



Creyos Dementia Protocol Science Overview

The science enabling Creyos to accurately and efficiently screen and assess patients for dementia



Important Information Before You Read This Document

Creyos provides a scientifically-validated and objective measure of an individual's cognition. It should be used in conjunction with other information and clinical judgments to reach conclusions regarding an individual's health. It is not a stand-alone diagnostic tool and cannot replace the judgement of a healthcare professional. Creyos does not assume responsibility for the outcome of decisions made based on Creyos data.

Table of Contents

Introduction	pg. 4
A. Aging and Cognitive Decline	pg. 5
Defining Mild Cognitive Impairment (MCI)	pg. 5
Advantages of Testing for MCI in Creyos	pg. 6
<i>Will Biomarkers Replace Cognitive Testing?</i>	
Progression From MCI to Dementia	pg. 7
<i>The Importance of Early Detection</i>	
B. The Creyos Dementia Screener	pg. 9
Training a Machine Learning Algorithm for Detecting Cognitive Impairment	pg. 9
C. The Creyos Dementia Assessment	pg. 11
Cognitive Tasks	pg. 11
<i>Tasks in the Creyos Dementia Assessment</i>	
<i>Task Performance Thresholds for Objective Cognitive Impairment</i>	
<i>Validation of the Creyos Dementia Screener and Assessment</i>	
<i>Sensitivity and Specificity of The Creyos Dementia Screener and Assessment</i>	
<i>Validity and Reliability</i>	
<i>The Creyos Normative Database</i>	
Questionnaires Included in the Dementia Protocol	pg. 20
Patient Classification in the Creyos Dementia Assessment	pg. 21

The Science Behind Creyos Dementia Screening and Assessment

The Creyos dementia protocol combines cognitive, functional, and behavioral testing to provide information about symptoms of mild cognitive impairment and dementia. This guide reviews the science behind the screener and assessment, including the link between age and cognitive decline, the tasks used in this protocol, and how patients are classified based on standard diagnostic criteria.

Creyos supports the full continuum of dementia testing and care:

- **Screening:** a 5-minute, two-task screener to identify impairment and determine if further testing is needed.
- **Assessment:** a 20-minute assessment with an additional four tasks and four questionnaires to help establish diagnostic criteria for mild or major neurocognitive disorders.
- **Care planning:** a collection of the results of the assessment and additional questionnaire results to help inform, design, and deliver a care plan suitable for patients with cognitive impairment.
- **Tracking:** the ability to easily re-administer the protocol for longitudinal tracking and monitoring of cognitive health.

[*Read more about the range of cognitive screening, testing, and care planning available in Creyos Health.*](#)

A. Aging and Cognitive Decline

Cognition declines with age, and everyone ages.

Despite the unique needs of older adults, many healthcare professionals, including primary care physicians, are uncomfortable assessing a patient's cognitive health. That leaves a problem: nearly all patients will notice symptoms of cognitive decline as they age, but their doctors are not equipped to tell them if the decline is normal or greater than expected. The latter could be an early sign of conditions like dementia.

The Creyos dementia protocol is designed to help solve this problem by making it easier for healthcare providers to identify mild or severe cognitive impairment.

This guide will review the scientific background behind the creation of the screener and assessment, define key terms needed to interpret the reports, and provide references for further reading. For the nitty-gritty details of each element of the report and interpretation advice, see the [Creyos Dementia Protocol Report Interpretation Guide](#).

Defining Mild Cognitive Impairment (MCI)

Mild cognitive impairment (MCI) is recognized in the medical and scientific communities as a potential early indicator of dementia risk. While not all people with MCI will go on to develop a neurocognitive disorder, **those with MCI are at a greater risk of developing Alzheimer's disease or a related dementia** (Prado et al., 2019). The Creyos dementia protocol is based on a working definition of mild cognitive impairment (MCI), also known as mild neurocognitive disorder, that combines consensus definitions from the NIA-AA and the DSM-5.

The National Institute on Aging and Alzheimer's Association (NIA-AA; see [Jack et al., 2018](#)), focusing on research-based criteria and pre-clinical Alzheimer's disease (AD) as a cause for impairment, proposed that MCI is present when a patient displays evidence of:

- Cognitive performance below the expected range for the individual, based on all available information; *and*
- Decline from baseline, reported by the individual, an observer, or via longitudinal testing; *and*
- Capacity for performing daily life activities independently

The DSM-5 is more clinically focused, but has similar criteria for mild neurocognitive disorder (the DSM-5's equivalent term for MCI):

- Modest decline in one or more cognitive domains, based on the concern of the individual, an informant, or the clinician and a decline in cognitive performance, preferably documented by standardized neuropsychological testing; *and*

- Deficits do not interfere with independence in everyday activities; *and*
- Deficits do not occur only in the context of delirium and are not better explained by another mental disorder

The Creyos dementia assessment adopts a definition of MCI that is compatible with both frameworks and clinically useful. To be identified as meeting the criteria for potential mild neurocognitive impairment, a patient must:

- ✓ **Express concern about decline** from a previous baseline (*subjective decline*, measured by the IQCODE-SR questionnaire); *and*
- ✓ **Demonstrate objective impairment** relative to age-matched population or an objective decline from a previous baseline, in at least one cognitive domain (*objective decline*, measured by a set of Creyos cognitive tasks); *and*
- ✓ **Be able to perform instrumental activities of daily living** independently (*functional independence*, measured by the IADL questionnaire)

Additional questionnaires are available through the Creyos platform to measure symptoms of anxiety and depression (with the GAD-7 and PHQ-9 questionnaire, respectively), and can be included with the dementia protocol to help clinicians rule out other mental disorders or neurobehavioral symptoms as the primary cause of deficits.

Advantages of Testing for MCI in Creyos

Typical tools for examining age-related cognitive decline may include pen-and-paper screeners (e.g., the MoCA, MMSE, and SLUMS) and/or a neuropsychological examination that includes multiple tests and batteries. The Creyos protocol offers both **a quick screener** to identify the need for further testing and **a dementia assessment** that offers more detailed information.

Creyos tasks are **strongly correlated with pen-and-paper screening tools, but have been demonstrated to add information about cognition over and above these simple tasks** (Sternin et al., 2019). They provide a wealth of detailed performance data beyond a simple total score. These data can be used to identify subtle patterns characteristic of impairment. The more comprehensive Creyos dementia assessment also provides information about specific domains that may be impaired, it can be administered multiple times, and it may be able to reveal subtle cognitive patterns that tools like the MMSE miss due to a ceiling effect (i.e., except in cases of severe impairment, many older adults score nearly perfectly) or low sensitivity to mild decline. For example, Hosseini et al. (2023) found that patients with Parkinson's disease were impaired on Creyos tasks, even when MMSE scores were within a normal range.

The Creyos tasks are also correlated with gold-standard neuropsychological assessments, including

the WAIS-IV, Trail Making Task, and more (Kochan et al., 2022, 2022b), indicating that they can capture much of the same information in an efficient set of computerized tasks, even when unsupervised, and in far less time than a full neuropsychological assessment. However, in some cases, a neuropsychological exam or referral to a neuropsychologist may still be justified after Creyos testing reveals cause for concern.



Will Biomarkers Replace Cognitive Testing?

Biomarkers are playing an increasingly important role in research and clinical work related to dementia, and especially Alzheimer's disease. Amyloid beta (A β) peptides are found in the brains of people diagnosed with Alzheimer's disease, and may be a target for future diagnosis tools and interventions. However, there will be a need for objective cognitive testing for the foreseeable future (Sabbagh et al., 2020). Reasons include:

- Cognitive deficits are the defining symptoms of MCI and dementia, regardless of potential physical signs or causes of decline.
- MCI can be established independently from Alzheimer's disease, and can have other causes.
- Biomarker testing is invasive, expensive, and not easily accessible to most patients.
- The diagnostic utility of A β testing is currently unclear, and must be combined with cognitive testing, subjective concerns, and expert clinical judgment in order to avoid issues like widespread false positives and undue patient stress.
- Anti-amyloid therapies for Alzheimer's disease may not be as effective as initially hoped, their use remains controversial, and they may not address MCI resulting from causes other than Alzheimer's disease.

When biomarker data are available, they may complement cognitive testing to help establish the presence, severity, and type of age-related conditions. Research has found that several dementia-linked biomarkers are associated with Creyos cognitive task scores.

Progression From MCI to Dementia

The ultimate goal of detecting MCI is often not about mild impairment itself. Rather, MCI is assessed to detect early signs of dementia—in other words, mild impairment is likely to get more severe as a patient ages, and potentially begin to interfere with activities of daily living.

Individuals diagnosed with MCI do tend to demonstrate an accelerated rate of progression to

dementia ([Petersen & Negash, 2008](#)), and neuropsychological test performance is higher in people who do not progress to dementia ([Prado et al., 2019](#)).

Major neurocognitive disorder is the term now used in the DSM-5 to refer to what is commonly known as dementia in medical literature and everyday usage. There are several possible causes for dementia. Alzheimer's disease is the most common, but the DSM lists numerous other etiologies, such as traumatic brain injury and Parkinson's disease.

The main factor that distinguishes minor and major neurocognitive disorder is interference with independence in everyday activities. If a patient requires assistance with complex or simple everyday activities, such as transportation, shopping, or managing medications, then their condition may have progressed to major neurocognitive disorder. In the Creyos dementia assessment, the Instrumental Activities of Daily Living Questionnaire (IADL) can help establish functional dependence or independence, and results are used to automatically provide a potential DSM-5-based classification for the patient ([see the Patient Classifications section below](#)).

The Importance of Early Detection

Over 70% of Americans would want to know about early signs of dementia if it could allow for timely intervention, [according to the Alzheimer's Association](#). Furthermore, early detection is crucial to maximize the effectiveness of the long-term lifestyle changes that remain the best hope for preventing or slowing dementia. Not all cases can be prevented, but detecting and tracking progression of cognitive decline can also help with care planning, living conditions, and strategies for living with reduced cognitive function. Creyos includes [care planning assistance](#) that can be initiated immediately if the dementia assessment raises cause for concern.

A 2017 paper from the Lancet Commission, [updated in 2024](#), identified 12 modifiable risk factors that account for about 40% of worldwide dementias. Some of these factors, such as managing blood pressure, using hearing aids, and increasing physical activity, are under the patient's control, and early detection of MCI may provide additional motivation for changes, or may identify the patients most in need of lifestyle interventions.

Research using Creyos has also found promising results for some early intervention programs, such as multimodal movement, diet, and stress coaching ([Sandison et al., 2023](#)) and intensive online modules targeting top risk factors ([Brodaty et al., 2023](#)).

B. The Creyos Dementia Screener

The **Creyos dementia screener is often the first step** toward detecting cognitive impairment.

It is a two-task, 5-minute cognitive testing protocol that determines if there are signs of cognitive impairment and whether further testing is needed.

A machine learning approach was used to determine which cognitive tasks, and which combination of results from those tasks, would best distinguish impaired people from healthy controls. The first step was to examine every possible combination of one, two, or three of the 12 Creyos core cognitive tasks to search for a battery that was as short as possible but could accurately identify impairment. The winning combination was a set of two tasks:

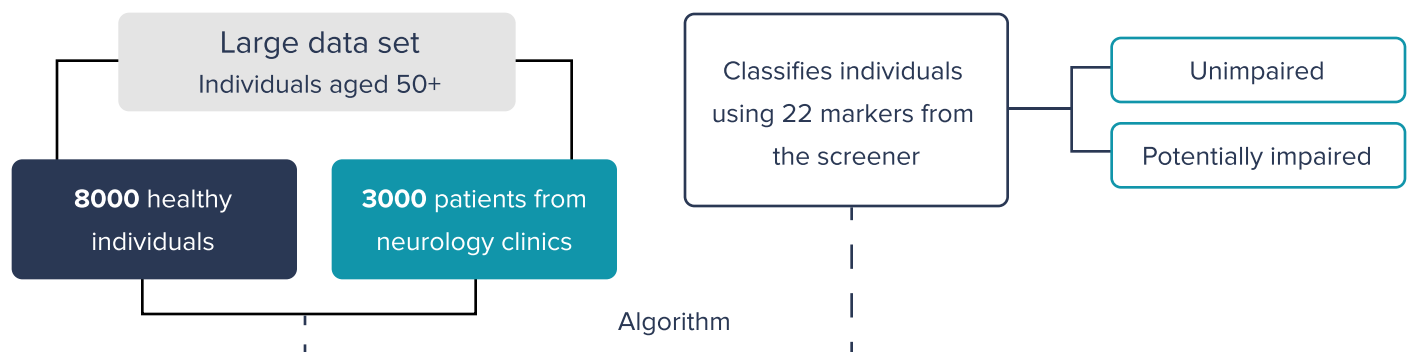
- **Number Ladder**, a test of visuospatial working memory
- **Feature Match**, a test of attention

See the [Patient Classifications](#) section below for more information about how each task is linked with cognitive decline.

Training a Machine Learning Algorithm for Detecting Cognitive Impairment

The Creyos dementia screener uses a sophisticated machine learning classifier that leverages multiple outcomes from each task, such as reaction times, error rates, and interference ratios. Together, Number Ladder and Feature Match have 22 such features that are used by the classifier to predict whether an individual is cognitively healthy, or potentially impaired.

The machine learning model was trained on a large data set consisting of over 8000 healthy individuals and over 3000 patients from select neurology clinics, all over the age of 50. Using only the data provided by the Number Ladder and Feature Match tasks, the model learned to distinguish between these two groups. Once this learning had taken place, the trained model could be used to make a prediction about whether the cognitive testing data from a new individual belonged to the healthy group or the patient group.



Further validation was performed to ensure that high classification accuracy could be achieved outside of the training data, in *different* groups of patients and healthy individuals. This validation ensures that the screener maintains its accuracy outside of the lab, effectively identifying impaired individuals in a diverse set of patient populations. See Section C for more information about sensitivity and specificity of the screener and assessment.

Further testing is suggested will appear on the dementia screener report if a patient is predicted to be similar to impaired patients (i.e., a positive result). In rare cases, **reassessment required** will appear if there was a technical problem with testing or patient behavior was so unusual that performance markers could not be calculated.

The screener is designed to have high sensitivity. Therefore, a large percentage of individuals with any type of cognitive impairment will be flagged for further testing. Some healthy individuals will also be flagged for further testing—as with any cognitive assessment that classifies patients, there will be some false positives, and results cannot be used in isolation. Additional Creyos tools, such as the full dementia assessment and questionnaires, when combined with clinical expertise, can assist in confirming or ruling out cognitive impairment with high accuracy and confidence.

See the [Creyos Dementia Protocol Report Interpretation Guide](#) for more information about the screener report and interpreting results.

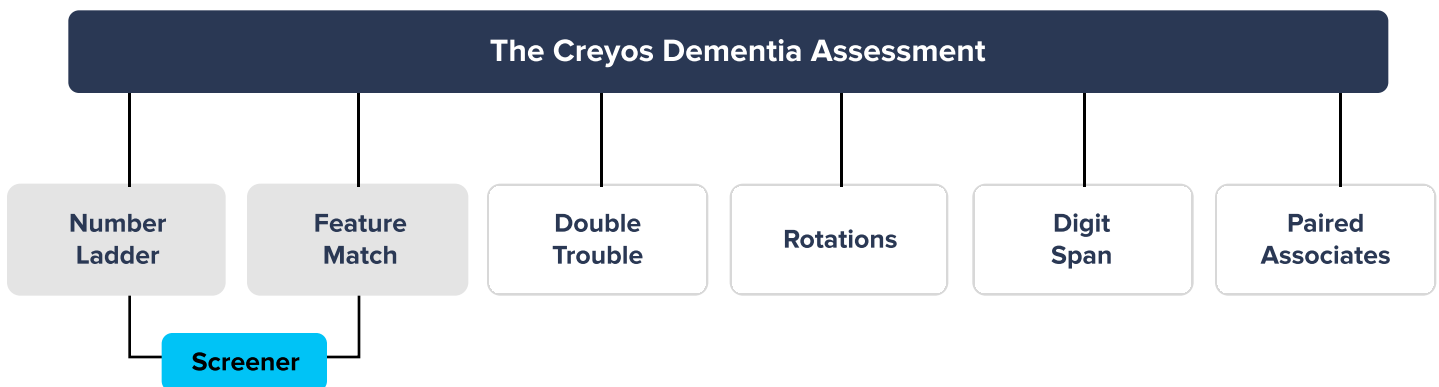
C. The Creyos Dementia Assessment

When results more detailed than a screener are needed, the Creyos dementia assessment provides **domain-specific information about a patient's cognition**, along with self-report information that helps confirm and document criteria for neurocognitive disorders like MCI and dementia.

Cognitive Tasks

Tasks in the Creyos Dementia Assessment

The Creyos dementia assessment consists of **six cognitive tasks**: the two tasks from the screener, plus four additional tasks. If the patient has already completed the screener, then the two tasks from the screener will not be repeated and will be included in the results for the assessment.



The six tasks in the assessment measure visuospatial working memory, episodic memory, attention, mental rotation, verbal short-term memory, and response inhibition. These fall into three broad domains: memory, reasoning, and verbal ability. Dementia and MCI are often seen as memory problems, but focusing on memory impairment alone can be less accurate than measuring memory alongside other domains (Brodaty et al., 2016), and the DSM-5 criteria for mild neurocognitive disorder do not single out memory. However, most neurologists distinguish between amnesic and nonamnesic MCI (Roberts et al., 2010), so impairments in short-term memory will be highlighted on the patient's report as potential amnesic MCI or amnesic major neurocognitive disorder (see [Patient Classifications in the Creyos Dementia Assessment below](#)).

The three domains come from a study by Hampshire et al. (2012), who showed, from behavioral and brain imaging data collected from participants completing the Creyos tasks, that at least three distinct cognitive domains (recruiting distinct brain networks) are involved to different extents in each of the tasks. In the Creyos framework, each task is assigned to the domain that it empirically loads on most highly.

Brief descriptions of studies linking dementia and MCI to each task are included below. See the [Creyos Science Overview](#) for general-purpose task descriptions and score calculations.

Memory Tasks



Visuospatial Working Memory (Number Ladder): Memory impairments are often seen as the most common sign of age-related cognitive decline. Indeed, visuospatial working memory is often impaired in patients with MCI or Alzheimer's disease ([Weissberger et al., 2017](#)). Performance on the Creyos Number Ladder task (formerly known as Monkey Ladder) has been associated with dementia biomarkers ([Thienel et al., 2023](#)) and genetic risk for dementia ([Lupton et al., 2023](#)). Number Ladder is also included in the two-task screener.



Episodic Memory (Paired Associates): Loss of the ability to recall events is a typical sign of cognitive decline. The Creyos Paired Associates task is an abstract representation of the ability to store and recall paired pieces of information. Episodic memory impairments are a sign of preclinical Alzheimer's disease ([Bäckman et al., 2005](#)), and paired associate learning tasks specifically can help distinguish patients with cognitive decline from healthy controls ([Edmonds et al., 2015](#)).

Reasoning Tasks



Attention (Feature Match): Attention is an early step in information processing, and deficits in attention can affect other cognitive functions. Attentional abilities are generally impaired in MCI and early dementia ([Bäckman et al., 2005](#)). Tasks like Feature Match may reveal abnormalities in attention, even in patients who are only *aware* of deficits in memory ([Tales et al., 2004](#)). Feature Match is also included in the two-task screener.

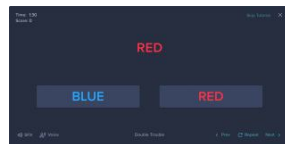


Mental Rotation (Rotations): Visuospatial abilities, including mental rotation, are not often the focus in dementia research, but some researchers have argued that visuospatial tests should be used to measure the parietal lobe changes seen in early Alzheimer's disease ([Salimi et al., 2018](#)). Slower reaction times may also explain deficits in simple visuospatial tasks like Rotations and Feature Match ([Bourrelier et al., 2015](#)).

Verbal Ability Tasks



Verbal Short-Term Memory (Digit Span): Deficits in verbal abilities may be more subtle in cases of age-related difficulties, but when impairments are present in this domain, it can help establish that decline is occurring in multiple areas. Reviews (e.g., [Bäckman et al., 2005](#)) find that although verbal ability is not the domain most impaired in early Alzheimer’s disease, it is still lower in patients than in healthy controls. Verbal short-term memory deficits in particular are measured by Digit Span, and often a self-reported early sign of cognitive impairment (e.g., trouble remembering phone numbers). Some studies have found subtle deficits in Digit Span performance in patients with MCI or dementia ([Ruchinskas, 2019](#); [Battista et al., 2020](#)), but reviews (e.g., [Martyr & Clare, 2012](#)) have found that Digit Span is not consistently impaired in Alzheimer’s disease. Nonetheless, information about verbal short-term memory contributes to the overall assessment’s sensitivity in dementia patients, and may help identify more severe cases affecting multiple domains.



Response Inhibition (Double Trouble): Inhibitory control is a part of executive functioning, which is frequently impaired in cases of MCI, and may contribute to everyday difficulties experienced by individuals with cognitive decline ([Rabi et al., 2020](#)). The Creyos Double Trouble task is based on the classic Stroop test, in which individuals with MCI and dementia perform more slowly and less accurately than healthy controls ([Bélanger et al., 2010](#)).

Task Performance and Thresholds for Objective Cognitive Impairment in the Dementia Assessment

Performance on each cognitive task is represented by a final overall score, which is then compared to the Creyos [normative database](#).

Criteria to be flagged for objective cognitive impairment: performing **one standard deviation** or more **below average in two or more cognitive tasks**.

Objective cognitive impairment:  **Detected**

There is no gold standard for criteria to determine objective impairment, but several classification schemes have been proposed ([Emmert et al., 2022](#)). The DSM-5 mentions one to two standard deviations (SDs) below norms as typical performance for mild neurocognitive disorder. The cutoff

of one standard deviation is quite lenient on a single task, classifying about 16% of healthy norms as impaired. However, by requiring multiple tasks to fall lower than one SD below average in order to be classified as objectively impaired, there is increased confidence, stability, and reliability of the classification (Edmonds et al., 2015). In one study of various diagnostic cutoffs (Taylor & Heaton, 2002), using a one SD cutoff on at least two factors resulted in good sensitivity and specificity for detecting impairment.


If both of the tasks within the same domain are below typical range, then that domain is flagged as potentially impaired. If two or more tasks from different domains are below typical range, then the patient is flagged for potential general impairment.

Objective Cognitive Impairment Creyos Cognitive Assessment	🚩 Potential memory and reasoning impairments	Impairment in one or more categories of cognitive performance, determined using standardized test results.
Objective Cognitive Impairment Creyos Cognitive Assessment	🚩 Potential memory and reasoning declines	Meaningful decline in one or more categories of cognitive performance, determined using longitudinal standardized test results.

Note that a patient can be positive on the quick screener without being impaired in both tasks in the full assessment—the screener is designed to be sensitive to subtle impairments that may not be present in the more stringent criteria of the assessment.

Which Scores are Used to Determine Impairment?

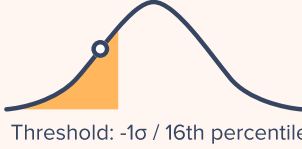
The Creyos dementia protocol uses *adjusted standard scores* to determine whether or not a task result is more than one standard deviation below the mean. The standard score and associated percentile are shown in the detail pages of the report.



Episodic Memory

Paired Associates

A measure of episodic memory — the ability to remember specific events, paired with the context in which they occurred.



Threshold: -1σ / 16th percentile

Percentile: **14**
Standard Score: **82**

🚩 **Below typical range**

For more on how standard scores are calculated and adjusted, see the [Creyos Health Report Interpretation Guide](#).

Objective Cognitive Decline

If a patient has completed more than one assessment, meaningful objective *decline* may be flagged on the report instead of or in addition to objective *impairment*.

Criteria to be flagged for objective cognitive decline: **a meaningful decline in two or more cognitive tasks.**

As with objective impairment, decline can be domain-specific (both tasks in a domain have declined) or general if two or more tasks from different domains have declined. If a patient's baseline performance is high, it is possible to be flagged for decline even if task performance is still within the typical range. Meaningful declines are indicated with an asterisk on the report:

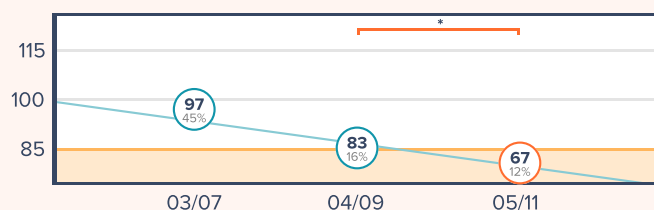


Visuospatial Working Memory

Number Ladder

A measure of visuospatial working memory — the ability to remember information about objects in space, and update memory based on changing circumstances.

- Below typical range
- Meaningful decline from last test

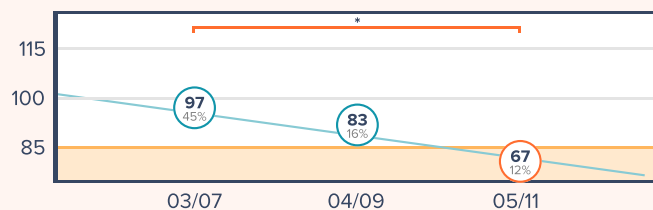


Episodic Memory

Paired Associates

A measure of episodic memory — the ability to remember specific events, paired with the context in which they occurred.

- Below typical range
- Meaningful decline from baseline



Meaningful decline is determined based on typical changes seen in the Creyos database. For calculation of meaningful change, see the [Creyos Health Report Interpretation Guide](#).

Validation of the Creyos Dementia Screener and Assessment

The first step in validating the Creyos dementia protocol was to choose the optimal combination of cognitive tasks to include. Analyses started with examining scores from all 12 of the Creyos core cognitive tasks in adults age 50 and above. Using criteria similar to those above for detecting objective impairment, the ability to distinguish patients from controls was calculated in two samples: 8,473 healthy individuals and 3,665 patients from select neurology clinics. Every possible combination of six tasks (all including the two from the screener) was compared to the full 12-task battery in order to find candidates for an abbreviated assessment that takes half the time of the full battery, but provides similar results. From these candidates, a six-task battery was selected to represent three distinct domains while taking as little time to complete as possible and being practical to administer to diverse patient populations (e.g., with any literacy level). The result is a short battery that is able to accurately distinguish healthy people from those who are potentially impaired. Together, the screener and the assessment provide a highly accurate set of tools for diagnosing and tracking dementia.

Sensitivity and Specificity of The Creyos Dementia Screener and Assessment

In dementia care, high sensitivity and specificity are vital to ensure accurate diagnosis and effective treatment planning. High sensitivity minimizes the risk of missed cases, catching even subtle early signs of cognitive decline. High specificity reduces false positives, preventing unnecessary patient anxiety, wasted provider time, and costly follow-ups. The Creyos dementia protocol is designed to maximize these metrics to empower providers with precise insights for confident decision-making. The screener stage focuses on sensitivity, ensuring that patients with even mild cognitive symptoms are flagged for further testing. The assessment stage focuses on specificity and detailed diagnostic information, ensuring that healthy individuals are not falsely identified as having dementia.

Dementia Screener

The Creyos dementia screener is optimized for sensitivity, so it does not miss patients who require more testing. The goal of the screener is to establish which patients are most likely to be impaired and flag them for a more in-depth neuropsychological evaluation that can help rule out false positives or provide more detail on truly impaired individuals, including impaired domains, specific performance metrics, and alignment with diagnostic criteria for dementia.

Sensitivity for the screener is very high. In the internal Creyos data used to train the algorithm (see Section B), the screener achieved over 80% sensitivity for identifying patients with at least mild cognitive concerns, while maintaining 80% specificity in data from healthy norms. When the same algorithm was applied to a completely different set of data from patients with cognitive concerns and healthy older adults, sensitivity was 77%, and specificity was 79%, demonstrating that the screener's results remain accurate in several different types of patient groups. Severe dementia can also be

detected. In a small sample of patients diagnosed with Alzheimer’s disease, sensitivity was 100%. These results are being prepared for publication.

Dementia Assessment

At the assessment stage (often used when patients are positive on the screener), the focus is on detailed dementia-related information and specificity. The assessment has criteria for identifying a patient as cognitively impaired or cognitively unimpaired. In short, impairment requires two or more neuropsychological tasks falling lower than one standard deviation below age-match norms. This cognitive information is bundled with questionnaire responses to assist clinicians with diagnostic decisions, especially when focusing on the DSM-5’s diagnostic criteria for major neurocognitive disorder (or dementia).

Because six neuropsychological tasks across multiple domains are included, this stage should help to rule out impairment in healthy people who slipped through the screen. Those who are flagged for cognitive impairment in the assessment have demonstrated significant impairment in several domains of cognition, meeting standard criteria for identifying impairment.

Specificity for the assessment is very high. In healthy populations, 94 to 99 percent of individuals are not flagged for impairment.

Because the assessment is designed as a diagnostic aid for specific criteria, sensitivity is problematic to calculate and interpret—the patient either meets criteria or doesn’t, and there is often no additional external “truth” to compare to. In internal Creyos data, over 30% of patients with mild concerns about cognition and 80% of patients with suspected dementia were flagged for impairment on the Creyos dementia assessment. Similarly, [Taylor and Heaton \(2001\)](#) looked at WAIS performance in patients independently diagnosed with various dementia-related disorders. Treating those diagnoses as truth, and using criteria very similar to the Creyos assessment, sensitivity was 80% or higher, while maintaining about 85% specificity. The Creyos assessment can be considered a similar neuropsychological testing approach, but it takes far less time to complete.

Some clinicians may choose to do repeated testing on patients who are positive on the screener but not flagged on the full assessment. In these borderline cases, the screener identifies candidates for longitudinal testing, where the assessment can identify meaningful declines compared to a personalized baseline, or capture data when a patient slips below thresholds. Thus, for patients on a trajectory of decline, sensitivity increases with repeated testing.

Validity and Reliability of the Cognitive Tasks

The six Creyos tasks used in the dementia protocol have been validated over the course of decades of research. Validity has been established in over [400 studies](#), including patient studies, brain imaging research, and large-scale online projects involving tens of thousands of participants.

Creyos tasks have been used extensively in aging and dementia research. Age is one of the strongest predictors of test scores on all Creyos tasks. Scores typically decline with age through adulthood, though the domain measured, sex, and sociodemographic factors can affect this trajectory ([Nichols et al., 2021](#)). For a review of the history of Creyos tasks in aging research, and data on comparisons with traditional assessments like the MoCA and MMSE, see [Sternin et al. \(2019\)](#).

In dementia research, Creyos has proven a valuable assessment tool. In studies demonstrating strong validation of the tasks for early detection of age-related impairment, biomarkers of dementia such as genetic risk, sulcal width, and amyloid status have been associated with task scores ([Thienel et al., 2023](#); [Lupton et al., 2023](#)). Early treatment also appears to have the expected effects on Creyos task scores ([Brodaty et al., 2023](#)).

More information about each task's validity and reliability can be found in the [Creyos Health Science Overview](#). Further validation through brain imaging can be found in the [Creyos Brain Regions Guide](#).

For advice on determining if a specific patient has provided valid data, or concerns about cheating or malingering, see the [Creyos Dementia Protocol Report Interpretation Guide](#).



Is online cognitive testing valid?

Computerized testing has become widespread, but there may be concerns that testing completed over the Internet and/or without supervision results in less valid or reliable data compared to in-person testing. However, Creyos has not detected systematic differences between in-person and online testing in patient populations or healthy controls ([Sternin et al., 2019](#)). Care should still be taken to ensure every patient devotes effort to the testing session, whether it is completed in-person or online. Creyos includes written instructions asking the participant to find an environment free of noise and distraction. Some clinicians provide their own guidance when introducing cognitive assessments, and verify that the patient has sufficient vision and motor control to complete computerized assessments without assistance. If there are concerns that an individual patient cannot complete testing without supervision, all Creyos assessments can be completed in person. The [Creyos Dementia Protocol Report Interpretation Guide](#) contains more tips for ensuring each testing session results in valid data.

The Creyos Normative Database


All standard scores are based on comparisons with age- and gender-matched norms. Due to its size and careful methodology to collect representative data, the Creyos database represents a generally healthy normal population. Therefore, a patient scoring below the typical range for their age group may indicate impaired functioning. For more information about the normative database that each patient is compared to, see [Understanding the Creyos Health Normative Database](#).

Note that norm comparison groups are broken down by age and gender, but not education. While education is correlated with cognitive test scores, and may provide a protective effect against dementia ([Livingston et al., 2020](#)), its role in dementia assessment is less clear.


Some researchers (e.g., [Ganon et al., 2013](#)) have found that **when traditional screening tools like the MoCA are corrected for education** (e.g., by adding points for individuals with lower education levels), **sensitivity decreases**, meaning an increased number of false negatives.

Clinical judgment about the patient's baseline cognition is valuable when interpreting the results of current cognition assessments. That judgment may be guided by the patient's education level, but also vocation, lifestyle, leisure activities, sociodemographic factors, and other information that could affect the patient's assumed "cognitive reserve." Attempting to automate this decision-making is not within the scope of any current software tool, including Creyos.

In addition to cognitive testing, the protocol also includes two questionnaires to help confirm diagnostic criteria for mild or major neurocognitive disorder. Each has established cutoffs for flagging potential concerns.

- BRAIN HEALTH CO.

IQCODE-SR Report



Assessment Details			
ID: 474983	Gender: Female	Completion Date: 2023/03/07	Page 1 / 2

Performance Summary

Overall Result

Indicative of subjective cognitive decline

Averaged score of 3.38, meets the 3.22 point threshold

This adapted self-report version of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE-SR) developed by Jorm et al. focuses on subjective change and is useful in screening and evaluating dementia. Combined with cognitive testing and functional scales, a useful overview is obtained.

To score the IQCODE, determine the average score by adding up the response scores for each question and dividing by 16. A score of 1 suggests considerable improvement, 3 no change, and 5 suggests sizeable deterioration. Scores above 3.22 indicate the possibility of MCI and longitudinal monitoring is warranted.

Raw Responses						
Item - Compared with 10 years ago how is this person at:	Response					
1. Remembering things about family and friends e.g. occupations, birthdays, addresses	1 Much improved	2 A lot improved	3 Not much change	4 A lot worse	5 Much worse	
2. Remembering things that have happened recently	1 Much improved	2 A lot improved	3 Not much change	4 A lot worse	5 Much worse	
3. Recalling conversations a few days later	1 Much improved	2 A lot improved	3 Not much change	4 A lot worse	5 Much worse	
4. Remembering your address and telephone number	1 Much improved	2 A lot improved	3 Not much change	4 A lot worse	5 Much worse	
5. Remembering what day and month it is	1 Much improved	2 A lot improved	3 Not much change	4 A lot worse	5 Much worse	
6. Remembering where things are usually kept	1 Much improved	2 A lot improved	3 Not much change	4 A lot worse	5 Much worse	
7. Remembering where to find things which have been put in a different place from usual	1 Much improved	2 A lot improved	3 Not much change	4 A lot worse	5 Much worse	
8. Knowing how to work familiar machines around the house	1 Much improved	2 A lot improved	3 Not much change	4 A lot worse	5 Much worse	
9. Learning to use a new gadget or machine around the house	1 Much improved	2 A lot improved	3 Not much change	4 A lot worse	5 Much worse	
10. Learning new things in general	1 Much improved	2 A lot improved	3 Not much change	4 A lot worse	5 Much worse	
11. Following a story in a book or on TV	1 Much improved	2 A lot improved	3 Not much change	4 A lot worse	5 Much worse	

IADL Report



Assessment Details

Sender: Male Completion Date: 2021/12/31

Performance Summary

Overall Result

5/5

Indicates independence in all activities

Interpretation

For each activity, the client selects a description that best resembles their functional level. Each response is **scored with a 0 or 1** and highlighted in the tables. Summary scores range from **0 (low function, dependent) to 5 (high function, independent)**. Studies have recommended a cutoff point of 1 functional deficit or more on the IADL.

Raw Responses	
	Response
s, etc.	1
	1
	1
	0
	Response

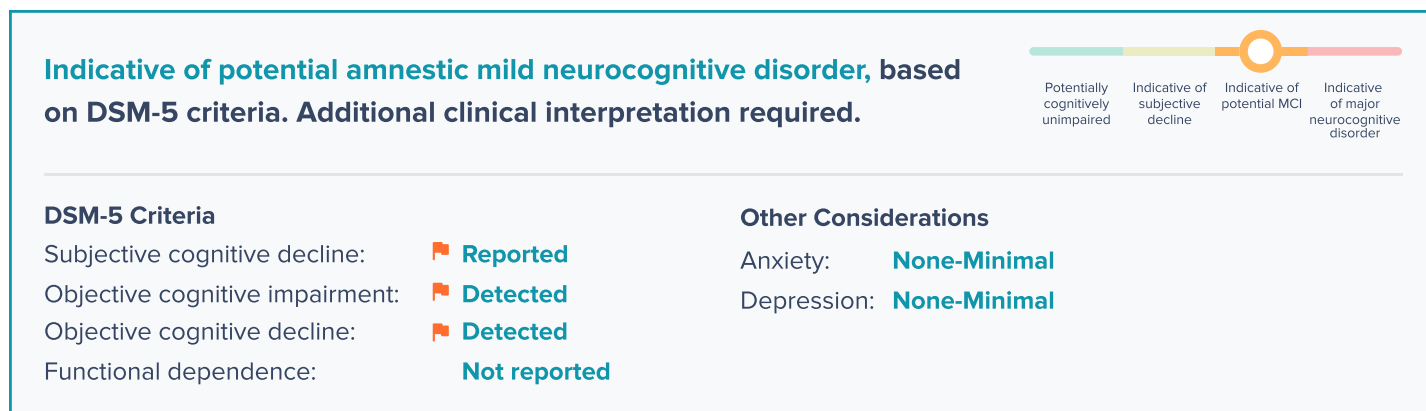
Two optional questionnaires can also be included to help quantify or rule out neurobehavioral symptoms as the primary cause of cognitive decline:

- **The Patient Health Questionnaire (PHQ-9)** is used to measure symptoms of depression.
- **The General Anxiety Disorder questionnaire (GAD-7)** is used to measure symptoms of anxiety.

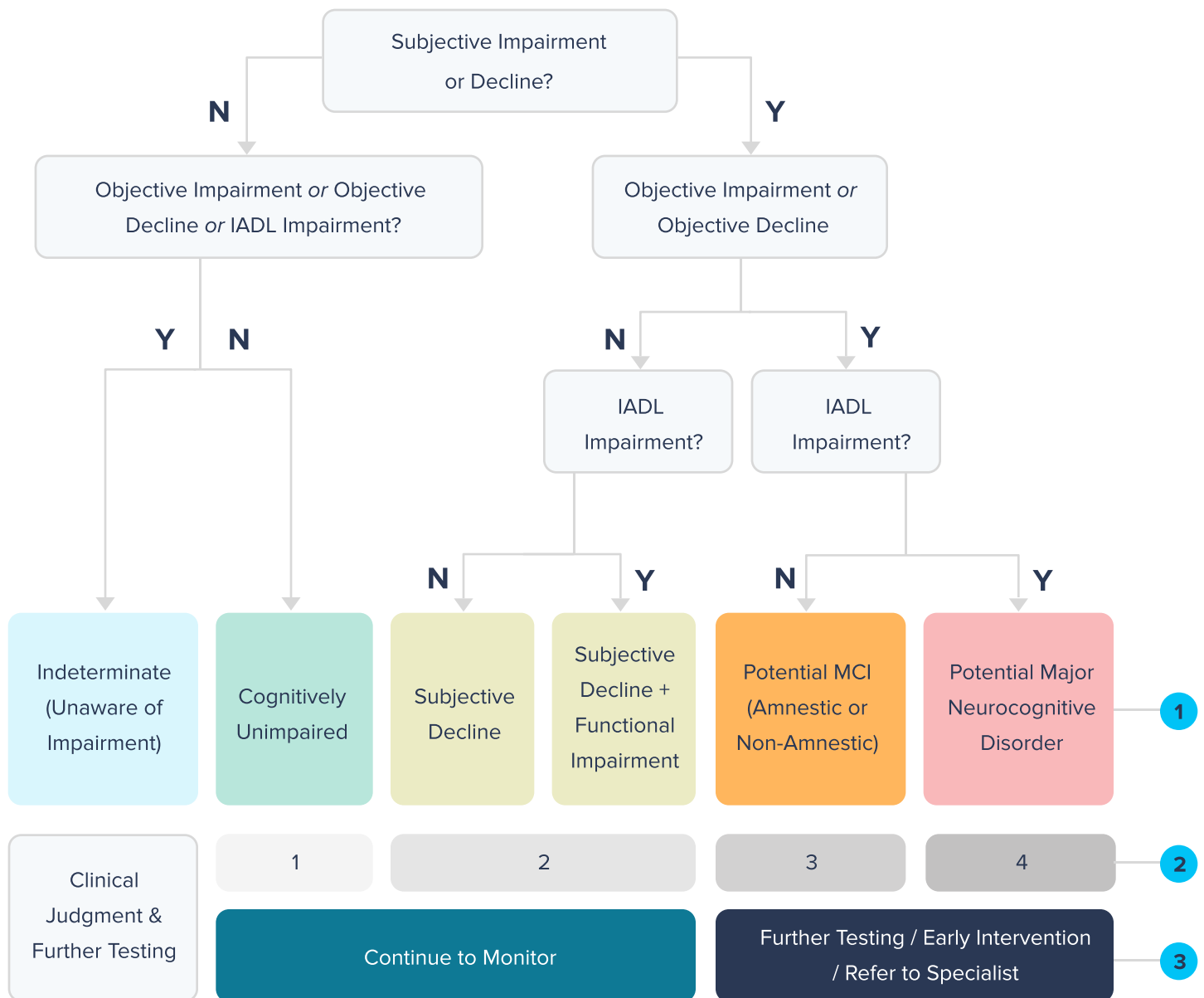
Each questionnaire is a standard third-party questionnaire commonly used to assess symptoms related to neurocognitive disorders. For more information on the origins of each questionnaire, psychometric properties, validation, and other information, see each of the articles linked above. See the [Creyos Dementia Protocol Report Interpretation Guide](#) for more information about how questionnaire results may contribute to a diagnosis or help track symptoms over time.

Patient Classifications in the Creyos Dementia Assessment

On the assessment report, each patient is labeled with a classification based on the results of cognitive testing and questionnaire responses. See the [Creyos Dementia Protocol Report Interpretation Guide](#) for a list of possible classifications and their meaning.



Classification is based on the patient's specific combination of subjective impairment, objective impairment / decline (amnesic or non-amnesic), independence in activities of daily living, and neuropsychiatric symptoms (anxiety and depression). The conceptual framework below illustrates possible patient classifications. Classification is based primarily on DSM-5 criteria for mild or major neurocognitive disorder, but the illustration also shows approximate alignment with the NIA-AA numerical clinical staging specifically for individuals in the Alzheimer's continuum ([Jack et al., 2018](#)).



1. DSM-5 Neurocognitive Disorder Criteria

2. NIAA Numerical Clinical Staging

3. Potential Next Steps

Occasionally, a classification will be indeterminate due to a mix of results that do not fit any particular set of criteria. This can often be a result of inaccurate self-report information on the IADL or IQCODE questionnaire. See the FAQs in the [Dementia Protocol Report Interpretation Guide](#) for advice on dealing with indeterminate results and additional tips for interpreting a patient's classification.

As indicated on the report, additional clinical interpretation is always required. The Creyos dementia protocols are based on research and established criteria, but clinical decision making cannot be automated—the rest is up to you.



Have Questions About The Creyos Dementia Protocol?

Already Using Creyos?

If you're using Creyos and are interested in getting started with the dementia protocol, contact your customer success manager or email help@creyos.com.

Not Yet Using Creyos?

If you're not yet using Creyos and are interested in getting it for your practice, visit creyos.com to learn more and book a personalized demo with one of our product specialists.