



Published in final edited form as:

*Schizophr Res.* 2008 February ; 99(1-3): 350–358. doi:10.1016/j.schres.2007.11.022.

## A Direct Comparison of Research Decision-making Capacity: Schizophrenia/Schizoaffective, Medically Ill, and Non-Ill Subjects

Philip J. Candilis, MD<sup>1</sup>, Kenneth E. Fletcher, PhD<sup>1</sup>, Cynthia M.A. Geppert, MD, PhD<sup>2</sup>, Charles W. Lidz, PhD<sup>1</sup>, and Paul S. Appelbaum, MD<sup>3</sup>

<sup>1</sup> *University of Massachusetts Medical School, Dept. of Psychiatry*

<sup>2</sup> *University of New Mexico Health Sciences Center, Dept. of Psychiatry and Religious Studies Program, University of New Mexico*

<sup>3</sup> *Columbia University College of Physicians and Surgeons, Dept. of Psychiatry*

### Abstract

To characterize predictors of impairment in research decision-making capacity, we undertook a direct comparison of schizophrenia/schizoaffective (n= 52), medically ill (diabetic; n= 51), and non-ill (n= 57) subjects. Scores on the MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR) were correlated with demographic variables and scores on the Positive and Negative Syndrome Scale (PANSS), Mini-Mental State Examination (MMSE), and Short-Form-36 (SF-36).

Across diagnoses, cognitive capacity, physical functioning, and a diagnosis of mental illness had the greatest impact on decision-making capacity, with level of education also having an impact. 69–89% of schizophrenia/schizoaffective subjects attained MacCAT-CR subscale scores achieved by almost all comparison (98–100%) and medically ill (94–100%) subjects. Positive, negative, and general psychotic symptoms correlated with poorer scores. Prior research experience, number of queries used during interview, and emotional functioning also predicted MacCAT-CR scores.

These data suggest that investigators and IRBs should consider a number of variables, many of which reach across diagnoses, as they decide which populations and individual subjects may require more intensive screening for decisional impairment or educational interventions to improve their abilities to make capable decisions about research participation.

### Keywords

research ethics; informed consent; decision-making capacity

### 1.1 Introduction

Recent empirical ethics research has underscored the similarities in decision-making capacity between medically ill and mentally ill research subjects. To be sure, studies have demonstrated a greater likelihood of decisional impairment among subjects with mental illnesses. However, they also show substantial overlap between mentally ill and non-mentally ill groups, so that

---

Corresponding author: Philip Candilis, MD, Associate Professor of Psychiatry, University of Massachusetts Medical School, 55 Lake Avenue North, Worcester, MA 01655; (508) 856-1473, philip.candilis@umassmed.edu.

**Publisher's Disclaimer:** This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

diagnostic category alone does not determine capacity status. There is also substantial overlap between mentally ill and non-mentally ill subjects in other aspects of informed consent. For example, motivation and willingness to participate in research are altruistic to a similar extent, elements of therapeutic misconception are prevalent across diagnoses, and risk-benefit assessments consider relevant personal experience in both groups (Appelbaum, 2004, 2006; Appelbaum et al, 1999, 2004; Candilis et al, 2006; Dunn et al, 2006; Jeste et al, 2006; Lidz and Appelbaum, 2002; Roberts et al, 2002, 2003). Although certain sub-groups of subjects diagnosed with mental illness may be at higher risk of impairment, specific weaknesses of those incapable of informed decisions, namely executive control dysfunction and cognitive impairment, are not limited to those with any specific illness (Moser et al, 2002; Palmer et al, 2005; Royall et al, 1993; Royall, 2002; Stanley et al, 1981).

The debilitating nature of illness in general also raises concerns with the decision-making of patients across diagnoses. Patients with diseases ranging from HIV and cancer to chronic illness, for example, may be affected by desperation and strong trust in their physicians (Fureman et al, 1997; Kodish et al, 1991; Logue and Wear, 1995; Minogue et al, 1995). Because diagnosis is not an adequate basis on which to expect limitations on the capacity to give informed consent, investigators and institutional review boards (IRBs) can benefit from information on factors beyond diagnosis that identify subjects at increased risk for impaired capacity. Appropriate remedies can then be devised, from more intensive screening to better educational efforts.

To further characterize predictors of impairments in capacity across diagnostic groups, we undertook a direct comparison of the decision-making of schizophrenia/schizoaffective disorder subjects, medically ill, and non-ill comparison subjects. We hypothesized that there would be substantial overlap in the capacities of the groups, and that cognitive capacity, education, psychosis, quality of life measures, research experience, length of illness and view of prognosis would affect decision-making. We anticipated that demographic factors such as ethnicity and sex would have no influence.

## 1.2 Methods

### 1.2.1 Subjects

Fifty-two mentally ill subjects were recruited from three sites: 45 stable patients from two Massachusetts state hospitals, and 7 outpatients from a site with greater expected ethnic diversity. Massachusetts state hospitals serve seriously and persistently ill patients, who had an average length of stay of 353 days during the years of subject recruitment. Subjects responded to announcements at community meetings or were approached through their physicians, who identified them as diagnosed with schizophrenia or schizoaffective disorder and capable of completing the interview. Subjects followed identical consent procedures as the diabetic subjects described below. All 52 subjects met DSM IV-R diagnostic criteria for either schizophrenia or schizoaffective disorder by clinical interview and/or chart review. The diagnoses of inpatient subjects who were not known to the principal investigator were confirmed with treating psychiatrists and clinical teams. Diagnoses of outpatient subjects were confirmed by accompanying family members or clinicians present who knew the subjects. The length of their illness varied from 1.0 to 42.0 years (mean = 16.79, sd = 11.89, median = 15 years). Demographic information is presented in Table 1.

Fifty-one medically ill subjects were recruited from a single medical school diabetes clinic whose physicians gave permission for their patients to be approached. Subjects were diagnosed with Type 1 or Type 2 diabetes mellitus, and were identified by their physicians as capable of completing a 45-minute interview. Patients approached by their own physicians were clearly instructed that they could refuse and that refusal would not affect their care. Refusal rates and

debriefing suggested strongly that subjects were not unduly influenced. The length of their illness varied from 0.1 to 47 years (mean = 17.0, sd = 9.54, median = 16.0 years).

Fifty-seven comparison subjects not being actively treated for any acute or chronic condition were recruited from the mental health staff of the state hospitals. This was a group likely to match patients in certain demographic characteristics (namely age, education, and ethnicity).

Twenty-three mentally ill subjects (30.7% of those approached) and seven comparison subjects (10.9%) refused the authors' requests for interviews. Diabetes clinic staff reported eight diabetic subject refusals (13.6%).

There were no significant differences between the groups in sex, completion of college education, ethnicity, or length of illness. This was not unexpected because researchers made specific efforts to match groups in the major demographic categories. Diabetic subjects were not significantly older than comparison subjects but were older than subjects diagnosed with schizophrenia/schizoaffective disorder ( $p \leq .05$  per Tukey's HSD follow-up tests of contrasts;  $F_{(2,157)}=5.80$ ,  $p=.004$ ). Mentally ill subjects scored significantly lower on the Mini-Mental State Examination (MMSE) than the other groups ( $F_{(2,152)}=5.91$ ,  $p=.003$ ). This is consistent with clinical and research expectations when comparing groups with schizophrenia and those without. Their mean score on the Positive and Negative Syndrome Scale (PANSS) was 64.6, (sd = 14.94, median = 62; above average impairment in the PANSS instrument's original normative sample).

Subjects were informed that a number of questionnaires would be administered after discussion of a hypothetical drug trial, and that they would be paid ten dollars for their participation. All provided written informed consent. The study was approved by both university and Department of Mental Health IRBs.

### 1.2.2 Measures

All subjects received the MacArthur Competence Assessment Tool – Clinical Research (MacCAT-CR), an instrument designed to assess decision-making capacity and adapted to the elements of a specific research protocol (Appelbaum and Grisso, 2001). MacCAT-CR administration involves disclosure of information about the study that subjects are being asked to consider, in this case a hypothetical medication trial, followed by questions that assess understanding, appreciation, reasoning, and choice. The hypothetical trial, designed for outpatients, involved random, blinded exposure to a new antibiotic for sore throat versus an established treatment; risks included those of blood draw and non-life-threatening side effects of the drug. The inability to guarantee direct benefit was explained as well. An antibiotic trial was chosen so that subjects might draw on a common treatment experience. It followed the design of mainstream protocols identified by colleagues conducting antibiotic research.

Specific rules for follow-up probing were developed. Interviewers were allowed to use up to five probes for each question. These involved repeating language from established MacCAT probes or feeding back the subjects' responses when answers were unclear. A repeated disclosure was permitted in the appreciation sub-section when subjects did not recall the study's lack of primary benefit to the subject. This departure from the usual MacCAT-CR procedure was designed to maximize subject performance.

The principal investigator (PC) conducted all but seven of the assessments and trained a co-investigator (CG) in use of the instrument. After observation of two interviews, the co-investigator interviewed four subjects with the principal investigator present, the surveys were scored independently, and any differences discussed. Interrater reliability scores were derived from eleven interviews, the four interviewed by the co-investigator and scored independently

by the two raters, and audiotapes of seven interviews by the principal investigator. Seven of the PI's interviews were reviewed for consistency by the one of the authors (PA), who co-developed the instrument.

For inter-rater reliability, interviewers attained an intraclass correlation of .87 on the MacCAT-CR Appreciation subscale (scored 0–6 points). For the Reasoning subscale (scored 0–8), inter-rater reliability measured by the intraclass correlation was .74.

For the Understanding subscale (scored 0–26), rate of agreement rather than intraclass correlations was used to assess reliability because ratings ranged over the same 3 scores – 24, 25, and 26 – for both raters. The two raters agreed on 8 of the 11 scores on the Understanding subscale, a 72.7% agreement rate, with 2 of the disagreements differing by only one point, and the third differing by two.

Raters agreed on 10 of the 11 ratings on the Choice subscale (scored 0–2), for a 90.9% agreement rate, with the one disagreement differing by one point. Therefore, in this study there appears to be good interrater reliability on the subscales of the MacCAT-CR.

Subjects also completed the SF-36 (Short Form-36) health-related quality-of-life instrument (Ware and Sherbourne, 1992), the MMSE (Mini-Mental State Examination, Folstein et al, 1975), PANSS (Positive and Negative Syndrome Scale, mentally ill subjects only; Kay et al, 1987), and a background information form asking about prior research experience, length of illness, and view of prognosis. These instruments were completed at the same encounter as the capacity assessment, in the same order for all subjects, and by the same unblinded interviewer.

### 1.2.3 Analysis

Statistical analyses were conducted using SPSS Version 13.0. Differences between groups on categorical data were analyzed using chi-square tests or Fisher's exact probability test. Differences between groups on ordinal or continuous data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey Honestly Significant Differences (HSD) tests of contrasts between all pairs of groups. Multivariate predictors of scores on Appreciation, Reasoning, and Understanding were examined using stepwise linear regression analyses. For these analyses, indicator variables were created for group membership, with the comparison group used as the reference group. It was not feasible to examine multivariate predictors of scores on Choice because 95.6% (153) of the 160 scores were the highest possible. Because of the number of significance tests, we used a more conservative significance level of .005.

In each regression analysis, the following variables were allowed to attempt to enter the equation: age, gender, perceived prognosis, length of illness, scores on the MMSE, t-scores on the SF-36 scales, and level of education.

## 1.3 Results

### 1.3.1 Diagnosis and MacCAT-CR scores

Subjects diagnosed with schizophrenia/schizoaffective disorder scored lower than the other two groups on all subscales (Table 2). For the purpose of comparison, cut-offs were set at the level attained by at least 98% of control subjects. 76.9% of mentally ill subjects scored 23 or above on the 26-point Understanding subscale (achieved by 98.2% of comparison subjects and 93.9% of diabetic subjects; Fisher's exact  $p < .001$  comparing mentally ill subjects to the other two groups combined).

80.8% of mentally ill subjects scored 6 or more points on the 8-point Reasoning subscale (achieved by 100% of comparison subjects and 100% of diabetics; Fisher's exact  $p < .001$  comparing mentally ill subjects to the other two groups combined).

69.2% of mentally ill subjects scored 4 or more points on the 6-point Appreciation scale (achieved by 98.2% of comparison subjects and 98.0% of diabetics; Fisher's exact  $p < .001$  comparing mentally ill subjects to the other two groups combined).

And 88.5% of mentally ill subjects scored 2 out of 2 points on the Choice subscale (achieved by 100% of comparison subjects and 98.0% of diabetics; Fisher's exact  $p < .001$  comparing mentally ill subjects to the other two groups combined).

Diabetic subjects scored comparably with comparison subjects on all subscales but Appreciation, where they scored lower than the comparison group.

The more probes necessary for any subject to answer a question fully, the lower the scores on Appreciation, Understanding, and Reasoning (Appreciation  $r = -.55$ ,  $p < .001$ ; Understanding  $r = -.67$ ,  $p < .001$ ; Reasoning  $r = -.60$ ,  $p < .001$ ). There was no significant correlation with Choice scores because of the relatively few subjects who scored 0 or 1 point out of 2 ( $t_{(6,17)} = 1.51$ ,  $p = .18$ ).

### 1.3.2 Bivariate Associations Between MacCAT-CR and Demographic Variables

MacCAT-CR scores were not significantly associated with age, ethnicity, sex, or number of years ill. Level of education was significantly correlated with scores on the Understanding ( $r = .33$ ,  $p < .001$ ), Appreciation ( $r = .35$ ,  $p < .001$ ), and Reasoning scales ( $r = .25$ ,  $p = .002$ ) among all groups considered together, as well as among mentally ill subjects ( $r$  with Understanding =  $.37$ ,  $p < .01$ ,  $r$  with Appreciation =  $.41$ ,  $p < .01$ , and  $r$  with Reasoning =  $.28$ ,  $p < .05$ ). At the same time, level of education was significantly correlated only with Understanding ( $r = .305$ ,  $p < .05$ ) among the comparison group, and was significantly correlated only with Appreciation ( $r = .315$ ,  $p < .05$ ) among the diabetic group.

Prior research experience was associated with higher Appreciation scores among all groups taken together (Mean if had prior research =  $5.61$ ,  $SD = 1.06$ ,  $n = 49$ ; Mean if no prior research =  $5.03$ ,  $SD = 1.50$ ,  $n = 110$ ; Mann-Whitney  $U$   $z = -2.89$ ,  $p = .004$ ), but not separately – although the trend was in the same direction.

For all groups taken together, higher MMSE scores (greater cognitive capacity) correlated with higher Understanding, Appreciation, Reasoning, and Choice scores (Table 3). Higher MMSE scores among mentally ill subjects correlated with higher Understanding, Appreciation, and Reasoning subscales of the MacCAT-CR. There were no significant correlations between MMSE and MacCAT-CR scores among the other two groups when examined separately.

PANSS subscale scores for mentally ill subjects correlated strongly with lower MacCAT-CR scores: with Positive Symptoms correlating with lower Appreciation ( $r = -.42$ ,  $p \leq .0005$ ) and Reasoning ( $r = -.48$ ,  $p = .001$ ); Negative Symptoms correlating with lower Understanding ( $r = -.70$ ,  $p \leq .0005$ ) and Appreciation ( $r = -.56$ ,  $p \leq .0005$ ); General Symptoms correlating with lower Understanding ( $r = -.71$ ,  $p \leq .0005$ ), Appreciation ( $r = -.55$ ,  $p \leq .0005$ ), Reasoning ( $r = -.57$ ,  $p \leq .0005$ ), and Choice ( $r = -.41$ ,  $p = .005$ ); and Anergia scores correlating with lower Understanding ( $r = -.41$ ,  $p = .005$ ). Higher PANSS Composite scores (a negative number) correlated with higher MacCAT-CR Understanding ( $r = .43$ ,  $p = .003$ ).

### 1.3.3 SF-36 Scores

For all subjects regardless of group, higher SF-36 scores on Physical Functioning and Role-Emotional correlated significantly with higher scores on MacCAT-CR Understanding ( $r = .32$ ,  $p < .001$ , and  $.31$ ,  $p < .001$ , respectively), Appreciation ( $r = .35$ ,  $p < .001$ , and  $.30$ ,  $p < .001$ ), and Reasoning ( $r = .31$ ,  $p < .001$ , and  $.24$ ,  $p = .003$ ). The MacCAT-CR subscales did not correlate significantly at the Bonferroni-adjusted significance level of .005 with any of the other SF-36 subscales. Only two of the remaining correlations attained a p-level of less than .05: SF-36 scores on Role-Physical correlated .19 ( $p < .02$ ) with MacCAT-CR Understanding and .21 ( $p < .01$ ) with MacCAT-CR Appreciation.

When analyzed by group, scores of comparison subjects showed no significant correlations with any SF-36 or MacCAT-CR scales. Among subjects with schizophrenia/schizoaffective disorder, the significant correlations were those between SF-36 Physical Functioning and MacCAT-CR Understanding ( $r = .45$ ,  $p < .001$ ), Appreciation ( $r = .54$ ,  $p < .001$ ), and Reasoning ( $r = .44$ ,  $p < .001$ ). There was a significant correlation between Role-Emotional and Understanding among diabetic subjects ( $r = .44$ ,  $p = .002$ ).

### 1.3.4 Stepwise Regressions

The final models for the stepwise regression of MacCAT-CR scales on other variables are shown in Table 4. In all final models, three variables – MMSE scores, SF-36 Physical Functioning scores, and schizophrenia/schizoaffective diagnosis – accounted for 57% of the variance in MacCAT-CR scores in Understanding, 48% of the variance in Appreciation, and 37% of the variance in Reasoning. Higher MMSE and physical functioning scores were associated with higher scores on each scale; while a diagnosis of schizophrenia/schizoaffective disorder was associated with lower scores. The standardized regression coefficients indicate that cognitive functioning was the most important predictor of decision-making scores (Beta = .63 when predicting Understanding, .51 when predicting Appreciation, and .40 when predicting Reasoning). Physical functioning was least important among the three factors when Appreciation (Beta = .18 vs  $-.28$  for schizophrenia/schizoaffective diagnosis) and Reasoning (Beta = .16 vs  $-.30$  for schizophrenia/schizoaffective diagnosis) were the outcomes, while demonstrating an impact on Understanding similar to that of a diagnosis of schizophrenia/schizoaffective disorder (Beta = .18 and  $-.17$ , respectively).

Since mentally ill patients differed significantly from the other two groups on their average MMSE scores (Table 1), hierarchical regression analyses were conducted predicting MacCAT-CR Appreciation, Reasoning, and Understanding. In these regressions, the three variables that formed the final stepwise regression models were entered one at a time, first entering SF-36 Physical Functioning scores, then MMSE scores, and finally the dummy variable indicating whether or not the subject was mentally ill. As indicated by the column labeled “R<sup>2</sup> Change” in Table 5, after entering SF-36 Physical Functioning into the equation, MMSE accounted for 39.3% of the total variance when predicting Understanding, 27.6% of the variance when predicting Appreciation, and 18.0% of the variance when predicting Reasoning (all significant at  $< .001$ ). With the other two variables in the equation, schizophrenia/schizoaffective disorder accounted for 3.7% of the total variance when predicting Understanding, 8.5% of the variance when predicting Appreciation, and 9.7% of the variance when predicting Reasoning (all significant at or below .001). Thus, although diagnosis remained significant after accounting for the other two variables, physical functioning and MMSE added prominently to the prediction of MacCAT-CR scores.

## 1.4 Discussion

In this direct comparison of schizophrenia/schizoaffective, medically ill, and non-ill subjects, cognitive capacity, physical functioning, and a diagnosis of mental illness had the greatest impact on decision-making capacity. These influences were most evident among subjects diagnosed with schizophrenia/schizoaffective disorder. Nonetheless, mental illness was not the only source of difficulty for our subjects. Overall, cognitive capacity and physical functioning both contributed to decision-making scores even after adjusting for diagnosis. Level of education also made a substantial impact on diverse elements of decision-making. These data suggest that investigators and IRBs should consider these variables as they decide which populations and individual subjects may require more intensive screening or education.

Impaired cognition is well-recognized as a limitation to the research participation of Alzheimer's, other geriatric, and neurology subjects, but its primacy among this study's predictors of poor decision-making underscores its importance as a risk factor independent of diagnosis. Although the MMSE is not a comprehensive assessment of cognitive functioning it is a well-established screen indicating here that cognition must be considered in capacity assessment, regardless of group.

The impact of physical health on research decision-making is an important health-related correlation across diagnostic groups, indicating that the effects of such impairment may appropriately be considered a barrier to adequate decisional capacity. Emotional health may also play a role. The recognition that health-related quality of life influences patient treatment decisions as well as clinician treatment choices provided the context for exploring its effects on research decision-making (Cohen et al, 2002; Ko et al, 2002; Maynard et al, 2003). The SF-36 has since shown correlations to elements of the therapeutic misconception – an important element of research decision-making (Appelbaum et al, 2004). Further research will be important to confirm that physical limitations in particular are an identified vulnerability for research subjects. That length of illness had no discernible effect on decision-making scores offers some hopeful data on the vulnerability of chronically ill patients in general. As may be expected, prior research experience appears to correlate with better appreciation for the differences of research from clinical care. A larger sample of sub-groups should establish whether the trends among different populations match those of the group analyzed here as a whole.

The capacity of 69–89% of schizophrenia/schizoaffective subjects to attain decision-making scores achieved by most comparison and medically ill subjects is an important reminder of the capacities of subjects with even significant mental illness. Nonetheless, mentally ill subjects demonstrating psychotic symptoms will require attention to both the positive and negative thought processes that affect their decision-making. Although negative symptoms and cognitive functioning have received recent attention as correlates of research decision-making, positive symptoms such as hallucinations and conceptual disorganization have been part of the literature since the inception of studies using the MacArthur tools (Grisso et al, 1997; Carpenter et al, 2000; Dunn et al, 2006). The conduct of consent interviews may have a particular impact here, as the greater number of queries needed to clarify subjects' thinking may identify those needing more time or information during consent discussions.

Medically ill and comparison subjects scored comparably on all decision-making subscales, except Appreciation. This supports earlier research that finds few differences in the capacities of non-ill and medical populations (Appelbaum and Grisso, 1997). The discrepancy in Appreciation (lower in diabetic subjects) appears to be an artifact of scoring guidelines: 8 of 51 diabetic subjects lost points for neglecting to mention that they could receive usual treatment if they withdrew from the research – a requirement of the scoring rules. Yet diabetic subjects

generally offered more complete responses to Appreciation questions – recognizing levels of research uncertainty more completely than other respondents – from “research is about improving things in general,” “I could benefit in the future,” to “doctors are scrutinizing responses to medicines closely in research.”

Conducted with subjects considering a single protocol, the study overcomes limitations of earlier studies that used multiple protocols and multiple interviewers. The use of a hypothetical protocol, however, invites replication with subjects entering actual research studies. Clinical assessments of capacity by blinded interviewers may also help to clarify the relevance of these group comparisons to the individual assessments of clinical researchers. Moreover, stable inpatients, although severely mentally ill, may not be as unstable as acutely ill subjects entering research protocols.

Cognition, education, and psychosis remain important factors in decision-making capacity, but future research should consider that physical and emotional functioning may also have an effect among different populations. Regardless of diagnosis, common vulnerabilities should encourage the continued attention of investigators and IRBs to the full range of variables affecting research decision-making.

## Acknowledgements

This work was supported by a grant from the NIMH (K01MH01850) to Dr. Candilis. The opinions expressed do not necessarily reflect those of the National Institutes of Health.

## References

- Appelbaum PS, Grisso T. Capacities of hospitalized, medically ill patients to consent to treatment. *Psychosomatics* 1997;38(2):119–125. [PubMed: 9063042]
- Appelbaum PS, Grisso T, Frank E, O'Donnell S, Kupfer DJ. Competence of depressed patients for consent to research. *Am J Psychiatry* 1999;156(9):1380–1384. [PubMed: 10484948]
- Appelbaum, PS.; Grisso, T. *MacCAT-CR: MacArthur Competence Assessment Tool for Clinical Research*. Professional Resource Press; Sarasota FL: 2001.
- Appelbaum PS, Lidz CW, Grisso T. Therapeutic misconception in clinical research: frequency and risk factors. *IRB* 2004;26(2):1–8. [PubMed: 15069970]correction and clarification, 2004;26 (5) 18
- Appelbaum PS. Commentary: willingness and competence of depressed and schizophrenic inpatients to consent to research. *J Am Acad Psychiatry Law* 2004;32(2):144–147. [PubMed: 15282873]
- Appelbaum PS. Decisional capacity of patients with schizophrenia to consent to research: taking stock. *Schiz Bull* 2006;32(1):22–25.
- Candilis P, Geppert C, Fletcher K, Lidz CW, Appelbaum PS. Willingness of subjects with thought disorder to participate in research. *Schiz Bull* 2006;32(1):159–165.
- Carpenter WT Jr, Gold JM, Lahti AC, Queern CA, Conley RR, Bartko JJ, Kovnick J, Appelbaum PS. Decisional capacity for informed consent in schizophrenia research. *Arch Gen Psychiatry* 2000;57(6):533–538. [PubMed: 10839330]
- Cohen L, Parker PA, Sterner J, De Moor C. Quality of life in patients with malignant melanoma participating in a Phase I trial of an autologous tumor-derived vaccine. *Melanoma Res* 2002;12(5):505–511. [PubMed: 12394193]
- Dunn LB, Candilis PJ, Roberts LW. Emerging empirical evidence on the ethics of schizophrenia research. *Schiz Bull* 2006;32(1):47–68.
- Folstein MF, Folstein SE, McHugh PR. “Mini-mental state.” A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12(3):189–198. [PubMed: 1202204]
- Fureman I, Meyers K, McLellan AT, Metzger D, Woody G. Evaluation of a video-supplement to informed consent: injection drug users and preventive HIV vaccine efficacy trials. *AIDS Educ Prev* 1997;9(4):330–341. [PubMed: 9376207]



- Grisso T, Appelbaum PS, Hill-Fotouhi C. The MacCAT-T: a clinical tool to assess patients' capacities to make treatment decisions. *Psychiatric Serv* 1997;48(11):1415–1419.
- Jeste DV, Depp CA, Palmer BW. Magnitude of impairment in decisional capacity in people with schizophrenia compared to normal subjects: an overview. *Schiz Bull* 2006;32(1):121–128.
- Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schiz Bull* 1987;13(2):261–276.
- Ko CY, Rusin LC, Schoetz DJ, Collier JA, Murray JJ, Roberts PL, Moreau L. Using quality of life scores to help determine treatment: is restoring bowel continuity better than an ostomy? *Colorectal Dis* 2002;4(1):41–47. [PubMed: 12780654]
- Kodish E, Lantos J, Stocking C, Singer PA, Siegler M, Johnson FL. Bone marrow transplantation for sickle cell disease. A study of parents' decisions. *NEJM* 1991;325(19):1349–53. [PubMed: 1922237]
- Lidz CW, Appelbaum PS. The therapeutic misconception: problems and solutions. *Med Care* 2002;40(9 Suppl):V55–63. [PubMed: 12226586]
- Logue G, Wear S. A desperate solution: individual autonomy and the double-blind controlled experiment. *J Med Philos* 1995;20(1):57–64. [PubMed: 7738459]
- Maynard SE, Whittle J, Chelluri L, Arnold R. Quality of life and dialysis decisions in critically ill patients with acute renal failure. *Intensive Care Med* 2003;29(9):1589–1593. [PubMed: 12819880]
- Minogue BP, Palmer-Fernandez G, Udell L, Waller BN. Individual autonomy and the double-blind controlled experiment: the case of desperate volunteers. *J Med Philos* 1995;20(1):43–55. [PubMed: 7738458]
- Moser DJ, Schultz SK, Arndt S, Benjamin ML, Fleming FW, Brems CS, Paulsen JS, Appelbaum PS, Andreasen NC. Capacity to provide informed consent for participation in schizophrenia and HIV research. *Am J Psychiatry* 2002;159(7):1201–1207. [PubMed: 12091200]
- Palmer BW, Dunn LB, Appelbaum PS, et al. Assessment of capacity to consent to research among older persons with schizophrenia, Alzheimer disease, or diabetes mellitus: comparison of a 3-item questionnaire with a comprehensive standardized capacity instrument. *Arch Gen Psychiatry* 2005;62(7):726–733. [PubMed: 15997013]
- Roberts LW, Warner TD, Brody JL, Roberts B, Lauriello J, Lyketsos C. Patient and psychiatrist ratings of hypothetical schizophrenia research protocols: assessment of harm potential and factors influencing participation decisions. *Am J Psychiatry* 2002;159(4):573–584. [PubMed: 11925295]
- Roberts LW, Warner TD, Nguyen KP, Geppert CM, Rogers MK, Roberts BB. Schizophrenia patients' and psychiatrists' perspectives on ethical aspects of symptom re-emergence in psychopharmacological research participation. *Psychopharmacology (Berl)* 2003;171(1):58–67. [PubMed: 12756518]
- Royall DR, Mahurin RK, True JE, Anderson B, Brock IP 3rd, Freeburger L, Miller A. Executive impairment among the functionally dependent: comparisons between schizophrenic and elderly subjects. *Am J Psychiatry* 1993;150(12):1813–1819. [PubMed: 8238635]
- Royall D. Back to the future of mental capacity assessment. *JAGS* 2002;50(11):1884–1885.
- Stanley B, Stanley M, Lautin A, Kane J, Schwartz N. Preliminary findings on psychiatric patients as research participants: a population at risk? *Am J Psychiatry* 1981;138(5):669–671. [PubMed: 7235066]
- Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30(6):473–483. [PubMed: 1593914]

Table 1

Demographics and MMSE for the three groups.

	Schiz/Schizo Aff Disorder	Comparison Subjects	Diabetes	Test of Overall Difference	P
<b>Age</b>					
Mean (SD)	n = 52 37.79 <sup>a</sup> (11.67)	n = 57 41.04 <sup>a,b</sup> (13.16)	n = 51 47.00 <sup>b</sup> (16.61)	F <sub>(2,157)</sub> = 5.80	.004
Median	38.5	41	48		
<b>Ethnicity</b>					
White	n = 52 80.8% (42)	n = 57 71.9% (41)	n = 51 88.2% (45)	Overall, $\chi^2_{(6)} = 5.99$	.42
African-American	9.6% (5)	19.3% (11)	5.9% (3)	White vs other, $\chi^2_{(2)} = 4.50$	.11
Hispanic Native American	7.7% (4) 1.9% (1)	7.0% (4) 1.8% (1)	3.9% (2) 2.0% (1)		
<b>Gender</b>					
Females	n = 52 23.1% (12)	n = 57 42.1% (24)	n = 51 35.3% (18)	$\chi^2_{(2)} = 4.48$	.11
Males	76.9% (40)	57.9% (33)	64.7% (33)		
<b>Education Less Than BA BA or More</b>					
	n = 51	n = 57	n = 51	$\chi^2_{(2)} = 4.26$	.12
Less Than BA	84.3% (43)	86.0% (49)	70.6% (36)		
BA or More	15.7% (8)	14.0% (8)	29.4% (15)		
<b>Length of Illness in Years</b>					
	n = 51	n = 21	n = 51	F <sub>(2,120)</sub> = 1.01	.37
Mean (SD)	16.79 (11.89)	13.19 (11.47)	17.00 (9.54)		
<b>Perceived Prognosis Stable or Getting Worse</b>					
	n = 51	n = 23	n = 51	Overall $\chi^2_{(2)} = 3.38$	.18
Stable or Getting Worse	72.5% (37)	91.3% (21)	74.5% (38)		
<b>Getting Better</b>					
	n = 51	n = 23	n = 51	F <sub>(2,152)</sub> = 5.91	.003
Mean (SD)	27.29 <sup>a</sup> (2.95)	28.56 <sup>b</sup> (1.34)	28.41 <sup>b</sup> (1.46)		
Median	28	29	29		

Note: Means with different superscripts differ significantly, per Tukey HSD follow-up contrasts at the .005 level. In Perceived Prognosis the categories of "Stable" and "Getting Worse" were collapsed because few subjects (1 schizizophrenia/schizoffective, 2 comparison, 7 diabetic) believed they were getting worse.

**Table 2**

MacCAT-CR Scores for the three groups.

MacCAT-CR Scale	Schiz/SchizoAff Disorder	Comparison Subjects	Diabetes	Test of Overall and Pair-wise Group Differences
<b>Understanding (0–26 points)</b>	n = 52	n = 57	N = 49	Overall: Kruskal-Wallis $\chi^2_{(2)} = 22.34$ , $p < .001$ .
Mean (SD)	22.42 (6.03)	25.46 (1.16)	25.47 (1.42)	Mental Illness vs Diabetes: Mann-Whitney U z = -4.14, $p < .001$ .
Median	25	26	26	Mental Illness vs Non-ill: Mann-Whitney U z = -3.66, $p < .001$ .
<b>Appreciation (0–6 points)</b>	n = 52	n = 57	N = 51	Overall: Kruskal-Wallis $\chi^2_{(2)} = 29.82$ , $p < .001$ .
Mean (SD)	4.35 (1.91)	5.81 (0.64)	5.43 (0.90)	Mental Illness vs Diabetes: Mann-Whitney U z = -2.90, $p < .004$ .
Median	5	6	6	Mental Illness vs Non-ill: Mann-Whitney U z = -5.28, $p < .001$ .
<b>Reasoning (0–8 points)</b>	n = 52	n = 57	N = 51	Diabetes vs Non-ill: Mann-Whitney U z = -3.11, $p < .002$ .
Mean (SD)	6.50 (2.31)	7.77 (0.54)	7.82 (0.43)	Overall: Kruskal-Wallis $\chi^2_{(2)} = 25.38$ , $p < .001$ .
Median	7	8	8	Mental Illness vs Diabetes: Mann-Whitney U z = -4.18, $p < .001$ .
<b>Expressing a Choice (0–2 points)</b>	n = 52	n = 57	n = 51	Mental Illness vs Non-ill: Mann-Whitney U z = -4.04, $p < .001$ .
Mean (SD)	1.83 (0.51)	2.00 (0)	1.98 (0.14)	Overall Kruskal-Wallis $\chi^2_{(2)} = 9.72$ , $p < .01$ .
Median	2	2	2	Mental Illness vs Diabetes Mann-Whitney U z = -1.94, $p < .052$ .
				Mental Illness vs Non-ill. Mann-Whitney U z = -2.62, $p < .009$ .

\* Difference is significant at a .005 level.

**Table 3**  
Correlations of MMSE with MacCAT-CR Scales.

	MacCAT-CR Understanding	MacCAT-CR Appreciation	MacCAT-CR Reasoning	MacCAT-CR Expressing a Choice
	<b>Among All Subjects</b>			
MMSE	.687 ≤ .0005* 151	.597 ≤ .0005* 153	.488 ≤ .0005* 153	.267 .001* 153
	<b>Among Mentally Ill Subjects</b>			
MMSE	.802 ≤ .0005* 45	.718 ≤ .0005* 45	.547 ≤ .0005* 45	.262 .083 45

\* Correlations significant at a .005 level.

Table 4

Final stepwise linear regression models.

	Unstandardized Coefficients		Standardized Coefficients		
	B	SE	Beta	t-value	P
<i>Predicting MacCAT-CR Understanding</i>					
MMSE	1.23	.13	.63	9.42	<.001
SF-36 Physical Functioning	.03	.01	.18	2.84	.005
Schiz/SchizoAff diagnosis	-1.52	.59	-.17	-2.57	.01
$R^2 = .57, F_{(3,107)} = 47.72, p < .001.$					
<i>Predicting MacCAT-CR Appreciation</i>					
MMSE	.34	.05	.51	6.95	<.001
SF-36 Physical Functioning	.01	.004	.18	2.51	.01
Schiz/SchizoAff diagnosis	-.87	.22	-.28	-3.98	<.001
$R^2 = .48, F_{(3,109)} = 39.70, p < .001.$					
<i>Predicting MacCAT-CR Reasoning</i>					
MMSE	.29	.06	.40	5.06	<.001
SF-36 Physical Functioning	.01	.005	.16	1.98	.05
Schiz/SchizoAff diagnosis	-.99	.26	-.30	-3.80	<.001
$R^2 = .37, F_{(3,110)} = 21.59, p < .001.$					

**Table 5**  
Hierarchical linear regression analyses.

	Cummulative R <sup>2</sup>	R <sup>2</sup> Change	F	P
<i>Predicting MacCAT-CR Understanding</i>				
SF-36 Physical Functioning	.106	.106	F <sub>(1,147)</sub> = 17.36	< .001
MMSE	.499	.393	F <sub>(1,146)</sub> = 114.60	< .001
Schiz/SchizoAff diagnosis	.536	.037	F <sub>(1,145)</sub> = 11.62	.001
<i>Predicting MacCAT-CR Appreciation</i>				
SF-36 Physical Functioning	.125	.125	F <sub>(1,149)</sub> = 21.34	< .001
MMSE	.402	.276	F <sub>(1,148)</sub> = 68.34	< .001
Schiz/SchizoAff diagnosis	.487	.085	F <sub>(1,147)</sub> = 24.44	< .001
<i>Predicting MacCAT-CR Reasoning</i>				
SF-36 Physical Functioning	.096	.096	F <sub>(1,149)</sub> = 15.90	< .001
MMSE	.276	.180	F <sub>(1,148)</sub> = 36.70	< .001
Schiz/SchizoAff diagnosis	.373	.097	F <sub>(1,147)</sub> = 22.85	< .001