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Brain Health: The Importance of Recognizing Cognitive Impairment: An IAGG Consensus Conference

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Abstract

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Cognitive impairment creates significant challenges for patients, their families and friends, and clinicians who provide their health care. Early recognition allows for diagnosis and appropriate treatment, education, psychosocial support, and engagement in shared decision-making regarding life planning, health care, involvement in research, and financial matters. An IAGG-GARN consensus panel examined the importance of early recognition of impaired cognitive health. Their major conclusion was that case-finding by physicians and health professionals is an important step toward enhancing brain health for aging populations throughout the world. This conclusion is in keeping with the position of the United States' Centers for Medicare and Medicaid Services that reimburses for detection of cognitive impairment as part the of Medicare Annual Wellness Visit and with the international call for early detection of cognitive impairment as a patient's right. The panel agreed on the following specific findings: (1) validated screening tests are available that take 3 to 7 minutes to administer; (2) a combination of patient- and informant-based screens is the most appropriate approach for identifying early cognitive impairment; (3) early cognitive impairment may have treatable components; and (4) emerging data support a combination of medical and lifestyle interventions as a potential way to delay or reduce cognitive decline.

Keywords

Cognitive impairment; Alzheimer disease; case finding; cognitive frailty; MCI

Cognition (the ability to learn, solve problems, remember, and appropriately use stored information) is a key to successful health and aging. A variety of conditions, many age-associated, adversely affect cognition. After the age of 70, numerous studies suggest that approximately 16% of persons have mild cognitive impairment (MCI) and 14% experience dementia. Approximately two-thirds of persons with dementia identified in population studies have Alzheimer disease (AD), either alone or in combination with other diseases. Because of the importance of the maintenance of cognitive health or brain health to both the individual and society, the International Association of Gerontology and Geriatrics (IAGG) and its Global Aging Research Network (GARN) convened an expert consensus panel to (1) determine the role of screening and/or case-finding to identify early cognitive impairment, (2) establish the minimum workup/advice that providers should give to a person with early cognitive impairment, (3) explore if the management of persons with subjective cognitive impairment should differ from that of persons with objective cognitive impairment, and (4) decide if cognitive frailty (a mixture of both mental and physical frailty) is a useful concept for research and clinical care. 10–12

An expert panel (referred to hereafter as "panel"), including neurologists, psychiatrists, geriatricians, social workers, and psychologists, was convened in St Louis, MO, in March 2015. The methodology followed a modified Delphi approach, which has been used previously to obtain consensus. 13,14 Before the conference, the panelists were surveyed using a series of questions pertinent to the objectives. During the panel meeting, the results of the survey were made available to the participants, along with results of focus groups of persons with dementia (n = 6), care partners (n = 8), and staff and volunteers (n = 9). The panel discussed in detail several key areas: Preferred terminology for early cognitive impairment; the distinction between screening and case-finding; screening instruments; post-

screening recommendations, including the role of antidementia drugs and treatment of potentially remediable components of cognitive impairment, possible nutritional and exercise (physical and cognitive) interventions, and utility of biomarkers for etiological diagnosis; the interaction between physical and cognitive failure; and possible next steps. A draft manuscript was then developed, circulated, and revised until the panelists arrived at consensus on the content.

Cognition is a Key to Good Health

Cognitive impairment is recognized as being either syndromic (eg, MCI, subjective cognitive decline, mild neurocognitive disorder, or cognitive frailty) or etiologic (eg, prodromal AD or early symptomatic AD). ¹⁵ The premeeting survey results identified that 60% of participants favored MCI as the term of choice, but panel members recognized the importance of framing the issue in the more positive terms of "cognitive (brain) health" to reduce public fears that may impede early detection and to encourage positive steps toward preserving cognitive function throughout the life course.

A stimulus in the United States toward providing guidelines relative to the recognition and management of cognitive health is the creation of a new Medicare benefit, the Annual Wellness Visit (AWV), under the Patient Protection and Affordable Care Act of 2010. 16 Among the reimbursable components of the AWV is detection of any cognitive impairment. In a 1996 study, physicians at the Mayo Clinic in Minnesota found the Mini-Mental State Examination (MMSE), 17 in 4000 persons 60 to 102 years of age to be of little value from the physician's point of view. 18 On the other hand, in southern France, family practitioners have found a very brief screen for memory problems and physical frailty to be highly useful to determine need for specialist referral when coupled with the ability to refer patients to a specialty clinic for further evaluation. 19 Screening for cognitive impairment has been carried out in primary care and community settings. 20–23

Cognitive impairment and dementia, when present, are either not recognized or recognized and not documented, in more than half of patients seen by primary care physicians. ^{24–28} The US Preventive Services Task Force, using a systematic review, determined that, "there is no empirical evidence that screening improves decision making." ²⁹ We note that this conclusion was based on limited studies reporting health outcomes in persons with dementia. The Gerontological Society of America (GSA) has issued a report providing 9 potential benefits of early diagnosis of dementia (https://www.geron.org/images/gsa/documents/gsaciworkgroup2015report.pdf). The GSA report also provided a 4-step approach to the diagnosis and management for detection of cognitive impairment and/or dementia, while recognizing that the approach still requires validation.

The panel recognized the important public health distinction between screening and case-finding. By definition, screening is universal and involves a brief assessment of all individuals within a certain category (for example, all of a certain age). It is well-established that the strongest risk factor for AD and other dementias is age. ³⁰ Although the panel was split on whether universal screening should be carried out, many members supported 70 years as an appropriate age threshold for screening. The focus groups (persons with

dementia, care partners, and direct practice staff and volunteers) were generally supportive of universal screening with several caveats, including the need for standardization of screening tools and adequate training for the provider administering the screening tool. Interestingly, the focus groups believed that screening at age 70 years was too late and advocated for earlier (by age 55 years) screening. In contrast to screening, case-finding is the assessment of a subgroup of individuals identified on the basis of known risk factors (eg, subjective cognitive concerns or family history of dementia) to be carried out by physicians and other health professionals. Table 1 depicts the way in which screening for cognitive impairment and dementia might fulfill the World Health Organization (Wilson's criteria) guidelines for screening.

The IAGG panel strongly endorses the viewpoint that international studies must determine the most cost-effective approach to identification and management of cognitive impairment in different settings and populations. However, like the GSA, the panel determined that, at a minimum, case-finding by physicians and other health professionals is important to enhance brain health throughout the world.

Screening Instruments

More than half of the panelists believe that an ideal screening instrument should be less than 5 minutes, although 5 to 7 minutes for screening was also considered reasonable. A number of validated screening instruments are available (Table 2). Of these, the Ascertain Dementia 8 (AD8) is an informant-based screening tool, which also may be useful in patients with MCI. ^{31–34} The items in the AD8 address memory, temporal orientation, judgment, and function. It has a sensitivity of 85% and specificity of 92%. Informant report has a better association with disease than self-rated report. ³⁵ The AD8 has been validated in Korea, Brazil, Spain, Japan, China, and Taiwan. ^{36–41}

A number of objective screening tests are available. The MiniCog meets the criterion of taking less than 3 minutes to administer. ^{42–45} The Rapid Cognitive Screen (RCS), developed from the Saint Louis University Mental Status (SLUMS) examination, also takes less than 3 minutes and validations are available in 2 studies. ⁴⁶ SLUMS has excellent receiver operating curves to distinguish both MCI and dementia. From an international perspective, the SLUMS is available in 24 languages (http://aging.slu.edu/index.php?page=saint-louis-university-mental-status-slums-exam). ^{47–49} "The 5-word test" has been validated in AD (specificity 87%). It has a positive predictive value of 83% and a negative predictive value of 93%. ⁵⁰ It takes 2 minutes to administer and is widely used in France. The panel agreed that all of these tools, as well as others, were acceptable for screening and selection should be left to the discretion of the provider.

Figure 1 illustrates that screening implementation requires a variety of components to allow for successful administration. These include training of the physicians and other health care professionals who administer the instrument, appropriate preparation of the patient/informant, immediate follow-up, and later follow-up.

Screening is typically accomplished by a simple test with a single score at a single point in time, to identify those patients who deserve a more complete diagnostic assessment by an

expert clinician. An individual's performance at a single point in time provides no information about the course of his or her cognitive functioning over time. The diagnosis of the progressive dementias, such as probable AD, depends on the patient experiencing cognitive decline over time. At the initial assessment, this information is typically obtained from the history. Ideally, decline should be identified based on serial objective assessments (repeated cognitive testing) over time (Figure 2). By using a well-validated cognitive test with established normative values for a range of age and educational groups, the clinician can compare a given patient's actual performance on the test, even on a single occasion, with the expected values for an individual of the same age and education. Test performance below the expected range strongly suggests that decline has occurred.

An example of an optimal, 2-pronged, approach to assessment might include administering an objective test to the patient, while the care partner or informant completes a questionnaire such as the AD8. Overall an "ideal" screening tool should be brief, have no copyrighted costs, and be able to be administered by any appropriately trained individual. There are limitations of many screening instruments in low education/illiterate populations. In addition, there is a need for culturally fair instruments.

The use of biomarkers (Table 3) for etiological diagnosis furthers our understanding of disease trajectories, but should be limited to use by specialists after an extensive clinical evaluation. ^{51–55} This emerging area of interest has led to different opinions from the National Institute on Aging/Alzheimer's Association and the International Working Group as to the role of biomarkers in the clinical evaluation of the patient. ^{56–58}

Potential Benefits of Early Diagnosis of Cognitive Impairment

When screening or case-finding reveals cognitive impairment, the health care professional can take the appropriate steps toward diagnosis and treatment. When testing fails to find cognitive impairment, this reassurance allows persons to re-focus on enjoying their "brain health." A negative screen may bring relief to older persons who fear that their normal agerelated cognitive changes represent the beginnings of AD.

Whether or not the screening information is shared with the patient and family, physicians and other health professionals should know that their patient is cognitively impaired. Management of chronic medical conditions requires the patient to enter into an active partnership with his or her health care professionals to obtain the best outcome. Besides failing to take their medications, cognitively impaired patients often fail to carry out other simple instructions from their physicians. These patients may not understand the explanation of their disease given to them by their physician or its implications. The same may be true of family members who are present when the diagnosis is given. ⁵⁹ Therefore, the clinician delivering the diagnosis should check for comprehension in both the patient and family members.

There also are numerous potentially reversible causes of cognitive impairment, including some which are clearly treatable when diagnosed early. These include anticholinergic medications, $^{60-62}$ polypharmacy, 63,64 depression, 65 metabolic disorders such as hypothyroidism and hypercalcemia, 66 normal-pressure hydrocephalus, 67 space-occupying

lesions in the brain, infections, and sleep apnea. 68,69 Defects in vision and hearing can lead to poor performance on cognitive screening and prolonged sensory isolation can result in cognitive impairment. 62

Patients with white matter hyperintensities on magnetic resonance imaging (MRI), suggestive of ischemic brain damage, may have treatable conditions that when controlled could slow down further ischemic brain damage and possibly the development of AD.^{70–73} These include hypertension, diabetes, hyperlipidemia, smoking, and atrial fibrillation.^{74–76} Both heart failure and chronic obstructive pulmonary disease are associated with an increased risk of cognitive impairment.^{77,78} This suggests early treatment and improvement of oxygenation may slow the development of cognitive impairment.

Persons with diabetes mellitus have early onset of cognitive impairment and a higher likelihood of developing dementia. ^{79–81} Hyperglycemia has been associated with reversible cognitive impairment in humans and animals. ^{82–84}

There are a number of lifestyle changes that have reasonable evidence for slowing down the rate of cognitive deterioration. Epidemiological studies support that persons consuming Mediterranean-style diets are less likely to have cognitive impairment. 85–87 In addition, the PREDIMED-NAVARRA study showed that a Mediterranean diet slowed the development of cognitive impairment after 6.5 years compared with a low-fat diet. 88 Extravirgin olive oil improves memory and reduces oxidative damage in the SAMP8 mouse 89 and extra-virgin olive oil was slightly better than nuts in improving cognition in the PREDIMED-NAVARRA study. 90 Mediterranean diet characteristics include fruit and vegetables, fish 2 times a week, olive oil, nuts, legumes, and whole grains. The "MIND-diet," which incorporates elements of both the Mediterranean diet and the "DASH diet," has been linked with a lower risk of cognitive impairment 91 and the development of AD. 92 It is recognized that association in epidemiological studies does not prove causality. The FINGER and PREDIMED-NAVARRA studies were controlled interventional studies, helping to confirm causality.

Although epidemiological studies have found that foods rich in antioxidant vitamins reduce the risk of AD, 93 intervention studies with antioxidant vitamins have been disappointing, 94,95 although 2000 IU per day of vitamin E did result in a slight, but significantly less, decline in the Alzheimer's Disease Co-operative Study/Activities of Daily Living Inventory. 96 Similarly, supplementation with B-vitamin supplements has not been effective except in cases of clear vitamin B deficiency or in countries where bread is not fortified with folate. 94,97–100 Preclinical studies have shown that a combination of nutrients involved in the Kennedy pathway for biosynthesis of neuronal membranes (including uridine monophosphate, choline and phospholipids) increased surrogate markers for synapse formation. In addition, in vivo studies showed that dietary enrichment with these nutrients improved neurotransmission, learning, and memory. 101 It has been shown that patients with AD may be partially deficient in some of these essential nutrients. ¹⁰² This led to the development of a specific nutrient combination (Souvenaid), which has been tested in humans. Although the results were negative in persons with established dementia, improvement in immediate and delayed verbal memory was seen in early cognitive dysfunction 103,104 and was sustained over a 12-month period without any safety issues being

observed. A European Union–funded trial (Lipidiet Consortium) is examining the effects in persons with prodromal AD. Medium-chain triglycerides (Axona), which are metabolized to ketone bodies, have been shown to have a small effect on memory in APOE4-negative individuals, but more studies are needed. ^{105,106} Overall, the consensus group concluded that a Mediterranean-type diet is a reasonable recommendation for persons with early cognitive dysfunction, whereas further evidence in early AD or MCI is awaited. Further studies are necessary to provide evidence for the efficacy for special dietary formulations.

An analysis of population-based data found that the population attributable risk for AD in the United States, Europe, and the United Kingdom was highest for physical inactivity. 107 A meta-analysis of prospective studies in persons without dementia (n = 33,816) found that physical exercise was protective against cognitive decline. ¹⁰⁸ The Cochrane meta-analysis suggested physical exercise had effects on delayed memory functions and auditory attention. 109 Another meta-analysis involving 14 randomized controlled trials (RCTs) found exercise had a very small significant effect on improving verbal fluency and no other significant effects. 110 Wang et al 111 found an effect of exercise on global cognitive function. Many of these studies were conducted over relatively short periods. A year-long aerobic exercise training study in older adults improved memory and hippocampal volume. 112 However, in another smaller study, the investigators failed to show an effect on cognition over a year. 113 In a study of resistance training in persons with MCI, there was a significant improvement in global cognitive function and maintenance of executive function over 18 months. 114 In the Fitness for Aging Brain study, physical activity enhanced cognitive scores, compared with an educational program over the 18-month follow-up. 115 A meta-analysis of 2533 participants found that Tai Chi enhanced both executive function and global cognitive function. 116 This was reinforced by a recent study. 117 Despite strong epidemiological evidence for a relationship between physical fitness and cognition, ¹¹⁸ the intervention studies have not shown large effects and none has shown protection against markers of neurodegenerative diseases, including AD. Moreover, none of the studies showed that the positive cognitive effects translated to everyday life; that is, the effects were not clinically meaningful. As physical exercise has many benefits for older persons and is generally recommended, the panel endorsed this recommendation for persons with cognitive impairment.

Epidemiologically, there is less cognitive decline in persons who have higher levels of engagement in intellectual activity, play a musical instrument, or dance. ^{119–122} The Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study provided cognitive exercises once a week for 10 weeks in 2832 older persons. ¹²² Participants in this intervention showed improvement in memory, reasoning, and processing even after 5 years of follow-up, although transfer of cognitive training benefits to improvements in real-world activities remains to be established. ¹²³ In persons with mild to moderate dementia, cognitive stimulation therapy (CST) has been shown to improve cognition. ^{124–130} CST also improves quality of life and is at least as effective as cholinesterase inhibitors in persons with dementia. ¹³¹ Reminiscence therapy has been shown to have a small effect on cognition and possibly quality of life. ^{132–135} Combinations of cognitive and exercise training can enhance cognitive function and functional status in older adults, but more studies are needed. ¹³²

Video game training produces positive effects on global cognition, memory, reaction time, and attention in older adults. 136,137

The Agency for Healthcare Research and Quality produced a meta-analysis examining factors associated with cognitive decline.²⁹ Overall, the evidence suggested that physical and cognitive activities were associated with lesser cognitive decline in aging. However, there is no evidence for a causal relationship, and the National Institute on Aging State-of-the-Science Conference could not make confident recommendations for preserving cognitive health based on existing evidence.¹³⁸

Given that cognitive impairment and dementia/AD are multifactorial disorders, targeting several risk factors simultaneously may be needed for optimal preventive effect. ¹³⁹ The Finnish geriatric intervention study to prevent cognitive impairment and disability (FINGER)¹⁴⁰ is the first large, long-term RCT showing that multidomain lifestyle-based intervention can maintain cognitive function and reduce cognitive decline in older at-risk individuals. In this study, 1260 persons aged 60 to 77 years were included and screened based on the Dementia Risk Score. ¹⁴¹ Half were randomly allocated to the multidomain intervention group (consisting of physical exercise, healthy diet, cognitive diet, and vascular risk monitoring), and half were allocated to a control group that received regular health advice only. After 2 years, the intervention group had significantly better

Neuropsychological Test Battery score (primary outcome) and lower risk for cognitive decline compared with the controls. ¹⁴⁰ Extended follow-up (up to 7 years) is ongoing to determine the effect on incidence of dementia and AD, other health outcomes, and long-term adherence to lifestyle intervention.

There are 2 other large, multidomain RCTs in Europe aiming to prevent cognitive impairment and dementia: The MAPT trial in France, and the pre-DIVA study in the Netherlands. ¹³⁹ Both of these trials have been recently finalized and results are awaited. Research groups from these 3 trials (FINGER, MAPT, pre-DIVA) have established European Dementia Prevention Initiative (EDPI; www.edpi.org) aiming to better use the available data. Through combined data analyses (totaling >6000 participants) and sharing of experiences about methodological issues, EDPI aims to improve multidomain preventive strategies that can be tested in larger studies.

The IAGG panelists recognized the paucity of high-quality randomized trials to make recommendations, but were in general agreement that positive lifestyle changes, such as those embodied in FINGER, should be recommended to all persons with early cognitive impairment.

Cholinesterase inhibitors do not improve cognition in persons with MCI (with the possible exception of prodromal AD). 142 Memantine should not be used in early AD.

Cognitive impairment at any level of severity creates significant challenges for both individuals and family members. ¹⁴³ Early recognition sets the stage for ongoing engagement of patients, family members, and clinicians in person-centered, individualized partnerships to optimize both medical and psychosocial outcomes over time. Early recognition of cognitive impairment allows the person to reprioritize personal life goals, and to develop

advanced directives for health, legal, and financial matters that fit with their preferences. This also allows the person to work with his or her family to identify and avoid major potential risks (eg, susceptibility to theft; wandering; unsafe use of tools, appliances, and guns; and operating motor vehicles). Early recognition also allows education for the person and the family on the effects of cognitive impairment and to engage both in activities that mitigate stress. Finally, early detection gives individuals the opportunity to make their own informed decisions about participation in research.

The recommendations that health care professionals should provide to persons with cognitive impairment are outlined in Table 4.

Cognitive Frailty

Cognitive frailty is a term that has recently emerged in the geriatrics literature inspired by potential parallel links to and possible common underlying mechanisms with the physical frailty syndrome. Physical frailty has been defined as "a medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death." ¹⁴ Recently it has been recognized that a subgroup of persons with cognitive impairment have reduced resilience and functional decline that interacts with physical frailty. Converging evidence suggests that the cognitive status represents an important dimension of the frailty syndrome. Epidemiological studies have shown an association between frailty and late-life cognitive decline, incident MCI and AD, and non-AD dementias. 144 It has been suggested that cognitive frailty can be defined as a reduced cognitive function (clinical dementia rating score = 0.5) with the cognitive impairment being due to either physical or brain disease, ^{29,145} or accelerated brain aging in the absence of evident brain disease. Physical frailty has to coexist to evoke the term cognitive frailty. It manifests commonly with executive dysfunction (frontal cortex) and less with pure amnestic defects (mesial temporal cortex). Others have suggested that the deficits in frail and prefrail patients in executive function and memory may be similar in size. 146

There is some evidence that, even with normal aging, both cognitive decline and physical frailty often coexist. 147–149 Cross-sectional studies find a high level of coexistence between rates of cognitive impairment and dementia and physical frailty. 150 Frailty predicts cognitive decline and incident dementia, 151,152 and cognitive impairment predicts frailty 153,154 in longitudinal studies. Loss of executive function and poor attention are particularly associated with slow gait. 155 There is increasing evidence that persons with white matter hyperintensities have poor balance, poor get up and go performance, slow gait speed, and increased falls. 156–158 White matter hyperintensities also predict functional decline. 159

The panelists agreed that persons with cognitive decline should be screened for physical frailty and vice versa. Although the concept of cognitive frailty may eventually yield useful insights and expanded predictability of function and disease outcomes, the panelists, however, considered it premature to incorporate cognitive frailty into the diagnostic lexicon and agreed that more studies on the interaction of the 2 entities and their pathophysiology are needed.

Conclusion

There was consensus that all persons 70 years and older should have their cognitive function (subjectively and objectively) evaluated when visiting their health care provider, at least once a year. The objectives of this assessment are to identify treatable disease, provide lifestyle guidance to try to slow cognitive impairment, to allow recognition of patients who may struggle understanding a physician's instructions, and to allow patients and their families to adequately prepare if they are at risk for developing dementia. Although this will vary by setting and circumstance, it was agreed that screening instruments should take less than 3 to 7 minutes to administer. The need to follow an individual longitudinally (ie, serial assessments) to demonstrate a deterioration in his or her performance was considered an important component of case-finding. The concept of cognitive frailty was viewed as being of interest but needs further research and development. The panel supports the Institute of Medicine's Report Brief that there is a need for a greater societal commitment to promote cognitive health (http://www.iom.edu/reports/2015/cognitive-aging.aspx). It is suggested that when communicating with the public, the term "cognitive (brain) health" may be more acceptable than talking about cognitive impairment or dementia.

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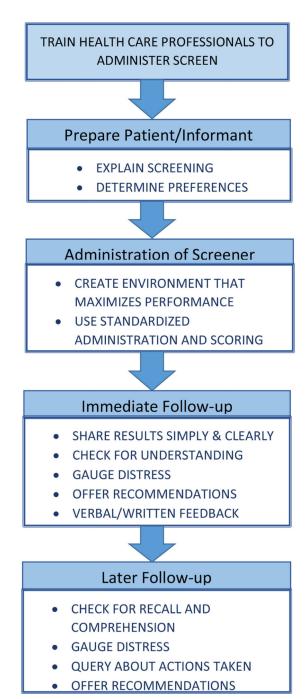


Fig. 1. Process for implementing screening.

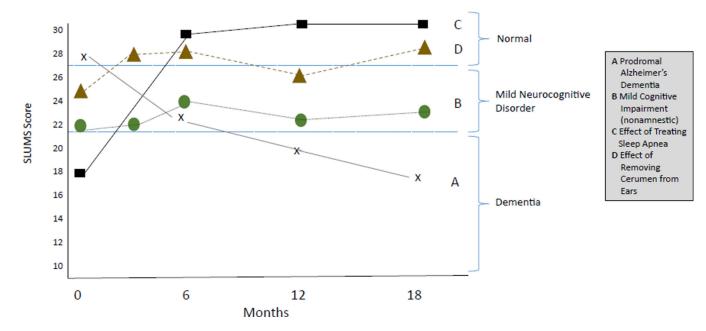


Fig. 2. Schematic demonstrating the importance of intra-individual change in confirming the diagnosis.

Table 1

Application of the World Health Organization (Wilson's Criteria) Screening Criteria to Cognitive Impairment and Dementia

	Cognitive Impairment	Dementia
1 The condition should be an important health problem	YES	YES
2 There should be treatment for the condition	Some	Slow Deterioration
3 Facilities for diagnosis and treatment should be available	Some	Some
4 There should be a latent stage of disease	Uncertain	YES
5 There should be a test or examination for the condition	YES	YES
6 The test should be acceptable to the population	YES	YES
7 The natural history of the disease should be adequately understood	Possibly	YES
8 There should be an agreed on policy of who to treat	Possibly	YES
9 The total cost of finding a case should be economically balanced	YES	YES
10 Case-finding should be a continuous process, not just a "once-and-for-all project"	YES	YES

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Table 2

Potential Screening Instruments for Early Cognitive Impairment

Ascertain Dementia 8 (AD8) Ascertain Dementia 8 (AD8) 1 Patic MiniCog 3 1 Patic The 5 Words 3 1 Patic Rapid Cognitive Screen (RCS) 4 3 Patic Memory Impairment Screen 4-5 4(P), 6(I) Patic General Practitioners Assessment of Cognition 4-5 4(P), 6(I) Patic Kokmen Short Test of Mental Status 5 8 Patic St Louis University Mental Status Examination (SLUMS) 7 14 Patic 7-Minute Screen (7MS) 7-10 Patic Patic	8 Informant 2 Patient 1 Patient 3 Patient 3 Patient	Yes Yes No Yes No	Yes Yes Yes Yes
3 3 3 4 4 4-5 5 5 7 7-10		Yes No Yes No	Yes Yes No Yes
3 3 4 4 4-5 5 5 77		No Yes Yes	Yes No Yes
3 4 4 4-5 5 5 7 7		Yes Yes No	No Yes Yes
4 4-5 5 5 7-10		Yes No	Yes Yes
4–5 5 7 7–10		No	Yes
fental Status 5 8 stal Status Examination (SLUMS) 7 14 7-10 11	4(P), 6(I) Patient/Informant]		
Ital Status Examination (SLUMS) 7 14 7-10 11	Patient	Yes	Yes
7–10 11	Patient	Yes	No
	11 Patient	No	Yes
Mini-Mental Status Exam (MMSE) 7-10 19 Patie	Patient	Yes	Yes
Telephone Interview for Cognitive Status 7-10 11 Patie	11 Patient	Yes	Yes
Informant Questionnaire on Cognitive Decline in the Elderly (Short IQCODE) 10–15 16 Informant Questionnaire on Cognitive Decline in the Elderly (Short IQCODE)	Informant	Yes	Yes
Addenbrook's Cognitive Exam 15 30+ Patie	Patient	Yes	Yes

*
The MMSE is both copyrighted and requires a fee to use in the United States. Most of the other copyrighted instruments require no fee at the present time.

Table 3
Potential Biomarkers for Persons With Cognitive Impairment

Biomarker	Utility
MRI	Ischemic disease (white matter hyperintensities), normal-pressure hydrocephalus, space-occupying lesions, vasculitis; AD (hippocampal volume, cortical thinning)
Cerebral spinal fluid Amyloid $\boldsymbol{\beta}$ and Tau	AD
Positron emission tomography	
Fluorodeoxyglucose	AD/Lewy body dementia
Pittsburgh compound β	AD
Florbetapir	AD
Florbetaben	AD; frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDR-17)
Tau	
Single-photon emission computerized tomography	
Dopamine transporter	Lewy body dementia

Table 4

Recommendations for the Management of Early Cognitive Impairment

• Spend enough time with the patient and, when appropriate, family members, to ensure maximum understanding of the condition and recommended care. Provide written instructions. When necessary, engage a care partner to help carry out recommendations.

- Identify all potentially reversible causes of cognitive impairment.
- Provide advice regarding lifestyle practices and follow-up on implementation:
 - i. The Mediterranean or similar diet including olive oil
 - ii. Physical exercise
 - iii. Intellectual activities
 - iv. CST for persons with early or moderate AD
- Discuss the potential use of cholinesterase inhibitors in persons with AD
- Encourage the person to develop advanced directives for health, legal, and financial matters, and follow-up on whether this was
 done
- Educate the patient and family through recognized specialty organizations (eg, the Alzheimer's Association in the US)
- Address, and take steps to avoid, major risks associated with cognitive impairment (eg, money management, "safe return" bracelet, appropriate disposition of unsafe tools and guns, driving)
- · Encourage identification and use of support services (eg, support groups, family and friend engagement activities)
- Talk about potential research participation and help the person to make his or her own informed decisions