

Assessing capacity to consent for research in cognitively impaired older patients

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Background: The number of clinical trials including older patients, and particularly patients with cognitive impairment, is increasing. While statutory provisions exist to make sure that the capacity to consent is assessed systematically for each patient, many gray areas remain with regard to how this assessment is made or should be made in the routine practice of clinical research.

Objectives: The aim of this review was to draw up an inventory of assessment tools evaluating older patients' capacity to consent specifically applicable to clinical research, which could be used in routine practice.

Methods: Two authors independently searched PubMed, Cochrane, and Google Scholar databases between November 2015 and January 2016. The search was actualized in April 2017. We used keywords (MeSH terms and text words) referring to informed consent, capacity to consent, consent for research, research ethics, cognitive impairment, vulnerable older patients, and assessment tools. Existing reviews were also considered.

Results: Among the numerous existing tools for assessing capacity to consent, 14 seemed potentially suited for clinical research and six were evaluated in older patients. The MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR) was the most frequently cited.

Conclusion: The MacCAT-CR is currently the most used and the best validated questionnaire. However, it appears difficult to use and time-consuming. A more recent tool, the University of California Brief Assessment of Capacity to Consent (UBACC), seems interesting for routine practice because of its simplicity, relevance, and applicability in older patients.

Keywords: aged, assessment tools, clinical research, decision-making capacity

Introduction

The prevalence of Alzheimer's disease (AD) and related disorders in the context of aging demographics is a major public health issue.¹ Dementia leads to several functional alterations responsible for a loss of bearings in time and space and impairment of the patients' capacity to perform activities of daily living or express their will without assistance.^{2,3} This progressive loss of autonomy drastically affects the life of patients (and those around them), making them vulnerable and reducing their quality of life.

One of the most important components of vulnerability in patients with cognitive decline is the loss of capacity to make decisions. This can progressively affect various domains of their everyday life and have implications in the legal or medical fields.^{3,4} The impairment of decisional capacity (DC) raises many questions for the patients' relatives or professional caregivers. According to a recent literature review, the prevalence of such impairment could reach 34% of hospitalized patients and up to 45% of patients in psychiatric settings.⁵

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In the case of alteration of their DC, the patients can easily find themselves deprived of fundamental rights. There is also a risk that they end up making decisions against their interest without realizing it. The loss of DC can, thus, affect the patients' autonomy and make them dependent on external help. Conversely, the DC of patients with mild cognitive impairment may also be excessively underestimated.^{6,7} In either situation, the potential legal or ethical consequences are considerable.^{3,4}

The field of clinical research is especially exposed to these risks. In spite of the existing bioethics laws and regulations designed to protect patients taking part in research,^{8,9} the means by which the inclusions to clinical trials are made can sometimes be put into question, especially regarding the evaluation of the patient's capacity to consent for research (CR). When the CR is in doubt, it is therefore common to consult a close relative such as the patient's support person, but there again, the means by which this person should be designated remain unclear, and the reliability of such surrogate consent is most often questionable.¹⁰⁻¹⁵

Various theoretical concepts have been developed for use in conceptualizing decision making specifically in informed consent contexts, merging from the fields of neuropsychiatry, psychology, sociology, or behavioral science.¹⁶ In the cognitive models, the consensus is that decision making is based on four different aptitudes.¹⁷⁻¹⁹ The patients need 1) to be able to understand the information and issues of the decision (comprehension), 2) to realize that the decision to be made applies to themselves and to personalize their decision in line with intimate values or beliefs (appreciation), 3) to be able to evaluate different alternatives and their consequences (reasoning), and 4) to communicate on a decision (choice). Furthermore, emotion and social factors also take a strong part in decision making.^{16,20,21} Short-term and semantic memory affect all four abilities but are more strongly associated with understanding and reasoning.^{22,23} Executive functions, which cover important domains such as attention, encoding of verbal and visual material, forward planning, organization, and cognitive flexibility, are also critical to decision making. They can be impacted even in early stages of AD- or Parkinson's disease-related cognitive impairment and alter understanding, appreciation, and reasoning.^{24,25} Finally, the expression of a choice can be influenced by language or behavioral and neuropsychiatric symptoms such as apathy.²⁶

There are two ways to assess DC in informed consent situations: assess cognitive capacities and their impairment (eg, mental status examinations and neuropsychological

instruments) and assess capacities as demonstrated within the context of content that is specific to the consent situation. However, usual global screening tests such as Folstein's mini-mental state examination (MMSE)²⁷ are indirect and, therefore, imperfect ways of inferring what a person might do if faced with the task of understanding or reasoning about being in a clinical trial study.^{28,29} Consequently, an objective and direct evaluation of patients' DC, in case of doubt as to the validity of the consent, ensures that the inclusion of subjects to clinical trials is ethical and respectful of their rights, which is the responsibility of researchers. However, it can be observed that research protocols are often vague on the means used to assess CR, suggesting that overall awareness of professionals and researchers, including those working in the field of dementia, is insufficient.

Previous reviews have essentially been focused on capacity to consent to treatment. Reviews focusing specifically on capacity to consent to research are scarce and seemed to have yielded only a few results in comparison to the numerous tools developed, especially in the psychiatric context.^{30,31} The aim of this review was to draw up an inventory of assessment instruments for evaluating the DC of older patients with cognitive impairment, which could be specifically applicable to the assessment of the CR.

Methods

Two authors (TG and OLS) independently consulted PubMed (Medline), Google Scholar, and the Cochrane databases in search for original articles describing tools for the assessment of DC. Existing literature reviews on the topic were also considered as additional information. The initial search was conducted between November 2015 and January 2016 and was actualized in April 2017.

The inclusion criteria were based on the tools themselves. To be included, the references had to make a description of tests specifically designed for assessing patients' DC, with a report of the methods for assessing validity and/or reliability (either from the original report or from other studies evaluating the same test). Second, a mention of applicability to research and to older people with cognitive impairment was sought.

Different search strategies were performed using in priority keywords from the MeSH thesaurus: "informed consent", "decision making", "neuro-cognitive disorders", "aged", "adult clinical protocols", and "research subjects". However, the following additional keywords completed the search strategy: "Alzheimer", "dementia", "protocol inclusion", "ethics", "consent for research", "consent to

research”, “inclusion in clinical trials”, “competency”, “capacity to consent”, “understanding”, and “neuro-psychological evaluation”. No language or publication date limit was set.

The article selection was based on titles, abstracts, and finally full text for relevant articles. Additional results were also retrieved from the bibliography of existing reviews. Second, the same two authors independently conducted the data extraction and the selection of suitable tests or tools for assessing patients’ CR. Finally, the results were combined, and consensus was reached through discussion between authors.

Results

The flow diagram in Figure 1 summarizes the number of articles accepted and rejected during the selection procedure. The search of the computerized databases identified a total of 226 articles. In the end, a total of 19 publications were identified as relevant to our research on instruments assessing DC for patients with cognitive disorders (Figure 1). In addition,

six literature reviews of instruments to evaluate CR were also considered as complementary information.^{30–35}

Thirty-eight instruments assessing DC were identified. However, the vast majority of existing tests were developed to assess the capacity of patients to consent to medical treatment and not for research purpose. For this particular context, 14 assessment tools were identified, the majority of which were initially developed or validated in psychiatric populations.^{30,32,34} The main characteristics of each test are summarized in Table 1. They differ by the method used (eg, self-administered questionnaire and structured interview), the abilities assessed (among the four dimensions of decision making), the population they were initially aimed for (sometimes focused on very specific populations), the administration time, and the robustness of their evaluation (validity and reliability) (Table 1).

In older patients with cognitive disorders, the following six tests have been evaluated, with variable consistency: the vignette method by Schmand et al,³⁶ the MacArthur

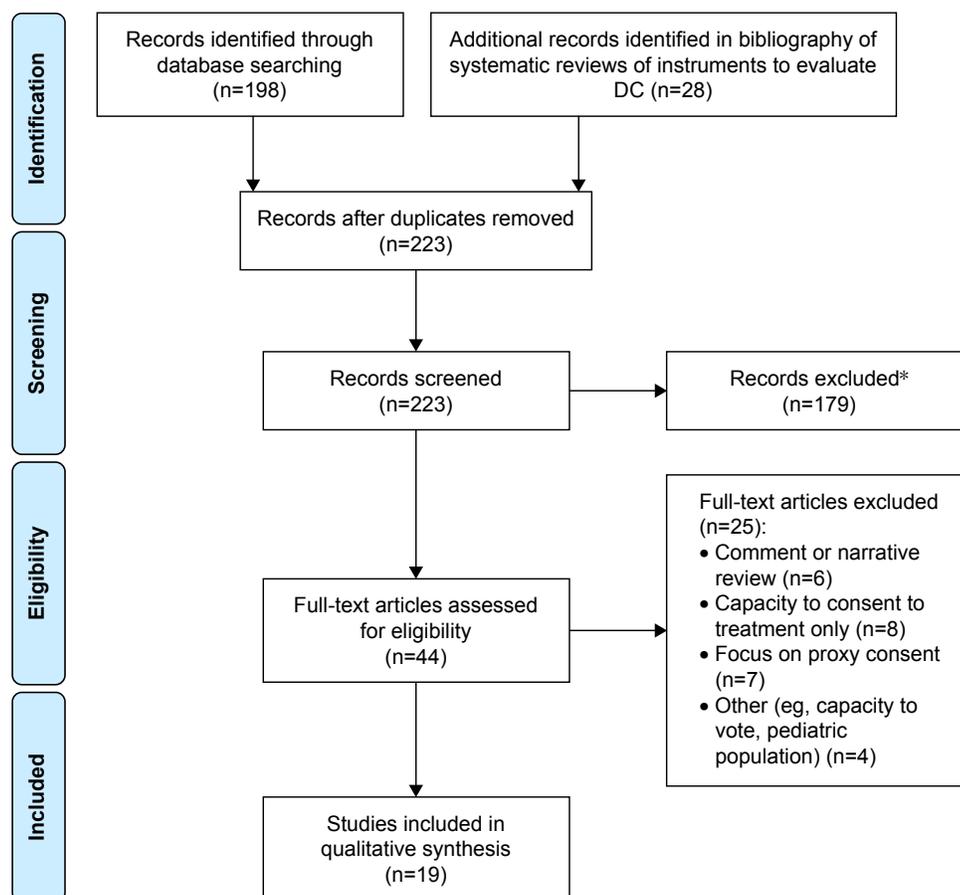


Figure 1 Flow chart of search results.

Note: *These were mainly comments, narrative reviews, or off-topic records.

Abbreviation: DC, decision capacity.

Table 1 Summary of included assessment tools (presented by year of publication)

| Assessment tool | Type | Abilities assessed | Administration time | Population | Validity | Internal consistency | Interrater reliability |
|------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|---------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| Two-part consent form ⁷⁶ | Self-administered questionnaire and semistructured interview | Understanding | Not reported | Psychiatric patients | Good agreement with expert judges; correlated with age, education, occupational level, and mental status | Test-retest $r=0.70-0.76$; | Interrater $r=0.94-0.96$; Kappa $=0.44-0.83$ |
| CIS ⁷⁷ | 15-item structured interview | Understanding, appreciation, reasoning and choice (four subscale scores) | Not reported | Patients undergoing electroconvulsive therapy | Correlation with the physician's judgment Pearson's $r=0.43-0.98$ | Cronbach's $\alpha=0.96$ | Interrater reliability was 0.95 for CIS total score excellent |
| Deaconess informed consent comprehension test ⁷⁸ | Structured interview Requires training | Understanding | <10 minutes | Trials evaluating anti-infective agents | Correlated with Wechsler Adult Intelligence Scale – Revised ($r=0.44$), reading ($r=0.38$), and education ($r=0.33$) | Test-retest reliability intraclass $r=0.79$ | Interrater $r=0.84$ |
| ESC ³⁸ | Five-item questionnaire delivered after information about the study, but before the formal consent process Requires training | Understanding | 5–10 minutes | Schizophrenia and HIV Also tested in 346 nursing home residents ⁴² | Correlated with MacCAT-CR Validity measured by item mapping with fit from 0.81 to 1.09 ⁴² | Not reported | Interrater reliability ($=0.81$) ⁴² |
| ICS ⁷⁹ | 36-item questionnaire Requires training | Choice, understanding, appreciation, and reasoning | Not reported | Schizophrenia | Correlated with the Brief Psychiatric Rating Scale $r=-0.17$ to -0.33 | Not reported | Not reported |
| Vignette methods described by Schmand et al (1999) ³⁶ | Vignettes, structured interview | Understanding, reasoning, and expression of a choice | 30–45 minutes | Older adults with or without dementia | Poor agreement with physician's judgment of competency; correlated with severity of dementia Kappa $=0.31$ | Cronbach's $\alpha=0.69$ | Not reported |
| CAT ⁸⁰ | Semistructured interview Requires training | Choice, understanding, appreciation, and reasoning | Not reported | Developed in primary care setting on a small patient sample | Good agreement with independent psychiatric assessment Kappa $=0.77-1.00$ | Not reported | Not reported |
| MacCAT-CR ³⁷ | 21-item structured interview | Appreciation, understanding, reasoning, and choice (four subscale scores) | 15–20 minutes | Developed initially on patients with mental illnesses (depression, schizophrenia) but also evaluated in dementia (Alzheimer's disease), ^{44,47} cancer, ⁸¹ HIV disease, diabetes, and control subjects | Correlations with Brief Psychiatric Rating Scale and MMSE; distinguishes between patients and control subjects Kappa >0.97 for each subscale ⁸¹ | Poor test-retest correlations: Kendall's Tau $=-0.15$ for reasoning, 0.26 for understanding, and 0.36 for appreciation ⁸² | High interrater reliability (ICC: 0.78–0.98) ^{44,47,83} Kappa $=0.53-0.79$ ⁸⁴ |

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|-----------------------------------------------------------|------------------------------------------------------------------------------------------------------------|----------------------------------------------------|----------------------------------------------|----------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|
| Quality of informed consent questionnaire ⁸⁵ | Self-administered 34-item questionnaire | Understanding (objective and subjective) | Mean completion time: 7.2 minutes (2.5–12.8) | Cancer patients | Consensus among independent experts: accuracy and comprehensiveness No correlation or agreement measure with expert panel conducted Correlated with psychopathology and cognitive impairment | Test–retest ICC: 0.66 for objective understanding and 0.77 for subjective understanding Cronbach's α : 0.83–0.88 | Not reported |
| CSA ⁸⁶ | 18-item structured interview (13 close-ended questions and five open-ended questions) Requires training | Appreciation | 10–20 minutes | Schizophrenia or related psychotic disorder and controls | | | Interrater percent agreement: 0.82–1.00 |
| Brief informed consent test, Buckles et al. ³⁹ | 11-item questionnaire (yes/no questions) Requires training | Understanding | 5–10 minutes | Older patients with dementia | Correlated with Clinical Dementia Rating (Spearman $r=-0.48$) and MMSE (Pearson $r=0.58$) Not compared with other tests such as MacCAT-CR Tested on 68 patients and correlated to psychiatric properties not given | Internal consistency: Cronbach's $\alpha=0.63$ or 0.70 (with one item removed) Not reported | Not reported |
| Capacity-to-consent screen ⁵² | 10-item questionnaire | Choice, understanding, appreciation, and reasoning | 20 minutes | Psychiatric populations | | | Not reported |
| UBACC questionnaire ⁴⁰ | 10-item questionnaire | Understanding, appreciation and reasoning | <5 minutes | Middle-aged and older outpatients with schizophrenia and healthy comparison subjects ⁴⁰ | Correlation with the MacCAT-CR scores Sensitivity 89% Specificity 100% | Internal consistency: Cronbach's $\alpha=0.77$ | Interrater reliability: ICC 0.84–0.98 |
| OACCR ⁴¹ | Four-item scale | Choice, understanding, appreciation, and reasoning | Brief, no time reported | Older patients in community and institutional settings | Validity evaluated in reference to the capacity to Consent Screen Score ⁵² Pearson's coefficient $r=0.939$ Sensitivity 99.2% Specificity 72.9% | Cronbach's $\alpha=0.85$ | Item-total correlation: 0.59–0.76 |

Abbreviations: CAT, capacity assessment tool; CIS, Competency Interview Schedule; CSA, California Scale of Appreciation; ESC, evaluation to sign consent; ICC, intraclass correlation coefficient; ICS, Informed Consent Survey; MacCAT-CR, MacArthur Competence Assessment Tool for Clinical Research; MMSE, mini-mental state examination; OACCR, older adults' capacity to consent to research; UBACC, University of California Brief Assessment of Capacity to Consent.

Competence Assessment Tool for Clinical Research (MacCAT-CR),³⁷ the evaluation to sign consent (ESC),³⁸ the brief informed consent test,³⁹ the University of California Brief Assessment of Capacity to Consent (UBACC) questionnaire,⁴⁰ and the older adults' capacity to consent to research (OACCR).⁴¹ These tools are described briefly hereafter in chronological order.

ESC

The ESC is a short questionnaire tailored to the research protocol.³⁸ The ESC presents the advantage of being short and simple to use. The patient reflects his understanding of the protocol by answering five questions, four of which require the assessor to make subjective judgments of the patient's capacity. However, the three other dimensions of DC assessment are not covered by this test. Furthermore, the evaluation may be at risk of examiner bias, as the scoring mainly relies on the subjective judgment of the examiner, without any explicit cutoff. The ESC was initially tested in schizophrenia and HIV patients but has also been evaluated in 346 older nursing home residents.⁴²

Vignettes method developed by Schmand et al

This method was developed in the 1990s and evaluated in aged Dutch people (70–90 years), who were cognitively intact ($n=176$) or had dementia ($n=64$; mostly AD).³⁶ Two vignettes were used as competency assessment instruments. A vignette is a description of an imaginary situation in which the subject is asked to decide on a proposed treatment or on participation in research. His/her understanding of the situation and the quality of the reasoning underlying that choice are tested by a short series of questions. The answers to the vignette questions were summed to form a competency score. The reliability (internal consistency) of this score was 0.82 for both vignettes combined. However, when assessing agreement between Schmand's vignette method and a physician's judgment in the group of patients with dementia, Cohen's kappa was only of 0.36 (fair agreement) and dropped to 0.04 (no agreement) when patients with "minimal dementia" were left out of the analysis.

MacCAT-CR

The MacCAT-CR was the most frequently cited existing tool, often referred to and used as a reference to assess capacity to consent to research and test the validity of other tools³⁷ as it is the most widespread and the most validated of all.^{3,30,32,43–45} It is a modified version of the MacCAT-T used to assess the

capacity to consent to treatment.⁴⁶ This is a 21-item structured interview with four subscales assessing the following four main dimensions of decision making: understanding, appreciation, reasoning, and expressing a choice. Each subscore is predictive of decision-making capacity. Thirteen questions are dedicated to understanding, three questions are dedicated to appreciation, four questions are dedicated to reasoning, and one question is dedicated to expressing a choice. Each item is scored 0 (inadequate), 1 (partially adequate), or 2 (adequate). Questions are tailored to the specific research context in which the patient is asked to participate. This test was developed in a wide variety of clinical situations and for different populations. Yet, the reliability and validation of derived versions are less established.³⁰ In particular, two groups of researchers adapted this test for use in patients with AD, in which they suggested dummy clinical trial protocols.^{44,47} The test comes with a user's guide and a precise rating manual. However, there is no threshold or limit score that would directly discriminate patients able to decide from those who are not. Rather, this tool was conceived as an aid to be used by the assessor for the appreciation of DC.³⁰ The other downsides of this test are its relative complexity, the need for specific training, the absence of specific cutoff scores, and the duration of the test of ~20 minutes, which could also be a barrier in the process of patient inclusions to clinical trials.^{30,48}

Brief informed consent test

This test was constructed to address the following eight elements of informed consent as stated in the Code of Federal Regulations:⁹ 1) explanation of the purposes of the research and the requirements of participation; 2) description of any reasonably foreseeable risks or discomforts to the participant; 3) description of any benefits to the participant or to others; 4) disclosure of appropriate alternative procedures or courses of treatment; 5) statement describing the extent, if any, to which confidentiality of records identifying the participant will be maintained; 6) for research involving more than minimal risk, an explanation/information as to whether any medical treatments are available if injury occurs; 7) contact information for the study investigator in the event of a research related injury to the participant and for questions; and 8) a statement that participation is voluntary and that refusal to participate will involve no penalty or loss of benefits. After a review process by ethical and research committees, 11 items were selected and closed-ended questions were used. This test shows only moderate correlation with the Clinical Dementia Rating scale (Table 1) and was not

evaluated against psychiatric expertise or other specific DC tools such as the MacCAT-CR.³⁹

UBACC

UBACC is a 10-item questionnaire.⁴⁰ This test uses a pragmatic approach using a teach-back process of the protocol and the potential risks and benefits of participating. The total score is determined by the accuracy of answers depending on expected answers for each question. It has the advantage of being short and does not require specific training. It can be tailored specifically to the clinical trial proposed to the patient. Yet, this tool does not evaluate the capacity to express a choice.⁴³ A validation study showed good performances of the UBACC in terms of external and internal validity, reliability, sensitivity, and specificity.⁴⁰ Although initially developed for all vulnerable patients, including those with schizophrenia, it has also shown promise in AD patients and showed good correlation with cognitive features such as verbal fluency and global cognition.⁴⁹ However, expression of a choice is not evaluated by this test. It has been translated and validated in different languages and should soon be recommended by European regulatory authorities.^{48,50,51}

OACCR

The OACCR was developed in nursing home residents and community dwelling older adults in South Korea.⁴¹ It was designed to cover the four dimensions of decision making with a short questionnaire of only four open questions. The strength of this questionnaire relies in its simplicity, which could make it interesting for use in routine practice. However, one could think such a simple test might not be enough to evaluate the complexity of the assessment of DC, and the validation procedure seems still insufficient, especially with regard to the gold standard chosen as reference. Rather than testing the correlation to psychiatric expertise or the MacCAT-CR (despite limitations enounced earlier), the authors have preferred to use the capacity-to-consent screen by Zayas et al,⁵² a test which is a less validated test.³¹ Finally, it is not clear whether an English version has been evaluated.

Discussion

In this study, we searched existing tools for assessing older patients' DC in the context of clinical research. Five reviews were identified.^{30,32-34,43} During our search, we listed 13 assessment tests specifically designed to evaluate the patients' capacity to consent to be included in a research protocol. Two of these appeared particularly relevant to us: the MacCAT-CR³⁷ and the UBACC.⁴⁰ No new instruments were

identified as having been developed in the past 6 years, and only two of the 14 were developed in the past 10 years.

While physiological aging does not normally affect communication and DC,^{34,48} many incident pathologies in aging, such as a decrease in sensory acuity, depression, stroke (especially in the case of aphasia), and of course dementia, can have a serious impact on DC.

There is no debate over the strong impairment of DC in severe stages of AD.^{28,53,54} Moreover, in the case of mild-to-moderate disease, many studies suggest that DC can be affected even at the early stages of cognitive decline.^{33,53,55-59} Understanding capacities would be affected the earliest, followed by reasoning and appreciation, while the capacity of choice would be preserved the longest.^{58,60} Indeed, understanding is mainly affected by an impairment of episodic and semantic memory, whereas reasoning and appreciation depend on both memory and executive functions.^{23-25,55,57}

Another particularity is that AD is often accompanied by anosognosia. Lack of awareness could alter the patient's capacity to anticipate and weigh the possible consequences of a decision or action (reasoning and appreciation). Patients may also paradoxically be able to reason situations for others but not as well for themselves. Lack of awareness is correlated with disease severity but can affect patients at an early stage. Some authors suggest using specific tests for anosognosia (such as the Anosognosia Questionnaire for Dementia⁶¹) when judging on a patient's competence, as awareness and DC could be affected differently in patients with cognitive impairment.⁶²

Many clinicians or researchers use their clinical impression or Folstein's MMSE²⁷ to give an opinion on the patients' DC. This attitude seems appealing, as it means there is no need for complementary investigations. In comparison with psychiatric expertise, this approach appears however imprecise.^{29,63} The interpretation of the results and the norms depend on the level of education of the patient and can thus vary from one patient to the another.⁶⁴ Additionally, besides extreme values, the MMSE score is not sufficiently reliable to evaluate the patients' comprehension and judgment ability.^{28,29} Moreover, there can be differences between individuals for a given MMSE score, and discrepancies can exist between the global assessment of cognitive functions and the DC of the patients as assessed by more specific evaluations.^{7,30} To a certain extent, this implies that the DC of patients can be affected, although the cognitive impairment remains mild, or oppositely, that the DC can sometimes be underestimated when the cognitive tests show greater impairment. Kim and Caine²⁸ have studied the reliability of Folstein's MMSE

to assess DC, in comparison to the MacCAT-CR, used as a reference. They concluded that MMSE was not a good predictor of incompetence. However, this test could still be useful if using two different thresholds: a score of >26 had a high sensitivity of 96%–100% to detect competent patients while a score of <19 had a specificity of 85%–94%.²⁸ The authors suggested that a score of >26 on the MMSE would allow to safely identify competent subjects with no need for further investigation.⁶⁵ In another study, Pucci et al⁶⁶ found that an MMSE score of ≤ 17 had a positive predictive value of incompetence of 95%, while only ~63% of patients above this threshold were rated sufficiently competent. Therefore, for patients with mild cognitive impairment (with MMSE values between 17 and 26), a gray area remains, with the need for more precise and specific assessment tools.

Standardized tools for assessing DC started to be developed in the 1990s.⁶⁷ We observed that the large majority of tests were developed to evaluate the patients' capacity to consent to a medical treatment or other everyday life situations, especially in the field of psychiatry.²⁰ However, there are some heterogeneities between schizophrenia and dementia with regard to DC⁶⁸ and clinical research is also a very specific domain. The distinction between consent to treatment and consent to research needs to be underlined. In the context of clinical trials, the patients need to be able to understand the aims of the research and other particularities such as randomization, the use of placebos, and the fact that they might not benefit from the treatment.⁶⁹ Patients with mild cognitive impairment may present with low understanding of the design, potential benefits, and risks of the study.⁷⁰ In fact, depending on the criteria considered, very few patients would be considered actually capable of giving consent with regard to the thresholds of the specific tests.^{55,60,68} However, patients with mild cognitive impairment remain able to participate in decisions affecting themselves.^{12,71} Among the numerous existing tests, only some^{36,40,51,72,74,75} enable simultaneous evaluation of the four dimensions of decision making (comprehension, choice, reasoning, and appreciation). Most of the tests only evaluate comprehension, while others are designed to evaluate other dimensions more specifically. Also, some tests explore certain components of understanding that are not studied by others. The notion of double blind is, for example, evaluated by the MacCAT-CR but not by the UBACC.

Another difficulty is that, during the evaluation of each tool, discrepancies in the evaluation of DC were found between the results of the tests and the point of view of experts.³⁰ Such differences could cause important interpretation

problems and complicate the development of assessment tools. For example, Schmand et al³⁶ have described a very low agreement between their vignette method and physicians' assessment ($\kappa = 0.04$ – 0.36) of capacity. While this initially appears like a flaw in the test's reliability, the authors attributed this to a lack of consistency of the subjective clinical evaluation and used this argument to warrant the use of their method.³⁶ Both psychiatric expertise and the large majority of assessment tools rely on subjective interpretation. This highlights the major difficulties of developing a reliable tool in the absence of an indisputable gold-standard evaluation. Many tools have been developed using the MacCAT-CR as a reference. Indeed, it is the most widely employed instrument and recognized as the most validated and reliable in this population.⁴⁵ However, it has limitations as a gold standard because it does not have a specific objective cut-point (clinical decision making is still required for interpretation) and was developed with reference to psychiatric expertise, which also lacks consistency. As there is currently no clear diagnostic reference to compare the reviewed diagnostic tests to, it becomes impossible to assess sensitivity and specificity of measures; this is also the main reason why the Cochrane systematic project was withdrawn from publication.³⁵ Furthermore, DC is ultimately a legal construct, which depends mainly on the external evaluation and also remains subjective, despite efforts toward standardization of procedures.

In this difficult context, the evaluation of interrater reliability appears very important, but this information was unfortunately lacking for six out of the 14 tests presented in Table 1. Among the six tools evaluated in the cognitively impaired geriatric population, interrater reliability was reported for only four and could be as low as 0.59 as for the OACCR.⁴¹

Following validation works from Kim et al⁴⁷ and Karlawish et al,⁴⁴ the MacCAT-CR can be applicable to the particular context of AD. However, in both of these studies, the MacCAT-CR tended to underestimate the patients' competency to decide, as compared to the judgment of experts.^{32,44,47} This could suggest that the MacCAT-CR is too "severe" for this type of population. However, this finding needs to be put into perspective, as it could also be argued conversely that the experts have overestimated the patients' competency, illustrating there again the interpretation problems due to the lack of a clear gold standard. In a study aiming to compare the DC of patients with schizophrenia and dementia, the same authors have developed a short three-item questionnaire derived from the understanding subscale of the MacCAT-CR, focused on understanding the purpose,

risks, and benefits of the protocol.⁶⁸ For a cut-point of 2.5, this simplified tool achieved a sensitivity of 100% and a specificity of 77.3% for detecting impaired understanding using the understanding subscale of the MacCAT-CR.⁶⁸ Such an approach could potentially help to rapidly discriminate patients with need for further assessment and make use of the MacCAT-CR more practical. However, this three-item questionnaire was only developed for the purpose of this study and would need further evaluation to be considered as a potential tool to be used independently.

Due to the prevalence of cognitive decline and multiple comorbidities in this population, older patients have, until recently, rarely been included in clinical trials – even though this age group accounts for a majority of overall medication consumption.⁷² Currently, clinical trials specifically oriented to aged patients are multiplying, especially in the field of dementia research. However, these studies are often forced to limit the inclusions to patients at very early and mild stages of the disease.⁷³ Scientific progress requires that clinical trials can be carried out and that potentially vulnerable patients can take part in the research in the most ethical and considerate way. Moreover, it appears important that patients recruited in clinical trials are representative of the target population. In order to improve the ethics of patient inclusion without altering participation rates to clinical trials, valid consent procedures are needed. In the event of incompetence, the means by which surrogate consent is used and the way the proxy is designated remain unclear.^{14,15,74,75} Finally, the awareness among professionals and researchers on this issue needs to be raised. Project reviewers and ethical boards should give particular focus to the procedures for patient inclusion when reviewing study protocols.

Disclosure

The authors report no conflicts of interest in this work.

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