ORIGINAL ARTICLE

# 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*

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**Context:** Considerable discussion surrounds issues related to the capacities of neuropsychiatric patients to consent to research, yet few empirical investigations have directly compared decisional capacity among patients with a serious mental illness with that among patients with neurologic or medical conditions. Also, as requirements for formal assessment of decisional capacity are becoming more common, there is a clear need to identify efficient screening methods.

**Objectives:** To compare decisional capacity among 3 diagnostic groups, and to examine the degree to which impaired understanding can be detected with a brief set of screening questions.

**Setting:** Outpatient veterans hospital clinic and university-based neuropsychiatric research centers.

**Design/Participants:** Cross-sectional comparison of decisional capacity among older (≥60 years) outpatients with schizophrenia (n=35), mild to moderate Alzheimer disease (n=30), and type 2 diabetes mellitus (n=36), and determination of sensitivity and specificity of a screening measure.

**Main Outcome Measures:** Three-item decisional capacity questionnaire and the MacArthur Competence Assessment Tool for Clinical Research.

**Results:** Patients with diabetes mellitus performed the best on the capacity instruments, patients with Alzheimer disease had the worst performance, and patients with schizophrenia were intermediate. However, there was considerable heterogeneity within each group. Even within diagnostic groups, the level of cognitive functioning (measured with the Mini-Mental State Examination) was generally the best predictor of decisional capacity (particularly in the understanding component). The 3-item questionnaire was sensitive to impaired understanding as measured with the MacArthur Competence Assessment Tool for Clinical Research understanding subscale.

**Conclusions:** Decisional capacity differed among the 3 groups; there was considerable heterogeneity even within each diagnostic group, so individualized consideration of capacity may be warranted. The level of cognitive deficits is 1 potential marker of which participants should receive comprehensive capacity evaluations, but sensitive brief questionnaires targeting key aspects of disclosed information may also provide an effective means of screening for participants warranting comprehensive capacity evaluations.

*Arch Gen Psychiatry. 2005;62:726-733*

THERE IS GROWING RECOGNITION of the need for efficient and valid methods of assessing the capacity of research participants to provide meaningful consent prior to entry into clinical trials. Patients with schizophrenia tend to have worse understanding of disclosed material than do healthy comparison subjects,[1,2] and patients with Alzheimer disease (AD) are also at risk for impaired decisional capacity.[3,4] However, there appears to be considerable heterogeneity in the levels of decisional capacity within groups. Aging is associated with declines in some cognitive abilities that might be relevant to decisional capacity,[5] yet most studies of capacity to consent to research participation among patients without dementia have focused on nonelderly groups. There have also been few comparisons of decisional capacity across older neuropsychiatric or medical groups. Thus, there is little information on the degree to which the relationship between various patient characteristics and decisional capacity generalize across diagnoses. Identifying the patient character-

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istics associated with impaired capacity could inform researchers of when formal capacity evaluations and/or enhanced consent procedures may be most appropriate.

The empirical literature includes a number of instruments designed to evaluate participants' understanding of consent forms and/or 1 or more components of capacity to consent to research.[6-13] Most of the published measures focus exclusively on the understanding of disclosed material; only 2 of the published measures, the MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR)[6] and the Informed Consent Survey,[7] are designed to evaluate all 4 commonly recognized dimensions of capacity to consent to research (understanding, appreciation, reasoning, and expression of a choice[14]). An advantage of the MacCAT-CR is that it has a published comprehensive administration and scoring manual. It also appears to be the single most widely used instrument for formal assessment of capacity to consent to research.[1,2,4,15-19] However, administration requires 15 to 30 minutes; except in populations with high base rates of impaired capacity, it may not be efficient to administer the MacCAT-CR to every potential participant. An alternative would be to screen potential participants with a brief but highly sensitive instrument. Those individuals identified as having questionable capacity could then receive more comprehensive capacity evaluations.

In the present study, we evaluated the capacity to consent to research among 3 groups of older outpatients with diagnoses commonly targeted for clinical research: (1) schizophrenia/schizoaffective disorder, (2) mild to moderate AD, or (3) type 2 diabetes mellitus. Given the levels of capacity seen in prior studies of outpatients with schizophrenia[16,20] and those of patients with mild to moderate AD,[3,4,15] we expected that patients with AD would have worse capacity than those with schizophrenia. Also, given that any cognitive effects of type 2 diabetes mellitus would be less salient or prevalent than those associated with the other 2 conditions, we expected the diabetes mellitus group to have less impairment in decisional capacity. In light of prior findings regarding predictors of treatment-related capacity[14,20] and capacity to consent to research among elderly patients with AD[21] and younger adults with schizophrenia,[2,16] we hypothesized that there would be significant correlations between cognitive functioning and decisional capacity even within specific diagnostic groups. Finally, we hypothesized that a 3-item questionnaire targeting the main elements of research disclosures would relate to a more comprehensive assessment of the patients' capacities to understand disclosed information.

## METHODS

### PARTICIPANTS

Participants included 35 clinically stable outpatients with *DSM-IV* diagnoses of schizophrenia or schizoaffective disorder (n=35; 30 patients with schizophrenia), 30 noninstitutionalized outpatients with mild to moderate probable AD (without psychosis), and 36 outpatients with type 2 diabetes mellitus. Participants were recruited through clinical research programs at the University of California, San Diego (primarily the Advanced Center for Interventions and Services Research, which focuses on studies of older people with psychotic conditions, and the Alzheimer Disease Research Center) and via referrals from physicians and clinical staff at a research-active diabetes mellitus outpatient clinic at the Veterans Affairs San Diego Healthcare System (physicians and nursing staff mentioned our study to patients meeting the inclusion and exclusion criteria, and those expressing interest in participation were referred to us for further information). Diagnoses were established by the patients' treating physicians and/or respective research program. Each consecutively referred or identified patient meeting the inclusion/exclusion criteria was invited to participate.

Inclusion criteria were (1) currently 60 years or older, (2) diagnosis matching 1 of the 3 targeted conditions, (3) fluency in English, (4) current score on the Mini-Mental State Examination (MMSE)[22] of 18 or higher, and (5) voluntary informed consent to participate in this study. We excluded patients with schizophrenia with comorbid diagnoses of dementia or diabetes mellitus, patients with AD with psychosis or diabetes mellitus, and patients with diabetes mellitus with psychotic or affective disorders or dementia. The study protocol and consent forms for this project were reviewed and approved by the Human Research Protections Program boards of the University of California, San Diego and the Veterans Affairs San Diego Healthcare System. We used an interactive consent process to ensure adequate understanding of the protocol basics. A study staff person met with the potential participant, reviewed the information in the consent form with him or her, encouraged the participant to ask questions about any aspects that seemed confusing, and clarified any points about which the potential participant appeared confused. The level of understanding needed to provide meaningful consent to participate in this procedurally simple and minimal-risk protocol was much lower than that required for a complex or higher-risk clinical trial, such as that described in the hypothetical protocol used to evaluate capacity in this study. No subject was excluded because of a lack of capacity to participate in this study.

### HYPOTHETICAL STUDY FOR CONSENT ASSESSMENT

We developed a hypothetical consent form describing a randomized controlled trial of an experimental compound (which we named "plakmin") being tested for cognitive-enhancing effects, which was modeled after one actually used for a local study of cognitive benefits of a cholinomimetic agent. The consent form described a 12-week randomized comparison of plakmin vs placebo. It was 5 single-spaced pages and had a Flesch-Kincaid reading level of 11.5 years. (Although that reading level is higher than the generally recommended eighth grade reading level, few consent forms actually achieve that goal.[23,24]) Procedures described to the patients included randomized assignment, medical and psychiatric interviews, blood draws, cognitive and functional capacity testing, and functional magnetic resonance imaging. The consent form also reviewed risks from the study procedures and medications (modeled after the risks for an actual cholinomimetic drug), potential benefits, treatment for compensation or injury, the voluntary nature of participation, procedures for withdrawal from the study, confidentiality, and procedures for addressing any questions or concerns.

### EVALUATION

#### Demographic and Clinical Information

Demographic information was obtained through patient interviews and review of available records. Among a subset of the

patients with schizophrenia and/or schizoaffective disorder (n=23), we also had contemporaneous data (within a 2-month window) on the severity of psychopathologic symptoms, as measured with the Positive and Negative Syndrome Scale.[25]

### Cognitive Screening

The level of cognitive impairment was assessed with the MMSE. The MMSE has a potential range of 0 to 30 points; we restricted the sample to those with MMSE totals of 18 or higher. Kim et al[15] previously used this cut score in a study of decisional capacity among patients with dementia, and we chose it so that we could focus on patients with AD who retain sufficient cognitive abilities such that questions of personal consent (rather than assent with surrogate consent) remain particularly germane.

## COMPREHENSION OF DISCLOSED INFORMATION/DECISIONAL CAPACITY

### Procedures

A trained research assistant conducted all the capacity evaluations during a single 60- to 90-minute visit with each individual patient. She explained the nature and purpose of this decisional capacity study to the potential participant and told the participant that he or she was not actually going to be asked to be included in the medication study but stressed that the participant should imagine that it was real so that we could evaluate the consent process. She then read the plakmin study consent form aloud while the participant read it silently to himself or herself. The research assistant stopped at appropriate points to answer the participant's questions (if any).

### Three-Item Questionnaire

After reviewing the plakmin study consent form, each participant was asked 3 questions about the plakmin study: (1) "What is the purpose of the study?" (2) "What are the risks?" and (3) "What are the benefits?" Our intention was to ascertain whether responses to these questions could serve as an efficient means of identifying people likely to have impaired understanding as determined by a more comprehensive evaluation. There are other elements that were not included in our short questionnaire, such as questions about the procedures, alternative treatments, and the voluntary nature of participation. We selected the present 3 questions because they cover arguably 3 of the most important aspects of consent form content mandated by federal regulations.[26] Also, some other important aspects that may be barriers to meaningful consent, such as presence of a therapeutic misconception, are implicit within these questions.

If a participant's initial response was vague or suggested misunderstanding of the question itself, the research assistant prompted for clarification or re-explained the question. She did not redisclose the relevant information at this point in the evaluation. The participants' responses were recorded verbatim, and these were then independently coded by 2 of us (B.W.P. and L.B.D.), who assigned each of the 3 items a score of 0 (incapable), 1 (questionable or intermediate), or 2 (capable). We followed the scheme used for scoring MacCAT-CR items, wherein a 2-point score reflects clear understanding of the disclosed material, a 0-point score reflects definite misunderstanding of the disclosed material, and a 1-point score reflects either partial but less than fully adequate understanding or, if this persists even after prompting for clarification, an uncertain level of participant understanding. So that we could evaluate the value of responses to these 3 items themselves without being influenced by other capacity-relevant information, the scorers were kept naive to each participant's diagnostic status, demographic and clinical characteristics, MMSE scores, and MacCAT-CR scores. It is possible that the raters might have been able to guess the likely diagnosis of a participant, but as the raters were kept unaware of the participant's MacCAT-CR responses, it is unlikely that the relationship seen between the 3-item questionnaire and the MacCAT-CR scores was biased by the content of the responses. We added the scores for each of the 3 items, creating a total score with a possible range of 0 to 6 (higher scores reflecting better understanding). The interrater reliability for the total scores was very good (ie, the intraclass correlation coefficient was 0.904). We used the mean of the 2 scorers' ratings for each participant for the statistical analyses.

## COMPREHENSIVE ASSESSMENT OF CAPACITY WITH A STANDARDIZED INSTRUMENT USING A SEMISTRUCTURED INTERVIEW

After completing the 3-item questionnaire and some additional questions about the hypothetical study (data not presented here), each participant was evaluated with the MacCAT-CR. The MacCAT-CR is a semistructured interview-based instrument that includes a series of questions related to decisional capacity. The disclosures and items were written in reference to the hypothetical study described earlier. As per standard MacCAT-CR administration and scoring,[6] and in contrast to the approach taken with the 3-item questionnaire, if a subject's initial response indicated that he or she misunderstood the relevant information, that information was re-explained and the item was readministered. Each item was scored as 0, 1, or 2, with higher scores reflecting better performance. Because MacCAT-CR administration and scoring are intended to be interactive, each item was scored by the research assistant during the interview. (We conduct semiannual interrater reliability checks with this and other MacCAT-CR raters for other research projects in our research center to ensure adequate interrater reliability [ie, an intraclass correlation coefficient of 0.80 or greater], and the research assistants meet regularly with B.W.P. and L.B.D. to review and discuss any scoring questions.) There are 4 subsections that correspond to the 4 commonly recognized dimensions of decisional capacity: (1) understanding (range, 0-26); (2) appreciation (range, 0-6); (3) reasoning (range, 0-8); and (4) ability to communicate a choice (range, 0-2). These subscale scores served as our primary units of analysis.

## STATISTICAL ANALYSES

The distribution of variables was checked to evaluate the presence of significant skew or kurtosis. The distributions of age and education met assumptions for parametric analyses, so differences among the 3 diagnostic groups were compared with 1-way analyses of variance with follow-up pairwise comparisons using the Tukey Honestly Significant Difference Procedure. Owing to significantly skewed distributions among 1 or more of the 3 groups, differences in MMSE total scores, the 3-item questionnaire total, and MacCAT-CR subscale scores were each evaluated with Kruskal-Wallis tests. When the Kruskal-Wallis test indicated the presence of significant differences, Mann-Whitney *U* tests were used for pairwise group comparisons. Group differences in categorical variables were compared with Pearson $\chi^2$ tests. Using Spearman $\rho$, we also examined the degree to which age, education, and MMSE totals (and in the schizophrenia/schizoaffective group, the Positive and Negative Syndrome Scale positive and negative subscale scores) were each significantly correlated with the total scores from the

**Table 1. Demographic, Clinical, Cognitive, and Decisional Capacity Assessments in Patients With Schizophrenia (SC), Alzheimer Disease (AD), or Diabetes Mellitus (DB)***

| Variable | Schizophrenia (n = 35) | Alzheimer Disease (n = 30) | Diabetes Mellitus (n = 36) | Test Value† | *P* Value | Significant Pairwise Differences |
|---|---|---|---|---|---|---|
| Age, y | 65.7 (5.2) | 77.0 (6.6) | 70.9 (6.2) | $F_{2,98} = 29.0$ | <.001 | SC<DB<AD |
| Education, y | 12.0 (3.0) | 14.6 (2.9) | 14.5 (2.2) | $F_{2,97} = 10.0$ | <.001 | SC<AD,DB |
| Men, % | 57.1 | 73.3 | 97.2 | $\chi^2_2 = 15.9$ | <.001 | SC = AD<DB |
| White, % | 80.0 | 90.0 | 72.2 | $\chi^2_2 = 3.6$ | .20 | |
| MMSE total score | 27.1 (2.1) | 23.0 (3.0) | 28.2 (1.8) | $\chi^2_2 = 43.1$ | <.001 | AD<SC<DB |
| Age of onset, y | 29.2 (12.4) | 71.9 (7.4) | 53.9 (12.6) | $F_{2,93} = 107.5$ | <.001 | SC<DB<AD |
| PANSS positive subscale score (n = 23) | 13.4 (5.8) | NA | NA | | | |
| PANSS negative subscale score (n = 23) | 12.4 (3.9) | NA | NA | | | |
| 3-Item questionnaire total score (potential range, 0-6) | 3.9 (1.6) | 1.9 (2.2) | 5.1 (1.2) | $\chi^2_2 = 32.7$ | <.001 | AD<SC<DB |
| MacCAT-CR | | | | | | |
| Understanding subscale score (range, 0-26) | 23.5 (4.0) | 16.4 (7.2) | 25.5 (1.4) | $\chi^2_2 = 38.7$ | <.001 | AD<SC<DB |
| Appreciation subscale score (range, 0-6) | 5.5 (1.0) | 5.2 (1.2) | 6.0 (0.2) | $\chi^2_2 = 11.2$ | .004 | AD = SC<DB |
| Reasoning subscale score (range, 0-8) | 6.6 (1.3) | 5.8 (1.9) | 6.9 (1.1) | $\chi^2_2 = 7.3$ | .03 | AD<DB |
| Expression of a choice subscale score (range, 0-2) | 1.9 (0.3) | 2.0 (0.2) | 1.9 (0.3) | $\chi^2_2 = 1.4$ | .503 | |

Abbreviations: MacCAT-CR, MacArthur Competence Assessment Tool for Clinical Research; MMSE, Mini-Mental State Examination; NA, not available; PANSS, Positive and Negative Syndrome Scale.

*Unless otherwise indicated, values are given as mean (SD).

†Owing to skewed distributions, Kruskal-Wallis tests (with pairwise comparisons via Mann-Whitney *U* tests) were used to compare groups on MMSE scores, 3-item questionnaire total scores, and MacCAT-CR scores.

3-item questionnaire and with each of the 4 MacCAT-CR subscale scores within the 3 diagnostic groups, and the degree to which the 3-item questionnaire correlated with each of the 4 MacCAT-CR subscales. Significance for all analyses was defined as $P<.05$ (2-tailed, where applicable).

We also examined the sensitivity and specificity of each potential cut score from the 3-item questionnaire to impaired vs intact understanding as measured with the understanding subscale of the MacCAT-CR. There is no established basis for defining impaired performance on the MacCAT-CR; however, in the National Institute of Mental Health–sponsored Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia study,[27] participants had to earn a score of 15 or more (of 26 possible points) on the understanding subscale to consent to participation. Also, in a study of younger patients with schizophrenia or human immunodeficiency virus, Moser et al[16] examined the ability of a 5-item (Evaluation to Sign Consent) questionnaire to detect impairment relative to this MacCAT-CR cut score. We used this precedent as our "gold standard" against which to evaluate the sensitivity and specificity of our 3-item questionnaire at each potential cut point.

## RESULTS

### GROUP CHARACTERISTICS AND DECISIONAL CAPACITY

Demographic, clinical, and decisional capacity characteristics of each group are described in **Table 1**. The schizophrenia group was the youngest and the patients with AD composed the oldest group. The patients with schizophrenia had fewer years of education than those in the other 2 groups. The proportion of male participants was highest among those with diabetes mellitus. The patients with AD had the most severe cognitive deficits (lowest mean MMSE total score), and the diabetes mellitus group had the highest mean MMSE total score. Age of onset of respective illness was earliest among the patients with schizophrenia and latest among the patients with AD.

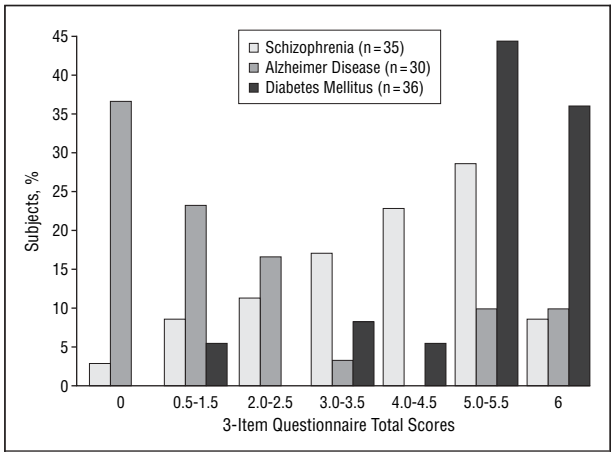


**Figure 1.** Three-item questionnaire total scores among older patients with schizophrenia, Alzheimer disease, or type 2 diabetes mellitus.

The patients with AD had the worst (lowest) mean scores and patients with diabetes mellitus had the best (highest) mean scores on the 3-item questionnaire (Table 1). However, as illustrated in **Figure 1**, there was also considerable heterogeneity within each group. While the modal score for patients with AD (11/30 [37%]) was 0 points, 6 (20%) of the patients with AD earned scores of 5.5 or 6.0. Conversely, 29 (80%) of 36 patients with diabetes mellitus obtained scores of 5 or higher (and none earned a score between 0 and 1.0), but 2 (6%) of these patients earned scores of 1.5 and 5 (14%) earned scores of 3.5 or lower. Among patients with

**Table 2. Spearman ρ Correlations Among Age, Education, Mini-Mental State Examination Total Scores, and Decisional Capacity Scores Among 35 Patients With Schizophrenia, 30 Patients With Alzheimer Disease, and 36 Patients With Type 2 Diabetes Mellitus**

| | Age | | | | Education | | | | MMSE Total Score | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | SC | AD | DB | All | SC | AD | DB | All | SC | AD | DB | All |
| 3-Item questionnaire score | 0.01 | –0.39* | –0.35* | –0.35† | 0.09 | –0.14 | 0.06 | 0.01 | 0.32 | 0.44* | 0.39* | 0.67† |
| MacCAT-CR | | | | | | | | | | | | |
| Understanding subscale score | 0.11 | –0.38* | –0.31 | –0.34† | 0.23 | 0.11 | 0.40* | 0.09 | 0.48* | 0.55* | 0.44* | 0.73† |
| Appreciation subscale score | –0.01 | –0.30 | –0.27 | –0.16 | 0.50* | 0.24 | 0.23 | 0.31* | 0.31 | 0.36 | 0.18 | 0.39† |
| Reasoning subscale score | –0.07 | 0.01 | –0.31 | –0.22* | –0.02 | –0.03 | –0.06 | –0.05 | 0.12 | 0.33 | 0.26 | 0.38† |
| Expression of a choice subscale score | 0.12 | –0.17 | –0.20 | –0.01 | –0.19 | –0.32 | –0.01 | –0.10 | 0.18 | 0.00 | 0.06 | –0.01 |

Abbreviations: AD, Alzheimer disease; DB, diabetes mellitus; MacCAT-CR, MacArthur Competence Assessment Tool for Clinical Research; MMSE, Mini-Mental State Examination; SC, schizophrenia.
*$P<.05$.
†$P<.001$.

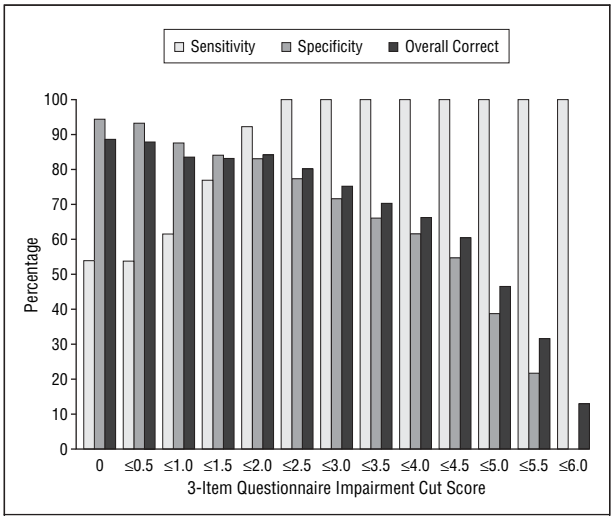


**Figure 2.** Sensitivity and specificity of each potential 3-item questionnaire impairment cut score to impaired understanding as defined on the MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR). Sensitivity refers to the number of patients impaired per 3-item questionnaire/number impaired per MacCAT-CR; specificity, to the number of patients intact per 3-item questionnaire/number intact per MacCAT-CR.

schizophrenia, 13 (37%) of 35 patients had scores of 5 or higher, but 8 (23%) obtained scores of 2.5 or lower.

We found a similar pattern on the MacCAT-CR subscales, with patients with AD garnering the lowest scores, particularly on the understanding and reasoning subscales. Compared with patients with diabetes mellitus, those with schizophrenia performed worse on the understanding and appreciation subscales. Most patients in all 3 groups had adequate performance on the expression of a choice subscale. The 3 groups also overlapped in their distributions of MacCAT-CR subscale scores. For instance, the median understanding subscale score for patients with schizophrenia was 25 points; 7 (23%) of the 30 patients with AD and 32 (89%) of the 36 patients with diabetes mellitus scored at or higher than this level. On the appreciation subscale, 26 (74%) of the patients with schizophrenia, 20 (67%) of the patients with AD, and 35 (97%) of the patients with diabetes mellitus earned full credit (6.0), although 2 (7%) of the patients with AD and 2 (6%) of the patients with schizophrenia scored 3 points or less on this subscale. The median reasoning score in both the schizophrenia and diabetes mellitus groups was 7.0; 13 (43%) of the patients with AD earned a reasoning score at or higher than this level.

Each of the bivariate correlations between age, education, and MMSE total scores with total scores on the 3-item questionnaire and each of the MacCAT-CR subscale scores are reported in **Table 2**. Age was sporadically associated with the 3-item questionnaire total score and MacCAT-CR understanding subscale score, particularly in the AD group but not in the schizophrenia group. With isolated exceptions, education was not significantly correlated with any of the measures of decisional capacity. The MMSE total score was a strong predictor of the 3-item questionnaire total score and the MacCAT-CR understanding subscale score. In the subsample of patients with schizophrenia or schizoaffective disorder for whom Positive and Negative Syndrome Scale scores were available, there were no significant correlations between severity of psychopathologic symptoms (Positive and Negative Syndrome Scale positive and negative subscale totals) and each measure of decisional capacity (all $P>.05$).

## RELATIONSHIP OF 3-ITEM QUESTIONNAIRE TO MACCAT-CR

The 3-item questionnaire total scores were significantly correlated with scores on the MacCAT-CR understanding subscale ($r=0.74$; $P<.001$) and, to a lesser degree, with the appreciation ($r=0.41$; $P<.001$) and reasoning ($r=0.44$; $P<.001$) subscales, but not with expression of a choice ($r=0.12$; $P=.10$).

Using the earlier cited criterion for categorizing subjects as impaired or intact on the MacCAT-CR understanding subscale, 13 (12.9%) of the 101 participants were impaired, including 2 patients with schizophrenia (5.7%) and 11 patients with AD (36.7%). The sensitivity and specificity of the 3-item questionnaire (at each potential cut score) relative to such impairment are illustrated in **Figure 2**. Owing to the low base rates of impairment, the highest overall proportion of correct classifications (89.1%) was achieved by defining impairment on the 3-item questionnaire as a score of 0. However, the intent of using the 3-item questionnaire was to identify par-

ticipants requiring further capacity assessment. Assuming false-negative errors are unacceptable, then the best balance of sensitivity and specificity was achieved with a cut score of 2.5 or less. All 13 of the patients impaired on the MacCAT-CR understanding subscale had 3-item questionnaire total scores of 2.5 or less, and specificity (1 – false positives) at this cut score was 77.3%.

In light of the observed relationship of cognitive functions to decisional capacity, we also calculated the sensitivity and specificity of different MMSE total scores as cut points relative to the CATIE-based MacCAT-CR understanding criterion. There was no instance where the MMSE achieved better specificity at an equivalent level of sensitivity and only 1 instance where the sensitivity and specificity achieved with the MMSE were equivalent to those with the 3-item questionnaire (an MMSE cut score of $<24$ and a 3-item questionnaire score of $\leq 1$ were each associated with 61.5% sensitivity and 87.5% specificity). We found that the area under the receiver operating characteristics curve (SPSS Receiver Operating Characteristics Graph option; SPSS Inc, Chicago, Ill) for the 3-item questionnaire was 0.92 (95% confidence interval, 0.86-0.97) whereas that for the MMSE was 0.88 (95% confidence interval, 0.79-0.96).

## COMMENT

This is, to our knowledge, the first study to compare levels of capacity to consent to research among older people who have schizophrenia with levels of that capacity among patients who have mild to moderate AD and patients in a medical comparison group. As expected, the patients with AD showed the worst performance on the measures of decisional capacity, particularly in terms of understanding disclosed information. Patients with diabetes mellitus performed the best, and patients with schizophrenia performed intermediately. Cognitive ability was the only consistent correlate of decisional capacity, with particularly strong correlations with understanding of the disclosed material.

Given the contextual nature of decisional capacity, as well as the nature of the MacCAT-CR, a comparison of results across studies is somewhat difficult. Mean levels of MacCAT-CR performance vary widely within diagnostic groups. In a study of patients with schizophrenia who have been institutionalized long-term in a state-run facility, Kovnick et al[1] found that the mean understanding total score was 12.1 (of 26 possible points); similar understanding scores in a mixed inpatient/outpatient sample were reported by Carpenter et al,[2] whereas the mean scores noted by Moser et al[16] were more similar to those found in the present schizophrenia sample. Yet while comparison of absolute levels across studies is difficult, the importance of cognitive functions in a decisional capacity is a very consistent finding across multiple disorders, including schizophrenia, AD, human immunodeficiency virus, and cancer.[2,14,16,19-21,28,29]

The present results show that it is inappropriate to draw conclusions about an individual patient's capacity for meaningful consent based solely on diagnosis. Even among patients with AD or schizophrenia, there was a wide range of decisional capacity scores. Although none of the patients with diabetes mellitus earned scores lower than 1.5 on the 3-item questionnaire or lower than 15 points on the MacCAT-CR understanding subscale, 5 (14%) did obtain scores of 1.5 to 3.5 points on the 3-item questionnaire, suggesting that they had at least initial difficulty comprehending some aspects of the hypothetical protocol relevant to providing meaningful consent.

Using 3 simple questions about the purpose, risks, and benefits of the protocol, we were able to identify a cut score (2.5 points) having 100% sensitivity, albeit with less than perfect (77.3%) specificity. A similar pattern was demonstrated by Moser et al[16] using a 5-item questionnaire with younger patients with schizophrenia and comparison subjects with human immunodeficiency virus. In the present study, there was no instance in which the balance of sensitivity and specificity associated with the MMSE exceeded that associated with the 3-item questionnaire. However, given that the range of the 95% confidence intervals for areas under the curves associated with 2 tests overlapped, the primary advantages of the 3-item questionnaire may be conceptual and pragmatic. The conceptual advantage of the 3-item questionnaire is that the capacity to consent to research is an inherently context-specific construct; the content of the 3-item questionnaire is directly relevant to making a meaningful choice in that it refers to information that participants actually need to make a valid choice, whereas the MMSE content has no inherent value in that choice. In addition, a pragmatic advantage is that the 3 questions can be readily integrated into every consent delivery process with virtually no added burden on the study or the participants, whereas the MMSE requires additional training and added time for administration and scoring.[28]

Routine evaluation of decisional capacity in studies of patient populations with high base rates of impaired capacity (such as AD) may be reasonable, particularly for greater-than-minimal-risk studies. Where base rates are lower, however, it may be impractical to administer the MacCAT-CR or other comprehensive capacity assessment measures to every potential participant. The present results suggest that a reasonable alternative might be to use shorter screening questions with high sensitivity and acceptable specificity, allowing researchers to identify those individuals for whom more comprehensive capacity evaluations are appropriate. Based on initial responses to a single disclosure, a cut point of 2.5 on the 3-item questionnaire provided the best balance of sensitivity and specificity when judged against the relatively low threshold (15 of 26 points on the MacCAT-CR understanding subscale) of the CATIE study. However, we think it would be inappropriate to enroll a participant if he or she could only achieve an understanding of 42% (2.5 of 6.0 points) of disclosed information after repeated explanations. A number of participants have difficulty on initial disclosure but can understand information on re-explanation.[30] Thus, we believe that it is crucial to at least query potential participants to make certain that they can explain the purpose, risks, and anticipated benefits (or lack thereof) of any study in which they are enrolling, and to use an interactive process by which initially misunderstood information is re-explained.

A potential limitation of the results of the 3-item questionnaire is the absence of an objective criterion against which the sensitivity and specificity of this questionnaire (or the MacCAT-CR itself) can be unambiguously evaluated. We used the criterion from the National Institute of Mental Health–sponsored CATIE study, which was also used by Moser et al,[16] but clearly a more stringent criterion might be appropriate depending on the risk-benefit ratio of a particular study. Also, the CATIE-based criterion and our 3-item questionnaire both focus solely on understanding. One's observed understanding of information in a particular context is only an indirect manifestation of his or her theoretical capacity for such understanding; one may have adequate understanding and yet have deficits in appreciation, reasoning, or expression of a choice. Thus, understanding is a necessary but insufficient condition for meaningful consent. Beyond the specific information queried in our 3-item questionnaire, there are clearly other elements that potential participants must understand, appreciate, and reason through to make a meaningful choice about research participation. In studies targeting populations at risk for impaired appreciation or reasoning, it may be particularly advisable to include screening questions that directly evaluate patients for deficits in these other aspects of decisional capacity. Further development and validation of questions to screen for deficits in appreciation and reasoning are needed to document the sensitivity and specificity of available and newly developed capacity measures.

The sample sizes of 30 to 36 participants in each of the 3 diagnostic groups were chosen to permit us to detect medium to large effect size differences and were generally comparable with those in recently published studies of decisional capacity.[1,2,4,15-17,31] Nonetheless, increased power from a larger sample size might have resulted in some of the nonsignificant correlations (such as those between the severity of psychopathologic symptoms and understanding) reaching statistical significance. A larger number of impaired patients might also have led to more stable estimates of the sensitivity and specificity of the 3-item questionnaire at each potential cut score. Also, patients evaluated in the present study were identified through university-affiliated research centers (each with close affiliations with the Veterans Affairs San Diego Healthcare System) and a research-active Veterans Affairs diabetes mellitus clinic. All 3 settings are in close physical proximity (within 0.5 mile), and each is directed by academically oriented physicians on the faculty of the University of California, San Diego School of Medicine. This focus on academic medicine clinics was intentional, as this is the type of setting in which many patients are invited to participate in clinical trials. On the other hand, our results may not generalize to less academically oriented settings or those where patient-participants have markedly different educational or other demographic, clinical, or cognitive characteristics.

Despite these caveats, the present results document that although certain neuropsychiatric conditions are risk factors for impaired decisional capacity, there is considerable heterogeneity within each group in the range of capacity. Simple screening questions such as those used in the present study may be developed as a routine part of the consent process with any population. For those exhibiting difficulty answering these initial questions, more comprehensive evaluation and further educational efforts to enhance decisional capacity may be warranted.[2,7,32,33] Through such a multistage process, the likelihood that research participants are capable of making meaningful choices when consenting to participate in research will increase.

**Submitted for Publication:** June 30, 2004; final revision received October 20, 2004; accepted November 10, 2004.
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**Funding/Support:** This study was supported by grants S07 RR 18238, R01 MH64722, P30 MH66248, and P50 AG05131 from the National Institutes of Health, Bethesda, Md.
**Acknowledgment:** We express our gratitude to Margaret Thompson, BA, for her assistance with recruitment and data collection and to Kerstin Lynam, MBA, for assistance in obtaining grant support to fund this research.

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