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CREYOS ADHD CLINICAL PROTOCOL AND REPORT

Report Interpretation Guide

Quickly gain validated and powerful brain health insights

Important Information Before You Read This Document

Creyos (formerly Cambridge Brain Sciences) provides a scientifically-validated and objective measure of an individual's cognition, however, it is not a diagnostic tool. Creyos Health should be used in conjunction with other information and clinical judgment to reach conclusions regarding an individual's health. Ultimately, Creyos Health does not replace the judgment of a practitioner and Creyos does not assume responsibility for the outcome of decisions made based on Creyos Health data.

Interpreting Creyos ADHD Assessment Results

This guide is meant to help you with the interpretation of the ADHD protocol report. In it you'll find a breakdown of how the protocol works, sample results, and instructions for report interpretation.

A. ADHD Protocol Overview

The Creyos Health ADHD protocol gathers objective attention and executive function data alongside optional subjective reports to assist clinicians working with patients concerned about ADHD. This guide reviews the elements of the protocol and report, reviews cognition markers associated with ADHD, and answers common interpretation questions.

For more information on the science behind the protocol, validity, and how each marker is related with ADHD, see the Creyos ADHD Clinical Report Science Guide.

About the Creyos Health ADHD Protocol and Clinical Report

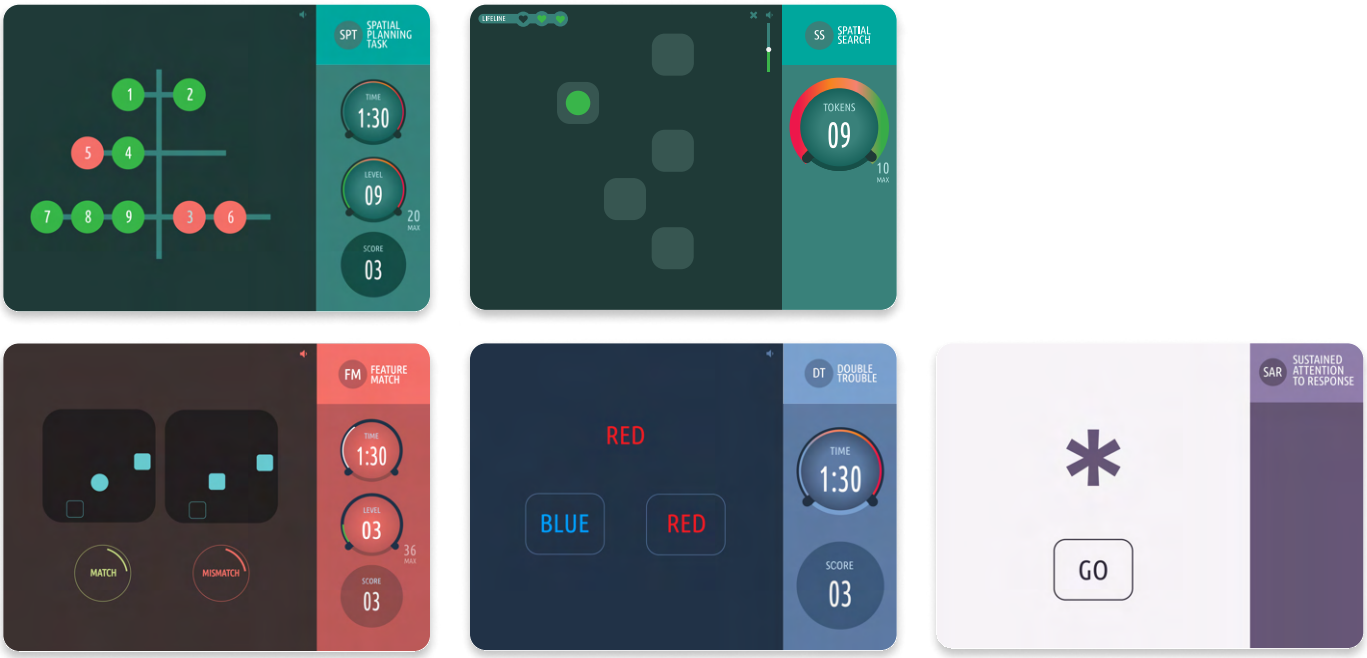
The Creyos ADHD protocol assesses cognitive function through a series of scientifically validated performance indicators, called markers, linked with attention deficit hyperactivity disorder. Ten of the markers come from the core Creyos cognitive tasks (Spatial Planning, Token Search, Feature Match, and Double Trouble). The remaining four markers are derived from the Sustained Attention to Response Task (SART)—a 6-minute task available exclusively as part of the Creyos ADHD protocol. Markers were validated through review of scientific literature on ADHD. Each marker is supported by multiple studies that report an association with a diagnosis. After the 20-minute protocol is complete, a validated, objective, and easy-to-interpret clinical report focused exclusively on ADHD is instantly generated.

The Cognitive Tasks

Cognitive challenges are a defining symptom of ADHD, and in some patients, serious deficits in intellectual function contribute to the problems at work, at school, and at home that accompany attentional difficulties.

There are a total of five cognitive tasks in the Creyos ADHD protocol. Each Creyos task was carefully selected for the protocol based on a significant relationship with ADHD, as demonstrated through peer-reviewed published papers. Each task has a clear relationship with ADHD, such that patients diagnosed with ADHD by a qualified professional perform differently from a healthy control group.

The tasks were also designed to complement one another. Double Trouble, Feature Match, and the SART each measure different aspects of attention itself. Spatial Planning and Token Search measure other aspects of executive functioning, which may not be core to the definition of ADHD, but are nonetheless impaired in many individuals diagnosed with the disorder (Patros et al., 2019; Alderson et al., 2013).



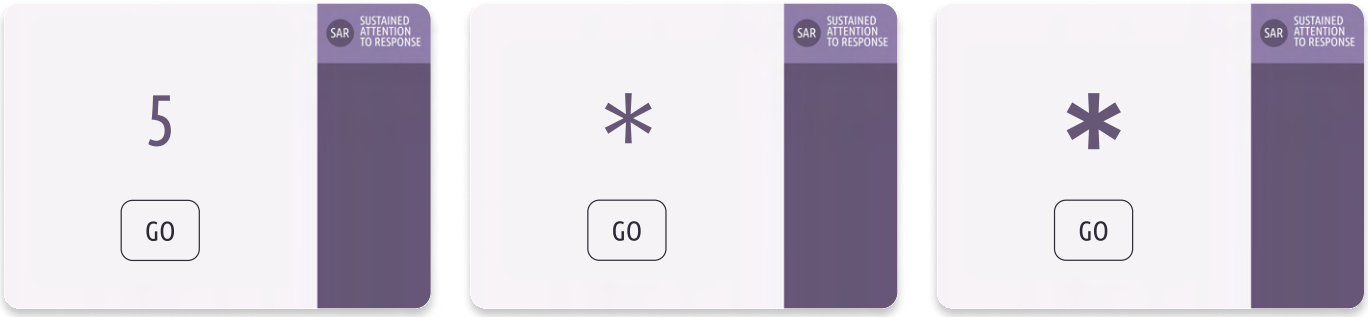
To learn more about each of the “core” cognitive tasks (Double Trouble, Feature Match, Spatial Planning, and Token Search), please refer to the Creyos Science Overview document. The SART is currently only available as part of the ADHD protocol, and described in more detail below.

The Sustained Attention to Response Task (SART)

The SART is a common task used to study and assess ADHD, and is part of the continuous performance task family—that is, tasks that measure attention and response inhibition over longer periods of time.

Created by Ian Robertson and colleagues in 1997, in the same unit at the University of Cambridge where most of the other Creyos tasks were conceived, the SART was designed to capture everyday “slips” in attention when performing routine tasks. That could include pouring cream in coffee even though it was requested black, saying “you too” when a server asks you to enjoy your food, or nodding along to a lecture then realizing you haven’t been paying attention.

The version of SART included in Creyos Health specifically measures the ability to sustain mindful, conscious information processing, even in repetitive, unstimulating, or distracting situations. The task works by having patients respond to numbers appearing on the screen. Using a spacebar, mouse, or tapping the “Go” button on a touchscreen, patients are instructed to respond to all numbers except the number “3”.



The task displays 225 trials with a random number from 1 to 9, followed by an asterisk. The participant is asked to respond as soon as the asterisk turns bold, unless the number 3 appears. Because the 3 is rare compared to other numbers, patients become accustomed to automatically responding after every number, but attentional difficulties can cause drifting in response times, failing to respond on time, responding even when the 3 appears, and other measurable differences. It takes about 6 minutes to complete in total, and requires a patient to maintain sustained attention for the duration.

In the decades since its creation, the SART has proven sensitive to a variety of disruptions to sustained attention. Inattention is a defining feature of ADHD and one of the symptom clusters identified in the DSM-5. Thus, the SART is a test commonly used to objectively measure deficits in sustained attention experienced by children and adults with ADHD.

ADHD Cognitive Task Markers

In the Creyos ADHD report, *markers* are specific cognitive performance metrics that are associated with an ADHD diagnosis. Each cognitive task results in at least one marker, and some tasks result in several markers. For example, the number of errors and average reaction time may be two separate markers from the same task, allowing clinicians to examine both accuracy and speed of responding.

Each marker is associated with a different aspect of attention or another cognitive function. All markers have been studied and featured in peer-reviewed papers that report a statistically significant difference between individuals diagnosed with ADHD and individuals considered to be typically developing or healthy controls. See the Creyos ADHD Clinical Report Science Guide for details.

Markers are presented in raw units—for example, reaction time markers are presented in milliseconds. The percentile rank of the marker is also displayed.

A marker is *outside the typical range* when it is unusual compared to the Creyos normative database, defined as more than one standard deviation away from the mean. To be flagged as

outside typical range, the patient must also have deviated from average in the same direction as people who are diagnosed with ADHD. For example, if people with ADHD tend to perform significantly slower on a task (i.e., take more milliseconds to respond), and a patient is unusually slow on a task, then the reaction time marker will be flagged as outside typical range.

Overall Reaction Time

Speed of responding, regardless of the complexity of the stimulus. People with ADHD tend to respond slower on short-term response inhibition tasks.

Result	2721ms
Typical Range	< 2684ms
Percentile	87

Pocklington, B., & Maybery, M. (2006). Proportional slowing or disinhibition in ADHD? A Brinley plot meta-analysis of Stroop Color and Word Test performance. *International Journal of Disability, Development and Education, 53,* 67-91.

This threshold is presented visually on the report. The orange region represents performance outside the typical range. This region is associated with ADHD, which may be on the left or the right side of the normal curve, depending on how people diagnosed with ADHD typically perform. In the example above, people with ADHD perform slower than average—that is, overall reaction time is *higher* in milliseconds. The shaded region is on the right, signifying that scoring outside the typical range means having an average reaction time *higher* than most individuals. The shaded region represents one standard deviation *above* the mean, or *above* the 84th percentile.

If people with ADHD have *lower* scores on the marker, then the shaded region will be on the left, representing one standard deviation *below* the mean, or *below* the 16th percentile.

The typical range is defined only by a normative database of generally healthy individuals—performance is not directly compared to individuals diagnosed with ADHD. Thus, a marker flagged as outside the typical range is simply an indication that performance was unusual enough to be considered atypical. More subtle deficits in attention and executive function may not reach this threshold, so clinician discretion is required to interpret each result (see Section D for common interpretation questions and tips).

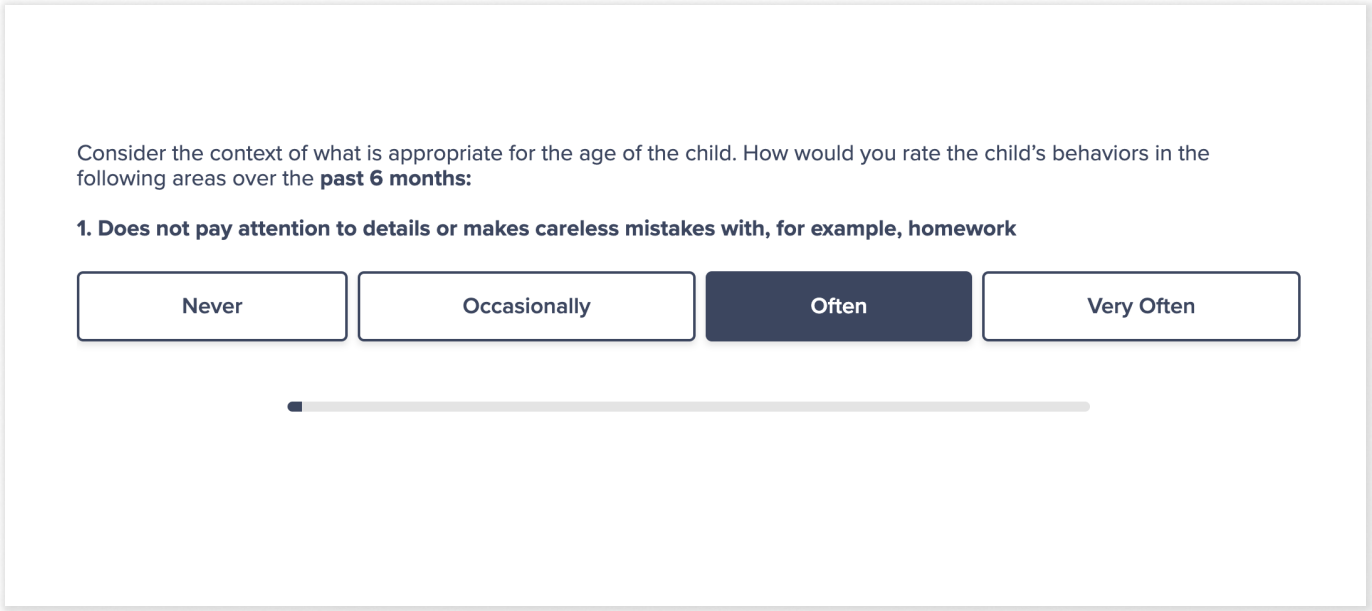
The results presented on the Creyos ADHD report can be compared to the blood biomarkers that share the “marker” terminology: they are compared to norms so they can be labeled as typical or atypical, and many markers have been linked to the presence or severity of a health condition. While no marker in isolation can definitively confirm or rule out a diagnosis, each result provides a piece of information that can be correlated with questionnaire results, clinical interviews, and other available patient data to assist in clinical decisions.

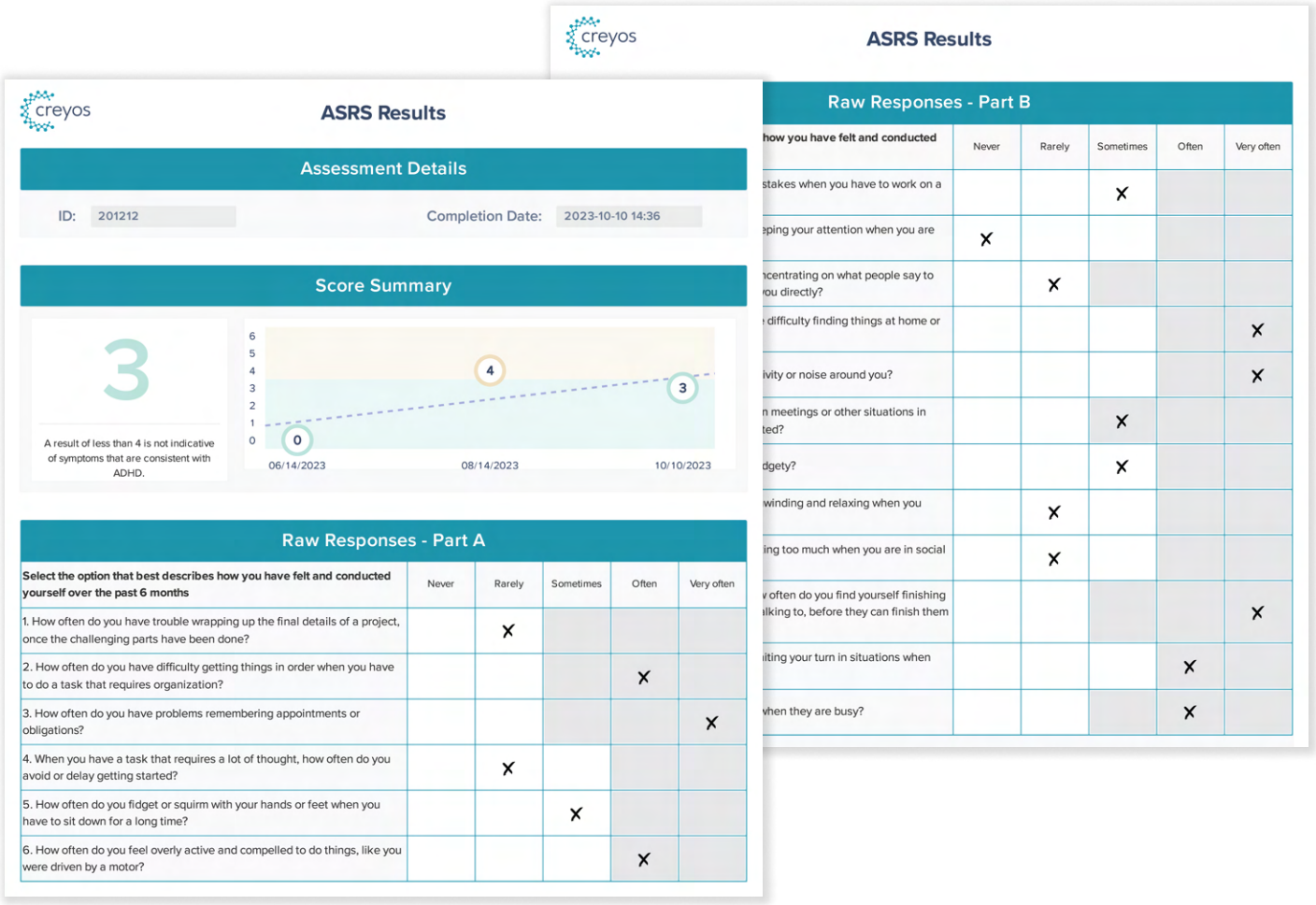
ADHD Questionnaires

The ADHD protocol includes an optional age-appropriate ADHD questionnaire, as per the specifications below:

- Age 6 to 11: The Vanderbilt ADHD Diagnostic Rating Scale (VADRS)
- Age 12 to 17: The Strengths and Weaknesses of Attention-Deficit/Hyperactivity-symptoms and Normal-behaviors (SWAN)
- Age 18+: The Adult ADHD Self-Report Scale (ASRS)

If included, the age-appropriate questionnaire will automatically appear in the assessment session based on your patient's age. When preparing an assessment, the questionnaire portion can be opted out of, in case questionnaire information is already available or a parent is not present to complete one.





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ASRS Results

Assessment Details

ID: 201212

Completion Date: 2023-10-10 14:36

Score Summary

3

A result of less than 4 is not indicative of symptoms that are consistent with ADHD.

Raw Responses - Part A

Select the option that best describes how you have felt and conducted yourself over the past 6 months	Never	Rarely	Sometimes	Often	Very often
1. How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?		X			
2. How often do you have difficulty getting things in order when you have to do a task that requires organization?				X	
3. How often do you have problems remembering appointments or obligations?					X
4. When you have a task that requires a lot of thought, how often do you avoid or delay getting started?		X			
5. How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?			X		
6. How often do you feel overly active and compelled to do things, like you were driven by a motor?				X	

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ASRS Results

Raw Responses - Part B

how you have felt and conducted	Never	Rarely	Sometimes	Often	Very often
stakes when you have to work on a			X		
eping your attention when you are	X				
ncentrating on what people say to ou directly?		X			
difficulty finding things at home or					X
ivity or noise around you?					X
n meetings or other situations in ted?			X		
dgety?			X		
winding and relaxing when you		X			
ing too much when you are in social		X			
often do you find yourself finishing alking to, before they can finish them					X
iting your turn in situations when				X	
when they are busy?				X	

Questionnaires provide subjective information reported by patients or their parents, complementing the objective data derived from cognitive testing. No source of information is better or worse than the other—questionnaires measure perceptions of symptoms and how they manifest in real-world scenarios, while objective measures assess core cognitive abilities in a controlled scenario. Both can clarify how symptoms are presenting in a specific patient, and may contribute information that assists in confirming or ruling out a diagnosis. See Section D for additional interpretation tips.

B. The Creyos ADHD Clinical Report

The Summary Page

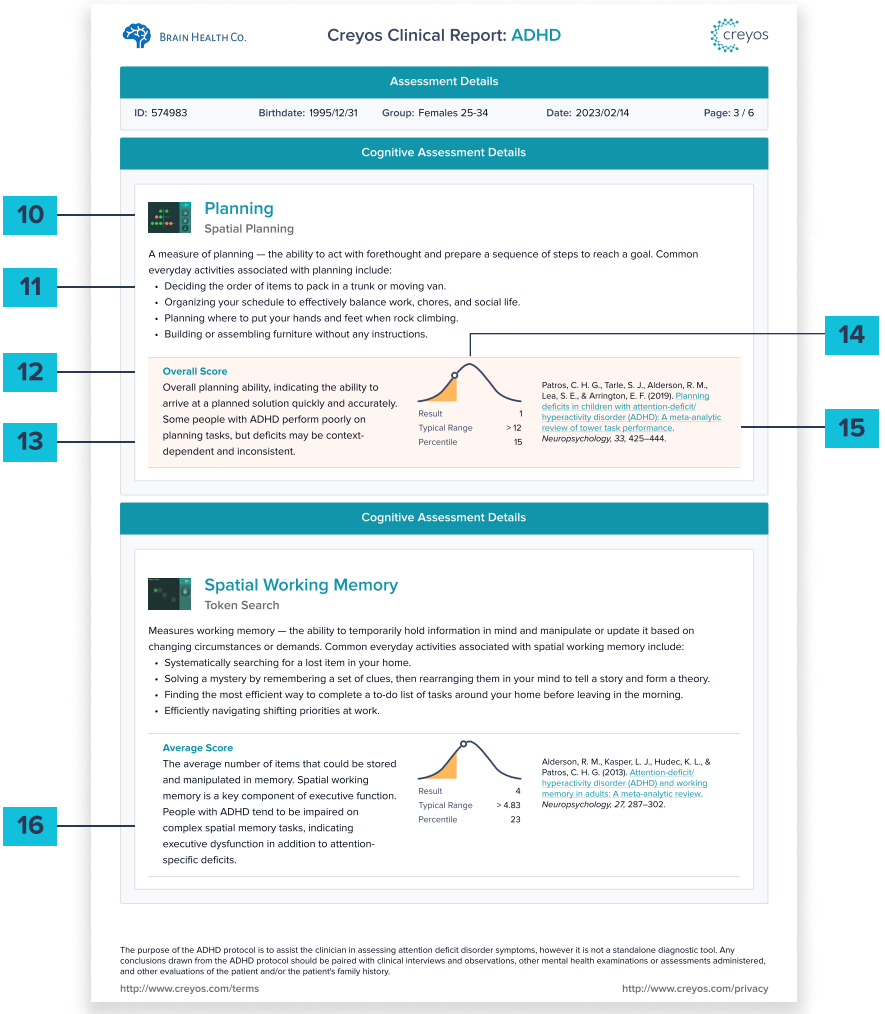
The Creyos ADHD Clinical Report is designed to be easy to read and shareable with the individual assessed. The summary page enables quick assessment of how a patient performed compared to the typical range for each ADHD marker. Falling outside the typical range refers to results that are approximately one standard deviation higher or lower than average, in the same direction as people diagnosed with ADHD in published studies. Age-specific questionnaires are also summarized on this page. Elements of the summary page are outlined below:

1. Unique identifier
2. Executive summary of all results (number of flagged markers in the cognitive assessment portion and overall results from the questionnaire)
3. Task name
4. Marker name
5. Marker score, cutoff for typical range, and percentile rank presented numerically and against the population
6. Page number for where to find further information on each marker
7. SART-specific markers
8. Questionnaire results
9. Questionnaire results plotted on a linear graph in relation to the threshold

Cognitive Assessment Details

The Details section of the report provides additional context for each task and its associated markers. More importantly, it presents the patient's performance metrics alongside additional task information to link performance with everyday activities and ADHD symptoms:

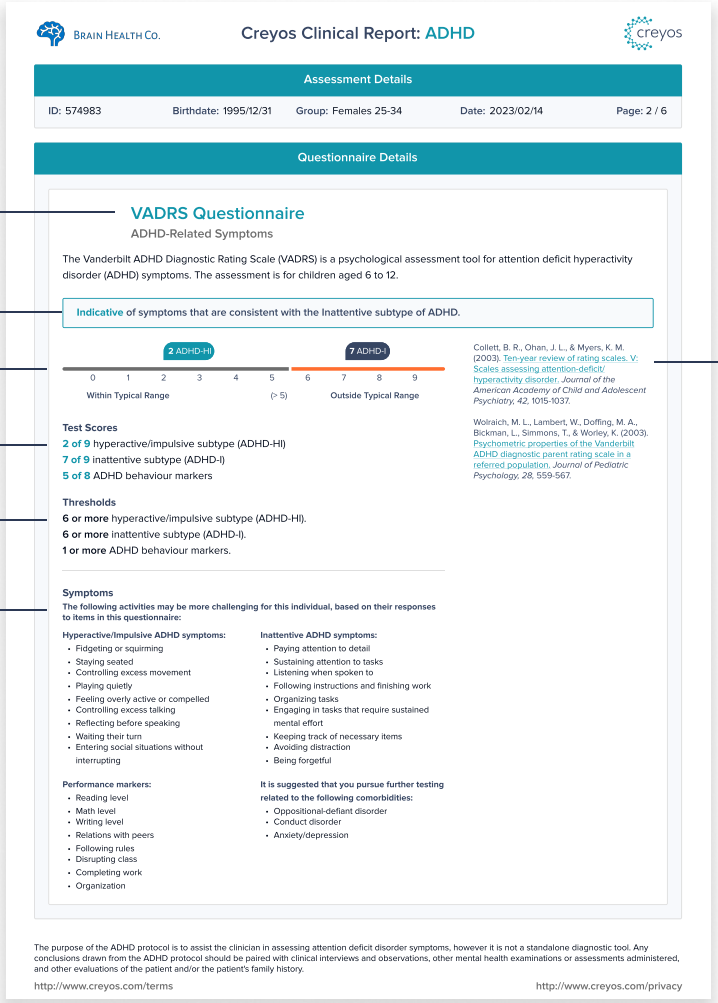
10. Task name
11. Task description and real-world examples of task-related behaviors
12. Marker name and description
13. Row fill in orange; represents a marker score falling outside the typical range
14. Marker score, percentile rank, and reference point for typical range
15. Reference
16. Row fill in white; represents a marker score falling within typical range



Questionnaire Details

The Questionnaire Details section provides more information about the questionnaire completed, including total scores and specific symptoms indicated.

17. Questionnaire name and description
18. Executive summary statement on questionnaire results
19. Visual representation of questionnaire scores in relation to typical range thresholds
20. Numerical value of questionnaire results
21. Threshold for the questionnaire
22. Symptoms patient or observer indicated based on their answers to each item in the questionnaire
23. References



C. Marker Performance Calculations

Each task completion results in performance metrics for one or more markers. This section describes how each marker is calculated, and the units that performance is displayed in. For more information on markers, including how they are linked with ADHD, see the Creyos ADHD Clinical Report Science Guide.

Spatial Planning

Marker	Units	Calculation
Overall Scores	Points	Total number of points scored during the task. Points are awarded to each correctly-solved puzzle, with more points awarded for more difficult puzzles.

Token Search

Marker	Units	Calculation
Average Scores	Number of boxes	Average number of boxes in which all tokens were located without error.

Feature Match

Marker	Units	Calculation
Number of Errors	Errors	Total count of incorrect responses. Higher is more errors.
Reaction Time	Milliseconds	Average of the reaction times of all correct responses. Higher is slower.
Impulsivity	Present/ Absent	If both reaction time and errors are outside of the typical range, impulsivity is marked as present (faster and less accurate).

Double Trouble

Marker	Units	Calculation
Number of Errors	Errors	Total count of incorrect responses. Higher is more errors.
Interference Ratio for Errors	Ratio	Ratio of incorrect responses in double incongruent trials (i.e., color is inconsistent with word in both stimulus and response options—e.g., the word red written in blue) to congruent trials (i.e., color is consistent with word in both stimulus and response options—e.g., the word red written in red). Higher is responding less accurately to incongruent stimuli.
Overall Reaction Time	Milliseconds	Average of the reaction times of all correct responses. Higher is slower.
Interference Ratio for Reaction Time	Ratio	Ratio of reaction time in double incongruent trials (i.e., color is inconsistent with word in both stimulus and response options—e.g., the word red written in blue) to congruent trials (i.e., color is consistent with word in both stimulus and response options—e.g., the word red written in red). Higher is responding slower to incongruent stimuli.
Interference Ratio for Reaction Time	Milliseconds	Standard deviation of reaction times of all correct responses. Higher is more variable.

SART

Marker	Units	Calculation
Commission Errors	Errors	Total count of inappropriate responses to a non-target stimulus (the number 3). Higher is more errors.
Omission Errors	Errors	Total number of times the participant failed to respond to a target stimulus (any number other than 3). Higher is more errors.
Reaction Time Variability	Milliseconds	Standard deviation of reaction times of all correct responses. Higher is more variable.
Slowing After Errors	Milliseconds	The difference between average reaction time after a correct response and average reaction time after a commission error. Higher is slower after an error, and negative values indicate speeding up after an error.

D. Common Interpretation Questions and Tips

What does the number of markers outside typical range mean? Is there a cutoff indicative of ADHD?

The Creyos ADHD protocol counts the total number of atypical markers as a quick indication of how many potential symptoms there are to review. However, this isn't a standalone diagnostic tool, and there is no cutoff. The report is analogous to a blood test, which shows each result separately. A high number of abnormal results could be more alarming than a low number, but even one abnormal result can reveal valuable information when correlated with other patient data.

ADHD is a multifaceted condition, so its diagnosis cannot be automated, but each marker can be combined with other patient details and subjective reports to help identify its presence and severity in a particular patient.

Can someone with few or no flagged markers have ADHD? Can markers be flagged for someone without ADHD?

All cognitive markers are associated with ADHD, but they are not only associated with ADHD. Therefore, flagged markers are only one piece of the puzzle, and additional information and expertise are required to diagnose ADHD or distinguish it from other conditions.

For example, an individual without ADHD may be outside typical range for other reasons, such as another disorder, distraction, or broader intellectual disabilities. Neuropsychological testing does not eliminate the need for a differential diagnosis procedure.

An individual with ADHD may be within the typical range on many or most markers. Attention issues can be specific to only a small number of areas, context dependent, or manifesting in aspects of ADHD like hyperactivity that are not fully captured in cognitive testing. Examining flagged markers alongside questionnaire results and other patient information may help

provide a full picture of a particular patient's symptoms.

> ***"Absence of evidence is not evidence of absence."***
> – Carl Sagan

Can ADHD types be identified by the Creyos ADHD report?

Some of the subjective questionnaires included in the Creyos ADHD protocol divide symptoms by ADHD type—inattentive, hyperactive/impulsive, or combined. For children, the SWAN provides a score for each type and the VADRS has a cutoff for each type. The ASRS for adults, however, only provides an overall score.

Studies on the links between ADHD and objective neuropsychological testing results do not generally distinguish between the types. Some papers report differences between types on specific variables (Mullins et al., 2005), but the differences can be subtle (Tucha et al., 2008), making implementation in clinical practice impractical. One study using the Creyos SART and Double Trouble tasks (Agha et al., 2023) found that lower performance was associated with both types of ADHD in adults.

Furthermore, symptoms that distinguish between types but cannot be measured by cognitive testing alone, such as hyperactivity, are likely best identified by self reports, informant reports, or direct observation.

Ultimately, questionnaire results and cognitive testing results must be interpreted alongside other patient information by a trained professional in order to diagnose a particular type of ADHD.

What does it mean if a patient is flagged on cognitive markers but doesn't reach an ADHD cutoff on a subjective questionnaire?

The Creyos ADHD report can include both cognitive tasks and questionnaires to provide different types of complementary information. Questionnaires have a subjective component, and typically ask about the patient's own perception of symptoms in everyday life. Cognitive tasks are more objective, and measure the patient's ability to perform within a controlled protocol. When questionnaires and continuous performance task results are compared directly in studies (e.g., Barakat et al., 2023), results are usually significantly but modestly correlated, suggesting that each result provides unique information about a patient.

Results will often match and bolster confidence in symptoms; that is, a patient who has trouble during cognitive tasks is likely to have subjective issues in everyday life as well.

However, patients with everyday difficulties will not always demonstrate deficits on objective tests, and vice versa. These differences can be informative. For example, some individuals may be capable of mustering attention and executive function for a brief amount of time in controlled conditions, but real-world factors like distraction and social anxiety can cause them to have everyday difficulties. When combined with clinical expertise, ruling out core attentional issues may contribute to decisions about the presence, nature, and/or severity of a diagnosis.

Do ADHD medications and other treatments affect cognitive testing performance?

Medications, lifestyle changes, and a patient's progress within any treatment program may be reflected in objective cognitive testing results.

For example, the effects of methylphenidate on ADHD symptoms are well documented when administering tests such as the SART and Stroop-based tasks like Double Trouble (Horowitz et al., 2020). The drug has been shown to improve scores on Token Search even in healthy volunteers (Mehta et al., 2000). Other treatments may also affect cognitive testing

results. For example, Wild et al. (2021) found that a multimodal training program for children with ADHD had a positive effect on multiple Creyos cognitive tasks.

Practitioners may take treatments into account when interpreting results—for example, some may choose to conduct testing when a patient is off medication, or administer assessments at multiple time points to measure progress through a treatment program and/or titrate medication dosages.

Does fatigue affect cognitive testing performance?

Tasks completed later in a battery may demonstrate more impairment (Erdodi et al., 2009, Horowitz et al., 2020), so the core attentional symptoms of ADHD, when present, may be more apparent in tasks completed later in a series of tasks. The Creyos ADHD protocol is presented in a fixed order designed to capitalize on the effects of fatigue to capture lapses in attention. Executive function tasks not directly related to attention (Spatial Planning and Token Search) come first, followed by engaging attention tasks (Feature Match and Double Trouble), then the sustained attention task (the SART). Questionnaires come last, to avoid possible effects of priming patients to think about ADHD when completing the objective assessments, and because they do not require real-time performance.

Effects of fatigue are generally subtle within a 20-minute assessment like the Creyos ADHD protocol, but the fixed order attempts to objectively capture attention deficits while also gathering accurate questionnaire responses.

Is the ADHD assessment susceptible to malingering or cheating?

Malingering is a possible concern in the ADHD space—for example, if a patient is seeking a prescription for medication, they may intentionally attempt to perform poorly. Cheating—attempting to perform exceptionally through illicit means—is less of a concern, but may also arise as a possibility.

The Creyos ADHD protocol does not contain a validity indicator for several reasons:

- The protocol is designed to identify extreme scores. Validity testing that removes extreme scores could mask deficits due to ADHD.
- Specific markers are thought to be less susceptible to malingering or cheating than overall scores from cognitive tests.

Clinicians are encouraged to explore the possibilities of malingering and cheating on a case-by-case basis, and perhaps a marker-by-marker basis.

For example, a patient may intentionally do poorly on Spatial Planning and Token Search by letting the timer count down or choosing incorrect responses, which would reflect in the overall final scores. However, a patient intending to do poorly would be less able to do so for more subtle markers. Double Trouble reports may show more errors and slower reaction times, but interference ratios are difficult to intentionally manipulate. Feature Match may show more errors as well, but almost no patients would know that faster reaction times are associated with ADHD in this simpler task. Reaction time variability and slowing after errors on the SART are other markers that are nearly impossible to intentionally perform atypically on.

As with all report interpretation, clinicians may wish to manually explore the possibility of malingering or cheating when unusual patterns or other reasons for suspicion arise.

How can overall intelligence be taken into account when interpreting results?

Overall intelligence (or IQ) is often distinguished from specific deficits in attention. Some academic studies correct for intelligence statistically, but clinical judgment is needed to correct for a specific patient's level of intellectual function.

If general intellectual function is suspected to be low, it could mean that general intellectual function is causing unusual

performance, rather than attentional issues specifically. If there are concerns that markers are being flagged purely due to other cognitive issues, then more investigation may be warranted. For example, the broader Creyos cognitive battery can help gain a fuller picture of a patient's intellectual strengths and weaknesses.

If general intellectual function is suspected to be high, attentional deficits can potentially be masked. Highly intelligent people may perform within a normal range on cognitive tasks (Milioni et al., 2016), even if they are struggling with attentional issues relative to their own expectations or baseline. Specific markers may be less susceptible to issues like this compared to overall average scores, but a patient's cognitive strengths should still be considered when interpreting results.

General intellectual function can be thought of as high performance in multiple cognitive domains. Creyos tasks have been used to examine the concept of intelligence, and have shown that it is not a unitary construct, making it even more essential to gather information about a patient's particular strengths and deficits. See Hampshire et al. (2012) for details.

Can the ADHD protocol be used alongside other Creyos assessments?

The Creyos Health platform contains multiple types of assessments, such as additional cognitive tasks and questionnaires unrelated to ADHD. Administering other assessments may enhance understanding of the patient's health. Examples include:

- Administering other questionnaires to assist in determining comorbidities or as part of a differential diagnosis.
- Administering all 12 core cognitive tasks to help estimate IQ or distinguish attention-specific deficits from general intellectual challenges.
- Administering a shorter battery on a schedule to quickly measure treatment progress, view longitudinal trends, watch for cognitive side effects, or automatically keep up with patients long-term.

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Already using Creyos and want to better understand the Creyos ADHD protocol and report? Email us at **help@creyos.com.**

Email **contact@creyos.com** to request a demo.