The Healthy Brain Checklist™: Identifying Mild Cognitive Impairment in Clinical Practice

Prepared by Medical Care Corporation

A number of studies have found that the prevalence of cognitive impairment, due to a variety of medical conditions, in persons over 65 years old, is on the order of 15-25% (**Table 1**). If left unchecked, many of these conditions can result in poor self-care, declining health, and increasing costs of care. Among the most prevalent causes of cognitive impairment is Alzheimer's disease, a progressive disorder for which the majority of patients is not diagnosed in a clinical practice setting, until the dementia stage,[1] which is more than halfway through the clinical course of the disease.

Table 1. Prevalence of Mild Cognitive Impairment

Study Location	Age Group	MCI Prevalence
China[2]	>60	9.7-16.5%
Korea[3]	>65	8-28%
Germany[4]	>75	26%
Spain[5]	>65	15%
Pennsylvania[6]	>65	28-35%
Minnesota[7]	>70	14-18%
Maine[8]	>65	25%

The Affordable Care Act of 2010 takes an important step towards addressing this problem. Effective 2011, physicians must "identify cognitive impairment" in their Medicare patients during annual wellness visits. This is a proactive step enabling earlier intervention against the many medical conditions that impair cognition.

While the intent of the requirement to identify cognitive impairment is clear and well justified, the mechanism by which physicians should accomplish this task is less clear. The most widely used and well-established instruments for assessing cognitive health in a primary care setting are not well suited to this task. Each of them is too long, too costly, or too insensitive to discern the earliest signs of disease-related cognitive impairment, during a routine exam, within the time allotted for a typical medical exam. **Appendix A** summarizes the published literature on the accuracy of instruments and tests that have been evaluated for their ability to distinguish normal aging from mild cognitive impairment; it does not include studies aimed at identifying dementia.

Normally aging patients often experience perceptible declines in their memory and cognitive abilities, but it is difficult to understand whether these changes are due to *normal aging* or to an *underlying medical condition*. As such, a well-designed assessment for cognitive impairment should address and consider all commonly reported cognitive changes, whether they correlate with normal aging or with medical conditions known to impair cognition. Approaches that focus solely on symptoms known to indicate an underlying problem, deny patients the opportunity to express their concerns. This can be problematic as some patients, in an effort to report a particular problem, will mischaracterize their symptoms when responding to a questionnaire that was not designed to identify complaints commonly associated with normal aging.

We have reviewed the literature to identify cognitive symptoms that are characteristic of normal aging, as well as those that are more likely to result from underlying medical conditions. This review, combined with the expertise of clinical specialists in memory and cognitive disorders, was used to construct the *Healthy Brain Checklist*, which can be completed in less than two minutes, by patients waiting to see their physician, to identify cognitive and affective concerns. It can also discriminate between those concerns that are likely due to normal aging and those that are likely due to underlying medical conditions. The layout of the *Healthy Brain Checklist* allows physicians to quickly determine if any reported symptoms are likely to be "QUALIFIED" concerns that require further evaluation, or "BENIGN" concerns that are common in normal aging.

The goals of the Healthy Brain Checklist are two-fold:

1) Early detection of cognitive impairment due to underlying medical conditions;
2) More efficient utilization of healthcare resources

The *Healthy Brain Checklist* enables physicians to identify patients expressing QUALIFIED memory, cognitive or affective concerns that are most likely related to one or more underlying medical conditions (e.g., any of the chronic diseases of aging, traumatic brain injury, depression, Alzheimer's disease, etc.). Such patients should have an objective evaluation of their cognition and, if impairment is confirmed, undergo a thorough evaluation and diagnosis of the cause. This approach enables a high standard of care, timely intervention, optimal treatment outcomes, and lower healthcare costs.

The *Healthy Brain Checklist* also enables physicians to identify patients expressing BENIGN memory, cognitive or affective concerns, that are most likely related to normal aging. Such patients should be annually or semi-annually reassessed with the *Healthy Brain Checklist,* but need not be further evaluated unless clinical judgment dictates otherwise. This discourages unnecessary diagnostic evaluation and promotes efficient use of healthcare resources.

The Risk for Cognitive Decline With Aging

The prevalence of mild cognitive impairment (**MCI**) among aging individuals is common, regardless of the operational criteria for MCI, or the geographic area studied (Table 1). The major etiologies that produce the syndrome of MCI include Alzheimer's disease (**AD**), depression, cerebrovascular and cardiovascular disease, metabolic syndrome, Parkinson's disease, Lewy Body Disease, Frontal Temporal Lobe Disease, Traumatic Brain Injury, hydrocephalus, epilepsy, and multiple sclerosis.

Because the majority of these disorders, including AD, can often be either stopped or delayed,[9,10] early detection and intervention provides the most immediate opportunity to improve healthcare outcomes. Detecting MCI is therefore essential. Table 1 suggests that physician vigilance toward memory loss should begin, at the latest, when patients have reached 60 years old.

Identifying When Cognitive Impairment Should Be Further Evaluated:

When impairment is mild, and does not meet criteria for dementia, disease-related memory decline is called mild cognitive impairment (**MCI**). Because distinguishing between *age-related* and *disease-related* memory decline can be difficult, concerns about memory loss are commonly

mishandled in clinical settings. Many legitimate signs of disease are dismissed as normal aging and left to progress without treatment, while many healthy but worried patients are guided through an expensive diagnostic work-up unnecessarily. Given the tremendous focus on efficient utilization of healthcare resources, physicians need reliable decision aids to properly direct their patient traffic. A simple and accurate assessment tool is therefore necessary, to distinguish between age-related and disease-related memory decline.

Developing the Healthy Brain Checklist (HBC)

Important characteristics of an effective instrument to aid physician decisions about the legitimacy of subjective memory concerns are that it:

- Should have high sensitivity for detecting MCI (or more severe deficit).
- Should allow normal aging persons to indicate memory concerns that are consistent with normal aging.
- Should detect common signs of major depression.
- Should be brief and simple enough for self-administration, without office staff assistance.
- Should be easily and rapidly interpreted by the physician.

Assessing For Cognitive Impairment

We surveyed the PUBMED database for subjective questionnaires that assess memory concerns. The search terms, "memory questionnaire", "AD8", "IQCODE", "Functional Activities Questionnaire", and "memory screen" were used. 59 of the articles discussed substantive results of specific memory questionnaires that characterized normal cognitive aging, MCI or their discrimination. Studies that included demented patients were excluded because the goal is to identify questions sensitive to discrimination between normal aging and MCI. The studies were reviewed to collect information on questionnaire length, population studied, sample size for normal and MCI, sensitivity, specificity, accuracy, validity, and reliability.

The questionnaires identified and reviewed included:

1. Multifactorial Memory Questionnaire (**MMQ**).
2. Prospective and Retrospective Memory Questionnaire (**PRMQ**)
3. Everyday Memory Questionnaire (**EMQ**)
4. Absentmindedness Questionnaire (**AMQ**)
5. The Memory Screen
6. The AD-8 Questionnaire
7. The IQCODE

Table 2 shows the questionnaires' performance statistics for discriminating between normal aging and MCI. Some of the questionnaires listed in Table 2 were designed to characterize memory concerns *among* normal aging or MCI individuals, and have not yet been evaluated for ability to discriminate *between* them.[11-15] For those instruments, a "?" appears in their performance statistics columns.

Table 2. Screening Performance Statistics of Subjective Memory Questionnaires

Questionnaire	Sensitivity (MCI)	Specificity (Normal)	Accuracy
Memory Screen[16,17]	93%	80%	89%
AD-8[18]	68%	90%	88%
IQCODE[19]	67%	60%	68%
AMQ[11]	?	?	?
EMQ[13,14]	?	?	?
PRMQ[12]	?	?	?
MMQ[15]	?	?	?

Memory Concerns Reported In Normal Aging or MCI Samples

Table 3 shows items with high or low factor loadings for questions from the MMQ[20] and AMQ,[11] which characterize memory concerns of normal aging persons.

Table 3. Factor Loading of Items From Candidate Memory Questionnaires

Test	Factor	Item	Statement	Loading
MMQ	Ability	2*	How often do you misplace something you use daily, like your keys or glasses?	0.52
MMQ	Ability	3	How often do you have trouble remembering a telephone number you just looked up?	0.55
MMQ	Ability	4*	How often do you not recall the name of someone you just met?	0.54
MMQ	Ability	6*	How often do you forget an appointment?	0.53
MMQ	Ability	7*	How often do you forget what you were just about to do; for example, walk into a room and forget what you went there to do?	0.67
MMQ	Ability	9*	How often do you have difficulty coming up with a specific word that you want?	0.67
MMQ	Ability	14*	How often do you forget what you were going to say in conversation?	0.74
MMQ	Ability	16	How often do you forget a telephone number you use frequently?	0.56
MMQ	Ability	17	How often do you retell a story or joke to the same person because you forgot that you had already told him or her?	0.45
MMQ	Ability	20*	How often do you forget details about a recent conversation?	0.54
MMQ	Strategy	1*	How often do you use a timer or alarm to remind you when to do something?	0.27
MMQ	Strategy	2*	How often do you ask someone to help you remember something or to remind you to do something?	0.30
MMQ	Strategy	9*	How often do you use a routine to remember important things, like checking that you have your wallet and keys when you leave home?	0.38
MMQ	Strategy	18*	18. How often do you write a note or reminder for yourself (other than on a calendar or in a notebook)?	0.39
AMQ	Forgetfulness	1*	Birthdays	0.25
AMQ	Forgetfulness	3*	“Appointments	0.43
AMQ	Forgetfulness	5	Miss TV show	0.35
AMQ	Forgetfulness	7	Addresses	0.09

AMQ	Forgetfulness	10*	Remote Family Events	0.26
EMQ	Retrieval	8*	Forgetting that you were told something yesterday	0.71
EMQ	Retrieval	14*	Completely forgetting to do things you said you would do	0.75
EMQ	Retrieval	15*	Forgetting important details of what you have done in the past few weeks	0.68

Table 3 also shows items with high or low factor loadings from the EMQ[13,14] for persons with MCI and stroke. For studies of normal aging samples, a high factor loading means the question captures a memory concern frequently reported by normal aging subjects. For example, Table 3 shows that questions 4 and 20 of the MMQ had high loadings for the factor described as "Ability" when a normal aging sample was assessed.[20] Similarly, for studies of MCI samples, a high factor loading on a question means that it captures a memory concern frequently reported by MCI subjects. For example, Table 2 shows that the EMQ had high loadings for questions 8, 14 and 15 for the factor described as "Retrieval" when an MCI sample was assessed.[13,14] Items with a high factor loading for either a normal aging or MCI memory concern became candidates for the HBC.

Deciding which of these questions to include in the HBC required consideration of *how* normal aging and MCI individuals commonly report their memory concerns to physicians. We therefore had an ADRD clinician, with more than 20 years of experience evaluating both MCI and normal aging patients, select the final questions for inclusion from those among the candidate questions listed in Table 2. The questions (or their content) selected by the ADRD clinician were those of the MMQ Ability factor (items 2, 4, 6, 7, 9, 14, 20), the MMQ Strategy factor (items 1, 2, 9, 18), the AMQ Forgetfulness factor (items 1, 3, 10) and the EMQ Retrieval factor (items 8, 14, 15). Also, an item with high, published accuracy, for characterizing difficulty performing complex tasks, was included to capture *cognitively related functional difficulties* seen during MCI and mild dementia.

Memory Concerns Discriminating Between Normal Aging and MCI Samples

Among the studies reviewed, a machine learning analysis of the Functional Activities Questionnaire, Blessed Orientation, Memory and Concentration Test, and Mini-Mental State Exam from a sample of 198 normal aging and 244 MCI subjects (Clinical Dementia Rating Scale scores of 0 and 0.5 respectively) at the UC Irvine Alzheimer's Disease Research Center identified a single question that detected MCI with 93% sensitivity, and detected normal aging with 80% specificity.[16,17] This question was *"Do you require assistance remembering appointments, family occasions, holidays or taking medications?"* Interestingly, this single question discriminated between normal aging and MCI as well as or better than the results of all other studies (Table 2). Also, as suggested by the results of the factor loadings for questions 1, 3 and 10 of the AMQ Forgetfulness factor (Table 3), this single question characterizes memory concerns not commonly reported among normal aging subjects (birthdays, appointments, remote family events). While this single question may not detect MCI subjects who are having trouble with these abilities, but do not yet require assistance, it captures a significant portion of them. The addition, into the HBC, of the aforementioned questions from the MMQ, AMQ and EMQ, which characterize memory concerns of either normal or MCI populations, may help identify subjects with degrees of MCI that are milder than that characterized by the single question.

Depression

Questions sensitive to major depressive disorder are also needed because depression is common among aging individuals, and can cause cognitive impairment. The Depression Scale (DEPS)

questionnaire has been validated across a broad range of individuals and ages, and has a diagnostic accuracy of ~88% for discriminating between major depressive disorder and depressive symptoms without psychiatric symptoms.[21] Questions from the DEPS questionnaire with high factor loadings for detecting major depressive disorder were selected (**see Question 3 in Appendix B**).

The Healthy Brain Checklist

The final form of the HBC used a mixture of useful questions, or their content, taken from well-studied questionnaires, plus clinical experience, for the types of cognitive or cognitively related functional concerns expressed by patients in clinical practice settings (**Appendix B**). For HBC question 2, the items in the "Symptoms of Medical Conditions" column typically characterize concerns expressed by individuals with MCI, whereas those in the "Symptoms of Normal Aging" column typically characterize concerns expressed by normal aging individuals.

Interpretation of the Healthy Brain Checklist

Along with the physician's clinical judgment, questions 1 and 2 are used to determine which patients should be further evaluated.

- **Question 1** indicates a fairly severe impairment (Do you *require assistance*…) and strongly suggests the need for further evaluation.
- **Question 2** is useful in distinguishing between QUALIFIED concerns and BENIGN concerns. Patients reporting "symptoms of medical conditions" have QUALIFIED concerns and need further evaluation. Patients reporting "symptoms of normal aging" are likely to be healthy and, unless the physician has additional concerns, need only to be monitored.
- **Question 3** can indicate major clinical depression and should trigger an evaluation in any patients who indicate symptoms of such.

The HBC is currently used in waiting rooms of physicians participating in the Orange County Vital Aging Program (www.OCVitalAging.org), and in any other clinical practice settings where physicians have adopted a proactive stance toward managing the cognitive health of their patients. It remains to be determined how frequently it will be used in these settings, to what extent it will increase identification of MCI patients, and to what extent it reassures normal aging patients with memory concerns. However, measurement of these outcomes is underway and will be submitted for peer-reviewed publication when the results have been analyzed.

Summary

The Healthy Brain Checklist is the first version of a waiting room instrument that can be self-administered in many clinical practice settings without office staff assistance. It was designed as a viable and effective mechanism enabling physicians to identify cognitive impairment during Medicare annual wellness visits, as required by the Affordable Care Act. More broadly, it can serve as a necessary first step in all primary care settings for selecting patients who need objective evaluation to determine whether they have cognitive impairment due to an underlying medical condition.

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APPENDIX A

Summary of all published studies reporting the unbiased measure of test performance, overall accuracy, for discriminating normal aging from MCI using ROC methods.

Excerpted from Appendix B of Trenkle et al. J Alzheimers Dis. 2007 Jun;11(3):323-35.

Test	AUC(NL vs. MCI)	NL	MCI	Total Cases
MCI Screen (called "CWL with CA" in article) [61]	97.3%	119	95	214
Alzheimer's disease Cooperative Study scale for ADL in MCI [44]	97.0%	30	45	75
MCI Screen (MCIS) [Present Study]	95.6%	130	53	183
Alzheimer's disease Assessment scale, cognitive subscale (ADAS-Cog) [44]	93.0%	30	45	75
Wechsler Logical Memory Delayed Recall (LM-II) [35]	91.7%	88	37	125
The Memory Screen [60]	89.0%	198	244	442
4-item Instrumental Activities of Daily Living Scale+Single-item informant report of memory problem [35]	87.2%	88	37	125
60 second verbal fluency task [14]	87.0%	46	45	91
MRI: Diffusion Tensor Left Hippocampal High Mean Diffusivity [41]	87.0%	18	18	36
Wechsler Logical Memory Delayed Recall:LM-II [35]	86.1%	88	37	125
AD8 Questionnaire [22]	84.7%	28	112	140
NeuroTrax Mindstreams [15]	82.3%	39	30	69
Wechsler Logical Memory Immed. Recall (LM-I) [35]	81.2%	88	37	125
Single-item informant report of memory problem [35]	79.5%	88	37	125
Mini-Mental Status Exam (MMSE) [8]	78.5%	25	26	51
NeuroTrax Mindstreams (Best Reported Result) [16]	78.3%	39	30	69
18FDG PET Hippocampal Glucose Metabolism [40]	78.0%	11	13	24
4-item Instrumental ADL Scale [35]	76.9%	88	37	125
Wechsler Logical Memory Immed. Recall (LM-I) [14]	76.0%	46	45	91
CNS Vital Signs (Best Result) [26]	74.1%	89	36	125
MRI: Left Hippocampal Low Normalized Volume [41]	72.0%	18	18	36
Mini-Mental Status Exam (MMSE) [35]	67.6%	88	37	125
MRI: Hippocampal Atrophy [43]	65.9%	59	65	124
AB Cognitive Screen (Verbal Fluency) [64]	64.6%	174	166	340
Enhanced Delayed Cued Recall [54]	62.5%	33	40	73
AB Cognitive Screen (Standardized MMSE) [64]	57.2%	174	166	340
Behavioral Dyscontrol Scale [6]	55.0%	40	40	80
California Verbal Learning Test [25]	NR	65	65	130
Hopkins Verbal Learning Test [57]	NR	54	19	73
Buschke Selective Reminding Test [45]	NR	76	234	310
Montreal Cognitive Assessment (MoCA) [42]	NR	39	49	88
Hopkins Verbal Learning Test+Placing Test [33]	NR	51	29	80

NL=Normal
AUC=Area Under the Curve
NR=Not Reported

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Appendix B: The Healthy Brain Checklist™

Name: _____ **Date**: _____

1. **Do you *require assistance* remembering appointments, family occasions, holidays or taking medications?**

   ☐ Yes ☐ No

2. **Check each symptom with which you are having *increasing difficulty*, compared to your past ability:**

Symptoms of Medical Conditions	Symptoms of Normal Aging
☐ Forgetting important details of things I have done in the past few weeks.	☐ Forgetting the name of someone I know well.
☐ Completely forgetting to do things I said I would do.	☐ Forgetting what I was going to say in a conversation.
☐ Forgetting recent events or conversations.	☐ Forgetting what I was going to do when going into another room.
☐ Retelling a story or joke to the same person because I forgot that I had already told them.	☐ Finding things I have recently put down.
☐ Completing complex tasks at work or home (i.e. balancing check books, planning projects).	☐ Recalling a specific word I want.

3. **Check each feeling that applies: "During the last month I have":**

   ☐ Felt that I cannot stop feeling "down" or "blue", even with help from family or friends.
   ☐ Felt all pleasure and joy has gone from life.
   ☐ Felt hopeless about the future.
   ☐ Felt that everything was an effort.
   ☐ Felt low in energy or slowed down a lot.

Please note any other memory or mood-related concerns to discuss the your doctor:

Due to rising awareness about progressive memory disorders like Alzheimer's disease, the public is increasingly expressing concerns about perceived memory loss. This has led to an increasing number of diagnostic tests performed on healthy patients with *benign* concerns. At the same time, research has shown that most early symptoms of cognitive decline, or *qualified* concerns, are overlooked in primary care settings. Physicians can provide better care if they are vigilant against such emerging problems.

The Purpose of the Healthy Brain Checklist

This Questionnaire will help physicians distinguish between QUALIFIED memory concerns that require further evaluation, and BENIGN memory concerns that are consistent with normal aging.

Which Patients Should Complete the Healthy Brain Checklist?

All patients aged 50 and older should complete this questionnaire at each physician visit, regardless of the purpose of their visit. Also, all patients undergoing a Medicare annual wellness visit should use this questionnaire, or a similar one, to detect any cognitive impairment.

How to Interpret Responses to the Healthy Brain Checklist

- **Question 1:** Requiring assistance with these tasks suggests an advanced level of impairment, so patients who respond "YES" to Question 1, are expressing a QUALIFIED concern. These patients are likely to have an underlying medical condition that is impairing their cognition, so further evaluation is recommended.
- **Question 2:** Increasing difficulties with tasks that correlate to **underlying medical conditions** (left column), indicate QUALIFIED concerns that should be further evaluated. Increasing difficulties with tasks that correlate to **normal aging** (right column), indicate BENIGN concerns. By themselves, BENIGN concerns do not warrant further evaluation, unless the physician clinically suspects cognitive impairment or depression.
- **Question 3:** These are common indicators of major depressive disorder, which could also interfere with memory and other cognitive abilities. Patients who indicate any of these symptoms should be evaluated for depression.

Recommended Next Steps

- Patients who are aging normally and expressed only BENIGN concerns (or no concerns), should be encouraged to monitor their cognitive health, and should be prompted to express any concerns at follow-up visits.
- Patients who expressed QUALIFIED concerns should undergo an objective assessment of their cognition. This can be completed in your office using the MCI Screen*, or by referring the patient to appropriate medical resources in your community.

* The MCI Screen is a well-validated, highly accurate test of cognition that a physician's staff can administer in the clinic. The test takes about ten minutes and requires Internet access. Using the MCI Screen to evaluate a memory concern is a reimbursable procedure in primary care and specialty settings. The MCI Screen is provided to physicians by Medical Care Corporation and can be evaluated free of charge at www.mccare.com.