

Canvas Dx: Harnessing the Power of Artificial Intelligence to Aid in the Identification of Autism Spectrum Disorder

The prevalence of autism spectrum disorder (ASD) has risen steadily since 2000 and is now estimated to affect 1 in 54 children in the United States.^{1,2}

Early initiation of ASD-specific intervention has been shown to improve long-term outcomes in several research studies.³⁻⁶ Receiving an ASD diagnosis is a key first step in that process. However, families of children who are at risk of developmental delay typically experience prolonged waits from initial concern to eventual diagnosis. Additional factors, including race/ethnicity, socioeconomic background, and geographic location, may exacerbate this issue.⁷⁻¹² These delays in diagnosis may prevent children from receiving ASD-specific intervention during a key neurodevelopmental window when there is greater potential for improved outcomes.

Inherent limitations of current ASD diagnostic approaches necessitate the need for efficient, equitable, and practical solutions that aid primary care physicians (PCPs) and families/caregivers to expedite diagnosis, improve access to intervention, and reduce confounding biases. Recent advances in technology, particularly those related to artificial intelligence, have the potential to improve diagnostic accuracy and reduce time to diagnosis.¹³

Barriers to ASD Diagnosis

On average, parents first report concerns about their child's development to their PCP when the child is 14 months old.¹⁴ Although screening for ASD is recommended starting at 18 months, parental concern is highly indicative of an ASD diagnosis; among children who eventually received an ASD diagnosis, 87% had a parent who reported developmental concerns by 36 months of age.^{15,16} Despite documented early developmental concerns, the average age of ASD diagnosis is 4 years, 3 months.² Girls, non-White children, and children from lower socioeconomic backgrounds are often diagnosed at later ages.^{8,11,17,18} Rural communities face significant challenges, including the availability of diagnostic

specialists and transportation barriers associated with geographic distance from specialized medical care, which may delay ASD diagnosis.^{7,18} Approximately 1 in 12 respondents in one study noted that they needed to travel more than 60 miles to receive an ASD diagnosis.¹⁹ The delay between caregiver's first concern and ASD diagnosis is approximately 3 years. Factors contributing to this delay may include a "wait-and-see" approach to developmental concerns, long wait-times for diagnostic appointments (ranging from 3 months to over a year), and a dependence on a growing shortage of specialists.^{7,20,21}

PCPs are generally the healthcare providers that children and families see most often. They are often the first point of contact for families with concerns about their child's development. As such, the American Academy of Pediatrics (AAP) recognizes the vital role pediatricians play in the early identification of autism, noting the importance of their ability to systematically assess the signs and symptoms of autism.^{15,22}

Although PCPs who are comfortable utilizing DSM-5 criteria and clinically assessing children to diagnose ASD are encouraged to do so by the AAP, they are estimated to currently be making approximately 1% of all diagnoses.^{15,23,24} This low rate may be explained by PCPs self-reported lack of training, knowledge, and confidence in assessing ASD, as well as the time necessary to administer the assessments and to counsel caregivers following a positive diagnosis.^{22,25,26} Although several programs have been created to train PCPs in identifying and managing ASD, developing diagnostic aids that are time efficient and practical to use in primary care settings may additionally bolster PCPs' ability to diagnose ASD and decrease strain on limited specialist services.^{10,27,28} Increasing capacity for ASD diagnosis in the primary care setting may allow for earlier diagnosis for some children, and, by extension, earlier ASD-specific interventions and optimal long-term outcomes.

Important Information Indications for Use

Canvas Dx is intended for use by healthcare providers as an aid in the diagnosis of autism spectrum disorder (ASD) for patients ages 18 months through 72 months who are at risk for developmental delay based on concerns of a parent, caregiver, or healthcare provider.

The device is not intended for use as a stand-alone diagnostic device but as an adjunct to the diagnostic process. The device is for prescription use only (Rx only).



Benefits of Earlier Autism-Specific Intervention

ASD is a disorder of hyper- and hypoconnectivity within different areas of the brain in which synaptic pruning occurs atypically during a key neurodevelopmental window in the first few years of life.^{29–31} Compared to those children who do not receive the same level of intervention, children who are provided with ASD-specific intervention within this window exhibit:

-  • Twice the cognitive developmental gains and a 12-point higher IQ^{5,6}
-  • Improvements in receptive and expressive language on the Mullen Scales of Early Learning that were 153% and 75% greater, respectively⁶
-  • Significantly higher scores for composite adaptive behavior on the Vineland Scales of Adaptive Behavior (VABS), with a mean difference of 9.4 points at age 6 years³
-  • Significantly better socialization, as assessed by VABS socialization score (mean difference of 9.8 points at age 6 years)³ and a 138% greater improvement in mean positive percentile change as measured by the Social Skills Rating System⁶

These developmental improvements can be more profound when children receive intervention at a younger age, with benefits lasting beyond the end of intervention.^{3,4,32–34}

Artificial Intelligence in ASD

Technological approaches, such as computer vision, biometrics and biomarkers, advanced imaging, and artificial intelligence (AI) hold promise to enable earlier identification and diagnosis of ASD.^{35–39} AI-based methods have been implemented in several ways for medical diagnostic purposes to augment clinical decision making. AI approaches can take large data sets (eg, radiological scans, video/audio recordings, or EHR information) and identify subtle patterns among patient characteristics, behaviors, and/or symptoms that inform a diagnosis or prognosis.^{40–42} AI-enabled tools may improve accuracy and efficiency of diagnosis, leading to treatment or intervention, and scalability by quickly managing repetitive processes, storing and handling large amounts of data, and

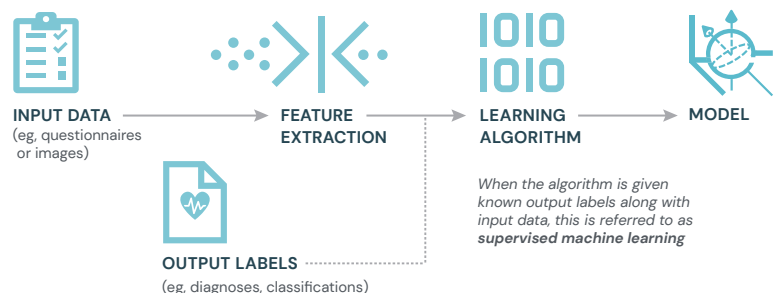
Important Information (continued) Contraindications

There are no contraindications to using Canvas Dx.
Please see full prescribing information.

providing support for diagnostic or treatment decisions that may reduce the probability for mistakes.^{42,43}

Machine learning is a type of AI where algorithms are applied to large datasets to look for patterns, and can be used to create models that encapsulate those patterns to help predict outcomes.^{44,45} These algorithms may be able to detect some of the most highly predictive and earliest behavioral features of ASD and further our understanding of its heterogeneity. For example, models using two-dimensional pose estimation trained on filmed ADOS assessments and children interacting with a virtual reality environment have reported >80% accuracy in distinguishing ASD from typical development.^{35,39} Studies investigating electroencephalogram and neuroimaging data have identified nonlinear features that may provide high predictive power in distinguishing ASD.^{36,37} Outputs from machine learning algorithms may be complex, which may require clinical expertise to translate the output (eg, a cluster of highly predictive features of ASD) into actionable information (eg, behavioral descriptors reflecting those features).⁴⁶

How Machine Learning Works^{43,47–49}



Cognoa utilizes machine learning in its diagnosis aid, Canvas Dx, which is intended for use by healthcare providers in the primary care setting as an aid in the diagnosis of ASD for patients ages 18 months through 72 months who are at risk for developmental delay based on concerns of a parent, caregiver, or healthcare provider. Canvas Dx is not intended for use as a stand-alone diagnostic device but as an adjunct to the diagnostic process and is for prescription use only.

Canvas Dx: An ASD Diagnosis Aid for Primary Care

Canvas Dx was granted marketing authorization by the FDA in June 2021. It falls under a class of products called software as a medical device (SaMD), which includes software or mobile apps that are intended to treat, diagnose, monitor, mitigate, or prevent disease or other conditions.⁵⁰ It makes use of a machine learning

algorithm that was initially developed using patient record data from thousands of children with diverse conditions, presentations, and comorbidities who were either diagnosed with ASD or confirmed not to have ASD based on standardized diagnostic tools and representing both genders across the supported age range.⁵¹⁻⁵⁷ The device integrates 3 independent inputs: a caregiver questionnaire; a video analyst questionnaire, which is completed by trained professionals with at least a master's degree and more than 5 years of experience diagnosing and/or treating children with ASD who score 2 videos of a child's natural behavior; and an HCP questionnaire.^{52,58} It then evaluates the information based on predictive features that are most indicative of autism and provides one of 3 outputs: positive, negative, or indeterminate. If the information is sufficient, Canvas Dx will provide a positive or negative result. If the information is insufficient, Canvas Dx provides an indeterminate output.^{52,58}

The accuracy of Canvas Dx was assessed in a multisite, prospective, double-blinded, active comparator cohort study that included 425 children, aged 18 to 72 months, with parental or HCP concern for developmental delay compared to the standard diagnostic approach of a specialist assessment based on DSM-5 criteria. The children in the study were broadly representative of the U.S. population in terms of race, ethnicity, and socioeconomic background. The primary endpoints included measurements of positive predictive value (PPV) and negative predictive value (NPV) among subjects with a determinate result, and the indeterminate rate. The secondary endpoints were sensitivity and specificity.⁵⁸⁻⁶⁰

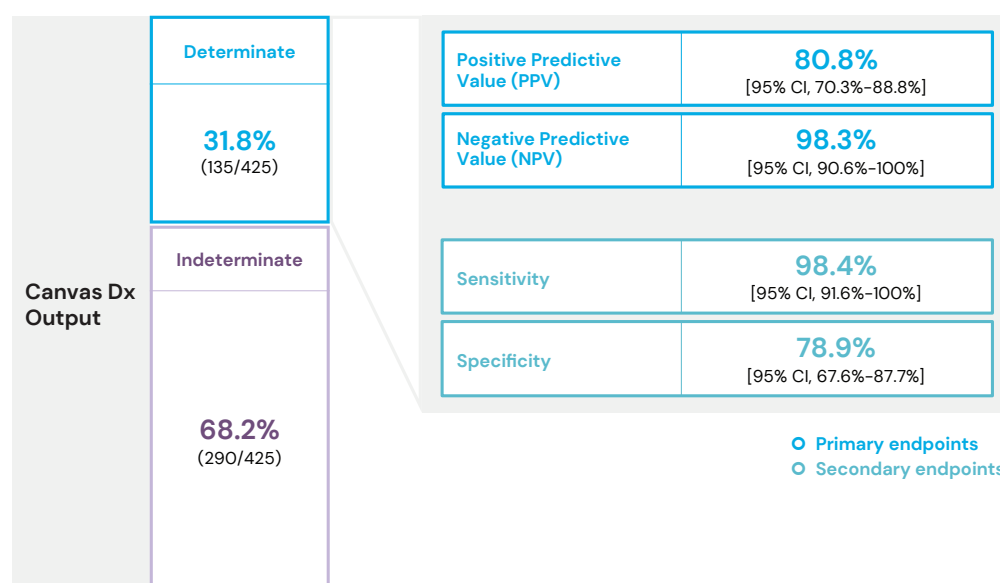
The output from Canvas Dx was compared against specialist diagnosis and shown to have a PPV of 81% (95% CI: 70%–89%) and an NPV of 98% (95% CI: 91%–100%) in those patients with a determinate device result (32%).⁵⁸

Among patients with a determinate result, Canvas Dx was shown to have a sensitivity of 98% (95% CI: 92%–100%) and specificity of 79% (95% CI: 68%–88%). In the Canvas Dx pivotal study, the average age of children diagnosed with ASD was 2.8 years, which is

approximately 1.5 years earlier than the average age of diagnosis in the U.S.^{2,58} No adverse events were reported. There was no evidence of device performance inconsistency across sex, race/ethnicity, income, or education level.^{58,60}

Among the 68% of subjects who received an indeterminate output, 91% were identified as having one or more neurodevelopmental conditions, including ASD (20%) and non-ASD neurodevelopmental conditions (71%). Given this result, PCPs may find that the indeterminate output from Canvas Dx is clinically relevant and could indicate a need for further evaluation.^{58,59}

Results for Determinate Output⁵⁸



The Potential for Earlier ASD Diagnosis

Many children with ASD are not being diagnosed during the period in which ASD-specific intervention provides greater benefits. Current standard ASD diagnostic approaches require intensive training and are time-consuming, which may be prohibitive for PCP assessment of ASD.^{22,25,26,61} Machine learning approaches utilized by Canvas Dx support PCPs in assessing children for ASD, which may allow for more efficient specialty referrals and streamlining of the diagnostic process. Results from the Canvas Dx pivotal study demonstrated the potential of Canvas Dx to help PCPs effectively diagnose or rule out ASD when used in conjunction with clinical assessment. Earlier diagnoses may enable initiation of intervention earlier than the current average age of diagnosis.^{2,58} Earlier ASD-specific intervention may, in turn, lead to better long-term developmental outcomes.^{3,5,6}

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Contraindications

There are no contraindications to using Canvas Dx.

Precautions, Warnings

The Device is intended for use by healthcare professionals trained and qualified to interpret the results of a behavioral assessment examination and to diagnose ASD.

The Device is intended for use in conjunction with patient history, clinical observations, and other clinical evidence the HCP determines are necessary before making clinical decisions. For instance, additional standardized testing may be sought to confirm the Device output, especially when the Device result is not Positive or Negative for ASD.

Canvas Dx is intended for patients with caregivers who have functional English capability (8th grade reading level or above) and have access to a compatible smartphone with an internet connection in the home environment.

The Device may give unreliable results if used in patients with other conditions that would have excluded them from the clinical study.

Among those conditions are the following:

- Suspected auditory or visual hallucinations or with prior diagnosis of childhood onset schizophrenia
- Known deafness or blindness
- Known physical impairment affecting their ability to use their hands
- Major dysmorphic features or prenatal exposure to teratogens such as fetal alcohol syndrome
- History or diagnosis of genetic conditions (such as Rett syndrome or Fragile X)
- Microcephaly
- History or prior diagnosis of epilepsy or seizures
- History of or suspected neglect
- History of brain defect injury or insult requiring interventions such as surgery or chronic medication

The Device evaluation should be completed within 60 days of the time it is prescribed because neurodevelopmental milestones change rapidly in the indicated age group.

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