Participants With Schizophrenia Retain the Information Necessary for Informed Consent During Clinical Trials

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ABSTRACT

Objective: Cognitive impairment is a characteristic of schizophrenia. This impairment may affect the retention of information required for ongoing knowledgeable participation in clinical trials. This study monitored retention of study-related knowledge—including assessment of therapeutic misconception—in people with stable, *DSM-IV* schizophrenia during participation in placebo-controlled clinical trials of adjunctive agents. Stability was defined as being on an antipsychotic with no change in medication or dose over the previous 4 weeks.

Method: This longitudinal study assessed retention of clinical trial–related consent information. Individuals enrolling in 1 of 8 clinical trials were approached for participation. Participants came from research clinics and community mental health centers. At baseline, clinical trial consent forms were reviewed and study knowledge assessed. Participants were randomized to follow-up assessments at weeks 1, 4, and 8; weeks 4 and 8; or at week 8 only. Clinical trial consent forms were not rereviewed at any follow-up visit.

Results: Fifty-nine participants were enrolled; analysis included 52 participants with at least 1 follow-up visit. Study knowledge did not decrease meaningfully in any group. Therapeutic misconception was not observed in participants during the study. The group assessed most frequently demonstrated significant improvement over baseline ($t_{44} = 3.43$, $P = .001$). Retention of study knowledge was not related to symptoms but had a weak correlation with cognitive capacity ($R = 0.28$, $P = .07$). Performance did not differ between participants from research clinics and those from community mental health centers.

Conclusions: Clinically stable people with schizophrenia enrolling in a placebo-controlled adjunctive medication study, once determined to have capacity to consent to a clinical trial, retained appropriate study knowledge for at least 8 weeks. In the absence of a specific reason to suspect a loss of decisional capacity, there appears to be no need to routinely reevaluate participants during this type of clinical trial.

J Clin Psychiatry 2013;74(6):622–627

Submitted: *July 3, 2012; accepted October 16, 2012 (doi:10.4088/JCP.12m07997).*
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As a group, people with schizophrenia perform worse than healthy controls on assessments of capacity to consent.[1,2] However, there is considerable variability in individual performance within this group,[3] and previous work has shown convincingly that many people with schizophrenia have capacity to consent to research.[4,5] Furthermore, people with schizophrenia who perform poorly on an initial assessment of decisional capacity can often considerably improve with the aid of training or other interventions.[4,6,7] A remaining concern is whether people with schizophrenia, once entered into a study, retain enough information about the study to participate knowledgeably—including making informed decisions about whether to terminate their involvement—as the study progresses.[8]

Stroup and colleagues[9] monitored changes in capacity to consent from enrollment to 6 and 18 months during the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study. Using the MacArthur Competence Assessment Tool—Clinical Research (MacCAT-CR),[10] they found nearly all (96%) of the 1,158 participants retained capacity to consent during the CATIE study. However, the CATIE study used US Food and Drug Administration–approved antipsychotics for their approved indication, without a placebo arm and with clinicians allowed to adjust doses according to participants' clinical needs.[11] Despite the use of blinding and randomization, the study's main parameters were very similar to what the participants experience in clinical care—in fact, one of the strengths of the CATIE study was this direct parallel to clinical care. As a result, however, it is unclear that the findings of Stroup et al[9] can be generalized to the novel situation of placebo-controlled trials of medications given in addition to an individual's regular antipsychotic treatment, a frequent model for research in schizophrenia.

Another concern related to ongoing participation in research is the therapeutic misconception.[12] Therapeutic misconception can be defined as the failure of study participants to recognize that research is meant to yield generalizable information and not primarily to benefit the individual.[13] It generally takes the form of misunderstanding the differences between clinical care and what occurs in a research study, such as not understanding random assignment, prescription of placebo or fixed doses of study medication, or that a study may be designed to investigate an illness without necessarily alleviating it. Therapeutic misconception is not restricted to psychiatric research participants but is a concern in any research setting—from critical care[14] to biobank-based genetic research.[15] However, people with schizophrenia may be particularly vulnerable to this type of confusion.

Schizophrenia is characterized by cognitive impairments affecting memory and attention[16,17] that remain static despite adequate control of psychosis. Although poor insight and prominent psychosis have been associated with decreased capacity to consent,[18–20] cognitive

Clinical Points

- People with schizophrenia who have stable psychotic symptoms have no meaningful loss of consent-related information during the first 8 weeks of participation in a clinical trial.
- Therapeutic misconception, or confusion between research and clinical care, was not prominent in this sample of people with stable schizophrenia.

impairment has been the strongest predictor of decisional capacity.[4,5,21–24] It is possible that difficulties with attention or memory could impair the ability of someone with schizophrenia to retain/recall the information needed to participate knowledgeably in an on-going study. This situation may be more likely when a clinical trial contains elements not previously experienced in clinical care, such as placebo. Additionally, cognitive impairment may make participants with schizophrenia more vulnerable to confusion between research and clinical care.

This study extends the findings of Stroup et al[9] by examining information retention during placebo-controlled clinical trials of adjunctive agents added to stable antipsychotic therapy. The goals of the study were to determine the following: (1) Do participants retain enough information for continued informed participation during the course of these clinical trials? and (2) If not, when do they lose this information? This work was designed to yield empirical data as to when and if researchers need to remind participants about the nature of their participation in a clinical trial. We hypothesized that there would be some meaningful information degradation at 8 weeks compared to baseline. We did not make specific predictions as to when this decrease would occur but tested some participants after 1 week and 4 weeks, as well as all participants at 8 weeks. An exploratory aim of the study was to evaluate whether therapeutic misconception was prominent at baseline or changed during the study.

METHOD

This study was approved by the institutional review boards of the University of Maryland, Baltimore, and the State of Maryland Department of Health and Mental Hygiene. Written documentation of informed consent for this study was obtained from each participant.

Participants

All participants were diagnosed with schizophrenia or schizoaffective disorder by best estimate approach (utilizing the Structured Clinical Interview for *DSM-IV* Axis I Disorders,[25] direct assessment, family informants, and past medical records). Individuals were approached for participation in this study after signing consent for a placebo-controlled clinical trial of at least 8 weeks' duration occurring at the Maryland Psychiatric Research Center. All participants were clinically stable on antipsychotic therapy and were enrolling in a study examining the addition of an adjunctive agent to their regular regimen. Participants came from Maryland Psychiatric Research Center research clinics and from community mental health centers. The clinical trials were augmentation of clozapine by risperidone versus placebo for treatment-resistant psychosis,[26] atomoxetine versus placebo for cognitive enhancement,[27] atomoxetine versus placebo for weight loss in people taking clozapine or olanzapine,[28] varenicline versus placebo for cognitive enhancement,[29] varenicline versus placebo for smoking cessation,[30] rimonabant versus placebo for weight loss,[31] davunetide versus placebo for cognitive enhancement,[32] and rasagiline versus placebo for persistent negative symptoms (trial recently concluded, ClinicalTrials.gov identifier: NCT00492336). Other than diagnosis and clinical trial participation, no inclusion/exclusion criteria were used for this study; however, each clinical trial had varying inclusion/exclusion criteria. All 8 clinical trials excluded potential participants for having acute psychiatric instability (operationalized as recent change in medication or dose), being mentally retarded, being medically unstable, or meeting criteria for substance abuse or dependence (other than for nicotine) in the past 3 months or 6 months, respectively.

Assessments

Retention of consent information was measured by the modified Evaluation to Sign Consent (mESC).[33] This 23-item Likert-type evaluation was developed with input from researchers, people with schizophrenia, and family members. The scale is used to assess participants in areas generally recognized as important in determining capacity to consent to a clinical trial: medication being studied, the symptom or illness for which it is indicated, and the method by which it will be assigned; the requirements of research participants (burdens of participation); the risks and benefits; and the process by which participants can withdraw from the study. This information is also regarded as vital for ongoing consent.[8] Items are scored 0–4, with anchors at 0, 2, and 4, yielding a maximum score of 92.

Unlike the original Evaluation to Sign Consent,[34,35] the mESC includes questions beyond a basic understanding of the facts. Participants are also asked to consider how the basic facts apply to their own situation and to manipulate those facts in order to make decisions. These latter exercises represent the domains of appreciation and reasoning, which, along with understanding, are assessed to determine decisional capacity. Additionally, 3 mESC items directly address the therapeutic misconception. The mESC is easily modified to reflect correct answers for particular clinical trials. Each clinical trial included in our study had appropriate mESC scoring anchors developed in conjunction with the clinical trial investigators (eg, for side effect questions: "Which side effects are important to know for this clinical trial?"). Cronbach α for the mESC was .83. (See supplementary material at PSYCHIATRIST.COM for a full copy of the mESC.)

The Brief Psychiatric Rating Scale (BPRS) total score and positive symptom items (conceptual disorganization, hallucinations, unusual thought content, and suspiciousness) were used to assess global psychopathology and positive

symptoms, respectively.[36] The BPRS items for emotional withdrawal, motor retardation, and blunted affect were used to evaluate negative symptoms. The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)[37] characterized participants' cognitive abilities.

Design

On the day participants received their first dose of clinical trial study medication, they completed a baseline assessment of study knowledge using the mESC. At this visit, the complete consent form for the clinical trial was read aloud to participants as they followed along. Afterward, they were offered an opportunity to ask questions or obtain clarification. The BPRS was then administered, followed by the mESC. For follow-up visits, only the BPRS and mESC were administered for our study of sustained knowledge about the trial. Although participants had free access to their copy of the clinical trial consent form, it was not rereviewed with them during follow-up.

Follow-up visits occurred after 1, 4, and 8 weeks to determine the timing of any loss of information. To evaluate the possible learning effects from repeatedly asking clinical trial-related questions, we randomly assigned participants to have follow-up assessments at all 3 time points (group 1), at weeks 4 and 8 only (group 2), or at week 8 only (group 3).

The investigators of this study were in regular communication with the clinical trial investigators. No formal criteria have been established as to what information a participant needs to retain to continue knowledgeable participation in the study. However, to address institutional review board concerns, it was decided a priori that any individual who seemed incapable of remaining in the clinical trial (based on the impression of our study rater) would be referred to the clinical trial investigator. The clinical trial investigator would then determine whether the participant would be withdrawn from the clinical trial or be reeducated about the clinical trial. Individuals withdrawn from the clinical trial could still remain in our consent study. However, to avoid biasing our results, we decided that if an individual received additional education regarding the information on the consent form during the clinical trial, he or she would be withdrawn from our study.

Statistical Methods

Paired *t* tests were used to assess within-group changes from baseline on mESC scores at all visits where it was administered. After adjusting for baseline score, we used analysis of covariance to test for differences at week 4 between groups 1 and 2 and at week 8 between groups 1, 2, and 3 in changes in the mESC, BPRS total score, and BPRS psychosis score. Spearman rank correlations were calculated between the baseline mESC total score and the RBANS total score and baseline BPRS symptom measures (total score, psychosis score, and negative symptom score), as well as between changes in the mESC score and changes in the symptom measures from baseline to week 8.

Table 1. Basic Demographics

Variable	Group 1 (retested at 1, 4, and 8 weeks), (n = 17)	Group 2 (retested at 4 and 8 weeks), (n = 17)	Group 3 (retested at 8 weeks), (n = 18)
Age, mean (SD), y	42.5 (10.2)	44.7 (8.9)	44.0 (11.1)
Male gender, n (%)	13 (76)	13 (76)	9 (50)
Nonwhite, n (%)	8 (47)	5 (29)	10 (56)
Education, mean (SD), y[a]	11.5 (2.4)	13.4 (1.7)	12.1 (2.1)
RBANS score, mean (SD)[b]	82.0 (12.5)	80.9 (12.3)	79.4 (12.6)[c]

[a]Years of education, group 2 > group 1 ($F_{2,29} = 3.92$, $P = .02$).
[b]RBANS ranges: group 1, 56–92; group 2, 60–102; group 3, 52–101.
[c]n = 14.
Abbreviation: RBANS = Repeatable Battery for the Assessment of Neuropsychological Status.

RESULTS

Demographics

Fifty-nine participants enrolled in the study. Data analysis was restricted to participants with at least 1 follow-up visit. Demographic characteristics are presented in Table 1. Group 2 was slightly more highly educated than group 1, but there were no other group differences.

Retention of Study Information

Changes in study knowledge for each group are presented in Table 2. Group 1 (assessed at 1, 4, and 8 weeks) improved from baseline at each assessment culminating in a 6.2-point improvement (about 8%) from baseline to week 8. This increase was both clinically meaningful and statistically significant ($t_{44} = 3.43$, $P = .001$). Group 2 (assessed at weeks 4 and 8) and group 3 (assessed at week 8 only) demonstrated no clinically meaningful change in their study knowledge (changes of 1% and 3%, respectively, at week 8).

Comparison of changes from baseline across groups revealed that the improvement in group 1 at week 8 was significantly greater than changes in both group 2 ($t_{45} = 2.66$, $P = .011$) and group 3 ($t_{45} = 3.22$, $P = .002$).

No participants performed so poorly on any mESC that they were referred to the clinical trial investigator for evaluation of the appropriateness of their remaining in the trial.

Interrater agreement for the mESC was good, with an intraclass correlation of 0.98 (95% CI, 0.96–0.99).

Therapeutic Misconception

Baseline mean ± SD values for the 3 mESC items representing the therapeutic misconception (maximum score of 12) were 9.0 ± 3.6 for group 1, 11.3 ± 1.0 for group 2, and 10.6 ± 1.9 for group 3. Mean changes from baseline over the 8 weeks ranged from −0.4 to 1.9, indicating no prominent worsening of therapeutic misconception during the study.

Symptoms

Little change in BPRS total score or psychosis subscore was observed during our study. No group differences were shown in change in symptom ratings at weeks 4 or 8.

Baseline BPRS total scores did not correlate with baseline mESC scores ($R = -0.02$, $P = .88$), nor did week 8 change in

Table 2. Retention of Study Information and Symptoms During Clinical Trials

	Group 1 (retested at 1, 4, and 8 weeks)		Group 2 (retested at 4 and 8 weeks)		Group 3 (retested at 8 weeks)				
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	*F*	*df*	*P*
Modified Evaluation to Sign Consent score									
Baseline	17	73.9 (14.1)	17	79.9 (7.5)	18	81.6 (6.5)	…	…	…
ΔWeek 1[a]	13	3.1 (5.9)	…	…	…	…	…	…	…
ΔWeek 4	14	2.6 (5.2)	13	−0.8 (5.1)	…	…	1.20	1,24	.28
ΔWeek 8	14	6.2 (5.5)[b]	17	−1.4 (6.6)	18	−3.1 (8.0)	5.58	2,45	.007[c]
BPRS total score									
Baseline	17	34.4 (8.0)	16	31.6 (7.2)	16	33.1 (7.8)	…	…	…
ΔWeek 1	13	−0.5 (3.8)	…	…	…	…	…	…	…
ΔWeek 4	14	−0.6 (5.1)	13	−0.8 (4.8)	…	…	0.03	1,24	.86
ΔWeek 8	14	−0.4 (4.9)	15	1.1 (6.4)	16	−0.6 (7.5)	0.23	2,41	.80
BPRS psychosis subscale									
Baseline	17	10.5 (4.7)	16	8.5 (4.1)	16	7.9 (3.3)	…	…	…
ΔWeek 1	13	0.3 (1.4)	…	…	…	…	…	…	…
ΔWeek 4	14	−0.8 (2.0)	13	0.4 (1.8)	…	…	1.35	1,24	.26
ΔWeek 8	14	−0.3 (1.4)	15	1.2 (3.3)	16	0.1 (3.2)	0.94	2,41	.40

[a]Δweek 1, Δweek 4, and Δweek 8 rows represent changes from baseline at each week.
[b]Group 1: Significant change from baseline ($t_{44} = 3.43$, $P = .001$).
[c]Group 1 had a significantly greater change in the modified Evaluation to Sign Consent from baseline to 8 weeks compared to both group 2 ($t_{45} = 2.66$, $P = .011$) and group 3 ($t_{45} = 3.22$; $P = .002$).
Abbreviation: BPRS = Brief Psychiatric Rating Scale.

Table 3. Participants From Research Clinics Versus Nonresearch Clinics

	Research Clinic		Nonresearch Clinic		Between-Group Comparisons		
	n	Mean (SD)	n	Mean (SD)	*F*	*df*	*P*
Modified Evaluation to Sign Consent							
Baseline	33	80.3 (8.4)	19	75.5 (12.5)	…	…	…
ΔWeek 1[a]	8	1.4 (6.7)	5	5.8 (3.0)	1.89	1,10	.20
ΔWeek 4	18	0.1 (5.2)	9	2.8 (5.3)	0.56	1,24	.46
ΔWeek 8	32	−0.1 (5.1)	17	0.6 (11.5)	0.06	1,46	.81

[a]ΔWeek 1, Δweek 4, and Δweek 8 rows represent changes from baseline at each week.

BPRS total score correlate to week 8 change in mESC score ($R = -0.19$, $P = .22$). The baseline BPRS psychosis subscore did not correlate with baseline mESC scores ($R = -0.13$, $P = .37$), nor did the week 8 change in BPRS psychosis subscore correlate with the week 8 change in mESC score ($R = -0.12$, $P = .42$). Baseline BPRS negative symptoms did not correlate with baseline mESC scores ($R = -0.13$, $P = .36$), nor did week 8 change in these items correlate to week 8 change in the mESC score ($R = -0.11$, $P = .48$).

Cognition

The RBANS correlation with baseline mESC score did not reach significance ($R = 0.28$, $P = .07$).

Research Experience

To assess the impact of having had prior research experience, participants recruited from the research clinics of Maryland Psychiatric Research Center were compared to participants recruited from nonresearch-related community mental health centers (Table 3). No significant differences in mESC change scores were noted over the 8 weeks between research-experienced and non–research-experienced participants.

DISCUSSION

Contrary to our hypothesis, participants did not show any appreciable, clinically relevant decreases in knowledge about the clinical trials in which they were enrolled. In fact, group 1, which was questioned about the study at weeks 1, 4, and 8, actually showed a significant improvement in study knowledge. This finding occurred despite the fact that the consent form was not rereviewed at any follow-up session.

The improvement in group 1 may indicate that repeatedly asking questions of the participant may enhance study-related knowledge in the absence of lengthy reviews of consent forms. Some problems people with schizophrenia may experience in the retention of consent-related information may therefore reflect memory retrieval impairment rather than impairment in initial encoding. Perhaps strengthening retrieval pathways by repeatedly asking the individual to remember previously reviewed information could be a strategy for enhancing capacity to consent. These data suggest that beginning the process soon after consent (ie, 1 week) is more efficacious than waiting longer. This finding merits further investigation.

Although we tested participants in a different type of clinical trial, our result is consistent with the overall findings of Stroup and colleagues.[9] An exception is that Stroup et al[9] found that positive and negative symptoms were correlated with change in the understanding subscale of the MacCAT-CR, while we found no relationship between symptoms and the mESC. This point of disagreement may exist because of the increased power to detect such correlations in the much larger CATIE study, the longer follow-up period in CATIE, or the different scales used in the studies (mESC versus MacCAT-CR and BPRS versus the Positive and Negative Syndrome Scale). Additionally, all of the participants in our consent study were clinically stable and on antipsychotic therapy. Patients in CATIE followed a randomized plan for switching medications when symptoms were not adequately controlled by the initial medication or patients stopped that medication. Patients with acute exacerbations[19,20] are one subgroup in which relationships have been observed between psychotic symptoms and decisional capacity. Stroup and colleagues[9] also found a relationship between performance on neuropsychological assessments and MacCAT-CR understanding subscores, and, similarly, we found a weak correlation approaching significance between the RBANS and the baseline mESC.

To our knowledge, this is the first study to examine therapeutic misconception in people with schizophrenia actually participating in clinical trials. Although Dunn and colleagues[38] reported on therapeutic misconception in older

adults with schizophrenia and found it somewhat prevalent, they used a hypothetical clinical trial rather than assessing people during real study participation. The indication from the present study is that therapeutic misconception—at least according to the definition we used—may not be prominent in people with schizophrenia when clinically stable and does not appear to change during the actual experience of a clinical trial.

This study has several limitations. The first is that while the mESC possesses excellent interrater reliability (intraclass correlation = 0.98), strong face validity, and good internal consistency (Cronbach $\alpha = .83$), it is not the gold standard for assessing capacity to consent, including understanding of study-related information. Additional research on the instrument needs to determine the relationship between the mESC and the MacCAT-CR. A larger sample size will also be needed to determine the internal factor structure of the scale and whether items representing "appreciation" or "reasoning" represent separable subscales. Furthermore, the mESC is an information-based assessment tied to the details of a consent form. It does not reflect the possibility that someone may choose to participate or remain in a study without full information, ie, respect for autonomy may require consideration of what level of information is truly sufficient for "informed consent." Second, this study was not designed to examine ongoing capacity to consent; rather, we examined the retention of consent-related information among research subjects. Even with regard to information retention, our findings may not be applicable to studies in which participants with schizophrenia may receive placebo instead of standard of care treatment or to symptom provocation studies (eg, placebo-controlled antipsychotic or ketamine challenge studies). Therefore, although these results extend the findings of Stroup et al,[9] the question of both knowledge retention and ongoing capacity to consent during a study in which psychotic exacerbation is expected remains unanswered. Likewise, as our assessments were conducted only up to 8 weeks, we cannot predict whether study-related knowledge would have significantly degraded beyond 8 weeks. Third, every participant had free access to their own copy of the clinical trial consent form and could have reviewed it in expectation of our follow-up visits. However, our experience in the study was that participants did not actively prepare for our follow-up visits and many only remembered that our assessment was due when we met with them after they finished their clinical trial assessments. Finally, although we found no difference between the participants recruited from research clinics and those recruited from community mental health centers, the sample was weighted toward research-experienced participants.

In summary, our finding that people with schizophrenia demonstrated no meaningful loss of consent-related information over the course of 8 weeks is reassuring. Assessment of decisional capacity at the time of consent is appropriate, but we found no evidence that people with schizophrenia require additional assessment of their understanding of a study within the first 8 weeks of a placebo-controlled clinical trial of an adjunctive agent, nor did we find prominent therapeutic misconception during the trials. Presuming these findings are confirmed, it appears that, as with any other adult, once a clinically stable participant with schizophrenia consents to a protocol, it can be assumed that he or she retains an understanding of the information related to participation unless there is a specific reason to suspect otherwise.

Drug names: atomoxetine (Strattera), clozapine (Clozaril, FazaClo, and others), ketamine (Ketalar and others), olanzapine (Zyprexa and others), risperidone (Risperdal and others), varenicline (Chantix).

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Potential conflicts of interest: None reported.

Funding/support: This work was supported by the National Institute of Mental Health, Grant R01MH058898 (principal investigator: Dr Carpenter).

Acknowledgments: The authors would like to thank the investigators of the clinical trials for their assistance: Robert W. Buchanan, MD; L. Elliot Hong, MD; Deanna L. Kelly, PharmD; James M. Gold, PhD; Elaine Weiner, MD; and M. Patricia Ball, RN, C, MS, all of the Maryland Psychiatric Research Center, University of Maryland School of Medicine, Baltimore; David Gorelick, MD, PhD, of the Intramural Research Program, National Institutes of Health, National Institute on Drug Abuse, Baltimore, Maryland; and Robert R. Conley, MD, Distinguished Scholar, Eli Lilly, Indianapolis, Indiana. The authors would also like to acknowledge the efforts of Patricia Greenberg, MA (now of the University of Maryland School of Social Work, Baltimore); Aneesha Garg (now a student at University of Pittsburgh, Pennsylvania); and Alison Murphy (now a student at Brown University, Providence, Rhode Island) for their help in data organization. None of these acknowledged individuals have a conflict of interest relevant to the contents of this article.

Supplementary material: The mESC is available as supplementary material for review at PSYCHIATRIST.COM. The scale is not copyrighted and is in the public domain.

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See supplementary material for this article at PSYCHIATRIST.COM.

THE JOURNAL OF CLINICAL PSYCHIATRY

Supplementary Material

Article Title: Participants With Schizophrenia Retain the Information Necessary for Informed Consent During Clinical Trials

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DOI Number: 10.4088/JCP.12m07997

List of Supplementary Material for the article

1. **Rating Scale** Modified Evaluation to Sign Consent

Disclaimer

This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Supplementary Material.

Note: [U]= Understanding, [A]= Appreciation, [R]= Reasoning, [TM]= Therapeutic Misconception items (based on face validity).

Modified Evaluation to Sign Consent (mESC) Template

Question:		**Anchors:**
Determine if the potential subject is able to communicate and maintain a meaningful conversation, and if the patient is willing to discuss the research project.	**Y N** (circle)	If **YES**, proceed If **NO**, consent cannot be validated at this time
Assignment of medication during research		
1. [U] What is being studied in this research project? (If patient responds "schizophrenia" ask, "What is it about schizophrenia that we/the researchers are trying to figure out?")	____	0: Does not know 1: 2: Some reference to schizophrenia treatment 3: 4: Clear knowledge that _____ (study medication) treatment is being studied
2. [U] What problems or symptoms is the project medication designed to help?	____	0: Does not know 1: 2: Some reference to relevant symptoms 3: 4: Clear knowledge of key symptoms (i.e. _____)
3. [A] Do you have any of these symptoms? (Briefly state key symptoms)	____	0: Does not admit to having the symptoms or problems 1: 2: States only that the doctors think he/she has the symptoms 3: 4: States has key symptom or problem
4. [A] Do you think the project medication could affect your symptoms? How?	____	0: No 1: 2: Maybe; unsure 3: 4: Believes the treatment could affect his/her symptoms
5. [U] In this research project, what is/are the experimental medication(s) being studied? What is a placebo or "sugar pill"? Could you get a placebo?	____	0: Does not know 1: 2: Knows about only _____(study medication) OR placebo, not both 3: 4: Specifies _____ (study medication) and placebo as possible treatments
6. [A] If you join the project, will you get to choose the medication you think is best for your problem?	____	0: Yes 1: 2: 3: 4: No
7. [TM] Will your doctor or therapist be		0: Yes; I think so or I hope so

able to make sure you get the project medication instead of placebo?	____	1: 2: 3: 4: No
8. [U] How do the researchers know which medication to give to the people in the project?	____	0: Subject does not know; "the one that works best" 1: 2: Research team decides 3: 4: Acknowledges random assignment; flip of a coin
9. [TM] (Clarify random assignment if necessary.) Is that how your doctor usually decides which medications you need most? How is it different?	____	0: Decision made in the same way; don't know if same or different 1: 2: Knows it is different, but vague about how 3: 4: Clear about the difference
Project Burden Issues		
10. [A] People in research projects are asked to do certain activities, like come for extra visits. Can you name some activities you would be asked to do if you joined this project?	____	0: Unaware of extra requirements 1: 2: Names some requirements but not ones which are very burdensome or painful 3: 4: Fairly clear view of burdensome or painful requirements (e.g. _____[time spent on study visits, blood draws, neuroimaging, etc.])
After above scoring is complete, show visual aid listing the extra activities the subject would be expected to participate in if enrolled in this project.		
11. [R] Are any of these project activities different from what you do in your normal routine? Why?	____	0: Does not relate to requirements in a personal manner/ No opinion 1: 2: Some awareness of personal effect/ Opinion but can't say why 3: 4: Realistic view of personal effect/ Opinion and can give examples of considering extra burdens
12. [TM] If you weren't in a research project, would you have to do these things? Are you doing them for your personal well-being or as part of the research?	____	0: To make sure he/she is getting well 1: 2: Does not know why 3: 4: Because it is part of what is being studied and not for clinical reasons

Risks and Benefits		
13. [U] What good things might happen to patients who join this project?	____	0: No benefit for participants; guaranteed clinical improvement 1: 2: Sees potential benefits, but overestimates potential for subjects to benefit –OR- only mentions monetary reward 3: 4: Realistic understanding of benefits (does not need to mention “closer monitoring” as benefit)
14. [A] How likely is it that good things will happen to *you* if you join this project?	____	0: Guaranteed 1: 2: Unrealistic Expectations 3: 4: Realistic; Chance
15. [R] How could those good things make it easier for you to do the things you like to do?	____	0: No concept of how life would be affected 1: 2: Knows it would help but unsure exactly how 3: 4: Can point to specific activities that could be improved
16. [U] What problems might people have because of joining this project? (Minor side-effects: _____ [List]; Major side-effects: _____[List])	____	0: Denies risk 1: 2: Partially understands risks 3: 4: Clear understanding of primary risks (_____ [List important risks])
After above scoring is complete, show visual aid listing important side-effects and other risks related to the project.		
17. [A] These are some things that might be a problem for people who join the project. If you join the project, do you think any of these could happen to you?	____	0: No 1: 2: Admits *some* risks but minimizes possibility unrealistically 3: 4: Acknowledges all are possible

18. [R] How could those experiences make it harder for you to do the things you like to do?	_____	0: No concept of how life would be affected 1: 2: Knows it would interfere but unsure exactly how 3: 4: Can point to specific activities that could be hindered
19. [U] Will this research benefit people in the future? How?	_____	0: No benefit to others; Don't know 1: 2: Acknowledges gain in information but not sure how that is beneficial 3: 4: Acknowledges that new treatment information can help future patients
20. [R] How do you decide whether to join a project or not?	_____	0: Doesn't know; doesn't think about those things 1: 2:Some appreciation of areas reviewed 3: 4: Weighs risks and benefits (Does not need to *say* that is what he/she does if it is obvious that is what is happening)
Project Withdrawal		
21. [U] Do the research participants *have* to remain in the project until the researcher says they have finished? Are participants allowed to leave the project before it is finished? How should they do that?	_____	0: Cannot quit 1: 2: Can quit but not sure how to do it 3: 4: Clear on right to withdraw; talk to Drs./Mr./Ms. _____ [List PI and study coordinator] (does not need to remember names if knows where to find them, i.e. consent form)
22. [A] If you join the project but you decide to pull out before it is finished, can you go back to your regular treatment?	_____	0: Cannot quit; cannot receive regular treatment if quit 1: 2: Realizes he/she can quit, but unsure how that affects treatment 3: 4: Acknowledges right to quit and still receive treatment
After above scoring is complete, show visual aid listing: symptoms getting worse, side-effects are uncomfortable, too much time in testing.		
23. [R] [Showing visual aid] These are some reasons why people leave research projects before the projects are finished. Would these things make you want to leave the project? What else might make you want to leave the project?	_____	0: Denies possibility of any adverse effect which would cause him/her to withdraw 1: 2: Vague thoughts about things that would lead to withdrawal 3: 4: Notes specific things that would make him/her uncomfortable continuing in the project (does not need to name something on the visual aid)