Table 3: Prospective Validation Studies of the Evolving Device and Algorithm

Evolving Device and Algorithm Description	Study Year/s	Methods	Participants	Key Findings	Peer Reviewed Publication
One input 1. Caregiver Questionnaire administered via an electronic platform with automatic scoring	2012-2013	Prospective clinical validation study Device administered to a clinical sample of children referred to a large pediatric medical center clinic for developmental/ behavioral concerns. Diagnostic determination of blinded clinicians compared to device output.	**n=222** Median age 5.8 years. Range 16 months to 17 years 76.1 % male, 31 % received a clinical diagnosis of ASD Concern for developmental delay	Device showed a sensitivity to detect ASD of 89.9 % [95 % CI = 82.7–97]; specificity of 79.7 % [95 % CI = 73.4–86.1].	Duda, Daniels & Wall. Clinical evaluation of a novel and mobile autism risk assessment. *J Autism Dev Disord* 2016; 466: 1953–1961.
Two inputs 1. Digital Caregiver Questionnaire 2. Digital Video Analyst Questionnaire	2016	Prospective, multi-center clinical feasibility trial Conducted across 3 large tertiary developmental medicine centers. Device completion followed by ASD diagnosis by clinicians who were blinded to the device output. Diagnostic recommendations compared. Objective: Sensitivity and specificity to detect ASD compared to other pre-existing screening tools.	**n= 230** *162 of whom completed the device inputs in addition to reference tests and diagnosis* Age: 18 - 72 months Referred to tertiary center for ASD related concern	Device found to perform similarly to other measures, accurately identifying children 71% of the time across the entire 18 to 72 month age range with an overall higher specificity in detecting ASD (62%) compared to the other measures ranging from 16% for the SRS-SA to 35% for the SCQ.	Kanne, S. M., Carpenter, L. A. and Warren, Z. (2018), Screening in toddlers and preschoolers at risk for autism spectrum disorder: Evaluating a novel mobile health screening tool. *Autism Research*. doi:10.1002/aur.1959 Abbas, H., Garberson, F., Glover, Eric., Wall, D. P. (2018), Machine learning approach for early detection of autism by combining questionnaire and home video screening, *Journal of the American Medical Informatics Association,* Volume 25, Issue 8, Pages 1000–1007, https://doi.org/10.1093/jamia/ocy039
Three inputs: 1. Caregiver Questionnaire 2. Video Analyst Questionnaire* 3. Healthcare Provider Questionnaire	2017	Prospective, blinded, multi-site clinical study Conducted across 3 large tertiary developmental medicine centers . Add-on to previous validation study. New participants received 3 device inputs. Roll-over participants received only 2 inputs (but an updated version of input 2 was used to re-analyze their videos). Device completion followed by ASD diagnosis by clinicians who were blinded to the device output. Objectives: • Device sensitivity and specificity compared to blinded best estimate clinical diagnosis • Device performance compared to 3 existing ASD screening instruments (CBCL, M-CHAT-R, and SRS) • Device concordance to ADOS • Impact of phenotypic characteristics such as age, IQ, and co-morbid disorders on device performance	**n=375** 213 of whom are new subjects, *data on all 3 device inputs available for this cohort,* and 162 roll-over subjects from previous validation study. *Only input 1 and 2 data available for this cohort* 18 - 72 months Referred to tertiary center for ASD related concern	Device outperforms baseline screeners administered to children by 0.35 (90% CI: 0.26 to 0.43) in AUC and 0.69 (90% CI: 0.58 to 0.81) in specificity when operating at 90% sensitivity. Compared to the baseline screeners evaluated on children less than 48 months of age, the device outperforms the most accurate by 0.18 (90% CI: 0.08 to 0.29 at 90%) in AUC and 0.30 (90% CI: 0.11 to 0.50) in specificity when operating at 90% sensitivity. Addition of input 2 and input 3 are shown to significantly improve algorithm performance, compared to use of input 1 alone. Allowing for a 30% abstention rate, the following performance improvements with the addition of extra inputs were reported: • Caregiver questionnaire alone (N=375): AUC= 0.791 • Caregiver and video analyst questionnaire (N=368): AUC 0.857 • Caregiver, video analyst and health care provider questionnaire (N=204): AUC 0.916	Abbas, H., Garberson, F., Liu-Mayo, S., Glover, E., & Wall, D. P. (2020). Multi-modular AI approach to streamline autism diagnosis in young children. *Scientific reports*, 10(1), 1-8.

*Independent research[12] has also demonstrated the feasibility of using home videos to support the diagnosis of ASD in young children