ORIGINAL CONTRIBUTION

Screening for Cognitive Impairment in Older Individuals

Validation Study of a Computer-Based Test

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Objective: This study examined the validity of a computer-based cognitive test that was recently designed to screen the elderly for cognitive impairment.

Design: Criterion-related validity was examined by comparing test scores of impaired patients and normal control subjects. Construct-related validity was computed through correlations between computer-based subtests and related conventional neuropsychological subtests.

Setting: University center for memory disorders.

Participants: Fifty-two patients with mild cognitive impairment by strict clinical criteria and 50 unimpaired, age- and education-matched control subjects. Control subjects were rigorously screened by neurological, neuropsychological, imaging, and electrophysiological criteria to identify and exclude individuals with occult abnormalities.

Results: Using a cut-off total score of 126, this computer-based instrument had a sensitivity of 0.83 and a specificity of 0.96. Using a prevalence estimate of 10%, predictive values, positive and negative, were 0.70 and 0.96, respectively. Computer-based subtests correlated significantly with conventional neuropsychological tests measuring similar cognitive domains. Thirteen (17.8%) of 73 volunteers with normal medical histories were excluded from the control group, with unsuspected abnormalities on standard neuropsychological tests, electroencephalograms, or magnetic resonance imaging scans.

Conclusions: Computer-based testing is a valid screening methodology for the detection of mild cognitive impairment in the elderly, although this particular test has important limitations. Broader applications of computer-based testing will require extensive population-based validation. Future studies should recognize that normal control subjects without a history of disease who are typically used in validation studies may have a high incidence of unsuspected abnormalities on neurodiagnostic studies.

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SUBTLE DEFICITS in cognitive function among older individuals are common, and many older persons function in the community with unrecognized difficulties of attention, memory, and judgment.[1-4] Individuals with cognitive impairment who remain unevaluated cannot benefit from current or future treatments or from other interventions that might reduce disability and postpone the need for institutional care.[5] The early detection of currently irreversible neurodegenerative disorders is likely to assume great importance as new treatment modalities are developed and tested[6-11] in an effort to slow progression.[12]

As older individuals continue to work past the previous traditional age for retirement, it also becomes increasingly important to consider the public health implications of unrecognized dementia such as the increased risk of motor vehicle accidents among cognitively impaired drivers.[13-15] Since the prevalence of cognitive impairment increases dramatically after age 60 years,[3,4,16] older physicians, airline pilots, and members of other occupations are at higher risk of subtle cognitive impairments that threaten the safety of others in society.

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SUBJECTS AND METHODS

SUBJECTS

Fifty-two impaired subjects (mean age, 71.2±10.1 years [±SD]; mean education, 14.7±2.3 years) and 50 age- and education-matched, highly screened control subjects (mean age, 68.7±5.0 years; mean education, 15.4±2.3 years) were enrolled. General information gathered from all subjects included a detailed medical history, with particular emphasis on neurologic, psychiatric, or visual problems.

The impaired subjects were drawn from the most mildly affected of approximately 375 patients referred for evaluation to the Emory University/Wesley Woods Memory Assessment Clinic in Atlanta, Ga. For each of the impaired subjects, the history supported a decline in cognitive abilities, and a Global Dementia Rating Scale[37] score of 2, 3, or 4 was obtained. Each patient within the impaired group was also required to score below the published age-based "normal" range on one or more of the following neuropsychological tests: Verbal IQ of the Wechsler Adult Intelligence Test–Revised (WAIS-R),[38] Performance IQ of the WAIS-R, the California Verbal Learning Test,[39] the Logical Memory Subtest from the Wechsler Memory Scale–Revised (WMS-R),[40] or the Visual Reproduction Subtest from the WMS-R. *Normal* was defined as performance within 1 SD of the mean, using age-scaled norms. For subjects older than the upper limit of available age norms, *normal* was defined as within 1.5 SDs of the mean for the oldest age norms. Patients with clinically significant depression by the *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition* (*DSM-III-R*) criteria[41] were not included in the impaired group. All of the 52 impaired patients had some form of dementia: 47 patients were diagnosed with probable Alzheimer's disease by standard criteria,[42] and five patients were diagnosed with multi-infarct or vascular dementia.

The control subjects were selected from volunteers solicited by word-of-mouth and by newspaper advertisement. Potential control subjects were rejected if they had any history of psychiatric illness requiring medication or of any central nervous system disease, including prior head trauma. Since an unknown and potentially substantial proportion of the elderly who consider themselves "normal" may actually have significant cognitive impairments, volunteers were intensively screened using all routinely available diagnostic procedures as described below.

Each control subject received a neurological examination and was excluded if there were any findings suggestive of cerebral disease. Control subjects were required to score within the normal range for age on the Verbal IQ and Performance IQ from the WAIS-R, the Logical Memory and Visual Reproduction subtests from the WMS-R, and to exhibit unimpaired performance on the Wisconsin Card Sorting Test.[43,44]

Individuals who met these criteria then underwent a routine 32-lead electroencephalogram read by a board-certified electroencephalographer. Subjects with abnormal electroencephalographic findings were excluded from further study (mild unilateral or bilateral temporal slowing was accepted). Finally, all remaining potential control subjects underwent brain magnetic resonance imaging on a 1.5-Tesla system (Philips, Best, the Netherlands). Axial T_1- and coronal T_2-weighted images were obtained and read by a neuroradiologist. Subjects were excluded if they had significant focal abnormality, although isolated small white matter hyperintensities were accepted. Atrophy varied widely among the control subjects and was statistically correlated with aging.[45]

Of 96 persons who volunteered to be control subjects excluded were 23 based on telephone interview revealing prior cerebral disease or psychoactive medication, six by neuropsychological scores below criteria, five by ab-

Despite the increased prevalence of cognitive impairment among the elderly, there is a decline in referral and treatment rates for mental impairments in persons over 65 years old.[5] While neuropsychological assessment is the most rigorous criterion standard for detecting and quantifying cognitive deficits, it is time intensive and expensive, requiring an average of 6.5 hours to interview, test, score, and report on a single patient, at an average cost of over $700.[17] Brief screening techniques that can be applied in the context of providing primary care are needed, as recommended in "Healthy People 2000."[18] Rapid, accurate screening tests for cognitive impairment would permit clinicians to direct at-risk individuals toward more complete neuropsychological testing, diagnostic neuromedical evaluation, and, if necessary, away from responsibilities that require full cognitive competency.

Although many conventional examiner-administered screening instruments have been proposed and tested,[19-24] computer-based testing has several potential advantages as a screening tool.[25-31] Self-administered, computer-based tests require minimal technical skill on the part of the administrator yet provide highly reproducible testing conditions. Test items can be generated randomly when necessary, or presented in creative audiovisual formats. Raw data may be scored quickly and accurately, and response latencies are easily recorded. Immediate feedback can be provided to subjects, and results can be rapidly reported to those interpreting the test. All of these features can maximize efficiency of use while minimizing the time investment of staff members, thus increasing the likelihood that such tests would actually be used in the offices of primary care providers if they were available and valid.

There are also disadvantages of computer-based testing. There is a strong emphasis on visual presentation

normal electroencephalographic findings of uncertain significance,[46] and two by occult strokes on magnetic resonance imaging scan. Two others could not complete the magnetic resonance imaging owing to claustrophobia. Five subjects dropped out of the testing protocol owing to personal or family illness, and three subjects dropped out without explanation.

TESTING PROCEDURE

The ACS is a computer-based, self-administered, multiple-choice test programmed in BASIC and designed for the MS-DOS environment. Minimum computer requirements are 512 kilobytes of memory, a hard disk, and a color graphics display monitor. The ACS begins with instruction and practice questions to determine that the subject is capable of responses using the keyboard. The ACS presents subtests that have been modeled after published neuropsychological tests, although they do not include specific items from these tests. Like many screening tests, the ACS is designed to cover major functional domains of intact adult cognition such as attention, verbal ability, visuospatial ability, and memory (**Table 1**). Keyboard response using only the numeric keypad, backspace, and enter keys is required. The ACS takes approximately 60 minutes in unimpaired individuals. Additional data on ACS design, rationale for subtest selection, and test-retest reliability are available on request from Powell Associates, a private consulting firm in Cambridge, Mass.

In this study, the test was explained by a geriatric nurse-practitioner (J.M.H.) who started the examination and was present nearby (but not in the same room) to offer assistance. Prior to starting the test, visual acuity was measured with a near card and corrected visual acuity of at least Jaeger 5 was documented in each subject. Conventional neuropsychological tests commonly used in the community to assess the cognitive domains tested by the ACS were administered to all subjects within 10 days to measure construct validity of individual ACS subtests (Table 1). The conventional neuropsychological tests were administered prior to the ACS in most cases, but occasionally the order was reversed.

Development of the ACS was funded by the Risk Management Foundation of the Harvard Medical Institutions through a contract with Powell Associates. We were subcontracted to quantify the validity of the test with written assurance that our data would be published independently. Funding was not implicitly or explicitly linked to results of the study or endorsement of the test. No one in our Program is insured by the Risk Management Foundation or is professionally affiliated with any of the test developers.

Scores on the computer-based test are automatically calculated for each subtest and for the total score, which is the sum of all subtest scores. Prior to analysis, frequency plots of the total score and of each subtest score were graphed to check the validity of a gaussian (normal) distribution assumption (histogram of total scores is presented in the **Figure**). To examine criterion-related validity,[47] scores were analyzed to determine how accurately the ACS distinguished the impaired from the control group. Construct validity was assessed by correlation of ACS subtest scores with domain-related conventional neuropsychological test scores. Threshold analysis of ACS total scores was performed to determine the cut-off score that optimized sensitivity and specificity.

Group differences in sex and keyboard experience were compared using χ^2 tests. The ACS scores between impaired and control subjects were compared using a two-tailed Student t test. Logistic regression analysis was used to predict impairment using the ACS score and controlling for sex and keyboard experience. Correlations between ACS subtests and conventional neuropsychological tests were obtained using Pearson product-moment estimates.

of stimuli, and patient response modes are limited. In most available tests, there is a heavy reliance on multiple-choice formats, and responses are indicated by a simple manual response, such as a keyboard, which may be unfamiliar or uncomfortable for older or less well-educated persons. Instructions are generally presented in the form of text material on a visual display, offering disadvantages to those with impaired visual acuity or lower reading ability. Many individuals are unfamiliar with computers and inexperienced in their use, and the anxiety of such individuals could diminish their test performance. However, appropriate orientation of patients to computer use as well as the development of more "user-friendly" computer-based tests is likely to alleviate this problem. Even among individuals with little exposure to computers, it has been shown that minimal practice periods can overcome initial differences in anxiety and mechanical facility.[32,33]

Recently, the Risk Management Foundation of the Harvard Medical Institutions, which offers malpractice insurance to over 5000 physicians and 14 institutions, funded the development of a computer-based neuropsychological screening instrument, originally designed to screen older physicians for cognitive impairments and their presumed consequent increase in malpractice vulnerability. Normative data on this test, designated the Assessment of Cognitive Skills (ACS), has been gathered in 1100 physician volunteers,[34-36] and the test is now being considered for use as a screening instrument in the general population. This article describes an independent validation study of the ACS involving carefully selected samples of impaired and unimpaired elderly nonphysicians. This study does not endorse the ACS, but it seeks to describe its advantages and limitations as a screening test. The methods employed in this evaluation may

Table 1. Correlation Coefficients Between ACS Subtests and Conventional Neuropsychological Tests*

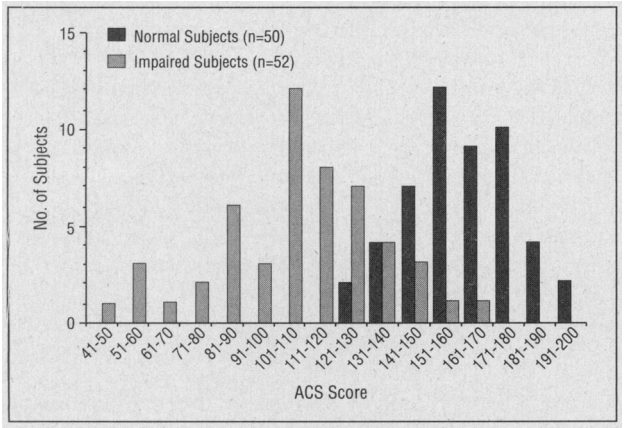
Cognitive Domain	ACS Subtests†	Conventional Test Measuring Similar Cognitive Attributes	Correlations of CNT With Relevant ACS Subtests‡
Attention	Mathematics	WAIS-R Mental Arithmetic	.62§
	Continuous performance	WAIS-R Mental Arithmetic	.36
	Digits forward	WAIS-R Digit Span	.43§
		WAIS-R Mental Arithmetic	.34§
	Digits reverse	WAIS-R Digit Span	.56
		WAIS-R Mental Arithmetic	.58
Executive Function	Rule identification	Wisconsin Card Sort	.43
Verbal Function	Analogies	WAIS-R Similarities	.41
Visuospatial Function	Cubes	WAIS-R Block Design	.49
	Clocks	WAIS-R Block Design	.41§
	Visual matching	WAIS-R Picture Completion	.50§
Verbal Memory	Story recall-immediate	WMS-R Logical Memory, Immediate	.63
	Story recall-delayed	WMS-R Logical Memory, Delayed	.63
	Word recognition	WMS-R Logical Memory, Immediate	.68
	Address recall	WMS-R Logical memory, Delayed	.48
Visuospatial Memory	Tic-tac-toe	WMS-R Visual Reproduction, Immediate	.50

*ACS indicates Assessment of Cognitive Skills; CNTs, conventional neuropsychological tests; WAIS-R, Wechsler Adult Intelligence Test–Revised; and WMS-R, Wechsler Memory Scale–Revised.

†An additional ACS subtest measuring Reaction Time is not listed here since this test was not performed by any "conventional" method that would permit validation. Some ACS subtests were presented in two forms, and, in those cases, only the first presentation is listed here and used in the correlational analysis.

‡For all correlations, $P<.001$.

§Value represents the highest correlation between this ACS subtest and any of the CNTs.



Histogram of the Assessment of Cognitive Skills (ACS) scores.

provide a starting point for rigorous validation of computerized cognitive tests among older persons.

RESULTS

ACCURACY AND PREDICTIVE VALUE OF THE ACS

Means of the ACS total scores obtained by the control subjects (160.7±16.8) and the impaired patients (107.7±26.1) were significantly different ($P<.001$). There were also significant group differences (all at least $P<.01$) for each of the ACS subtests and each of the conventional neuropsychological tests (CNTs), with the impaired group performing more poorly. **Table 2** shows the sensitivity and specificity of the ACS total score for accurate discrimination of impairment in the 102 subjects tested. The minimum number of misclassifications occurred using a cut-off score of 126 and above to designate "normal." As shown in Table 2, in actual practice, the cut-off score may be raised to increase the sensitivity of the test or lowered to decrease the number of false-positives.

Although matched for age and education, the control group had significantly more females ($P<.04$) and prior keyboard experience ($P<.001$) than the impaired group. However, logistic regression analysis revealed that neither sex nor prior keyboard experience significantly altered the predictive power of the scores.

Current estimates of the prevalence of dementing illness among the elderly range from 2% to 47%, depending on the investigator and the age group.[1,3,4,48] We conservatively estimated a prevalence of 10% and used this figure to calculate a predictive value positive and negative for each ACS score (Table 2).

The correlation coefficients between scores obtained on each ACS subtest and its domain-specific conventional neuropsychological test were also calculated (Table 1). The correlations ranged between .34 and .68, all of which were statistically significant ($P<.001$). However, for 11 of 16 of the ACS subtests, the correlation with the CNT designated as measuring similar cognitive attributes was not the highest correlation. For example, although tic-tac-toe, a test of immediate visual memory,

Table 2. Sensitivities, Specificities, and Predictive Values of the ACS With Various Cut-off Scores*

Total ACS Cut-off Score	Sensitivity	Specificity	Misclassifications	PV (+)†	PV (−)†
<121	0.71	1.00	15/102=0.15	1.0	0.97
<126	0.83	0.96	11/102=0.11	0.70	0.98
<132	0.85	0.92	12/102=0.12	0.54	0.98
<141	0.90	0.86	12/102=0.12	0.42	0.99
<147	0.94	0.78	14/102=0.14	0.32	0.99
<159	0.98	0.56	23/102=0.22	0.20	0.99
<163	1.00	0.42	29/102=0.28	0.16	1.0

*ACS indicates Assessment of Cognitive Skills; PV, predictive value positive (+) and negative (−), respectively.
†Predictive values are based on an estimated dementia prevalence of 10%.

had a correlation of .50 with WMS-R Visual Reproduction, Immediate, tic-tac-toe also showed a correlation of .52 with WAIS-R Block Design, .50 with WAIS-R Picture Completion, .52 with WMS-R Logical Memory, Immediate, and .54 with WMS-R Logical Memory, Delayed. In this case, tic-tac-toe correlated highly with a variety of tests, all of which depended on visuospatial ability and memory. In other cases, however, ACS subtests were significantly correlated with CNTs that seemed less functionally related. For example, Cubes had a correlation of .49 with its similar CNT, WAIS-R Block Design, but also had a correlation of .51 with WAIS-R Similarities, a verbal test of inferential ability.

COMMENT

ACS VALIDATION

These data suggest that the total score of the ACS computer-based screening test accurately distinguished patients with mild-to-moderate cognitive impairment from age- and education-matched normal control subjects, ie, that the ACS has criterion-related validity in the subgroups that are examined in this study. The choice of cut-off score is important since raising the cut-off score decreases the number of false-negatives but increases the number of false-positives. For example, using a cut-off score of 126, the ACS had a sensitivity of 0.83 and a specificity of 0.96. Based on a hypothetical 10% prevalence of cognitive impairment among the elderly, the estimated predictive value positive of the ACS for this cut-off score was 0.70, suggesting that of every 100 persons scoring lower than the cut-off, 70 would be correctly identified as impaired. The estimated predictive value negative of the ACS for the same cut-off score was 0.96, indicating that of 100 people scoring higher than the cut-off, only four will be incorrectly labeled as normal. The actual predictive value positive of this test would probably be lower among individuals under 65 years of age in whom the prevalence of cognitive impairment is thought to be less than 5%.

The correlations between ACS subtests and designated, similar conventional neuropsychological tests were significant. However, convergent-divergent construct validity was not supported in that most of the ACS subtests were related at least as strongly to other, less similar CNTs as they were to the CNT designated as most similar. This raises questions about the specificity of neuropsychological functions tapped by particular ACS subtests and cautions against the use of individual subtests to make inferences about specific intellectual abilities. Moreover, it is generally agreed that screening tests with excellent efficiency when applied to highly selected individuals can perform much more poorly in an unselected population.[24] Thus, even with favorable sensitivity and specificity, the validation of this test must be considered preliminary. Racial and socioeconomic heterogeneity, limited education, test anxiety, lifelong learning disabilities, static neurologic impairment, depression, or medication effects are far more common in the general population than in this study sample and would almost certainly increase the error variance of the ACS. Additional validation studies based on a representative sample of community-dwelling elderly would certainly be necessary before the ACS or any new screening test could be accepted for general clinical use.

The definition of normal control groups in cognitive studies of aging is controversial[49] and, to our knowledge, ours is the first neuropsychological test validation study to apply such rigorous standards to the selection of the normal control population. In our population, even after telephone screening of volunteers, 13 (17.8%) of 73 potential "normal" control subjects were excluded by unsuspected abnormalities on cognitive testing, electroencephalograms, or magnetic resonance imaging scans. Many conventional neuropsychological instruments do not have norms for older age groups, and, even when norms are available, their validity may be questionable since their "normal" populations are not fully evaluated to rule out unsuspected abnormalities that might cause subtle cognitive impairment. The control data in this article were not gathered from a representative popula-

tion of older individuals but, rather, from a population of volunteers. Nevertheless, these results suggest that in older age groups in which the prevalence of cognitive impairments is high,[3,4,16] potential subjects must have extensive evaluation before being included in a "normal" control group that is being used to validate clinical instruments or to establish norms.

APPLICATIONS OF COMPUTER-BASED SCREENING

A large number of examiner-administered instruments are currently used to screen the elderly for cognitive impairment.[19,50-52] The most popular of these, such as the Folstein Mini-Mental State Examination,[53] and the Short Portable Mental Status Questionnaire,[54] are brief and require little training to administer but are insensitive to mild impairments or to fluctuations in performance.[55-60] Other notable brief instruments, such as the Mattis Dementia Rating Scale[61,62] and the recently developed CERAD (Consortium to Establish a Registry for Alzheimer's Disease) battery,[63] are designed to measure a wide range of cognitive performance in identified patients rather than screen for cognitive impairments within the community.

Computer-based neurobehavioral tests have been most vigorously applied to studies of cognitive and human performance measures associated with unusual environmental conditions[30,64-66] and exposure to neurotoxins.[26,67-73] Despite the potential advantages of computer-based administration, there have been only a few systematic applications of automated testing, scoring, or diagnosis in the elderly.[21,74,75] Brief computer-based tests have been administered to both demented patients[25,69,76] and minimally screened, presumably normal older subjects,[27] but evaluation of test validity was limited in these cases. An innovative computer-based testing system with particular emphasis on ecologic or "face" validity of the memory tasks has been designed to investigate the controversial phenomenon of age-associated, nonpathological memory impairments.[77,78] This test has been standardized in thousands of apparently normal older persons in several countries,[79-82] but in these studies the presumably normal control subjects were also not stringently screened to detect those with subtle dementia. A recent review[83] describes many of the available computer-based neuropsychological tests.

Despite the encouraging evidence of validity in this preliminary study, a number of important concerns may be raised about the ACS. This version of the ACS required 1 hour for most unimpaired subjects and much longer for some patients; thus, it was not an optimal length for a screening tool. Patients with cognitive impairments had some difficulties learning the keyboard input despite the practice items provided at the start of the test, and their frequent expressions of anxiety and frustration made it clear that the test was an unpleasant experience for them. The heavy reliance of the test on reading skills is consistent with the original design of the test for use in physician populations, but this feature makes the test less useful in educationally disadvantaged populations.

In our study, analysis of the data using keyboard experience as a covariant did not alter the predictive accuracy of the test, and this is consistent with prior studies[33] showing that brief keyboard practice can overcome errors due to unfamiliarity. However, keyboard input is also likely to introduce much more variance among educationally and culturally less homogeneous populations.[80,84-87] We believe that some of these limitations may be overcome by creating shorter computer-based testing instruments that use touch-screens, verbal responses, or that monitor movements of the head, eyes, or limbs.[28,80,88]

SCREENING THE AGING PROFESSIONAL FOR COGNITIVE IMPAIRMENTS

The ACS is unique among computer-based tests in that its original development was funded by a malpractice insurance company to screen aging physicians for cognitive impairments that might signal risk for medical malpractice. Several logical links remain unsupported in this particular rationale that illustrate the problematic nature of attempting to screen aging professionals for diminished competency. For example, there are no data to suggest that aging physicians as a whole are at increased risk for physician errors, that malpractice suits against elderly physicians are related to cognitive impairments, or that practicing physicians with mild cognitive impairments make more physician errors. Neither the ACS nor any other neuropsychological instrument has been validated in impaired physicians, although norms for a large population of presumed normal older physicians have been gathered.[34]

In the absence of meaningful data of this type, discussion of even voluntary use of a cognitive screening test will arouse legitimate resistance among physicians or any other occupational group. Any notion of mandatory physician testing with such an instrument by the insurance industry would evoke profound legal and ethical questions: Should screening of only aged physicians be considered age discrimination? If so, should physician screening for cognitive impairment extend into younger age groups and be broadened to detect cognitive impairments associated with alcoholism, drug abuse, depression, acquired immunodeficiency syndrome, or head trauma? Should the privilege of malpractice insurance coverage (and indirectly the privilege of medical practice) depend on screening by an industry that is inherently more interested in sensitivity than specificity? If physicians at risk do need to be screened in some way, what should be the role of current licensing boards?

In our society, military commanders[89] and airline pilots[90,91] undergo mandatory retirement or demotion after a certain age, despite allegations and that such policies violate the rights and squander the skills of the elderly. Protecting the rights of older individuals to continue working in responsible positions, while at the same time protecting society from errors due to cognitive impairment, is a difficult task. It could be argued that physicians; pilots; military, political, and business leaders; and perhaps anyone who drives must be held to a high standard of cognitive competency regardless of age. If so, then the issue of screening among the elderly becomes urgent since the prevalence of cognitive impairment increases so dramatically between the sixth and eighth decades.[4,16]

The American Medical Association, Chicago, Ill, reports that there are 90 406 practicing physicians over the age of 60 years.[92] Older physicians typically remove themselves from high-risk activities toward the end of their careers, but even if the prevalence of cognitive impairment is only 5% in this age group, it may be estimated that there are over 4500 practicing physicians with some degree of cognitive impairment in the United States. While competent medical practice is surely too complex to be policed by cognitive fiat, as the demographic profile of our society changes into one in which those over 65 years old will represent 13.9% of the American population by the year 2010,[93] the issue of screening for cognitive compromise must be addressed, not just in medicine but throughout our society.

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