychotic symptoms; 5 = Psychotic depression; 6 = Dissociative disorder; # Clinically judged as lacking capacity

Table 2

Patients' and key relatives' comprehension and recall of information on the domains assessed in the two hypothetical trials

Domain	Questions	Correct responses*	
		Patients N (%)	Relatives N (%)
Hypothetical RCT 1			
Higher risk, fewer burdens:			
<i>Usual drugs withdrawn; new drug versus placebo for eight weeks; in-patient for four weeks; weekly clinical assessments; no other investigations; free admission; free treatment (drugs); travel expenses reimbursed.</i>		N = 7	N = 10
Equipoise	Q1. The new drug has been shown to be better than the usual drugs in previous research	3 (43)	4 (40)
	Q 6. Both medicines (new drug or placebo) are likely to make you feel better	3 (43)	5 (50)
	Q 10. The placebo will make you feel worse than the new drug	3 (43)	5 (50)
Randomisation	Q 2. Doctors will decide whether the new drug or placebo is given	4 (57)	3 (30)
Blinding	Q 4. You can find out from the hospital staff whether you have been given the drug or placebo	4 (57)	6 (60)
Appreciation of risks	Q 7. The new medicine is not likely to make you feel worse in any way	2 (29)	3 (30)
Study details	Q 3. Study medicines and usual medicines will be given	2 (29)	5 (50)
	Q 5. Study medicines will be given for four weeks	2 (29)	6 (60)
	Q 8. Participants will get free food and Rs 200 per day	5 (71)	7 (70)
	Q 9. Blood tests will be done every week while in hospital	5 (71)	4 (40)
*Correct answer: False for Q 1 to Q 10			
Hypothetical RCT 2			
Lower risk, more burdens:			
<i>Usual drugs continued; new drug versus placebo for eight weeks; in-patient for four weeks; weekly clinical assessments; ECG and EEG at baseline and at eight weeks; weekly blood tests for four weeks and at eight weeks; free admission; free treatment (drugs); travel expenses reimbursed.</i>		N = 7	N = 8
Equipoise	Q 1. In previous research, the new drug was safe when combined with the usual treatment for psychiatric disorders	5 (71)	3 (38)
Appreciation of risks	Q 3. The new medicine is not likely to make you feel worse in any way	5 (75)	4 (50)
Study details	Q 2. Study medicines and usual medicines will be given	4 (57)	6 (75)
	Q 4. Usual medicines will be given free for the period of the study	3 (43)	6 (75)
	Q 5. An EEG and an ECG will be done weekly while in hospital.	2 (29)	2 (25)
*Correct answer: False for Q 1, Q3, Q5; true for Q 2, Q 4			

N = Number; RCT = Randomised controlled trial; Q = Question

information on the trial and were clinically assessed as lacking the capacity to consent. Overall, three patient–key relative dyads (4, 8 and 9) were deemed to clinically lack the capacity to provide consent / proxy consent.

Competence assessments using the MacCAT-CR

The MacCAT-CR was administered independently, and within 48 hours of the other assessments carried out as part of this study (14). They were conducted over many sessions. Due to practical difficulties in scheduling these interviews, formal competence assessments using the MacCAT-CR were carried out for only eight participants (three patients – 1, 2 and 3; and five relatives – 1, 2, 3, 5 and 10) for hypothetical RCT 1. In the case of hypothetical RCT 2, they were conducted for seven participants (three patients – 1, 2 and 3; and four relatives – 1, 2, 5 and 10).

The patients' and relatives' scores on the four domains of the MacCAT-CR for both RCTs are provided in Table 3a. Table 3b lists those who were judged to be competent on the basis of different standards used to define competence. One of the three patients assessed (patient 1: 38 years old, female, graduate; diagnosis – schizophrenia; CGI-S score

moderate) was incompetent to consent even according to the least stringent standard (1a, scoring 50% or > of the maximum possible on the domains "expressing a choice" and "understanding") for both hypothetical trials (Table 3b). Of the five relatives formally assessed, one (the grandfather of patient 3) did not meet the least stringent competence standard for RCT 1 (and could not be assessed for RCT 2); while another (the father of patient 10) was competent to consent to RCT 1, but not RCT 2, by this standard (Table 3b). As the standards became more stringent, more patients and relatives were deemed not competent to consent. Reasoning was the domain that most patients and relatives had difficulty with, and their consequential and comparative reasoning skills were found to be inadequate. Only one patient (patient 2: 27 years old, male, graduate; diagnosis – schizophrenia; CGI-S score severe) and one relative (the husband of patient 5) were assessed as competent using the most stringent of the standards (3b, scoring 75% or > on all four domains) for RCT 1. A different patient (patient 3: 18 years old, male, 12th standard student; diagnosis – schizophrenia; CGI score moderate) and a relative (father of patient 2) met this standard of competence for RCT 2 (Table 3b).

Table 3

MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR) domain scores and proportions of patients and key relatives

a. Scores on the MacCAT-CR domains (% of total score for each domain)

SN	Patients				Key relatives			
	Understanding (0 to 26)	Appreciation (0 to 6)	Reasoning (0 to 8)	Choice (0 to 2)	Understanding (0 to 26)	Appreciation (0 to 6)	Reasoning (0 to 8)	Choice (0 to 2)
Hypothetical RCT 1								
1	4 (15)	0 (0)	2 (25)	2 (100)	17 (65)	4 (66)	4 (50)	2 (100)
2	24 (92)	6 (100)	7 (88)	2 (100)	21 (80)	5 (83)	3 (38)	2 (100)
3	25 (96)	5 (83)	2 (25)	2 (100)	5 (19)	2 (33)	2 (25)	2 (100)
5	NA	NA	NA	NA	23 (88)	6 (100)	6 (100)	2 (100)
10	NA	NA	NA	NA	20 (77)	3 (50)	2 (25)	2 (100)
Hypothetical RCT 2								
1	1 (4)	0 (0)	(0)	2 (100)	15 (57)	2 (33)	4 (50)	2 (100)
2	20 (77)	5 (83)	3 (38)	2 (100)	26 (100)	6 (100)	6 (75)	2 (100)
3	20 (77)	5 (83)	2 (75)	2 (100)	NA	NA	NA	NA
5	NA	NA	NA	NA	24 (92)	6 (100)	4 (50)	2 (100)
10	NA	NA	NA	NA	8 (30)	3 (15)	1 (30)	2 (100)

b. Competent to consent on the basis of different scoring standards

Domains*	Scoring standard	Patients		Relatives	
		RCT 1 P 1, 2, 3	RCT 2 P 1, 2, 3	RCT 1 R 1, 2, 3, 5, 10	RCT 2 R 1, 2, 5, 10
Understanding	1.a: 50% or >	2, 3	2, 3	1, 2, 5, 10	1, 2, 5
	1.b: 75% or >	2, 3	2, 3	2, 5, 10	2, 5
Understanding + appreciation	2.a: 50% or >	2, 3	2, 3	1, 2, 5, 10	2, 5
	2.b: 75% or >	2, 3	2, 3	2, 5	2, 5
Understanding + appreciation + reasoning	3.a: 50% or >	2	3	1, 5	2, 5
	3.b: 75% or >	2	3	5	2

SN = Patient number; RCT = Randomised controlled trial; P = Patient; R = Relative of patient; NA = Not assessed;

* All participants expressed a choice (3a), hence the scoring standards in 3b considered this domain as adequate for all participants.

Comparing clinical assessments for capacity and formal competence assessments

Of the three patients assessed formally with the MacCAT-CR, one (patient 1) was judged clinically to lack the capacity to consent, and also did not meet the least stringent criteria for competence during the formal assessment. The other two (patients 2 and 3) were considered clinically capable of providing valid consent and were deemed competent according to the intermediate criteria using the MacCAT-CR in the case of both RCTs. Both of them also fulfilled the most stringent criteria for competence for one of the two RCTs, though not for the same trial (Table 1 and Table 3b).

Of the five relatives who underwent formal competence assessments, one (the grandfather of patient 3) was deemed not competent using even the least stringent criteria (Table 1 and Table 3b). He had poor comprehension and recall scores for RCT 1, and declined to be interviewed on RCT 2 (Table 1). However, his capacity to provide proxy consent was clinically judged as adequate, on the basis of his responses during detailed clinical interviews (14). The other relatives (of patients 1, 2, 5 and 10) were deemed clinically capable of providing proxy consent, but only two fulfilled stringent criteria for competence for at least one of the RCTs (Table 3b).

Discussion

An important finding of this study was that the comprehension of the information provided during the informed consent process for the two hypothetical RCTs was suboptimal in the case of some consenting patients and their key relatives. In addition, seven patients and three relatives were clinically judged to lack the capacity to consent to participate in the hypothetical clinical trials. Most patients and relatives clinically assessed as having the capacity to provide consent were not deemed competent when using the more stringent criteria of the formal competence assessments. The results presented in this report need to be interpreted in the light of the other qualitative results of this study (14), which showed that though the majority of patients and relatives generally had positive attitudes to research and RCTs, they were discerning about participation in trials; 50% of them were unwilling to participate in the two hypothetical trials. When asked about their motivations for participating or not participating in the trials, the patients and relatives indicated that their decisions were made on the basis of individualised assessments of risks, burdens and pragmatic considerations versus the benefits of participation in the trials. However, the results presented in this report could cast doubts on the validity of the decisions on consent as presented in the previous report (14). This

merits more detailed discussion to help us in the overall interpretation of our study's results.

The relationship between comprehension and competence to consent

It is unclear whether the findings of suboptimal comprehension and inadequate competence (particularly in the reasoning domain) on the MacCAT-CR, for those assessed as clinically having the capacity to consent, fully captured the capacity to consent in all cases. Among the possible reasons for poor comprehension in an otherwise seemingly competent person were: (i) the process of providing information was suboptimal, as it was poorly conveyed in a complex information sheet, or involved a rushed consent process that gave the patient insufficient time to seek clarifications; (ii) the assessment of comprehension was inadequate or otherwise flawed, leading to incongruity in the assessments of competence; and (iii) clinical decisions on the capacity to consent were impressionistic and lacked the objectivity of formal competence assessments. On the other hand, it is also possible that (iv) the information provided was sufficient for the participants to make an informed decision, even though they may have appeared, in the opinion of the researcher, to show suboptimal comprehension; and/or that (v) clinical decisions on the capacity to consent captured aspects of competence that the scores on the formal competence tool did not fully incorporate.

Was the informed consent process suboptimal?

The information sheets were designed to be simple and were pilot tested. The English and Tamil versions were approved as adequate for the purposes of the study by the institutional research and ethics committees. The information sheet for the main study was six pages long and the two information sheets for the hypothetical RCTs were about four pages long. The average readability level of the English versions (assessed via the online calculator available at <https://readability-score.com/> by the Flesch-Kincaid Reading Ease scores: 54.5 for study participation; 53.9 for RCT 1; 58.2 for RCT 2; and the SMOG Index: 10.3 for study participation, 10.2 for RCT 1 and 9.3 for RCT 2) was around 12, which is roughly the reading level on the completion of high school. While a grade level of 8 would be more readable, the readability levels of the forms used in this study are representative of the reading levels in forms generally used for research (24). We are not aware of any formal and validated ways of assessing the reading level of the Tamil versions of the information sheets, and we depended on the opinions of the bilingual translators and the ethics reviewers to confirm equivalence in the readability of the two versions. However, most participants in this study preferred to have the information read out and explained to them. Sufficient time was allotted for the interviews, and the participants were given opportunities to seek clarifications till they claimed to be satisfied with the adequacy of the information imparted. Of the patients whose comprehension was assessed, two (patients 2 and 3) were educated up to the 12th standard or above and were assessed clinically as having the capacity to consent. Their comprehension scores were 50% or > for RCT 1, and one scored

even more than 75% for one of the RCTs. These two patients were also deemed competent using the more stringent criteria for the assessment of competence on the MacCAT-CR.

Were the assessments of comprehension adequate?

The assessment of comprehension undertaken by the first author tested immediate recall, using a "true/false/unsure/do not know" format for responses. This was supplemented by free enquiry to probe into the reasons for the choices. The formal assessment of competence using the MacCAT-CR tested delayed recall, and there was a delay of around 48 hours between formal assessments and the completion of the interviews. The formal assessment used open-ended questions rather than providing fixed choices. There was greater congruence between the competence assessments utilising the two approaches as far as the domain of understanding was concerned. In research involving patients actually participating in a clinical trial, the MacCAT-CR understanding subscale had the best ability to discriminate between those competent or incompetent to give informed consent (23,30). In the present study, as in the previous research (23,30), the additional domains assessed in the MacCAT-CR (particularly reasoning) resulted in incongruence between the two assessments.

Were clinical decisions on the capacity to consent solely impressionistic and did they lack the objectivity of formal competence assessments?

While the approach of the MacCAT-CR is inherently more structured, clinical judgments still need to be made while scoring responses in the various domains. The clinical assessments of the capacity to consent utilised information from multiple sources, which were derived from administering the study instruments and evaluating the participants' responses to them. This gave the clinical assessments a formal structure on which to base clinical judgments about capacity.

Was the information provided sufficient for participants to make valid and informed decisions?

One of the questions often raised regarding valid informed consent pertains to the extent of comprehension that would be deemed sufficient to make informed decisions. In previous research carried out in India and elsewhere, voluntary participants in clinical trials (25) and long-term observational studies (26) have expressed satisfaction with the informed consent process and the amount of information provided, but have displayed suboptimal understanding of the required elements of informed consent. There are also suggestions that people who value modern research tend to trust that their doctors (the research team and the institutions that conduct research, including the ethics review process) will consider their interests seriously; therefore, they listen selectively to the information provided on the non-essential (in their opinion) details of the study (27). As a result, these participants may appear to have a poor comprehension of some of the details of the study. This denotes therapeutic misconception; it does not necessarily mean that they are not competent to consent to research. In this context, one viewpoint is that requiring comprehension of all details of the information provided

“confuses an ethical aspiration with a minimum ethical standard” (28). The viewpoint posits that if the customary disclosures in a clinical trial satisfy the local regulations and otherwise conform to ethical requirements, such as a favourable risk–benefit ratio, an independent review and the possibility of direct benefit to the participants, voluntary participation by otherwise competent people who do not have a complete understanding would not be unethical or invalid (28). The two hypothetical trials in our study presented different risk–benefit ratios, which were identified correctly by many participants, as evidenced by the qualitative results regarding their motivations to participate in the trials (14). Moreover, 50% of the patients and key relatives interviewed declined to participate in either hypothetical RCT, even though they had a generally positive attitude towards the methods and goals of modern research (14). This suggests that in spite of their suboptimal understanding of other aspects of the trials, these participants’ decisions on consent indicated that they had sufficient competence to meet standards that are practical, rather than aspirational.

Did the clinical assessment of the capacity to consent utilise other important aspects that were not fully captured by the competence assessment tool?

Empirical research on validating cut-off scores on the MacCAT-CR to predict decisional incapacity among participants in psychiatric research has consistently demonstrated that the proportion with impairment depends on the domain assessed. The scores on understanding show the best correlation with the experts’ judgment on capacity, and those on reasoning show the least concordance (23, 30). The research also indicates that the sub-scales on the MacCAT-CR do not have a single cut-off reflecting a high sensitivity or specificity to discriminate between decisionally impaired and competent research participants (30). This implies that it might be unrealistic to expect any standardised instrument to possess the extreme precision and predictability that would enable one to make complex, value-laden judgments on a person’s decision-making capacity (30). In the clinical capacity assessments used in this study, we obtained rich information from multiple sources. These included interaction with the participants during the rapport-building sessions, discussion of their freely elicited responses regarding the hypothetical trials and their attitudes to the research questionnaire (14), an assessment of their understanding of both trials, reconciliation of their lack of understanding of some aspects of each trial with their adequate understanding of other aspects of each trial, and an assessment of their changing clinical status. The integration of this information facilitated the clinical assessments of capacity.

This suggests that comprehending information on consent is but one part of “health literacy”. It includes the “ability to understand health information well enough to know what to do”, as well as the “ability to actively engage with healthcare providers” (29). The participants judged to be clinically competent presented a gestalt of these two aspects of health literacy. Both aspects were utilised by the first author to make clinical assessments. This would not be reflected in

the judgements of competence that used mainly the scores on the MacCAT-CR domains of the degree of understanding, appreciation of consequences and reasoning abilities pertaining to the hypothetical trials to differentiate between those judged as competent/incompetent, since all participants were able to express a choice (i.e. they understood enough information to be able to know what to do). This conclusion is also in keeping with recommendations that while the MacCAT-CR offers a method to standardise the process of assessing competence, the scores on the MacCAT-CR should be supplemented with other important information when deciding competence (15).

Limitations

This study’s relatively small sample size is a major limitation. Not all of the 24 consenting study participants contributed to all assessments. In particular, the small number of relatives and even smaller number of patients who could be assessed on the MacCAT-CR limit the generalisability of the findings.

In addition, this study included only psychiatric patients with non-organic disorders and the sample did not include the elderly participants.

The fact that the MacCAT-CR scores have not been validated in the Indian context may also be considered a limitation of the study. However, even in countries where the MacCAT-CR has been validated, none of the subscale scores have a single cut-off score with a high sensitivity or specificity (23,30), and consequently, this tool’s ability to accurately predict decisionally impaired research participants is low, compared to experts’ judgements of capacity (30).

In spite of the limitations of this study (that can only be considered as exploratory), the findings provide insights into the requirements of valid informed consent, which are of heuristic value in aiding future research.

One of the implications of these findings is that any attempt to validate MacCAT-CR scores in India should compare judgements of competence with the MacCAT-CR with those of a panel of clinical experts (31). This could establish a range of scores on the domains of the MacCAT-CR that could be used in research protocols involving populations with differing prevalences of decisional incapacity, since the positive and negative predictive value of any cut-off will vary with prevalence (30). In addition, the range of scores to determine incapacity among participants who may have some decisional impairment may differ in research protocols with a higher risk (as in the hypothetical RCT 1 in this study). The threshold for defining competence may be set higher in such instances than in protocols with a lower risk but a higher burden due to additional investigations (as in RCT 2). These need to be determined in the Indian context.

Conclusions

In summary, the findings of this study indicate that there is a need to routinely assess psychiatric patients’ capacity to consent to participate in research, particularly interventional

research. In the case of those found to lack the capacity to consent, their key relatives should be assessed for their capacity to provide proxy consent.

The findings of this study also suggest that incomplete understanding of the information provided in information sheets and the consent process need not reflect incompetence if other facets of the clinical encounter indicate that the participant has adequate capacity to understand the information provided and make a choice. Hence, capacity assessments should not be restricted to assessing recall of information using structured questions or a checklist, but should incorporate clinical assessments and other sources of information as well. This approach would possibly be more appropriate for interventions that do not have an unfavourable risk-benefit ratio than for ones that do. In the latter case, it would be more important to ensure an adequate understanding and appreciation of the risks (29). Our findings warrant prospective research that utilises qualitative and quantitative methods to evaluate how incorporating the participants' health literacy and overall clinical assessments could supplement the assessment of competence. This would help to determine optimal standards for defining competence in formal assessment using tools such as the MacCAT-CR.

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