Exploring the value of a novel health technology tool to support diagnosis of autism spectrum disorder

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BACKGROUND

> Autism Spectrum Disorder (ASD) is one of the most common neurodevelopmental disorders in children that affects 1 in every 36 child in the US[1]

> ASD is more prevalent among boys, and it affects all races and ethnicities, however, the time to diagnosis and treatment varies across different racial and socioeconomic groups[1]

> The diagnosis of ASD is challenging, as patients are identified based on their symptoms. if presentation of the behavioral symptoms are not highly expressed. There could be delay in treatment

> The American Academy of Pediatrics (AAP) has recommended universal screening of pediatrics at the age of 18 months and 24 months during child wellness visits. The most common tool for screening is the Modified Checklist for Autism in Toddlers, Revised with Follow-up (M-CHAT-R/F)[2]

> In reality, universal screening is not effective given the variability in use of published, validated tools by physicians to identify early markers of ASD

> Therefore, there is a need for a novel health technology tool to support the diagnosis of ASD in children

OBJECTIVE

To examine the potential cost-utility of a novel pupillometry screening device for early diagnosis of autism spectrum disorder (ASD) compared to the Modified Checklist for Autism in Toddlers, Revised with Follow-up (M-CHAT-R/F)

METHODS

> We simulated a hypothetical cohort of children of average age 24 months receiving either the novel screening tool, or the standard M-CHAT-R/F

> We calculated the incremental cost-utility ratio (ICUR) and incremental net monetary benefit (INMB) under societal perspective by using a decision tree model for 5-year and 10-year time horizon

> Given the great variability in the utilization of the M-CHAT-R/F tool among providers, we considered two scenarios (Table 1)

- Scenario one: Low utilization of M-CHAT-R/F ~ 9.4%
- Scenario two: High utilization of M-CHAT-R/F ~80%

> Our base case scenario assumed that the utilization rate of the novel screening tool will be around 90%

> Some children do not receive screening during their child-wellness visits, in that case, we assumed that physicians would be able to detect the presence of ASD Restricted Repetitive Behaviors (RRB) red flags

> The model partitioned the simulated patient cohort into subgroups based on the intervention strategy and the metrics of the screening tool

> Children were categorized into different health states: true positive (TP), true negative (TN), false positive (FP), early screening (ES), and no early screening (NS). The early screening and no early screening states belong to children who receive a false negative screening result (Figure 1)

> We used a discount rate of 3% and all costs were inflation-adjusted to 2022 US dollars using the medical care component of the US Consumer Price Index

> We conducted a one-way (OWSA), two-way, and probabilistic sensitivity analyses (PSA)

> For the PSA, we ran a monte-carlo model with 5000 simulations. We used a normal distribution to vary average age, beta distribution for prevalence, probabilities, and utilities, gamma distribution to vary costs, and a log-normal distribution for time from first evaluation to diagnosis

TABLE 1: INPUTS OF THE MODEL

Model parameter	Input	Lower Range	Upper Range	Source
Average age of ASD children in months	24	18	48	Assumption
Prevalence of ASD in children	0.028	0.027	0.028	
Boys	0.043	0.042	0.044	
Girls	0.001	0.011	0.012	CDC Surveillance 2023[1]
White non-Hispanic children	0.024	0.023	0.025	
Black non-Hispanic children	0.029	0.028	0.031	
Hispanic children	0.032	0.030	0.033	
Asian/Pacific Islander children	0.033	0.031	0.036	
Proportion of children completing				
The novel screening tool	0.90	0.72	1.00	Assumption
The M-CHAT in a pediatrician setting	0.80	0.72	0.88	Carbone et al 2020[3]
The M-CHAT in a family physician setting	0.09	0.08	0.10	Carbone et al 2020[3]
The follow-up interview after M-CHAT	0.42	0.34	0.50	Guthrie et al 2019[4]
Probability of being evaluated by 36 months	0.49	0.39	0.59	CDC Surveillance 2023[1]
Boys	0.45	0.34	0.51	CDC Surveillance 2018[5]
Girls	0.48	0.39	0.58	CDC Surveillance 2018[5]
White non-Hispanic children	0.45	0.36	0.54	CDC Surveillance 2018[5]
Black non-Hispanic children	0.40	0.32	0.48	CDC Surveillance 2018[5]
Hispanic children	0.43	0.34	0.51	CDC Surveillance 2018[5]
Asian/Pacific islander children*	0.49	0.39	0.59	CDC Surveillance 2018[5]
Time between first evaluation and diagnosis (months)	12	4	19	CDC Surveillance 2023[1]
Metrics of the screening tools				
Sensitivity of novel screening device	0.75	0.60	0.90	Dr. Lynch
Specificity of novel screening device	0.72	0.62	0.81	Dr. Lynch
Sensitivity of RRB red flags only	0.79	0.63	0.95	Dow et al[6]
Specificity of RRB red flags only	0.52	0.42	0.62	Dow et al[6]
Probability of a positive M-CHAT	0.09	0.03	0.11	Guthrie et al 2019[4]
Probability of M-CHAT score >8	0.11	0.09	0.13	Guthrie et al 2019[4]
Probability of M-CHAT score 3-7	0.89	0.71	1.00	Guthrie et al 2019[4]
Probability of a positive M-CHAT after follow-up	0.05	0.04	0.06	Guthrie et al 2019[4]
Negative predictive value of M-CHAT	0.99	0.79	1.00	Guthrie et al 2019[4]
Positive predictive value of M-CHAT score > 8	0.35	0.28	0.42	Guthrie et al 2019[4]
Positive predictive value of M-CHAT score 3-7 (no follow-up administered)	0.10	0.08	0.12	Guthrie et al 2019[4]
Positive predictive value of M-CHAT with Follow-up	0.38	0.30	0.46	Guthrie et al 2019[4]
Negative predictive value of M-CHAT with Follow-up	0.96	0.77	1.00	Guthrie et al 2019[4]
Utilities				
Children with ASD	0.67	0.62	0.72	Hoopen et al 2020[7]
Children with ASD receiving early intervention	0.7	0.63	0.77	Assumption
Children without ASD	0.94	0.93	0.96	Hoopen et al 2020[7]
ASD caregiver aged 18 - 44 years old	0.82	0.80	0.85	Brown et al 2019[8]
US general population aged 18 - 44 years old	0.91	0.89	1.00	Khanna et al 2013[9]
Medical and Healthcare related services costs in USD ($)				
Cost of novel screening	$10	$8	$15	Dr. Lynch
Cost of M-CHAT-R/F (office visit/ Child wellness visit) and M-CHAT	$46	$5	$87	NASHP 2021[10]
Yearly Costs of HRU associated with ASD in ages 0-5 years old	$8,340	$6,672	$10,008	Buescher et al 2014[11]
Yearly Costs of HRU associated with ASD only ages 6-17 years old (Yearly)	$11,675	$9,340	$14,010	Buescher et al 2014[12]
Cost of early intensive behavioral intervention in USD ($)	$62,294	$55,628	$94,385	Amendah et al 2011[13], Cidav et al 2017[14], Butter et al 2003[15], Sallows et al 2005[16], Chasson et al 2007[17]
Productivity associated costs & Caregiver burden costs in USD ($)	0.560	0.448	0.672	Cidav et al 2012[15]
Maternal productivity loss for ASD children 0-17 years	$56,170	$50,553	$61,787	US census Bureau[16]
Women aged 25- 34 years old median income for year 2021	$63,873	$57,486	$70,261	US census Bureau[16]
Women aged 35- 44 years old median income for year 2021				
Yearly Special education costs associated with ASD in USD ($)				
0-5 years old	$40,570	$32,456	$48,684	
6-21 years old	$18,028	$14,422	$21,634	Buescher et al 2014[12]
Costs of Accommodation, Employment Support, and non-medical services for ASD ($):				
0-2 years old	-	-	-	
3-6 years old	$4,614	$3,691	$5,537	Blaxil et al 2021[16]
7-11 years old	$4,614	$3,691	$5,537	
12-21 years old	$7,944	$6,355	$9,533	

Abbreviations: ASD, autism spectrum disorder; M-CHAT, Modified Checklist for Autism in Toddlers; RRB, restrictive and repetitive behavior; M-CHAT-R/F, Modified Checklist for Autism in Toddlers – Revised with Follow-up; HRU, Healthcare resource utilization
* No information provided, so overall prevalence was used

RESULTS

> **Low utilization M-CHAT setting:** The novel screening device is dominant and cost-saving under both 5-year and 10-year time horizon analysis generating an INMB of $6,400 and $6,000 respectively (Table 2)

> **High utilization M-CHAT setting:** The novel screening device is dominated under both 5-year and 10-year time horizon analysis (Table 2)

> **OWSA:** Utility of children without ASD, negative predictive value of M-CHAT, and time between evaluation and diagnosis are key drivers of the model in both setting. In 10-year time horizon under low utilization of M-CHAT, specificity of the novel device and RRB are influential parameters in the model.

> Varying the specificity of the novel screening device and proportion utilizing M-CHAT (Figure 2) shows that as utilization of M-CHAT increases, the novel device becomes less cost-effective

> At a WTP equal to $150,000, the minimum specificity required for the novel screening tool to be cost effective is around 56% in settings of low utilization to M-CHAT

FIGURE 1: MODEL OVERVIEW

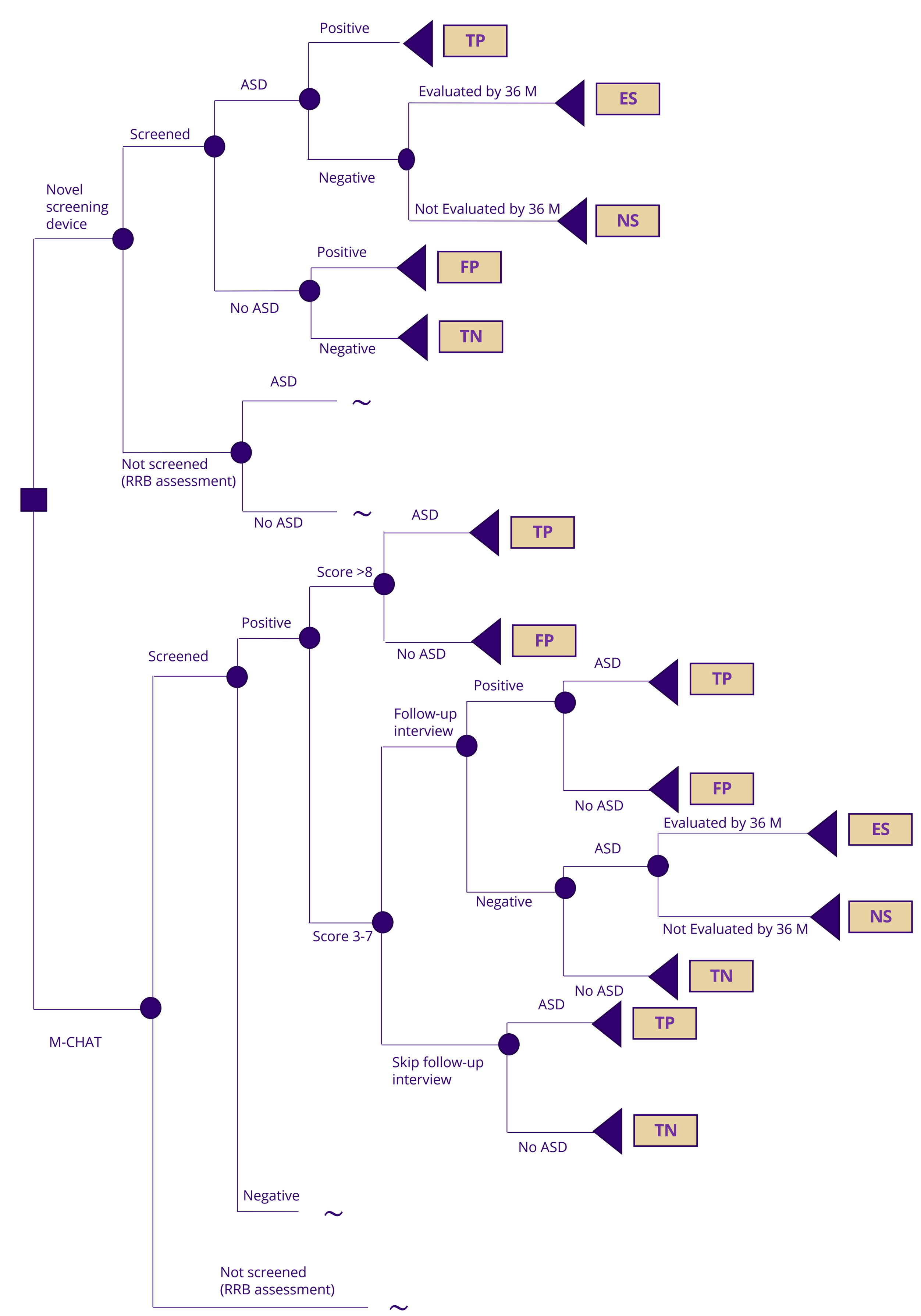
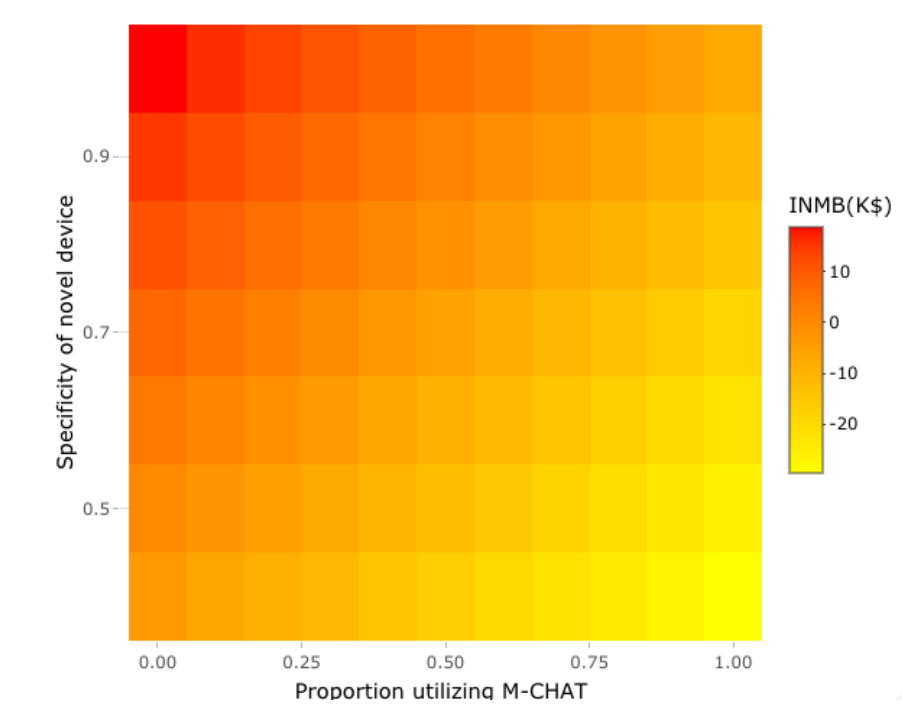


TABLE 2: BASECASE SCENARIO RESULTS

Outcome	5-year: Novel screening tool	5-year: M-CHAT screening	5-year: Incremental	10-year: Novel screening tool	10-year: M-CHAT screening	10-year: Incremental
Low utilization M-CHAT setting						
QALY in children	4.395	4.389	0.006	8.190	8.185	0.005
QALY in caregiver	4.241	4.230	0.011	7.920	7.910	0.011
Total Cost	$18,500	$22,400	-$3,900	$25,100	$28,800	-$3,700
ICUR			Dominant			Dominant
INMB			$6,400			$6,000
High utilization M-CHAT setting						
QALY in children	4.395	4.395	0.00	8.190	8.194	-0.004
QALY in caregiver	4.241	4.257	-0.016	7.920	7.939	-0.018
Total cost	$18,500	$11,100	$7,400	$25,100	$16,100	$9,000
ICUR			Dominated			Dominated
INMB			-$9,800			-$12,300

> The novel screening tool remained the cost-saving strategy in settings that have up to 37% utilization of M-CHAT under 5-year time horizon, and 32% under 10-year time horizon

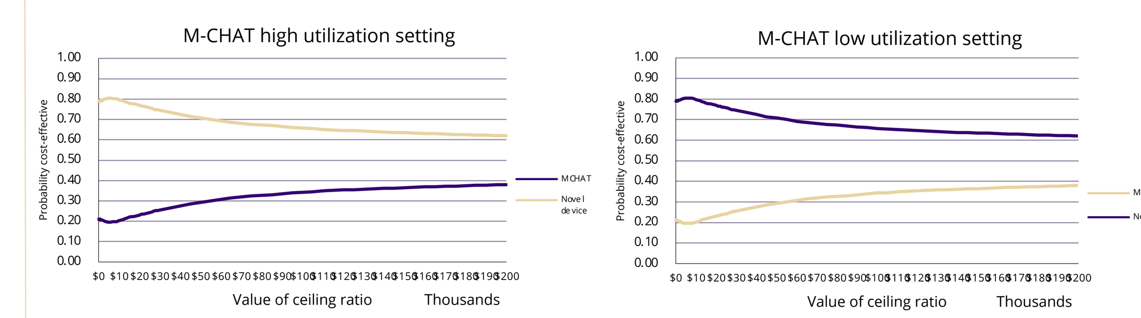
FIGURE 2: TWO-WAY SENSITIVITY ANALYSIS



> At the WTP of $50,000 per QALY, the novel device had only 16.5% probability of being cost-effective in M-CHAT high utilization setting, and 31% probability at WTP of $150,000 per QALY (Figure 3)

> In M-CHAT low utilization setting, The novel device had a 71%, and 64% probability of being cost-effective at WTP of$50,000 and $150,000 per QALY, respectively (Figure 3)

FIGURE 3: COST-EFFECTIVENESS ACCEPTABILITY CURVES



LIMITATIONS

> Children who do not receive screening at their first child-wellness visit are assumed to receive screening later with a probability of being evaluated within 36 months

> Due to lack of information about utility of children with ASD in the US, we used the utility of children with ASD residing the Netherlands

> We also assumed the utility associated with the efficacy of receiving early behavioral intervention

> The "false positives" were assumed to bear the same costs as those in the "true positive" health state until the children receive an accurate diagnosis

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