

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Diagnostic Accuracy of the M-CHAT(-R/F)

The overall diagnostic accuracy of the M-CHAT(-R/F) was assessed using the hierarchical summary receiver operating characteristic (HSROC) model.^{18,19} This model was chosen for its ability to account for the inherent relationship between sensitivity and specificity, as well as high heterogeneity of the sample (as is often the case with diagnostic test accuracy studies) through use of a Bayesian model to determine random effects. HSROC models were run on included studies (n=49) using the MetaDAS SAS macro²⁰, which outputs HSROC parameters, the diagnostic odds ratio (DOR; an overall estimate of diagnostic test accuracy that can be used to compare across tests and models), and pooled sensitivity and specificity. The HSROC model was run with and without covariates (added individually) to assess if these study characteristics affected the accuracy, threshold, or shape of the HSROC curve. Covariates included the ASD likelihood level of sample (low-likelihood, high-likelihood), case confirmation strategy classification (concurrent, prospective), sample size (<500, 500-5000, >5000), M-CHAT(-R) version (M-CHAT, M-CHAT-R), use of structured Follow-Up (Follow-Up, initial screen only), and language (English/ primarily English, other language). When study characteristics indicated more than one of these categories, they were re-classified based on predominant data. Four studies that reported mixed-likelihood level were reclassified as low-likelihood, as a large majority of participants were low-risk.^{25,32,58,66} In addition, two studies reported mix of initial screen and use of Follow-Up interview. One study⁸ was classified as initial screen only, as only 1 out of the 12 practices completed the Follow-Up in the standardized interview form. The other study⁹ was classified as using structured Follow-Up, since Follow-Up was built into the electronic health record, and intended to be used when indicated based on initial score; 41% of expected sample received the Follow-Up interview, consistent with other studies that attempted to administer the interview but were not always successful. Three studies classified as “mixed” or “unknown” in any category were excluded from the analyses^{62,68}. The HSROC parameters output by each model were input into RevMan 5 software to create the HSROC summary curves.

eTable 1. Database Search Terms

| Database | Search terms |
|-----------------|--|
| PubMed | ((M-CHAT*[Title/Abstract]) OR (MCHAT*[Title/Abstract]) OR ("Modified Checklist for Autism in Toddlers"[Title/Abstract]) OR ("Modified-Checklist for Autism"[Title/Abstract]) OR ((screen*[Title/Abstract] AND autis*[Title/Abstract] AND toddler*[Title/Abstract]))) AND ((Autis*[Title/Abstract]) OR (Asperger*[Title/Abstract]) OR (ASD[Title/Abstract]) OR (PDD[Title/Abstract]) OR ("Pervasive Developmental Disorder*[Title/Abstract])) AND ("2001/01/01"[Date - Publication] : "3000"[Date - Publication]) |
| Web of Science | AB=((M-CHAT*) OR (MCHAT*) OR ("Modified Checklist for Autism in Toddlers") OR ("Modified-Checklist for Autism") OR ((screen* AND autis* AND toddler*))) AND AB=((Autis*) OR (Asperger*) OR (ASD) OR (PDD) OR ("Pervasive Developmental Disorder*")) AND LANGUAGE: (English); Timespan: 2001-2022 |
| SCOPUS | TITLE-ABS-KEY((M-CHAT*) OR (MCHAT*) OR ("Modified Checklist for Autism in Toddlers") OR ("Modified-Checklist for Autism") OR (screen* AND autis* AND toddler*)) AND TITLE-ABS-KEY((Autis*) OR (Asperger*) OR (ASD) OR (PDD) OR ("Pervasive Developmental Disorder*")) AND (PUBYEAR > 2001) |

eTable 2. QUADAS-2 Description and Adapted Signaling Questions

| | |
|---|--|
| Domain 1: Patient Selection | |
| QUADAS-2 description and signaling questions adapted for this study | |
| Risk of Bias | Could the selection of patients have introduced bias? 1. Were participants randomly selected? 2. Were all exclusion appropriate and defined a priority? |
| Applicability | Are there concerns that the included patients and setting do not match the review question? *Any such studies would have been excluded for the purpose of this review, and therefore we have no applicability concerns in this area |
| Domain 2: Index Test | |
| Risk of Bias | Could the conduct or interpretation of the index test have introduced bias? 1. Was interpretation of M-CHAT(-R/F) done prior to knowing child’s diagnosis? 2. Were standardized M-CHAT(-R/F) methods used? 3. Was an appropriate threshold used to indicate risk? |
| Applicability | Are there concerns that the index test, its conduct, or its interpretation differ from the review question? 1. Was correct criteria used for scoring? 2. Was correct threshold used to calculate sensitivity and specificity? |
| Domain 3: Reference Standard | |
| Risk of Bias | Could the reference standard, its conduct, or its interpretation have introduced bias? 1. Was provider who gave diagnosis blind to M-CHAT(-R/F) score? 2. Was appropriate ASD measure used to diagnose ASD (i.e., ADOS, ADI-R, or CARS), or was provider qualified to give ASD diagnosis? * If community diagnosis given and no additional information was used, marked as unclear bias. |
| Applicability | Are there concerns that the target condition as defined by the reference standard does not match the question? 1. Were all participants identified as having ASD diagnosed with ASD as based on DSM or ICD criteria? 2. Was appropriate criteria for diagnosis utilized? |
| Domain 4: Flow and Timing | |
| Risk of Bias | Could the patient flow have introduced bias? 1. Did all participants receive the same reference standard? 2. Was time between screen and diagnosis within 1 year? 3. Were all recruited participants screened with M-CHAT(-R/F) and evaluated for ASD? |

eTable 3. Quality Assessment of Studies Included in the Systematic Review

| Reference | Risk of Bias | | | | Concerns of Applicability | | |
|---|-----------------------|------------|--------------------|-----------------|---------------------------|------------|--------------------|
| | Participant Selection | Index Test | Reference Standard | Flow and Timing | Participant Selection | Index Test | Reference Standard |
| Baduel et al, ²² 2017 | Low | Low | Low | High | Low | Low | Low |
| Beacham et al, ⁴² 2018 | Low | Low | Unclear | Low | Low | Low | Low |
| Canal-Bedia et al, ⁵⁸ 2011 | Low | Low | Low | High | Low | Low | Low |
| Carbone et al, ⁸ 2020 | Low | Low | Unclear | High | Low | Low | Low |
| Chang et al, ²³ 2021 | Low | Low | Low | High | Low | Low | Low |
| Charman et al, ⁴³ 2016 | Low | Low | Low | High | Low | Low | Low |
| Chlebowski et al, ²⁴ 2013 | Low | Low | Low | High | Low | Low | Low |
| Choueiri et al, ⁴⁴ 2021 | Low | High | Low | Low | Low | Low | Low |
| Christopher et al, ⁴⁵ 2020 | Low | Low | Low | Low | Low | Low | Low |
| Coelho-Medeiros et al, ²⁵ 2019 | High | Low | High | High | Low | Low | Low |
| Dereu et al, ²⁶ 2012 | Low | Low | Low | High | Low | Low | Low |
| DiGuseppi et al, ²⁷ 2010 | Low | Low | Low | High | Low | Low | Low |
| Dudova et al, ²⁸ 2014 | Low | High | Low | High | Low | Low | Low |
| Eaves et al, ⁴⁶ 2006 | Low | High | Low | Low | Low | Low | Low |
| Guo et al, ²⁹ 2019 | Low | Low | Low | High | Low | Low | Low |
| Guthrie et al, ⁹ 2019 | Low | Low | Unclear | High | Low | Low | Low |
| Harris et al, ³⁰ 2021 | Low | Low | Low | High | Low | Low | Low |
| Hoang et al, ³¹ 2019 | Low | Low | Low | High | Low | Low | Low |
| Inada et al, ⁶⁴ 2011 | Low | Low | Low | High | Low | Low | Low |
| Jonsdottir et al, ⁶⁰ 2021 | Low | Low | High | High | Low | Unclear | Low |
| Kamio et al, ⁶⁵ 2014 | Low | High | Low | High | Low | High | Low |
| Kanne et al, ⁴⁷ 2018 | Low | Low | High | Low | Low | Low | Low |
| Kara et al, ³² 2014 | Low | Low | Low | High | Low | Low | Low |
| Keehn et al, ⁴⁸ 2021 | Low | Low | High | Low | Low | Low | Low |
| Kerub et al, ⁶¹ 2020 | Low | High | Low | High | Low | Low | Low |
| Kim et al, ⁶⁷ 2016 | Low | Low | Low | High | Low | Low | Low |
| Kleinman et al, ⁶⁶ 2008 | Low | Low | Low | High | Low | Low | Low |

| | | | | | | | |
|--|-----|-----|---------|---------|-----|-----|-----|
| Koh et al, ⁴⁹ 2014 | Low | Low | Low | High | Low | Low | Low |
| Magan-Maganto et al, ³³ 2020 | Low | Low | Low | High | Low | Low | Low |
| Matson et al, ⁵⁰ 2013 | Low | Low | Low | Low | Low | Low | Low |
| Oner et al, ⁵⁹ 2020 | Low | Low | Low | High | Low | Low | Low |
| Robins et al, ³⁴ 2014 | Low | Low | Low | High | Low | Low | Low |
| Salim et al, ⁵¹ 2020 | Low | Low | Unclear | Unclear | Low | Low | Low |
| Salisbury et al, ⁵² 2018 | Low | Low | Low | Low | Low | Low | Low |
| Samadi et al, ³⁵ 2015 | Low | Low | Low | High | Low | Low | Low |
| Schjolberg et al, ⁶³ 2022 | Low | Low | Low | High | Low | Low | Low |
| Smith et al, ⁵³ 2013 | Low | Low | Low | High | Low | Low | Low |
| Snow et al, ⁵⁴ 2008 | Low | Low | Low | Low | Low | Low | Low |
| Srisinghasongkram et al, ²¹ 2016 (Sample 1) | Low | Low | Low | Low | Low | Low | Low |
| Srisinghasongkram et al, ²¹ 2016 (Sample 2) | Low | Low | Low | High | Low | Low | Low |
| Sturner et al, ³⁶ 2016 | Low | Low | Low | High | Low | Low | Low |
| Sturner et al, ³⁹ 2022 | Low | Low | Low | High | Low | Low | Low |
| Taylor et al, ⁵⁵ 2014 | Low | Low | Low | Low | Low | Low | Low |
| Toh et al, ⁶² 2018 | Low | Low | Low | High | Low | Low | Low |
| Tsai et al, ⁶⁸ 2019 | Low | Low | Low | Low | Low | Low | Low |
| Vui et al, ⁴⁰ 2022 | Low | Low | Low | High | Low | Low | Low |
| Weitlauf et al, ³⁷ 2015 | Low | Low | Low | High | Low | Low | Low |
| Wieckowski et al, ³⁸ 2021 | Low | Low | Low | High | Low | Low | Low |
| Windiani et al, ⁵⁶ 2016 | Low | Low | Unclear | Low | Low | Low | Low |
| Wong et al, ⁵⁷ 2018 | Low | Low | Low | Low | Low | Low | Low |
| Zhang et al, ⁴¹ 2022 | Low | Low | Low | High | Low | Low | Low |

Note. Low: Low concern; High: High concern; Unclear: concern is unclear.

eTable 4. Additional Study Characteristics and Psychometric Properties for M-CHAT(-R/F)

| Reference | Screen Age ^a | Eval. Age ^a | Sample description | Study Location | M-CHAT Version ^b | Single/Repeat ^c | FN Strategy Description ^d | Spec. Original ^e | Spec. New ^f |
|---|--------------------------|--------------------------|--|-------------------|-----------------------------|----------------------------|---|-----------------------------|------------------------|
| Baduel et al, ²² 2017 | 24.2 (0.6); 22.2-26.0 | 25.1 (1.9); 24-34 | Primary care and daycare population | France | M-CHAT/F | Single | Use of second screener | 0.99 | 0.993 |
| Beacham et al, ⁴² 2018 | 27.8 (6.6); 16-45 | 27.8 (6.6); 16-45 | High likelihood for ASD | US | M-CHAT-R | Single | All evaluated | 0.533 | 0.533 |
| Canal-Bedia et al, ⁵⁸ 2011 | 18-36 | 18-48 | Primary care population and EI centers / psychiatric units | Spain | M-CHAT/F | Single | All HL children evaluated | 0.98 | 0.980 ^g |
| Carbone et al, ⁸ 2020 | 16-30 | 46.8 (17.7) ^h | Primary care population | US | M-CHAT/F | Repeat | Medical record review | 0.978 | 0.978 |
| Chang et al, ²³ 2021 | 17-37 | 17-37 | Primary care population | US | M-CHAT-R/F | Single | Physician or caregiver concern | 0.988 | 0.988 |
| Charman et al, ⁴³ 2016 | 35.2 (8.3); 18-56 | 51.6 (8.8); 32-73 | High likelihood for developmental concerns | London | M-CHAT | Single | All evaluated | 0.5 | 0.500 |
| Chlebowski et al, ²⁴ 2013 | 20.4 (3.1); 16-30 | 25.8 (4.5) | Primary care population | US | M-CHAT/F | Repeat | Use of second screener after concern | 0.995 | 0.995 |
| Choueiri et al, ⁴⁴ 2021 | 18-36 | 18-36 | Children in early Intervention | US | M-CHAT-R/F | Single | All evaluated | 1.00 | 1.00 |
| Christopher et al, ⁴⁵ 2020 | 18-48 | 31.9 (8.3); 18-48 | High likelihood for ASD | US | M-CHAT-R/F | Single | All evaluated | 0.33 | 0.333 |
| Coelho-Medeiros et al, ²⁵ 2019 | 22.5 (4.2); 16-30 | 22.5 (4.2); 16-30 | High likelihood for ASD and randomly selected controls | Chile | M-CHAT-R/F | Single | Subsample of negative screens evaluated | 0.833 | 0.960 |
| Dereu et al, ²⁶ 2012 | 21.2 (2.6); 16.7-31.0 | 28.8 (7.0); 13.5-51.4 | High likelihood for ASD or language delay | Flanders, Belgium | M-CHAT | Single | Use of a second screener | 0.88 | 0.881 |
| DiGuseppi et al, ²⁷ 2010 | 52.7(14.8); 20-86 | 52.7(14.8); 20-86 | Diagnosis of Down syndrome | US | M-CHAT | Single | Subsample of negative screens evaluated | 0.468 | 0.593 |
| Dudova et al, ²⁸ 2014 | ~24 | N/A | Preterm birth with low birth weight | Prague | M-CHAT | Single | Use of a second screener | 0.926 | 0.926 |

| | | | | | | | | | |
|--|-------------------------------------|----------------------------|--|---------------------|------------|--------|---|-------|--------------------|
| Eaves et al, ⁴⁶ 2006 | 37.2; 17-48 | 40.3 (6.9); 22-53 | High likelihood for ASD | British Columbia | M-CHAT | Single | All evaluated | 0.27 | 0.267 |
| Guo et al, ²⁹ 2019 | 22.7 (4.1); 16-30 | 23.2 (4.4) | Primary care population | China | M-CHAT-R/F | Single | Use of second screener after parent or provider concern | 0.865 | 0.986 |
| Guthrie et al, ⁹ 2019 | 16 - 26 | 41.3(13.6); 17.7- 87.7 | Primary care population | US | M-CHAT/F | Repeat | Medical record review | 0.937 | 0.937 [§] |
| Harris et al, ³⁰ 2021 | 42.6 (2.2); 24-48 | N/A | Children in Head Start | US | M-CHAT-R/F | Single | Use of two other screeners | 0.99 | 0.99 |
| Hoang et al, ³¹ 2019 | 18-30 | 18-30 | Population-based sample | Vietnam | M-CHAT | Single | Subsample of negative screens evaluated | - | 0.993 |
| Inada et al, ⁶⁴ 2011 ⁱ | 18.6 (0.5); 17-23 | 37.1 (1.1); 35-44 | Primary care population | Japan | M-CHAT | Single | Diagnosis confirmed at age 3 through interviews | 0.961 | 0.961 |
| Jonsdottir et al, ⁶⁰ 2021 | 31.7(1.7) | N/A ^j | Primary care population | Iceland | M-CHAT-R/F | Single | Medical record review | 0.996 | 0.996 |
| Kamio et al, ⁶⁵ 2014 | 18.7 (0.6); 17-26 | 49.4(11.5); 33-73 | Primary care population | Japan | M-CHAT/F | Single | Follow-up primary care of all children | 0.986 | 0.986 |
| Kanne et al, ⁴⁷ 2018 | 18-48 | 32.5 (8.3); 24-42 | High likelihood for ASD | US | M-CHAT-R/F | Single | All evaluated | 0.385 | 0.385 |
| Kara et al, ³² 2014 | 18 - 36 | 24-42 | High likelihood for ASD and primary care population | Turkey; Istanbul | M-CHAT/F | Single | All HL and subsample of LL children evaluated | - | 0.973 |
| Keehn et al, ⁴⁸ 2021 | 30.4(6.5); 18-48 | 30.4(6.5); 18-48 | Referred by physician for ASD concern | US | M-CHAT-R/F | Single | All evaluated | 0.378 | 0.378 |
| Kerub et al, ⁶¹ 2020 | 22.5(3.8); 18-36 | N/A ^k | Primary care population | Israel | M-CHAT/F | Single | Medical record review | 0.982 | 0.973 |
| Kim et al, ⁶⁷ 2016 | 24.8(2.5); 4.8-43.1 ^l | 120.4(8.8); 110-151 | Preterm birth | US | M-CHAT | Single | Use of second screener at 10- year follow-up | 0.84 | 0.840 |
| Kleinman et al, ⁶⁶ 2008 ^m | 16-30 | 52.2 (8.0) ^h | High likelihood for developmental concerns and primary care | US | M-CHAT/F | Repeat | Re-screening and surveillance at a second timepoint | N/A | 0.962 |
| Koh et al, ⁴⁹ 2014 | 34.0 (7.9); 16.8-48.1 | 42.1(10.0); 17.8 – 69.2 | High likelihood for developmental concerns | Singapore | M-CHAT | Single | All evaluated | 0.667 | 0.667 |

| | | | | | | | | | |
|--|-----------------------|-----------------------|---|---------------------|------------|--------|---|-------|-------|
| Magan-Maganto et al, ³³ 2020 | 14-36 | 23-36 | Primary care population | Spain | M-CHAT-R/F | Single | Surveillance from EI centers | N/A | 0.996 |
| Matson et al, ⁵⁰ 2013 | 16-30 | 16-30 | Enrolled in early intervention | US | M-CHAT | Single | All evaluated | 0.502 | 0.502 |
| Oner et al, ⁵⁹ 2020 | 26.8 (5.8); 16-36 | 27.4 (5.9); 16-41 | Primary care population | Turkey; Istanbul | M-CHAT-R/F | Single | Subsample of negative F/U screens evaluated | 0.67 | 0.985 |
| Robins et al, ³⁴ 2014 | 20.9 (3.3); 16-30 | 26.2 (5.5) | Primary care population | US | M-CHAT-R/F | Repeat | Provider surveillance and a subsample of negative screens evaluated | 0.993 | 0.993 |
| Salim et al, ⁵¹ 2020 | 18 - 48 | 18-48 | High likelihood for developmental concerns | Bali, Indonesia | M-CHAT | Single | All evaluated | 0.786 | 0.786 |
| Salisbury et al, ⁵² 2018 | 16 -48 | 16-48 | High likelihood for developmental concerns | US | M-CHAT | Single | All evaluated | 0.564 | 0.564 |
| Samadi et al, ³⁵ 2015 | 24-60 | 24-60 | Primary care, preschool, and kindergarten centers | Iran | M-CHAT | Single | Use of a second screener | 0.817 | 0.981 |
| Schjøberg et al, ⁶³ 2022 | 19.02 (1.2) | ~42 | Population-based study | Norway | M-CHAT | Single | Medical record review | 0.925 | 0.925 |
| Smith et al, ⁵³ 2013 | 18-48 | 18-48 | High likelihood for developmental concerns | US | M-CHAT | Single | All evaluated | 0.617 | 0.617 |
| Snow et al, ⁵⁴ 2008 | 43.1(14.2); 18-48 | 43.1(14.2); 18-48 | High likelihood for ASD | US | M-CHAT | Single | All evaluated | 0.385 | 0.385 |
| Srisinghasongkram et al, ²¹ 2016 (Sample 1) | 31.2 (6.7); 18-48 | 18-48 | High likelihood for language delay | Thailand | M-CHAT/F | Single | All evaluated | 0.984 | 0.984 |
| Srisinghasongkram et al, ²¹ 2016 (Sample 2) | 24.6 (8.4); 18-48 | 18-48 | Primary care population | Thailand | M-CHAT/F | Single | Telephone F/U, EHR review, or evaluation | 0.999 | 0.999 |
| Sturner et al, ³⁶ 2016 | 18-24 | 22.9 (6.1); 14.7-40.8 | Primary care population | US | M-CHAT/F | Single | Negative F/U screens evaluated | 0.712 | 0.996 |
| Sturner et al, ³⁹ 2022 | 18.0 (0.53); 16-20 | 20.5 (1.9) | Primary care population | US | M-CHAT-R/F | Single | Subsample of negative screens evaluated | 0.658 | 0.658 |

| | | | | | | | | | |
|---|--------------------------|----------------------|---|-----------|------------|--------|--|-------|-------|
| Taylor et al, ⁵⁵ 2014 | 28.1 (4.8); <36 | 28.1 (4.8); <36 | High likelihood for developmental delay | US | M-CHAT | Single | All evaluated | 0.559 | 0.559 |
| Toh et al, ⁶² 2018 | 20.8 (4.1); 15.0–36.0 | N/A | Primary care population | Malaysia | M-CHAT | Single | Medical record review | 0.999 | 0.999 |
| Tsai et al, ⁶⁸ 2019 | 24.3 (4.4); 16-32 | 36.0 (0.1); 36-37 | Community and clinical settings | Taiwan | M-CHAT-R/F | Single | All evaluated | 0.935 | 0.935 |
| Vui et al, ⁴⁰ 2022 | 18-30 | N/A | Population-based study | Vietnam | M-CHAT | Single | Subsample of negative screens evaluated | 0.977 | .995 |
| Weitlauf et al, ³⁷ 2015 | 16-36 | 18–43 | Younger siblings of children with ASD | US | M-CHAT-R/F | Single | Subsample of negative screens evaluated | 0.806 | 0.806 |
| Wieckowski et al, ³⁸ 2021 ⁿ | 18.8(0.93); 17-22 | 23.8(6.87); 18-60 | Primary care population | US | M-CHAT-R/F | Repeat | Physician concern | 0.972 | 0.972 |
| Windiani et al, ⁵⁶ 2016 | 30.6 (9.6); 18-48 | 30.6 (9.6); 18-48 | High likelihood for developmental delay | Indonesia | M-CHAT-R/F | Single | All evaluated | 0.946 | 0.946 |
| Wong et al, ⁵⁷ 2018 | 18-47 | 30.2 (8.1); 18-47 | High likelihood for developmental delay | Taiwan | M-CHAT | Single | All evaluated | .528 | .528 |
| Zhang et al, ⁴¹ 2022 | 18-24 | 23.1(4.6) | Primary care population | China | M-CHAT-R/F | Single | Use of a second screener and follow-up of negative screens | 0.995 | 0.995 |

Note: ^a Mean, Standard Deviation, and Range in months reported for entire sample that received M-CHAT(-R/F) or evaluation, when available. If not available, an estimate from the manuscript or from communication with authors is reported in months. ^b Version of M-CHAT; M-CHAT = original M-CHAT without Follow-Up; M-CHAT/F = original M-CHAT with Follow-up; M-CHAT-R = revised version of M-CHAT without Follow-Up; M-CHAT-R/F = revised version of M-CHAT with Follow-Up ^c Single or repeat timepoint screening schedule. Studies were classified as repeat even if only a subset of children completed screener more than once. ^d Description of strategy used to detect False Negative (FN) cases. ^e Original specificity reported in the manuscript. ^f Specificity was recalculated using the recalculated TN. TN was recalculated to include presumed true negatives (i.e., including children who screened negative but were not further evaluated), for consistency across studies, unless noted otherwise. Negative screens were presumed to be TN unless there was other presented evidence. ^g TN and Spec taken from directly from paper and not recalculated due to missing information. ^h Age of evaluation is for ASD sample only; age for non-ASD sample is unknown. ⁱ Discriminant validity sample only reported due to not enough information provided for the concurrent validity sample. ^j Evaluation occurred up to 18 months after the screening. ^k Age of evaluation was within 10 months of screen. ^l Age reported is uncorrected for prematurity. ^m Study 2 sample only presented and analyzed due to overlap of sample 1 with Chlebowski et al. ⁿ Information is reported for 18 month screening start age only.

eTable 5. Sensitivity and Specificity for Younger and Older Samples

| References | FN Strategy | Screen Age (m) | N | Sens. | Spec. | TP | TN | FP | FN |
|--|--------------------|-----------------------|----------|--------------|--------------|-----------|-----------|-----------|-----------|
| Beacham et al, ⁴² 2018 | C: All Eval | 16-30 | 99 | .87 | .58 | 65 | 14 | 10 | 10 |
| | | 31-45 | 55 | .82 | .33 | 40 | 2 | 4 | 9 |
| Christopher et al, ⁴⁵ 2020* | C: All Eval | 18-30 | 115 | .90 | .22 | 79 | 6 | 21 | 9 |
| | | 31-48 | 173 | .70 | .41 | 90 | 18 | 26 | 39 |
| Kanne et al, ⁴⁷ 2018 | C: All Eval | 18-30 | 72 | .90 | .30 | 47 | 6 | 14 | 5 |
| | | 31-48 | 86 | .73 | .47 | 49 | 9 | 10 | 18 |
| Koh et al, ⁴⁹ 2014 | C: All Eval | 18-30 | 173 | .89 | .59 | 47 | 71 | 49 | 6 |
| | | 31-48 | 407 | .76 | .72 | 111 | 187 | 74 | 35 |
| Salisbury et al, ⁵² 2018 | C: All Eval | 16-30 | 271 | .78 | .54 | 134 | 53 | 45 | 39 |
| | | 31-48 | 214 | .69 | .59 | 86 | 53 | 37 | 38 |

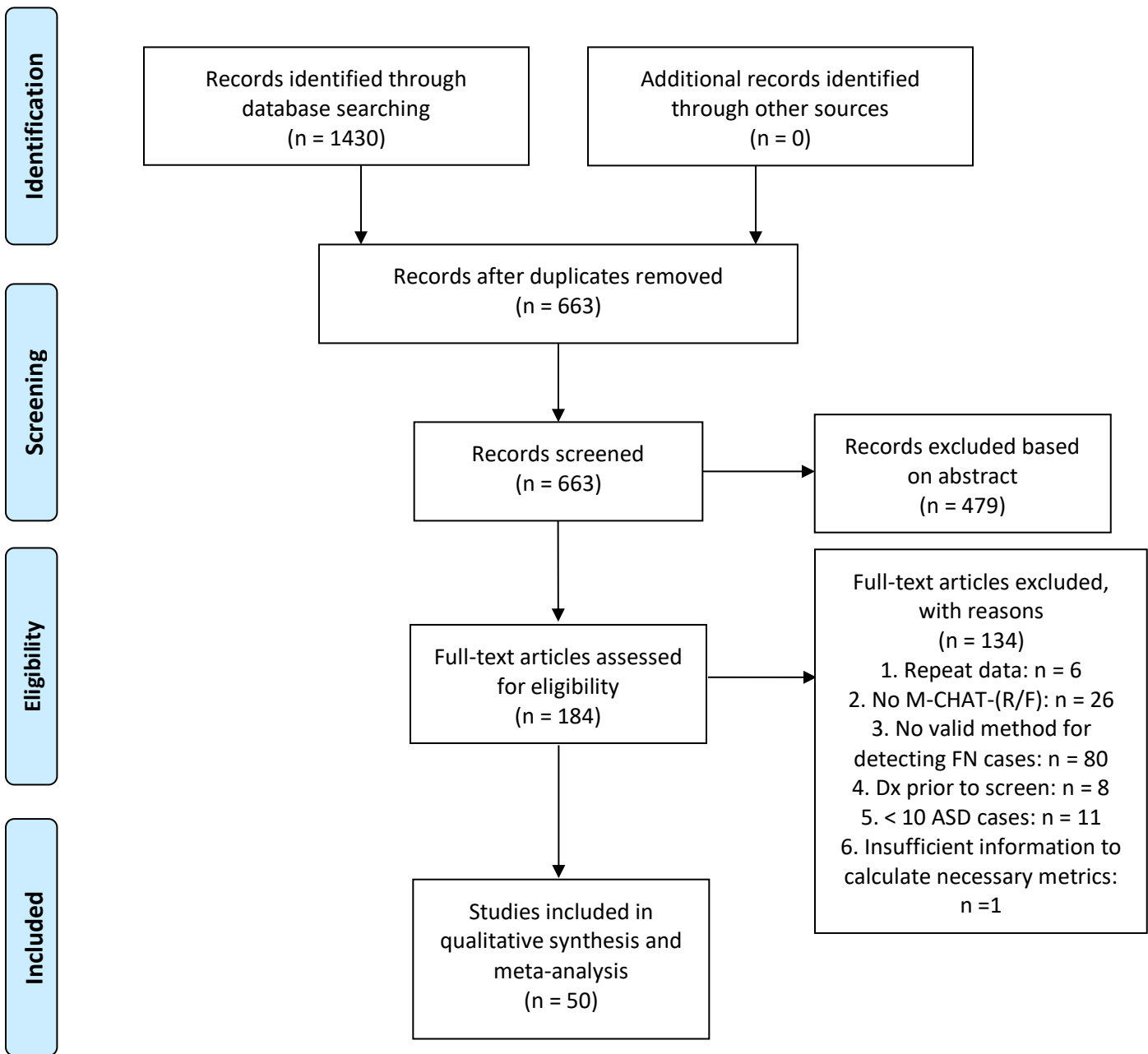
*Data obtained from personal communication with one of the authors.

eTable 6. Sensitivity and Specificity for Single and Repeated Screening

| | | Single (18 or 24 months) | Repeat (18 and 24 months) | Combined (18 and/or 24 months) |
|--|-------------|---|--|---|
| Carbone et al, ⁸ 2020 | Sensitivity | .28 | .41 | .33 |
| | Specificity | .98 | .98 | .98 |
| Guthrie et al, ⁹ 2019 ^a | Sensitivity | .39 | .51 | .50 |
| | Specificity | .95 | .95 | .94 |
| Wieckowski et al, ³⁸ 2021 ^b | Sensitivity | .74 | - | .82 |
| | Specificity | .97 | - | .97 |

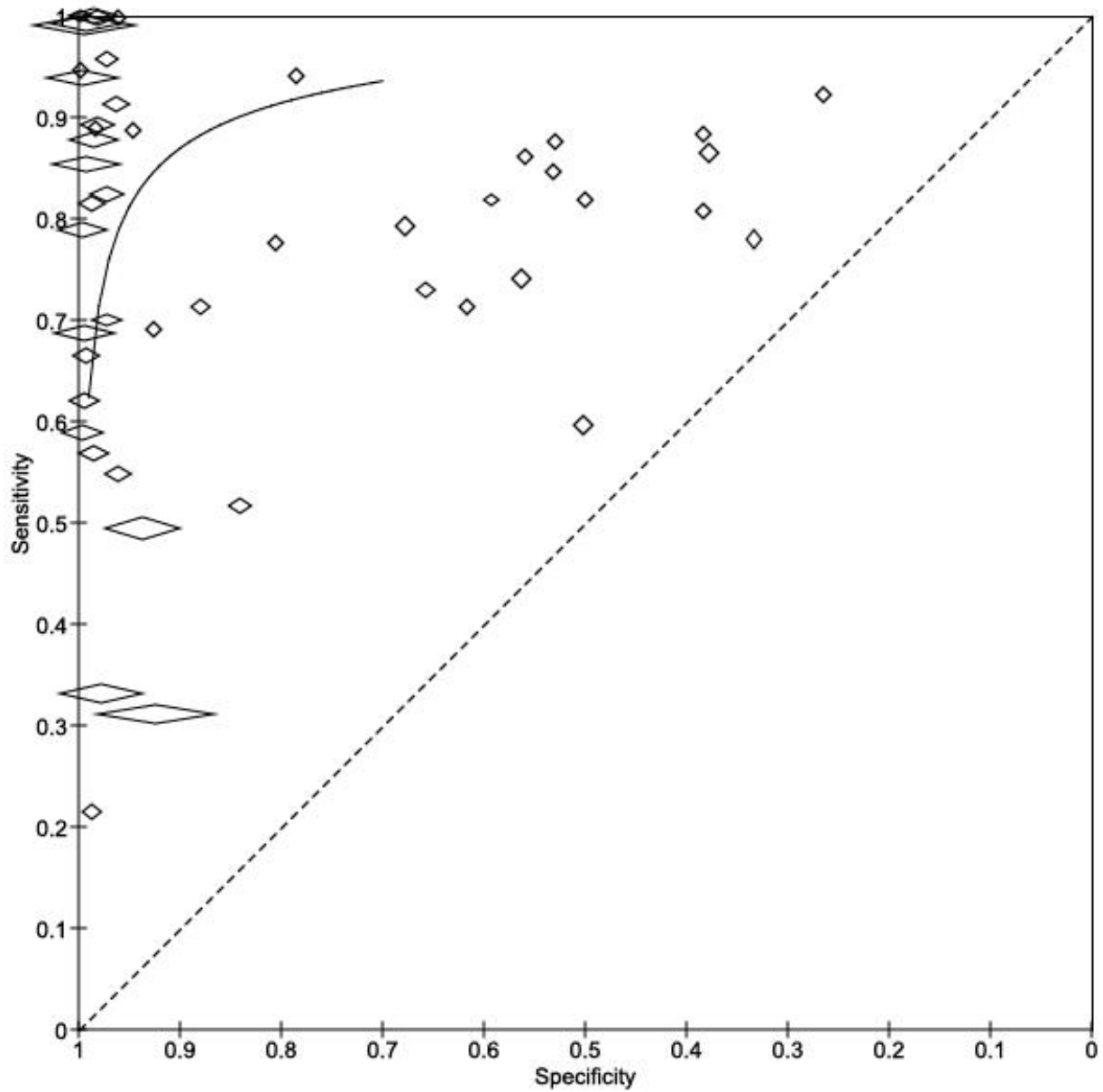
^a Data obtained from personal communication with one of the authors.

^b Data for 18 month screening and rescreening at 24 and/or 36 months is reported



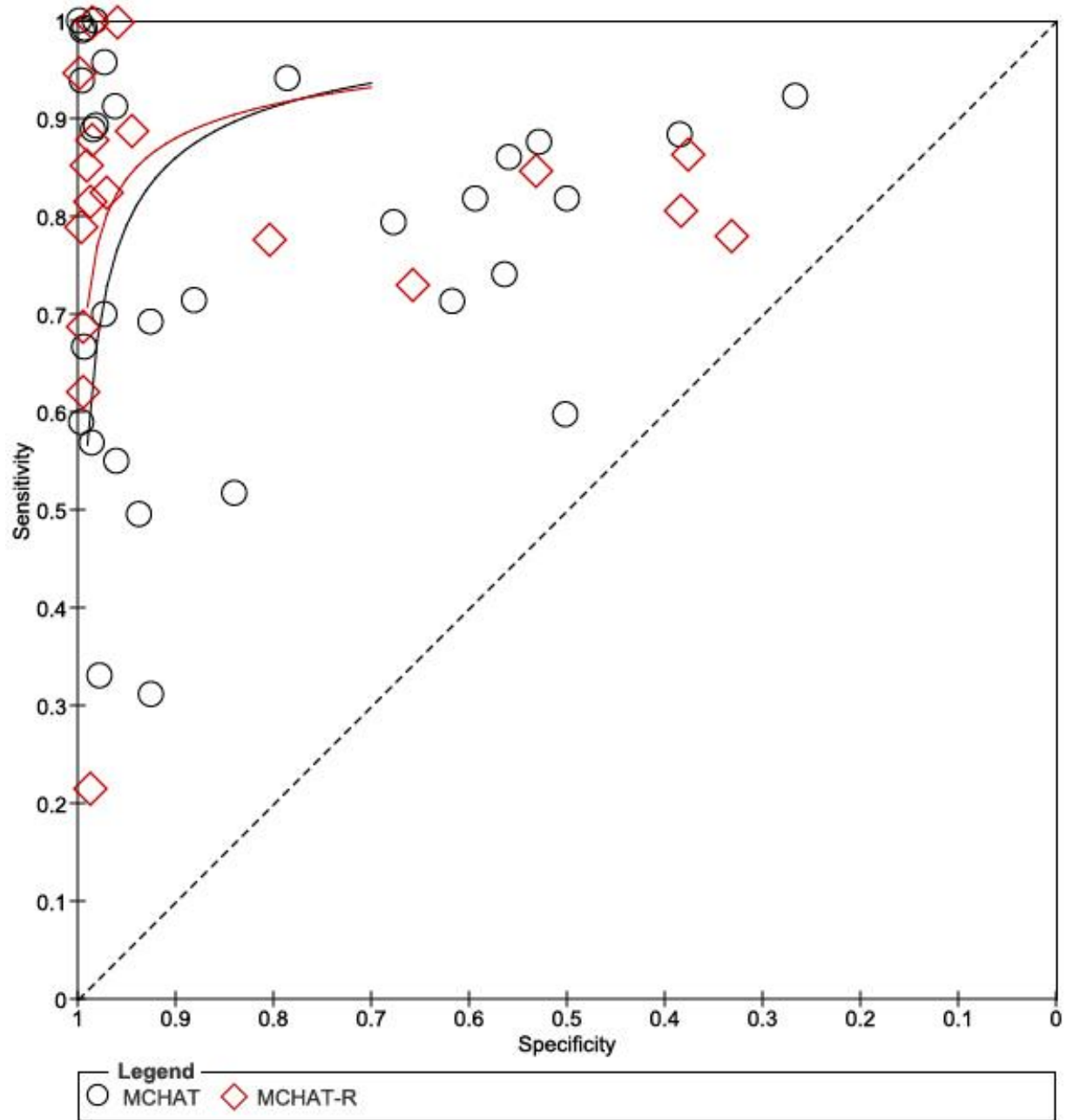
eFigure 1. Study Selection Flow Chart Following PRISMA Guidelines

eFigure 2. Overall SROC of M-CHAT(-R/F) (n = 49¹ Studies)
Diamond width reflects sample size.

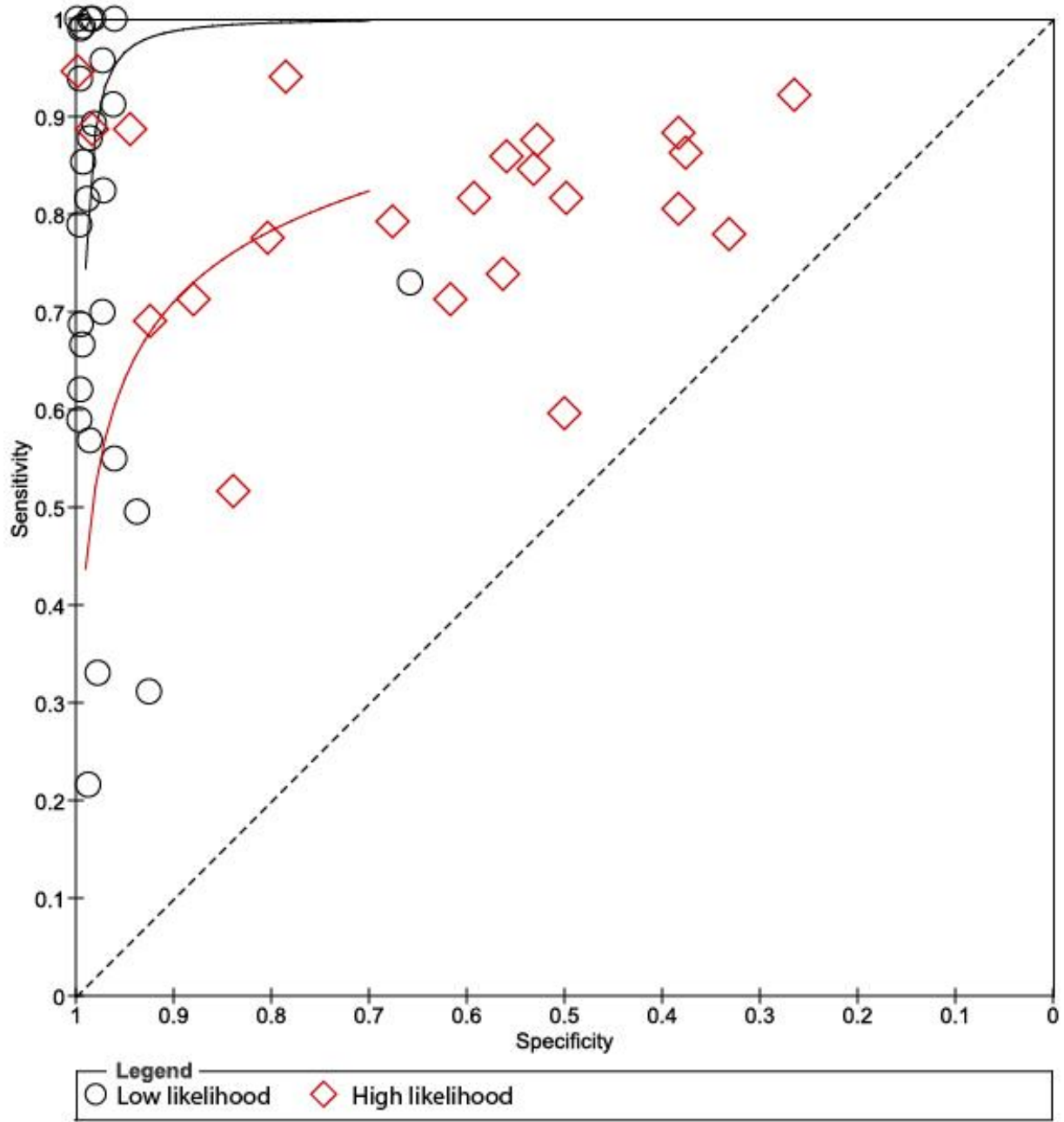


¹ Studies classified as “mixed” or “unknown” in any category were excluded from the analysis (n=2)^{62,68}

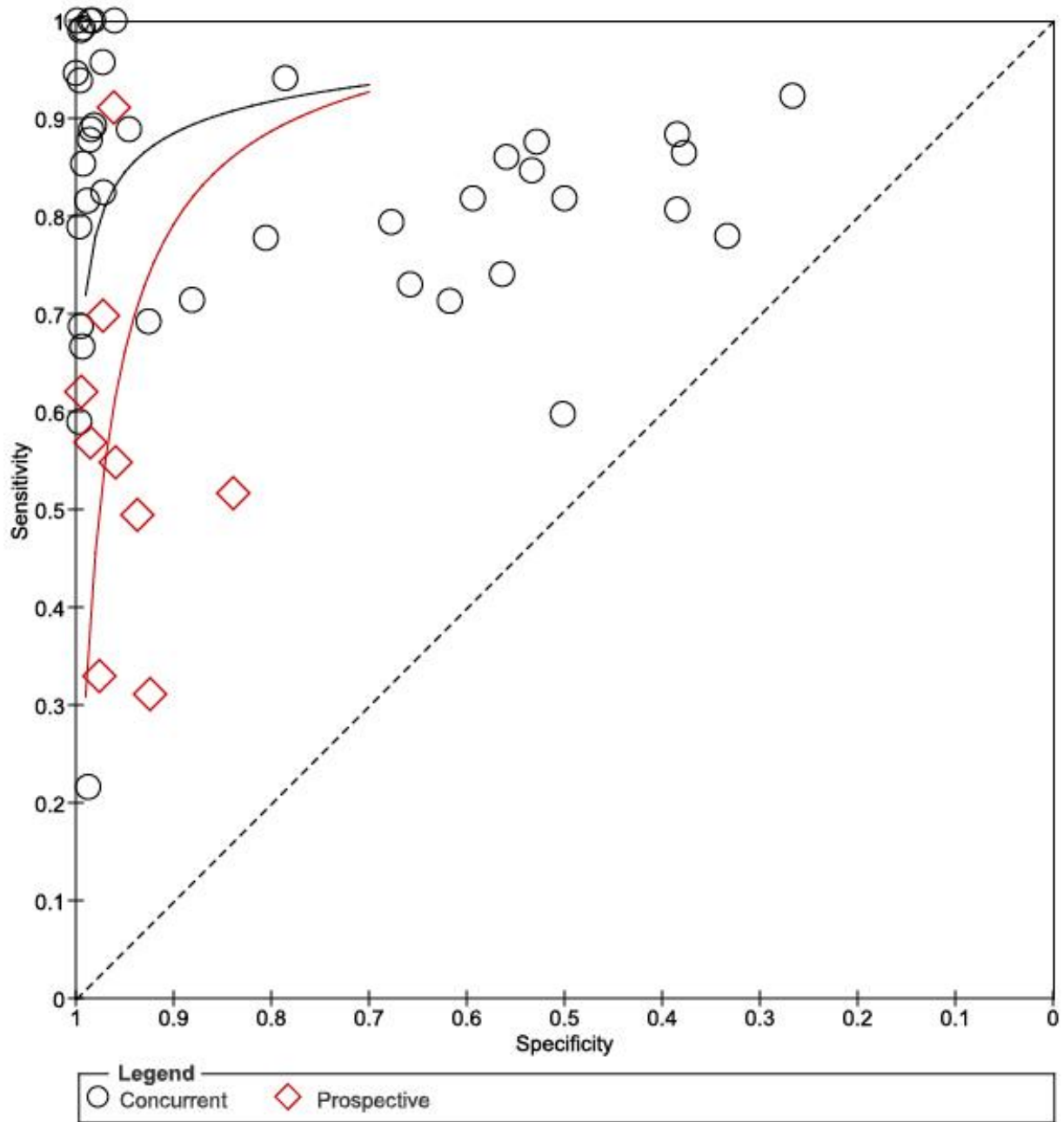
eFigure 3. SROC Plot of M-CHAT(-R/F) by M-CHAT Version (M-CHAT n = 31, M-CHAT-R n = 18)



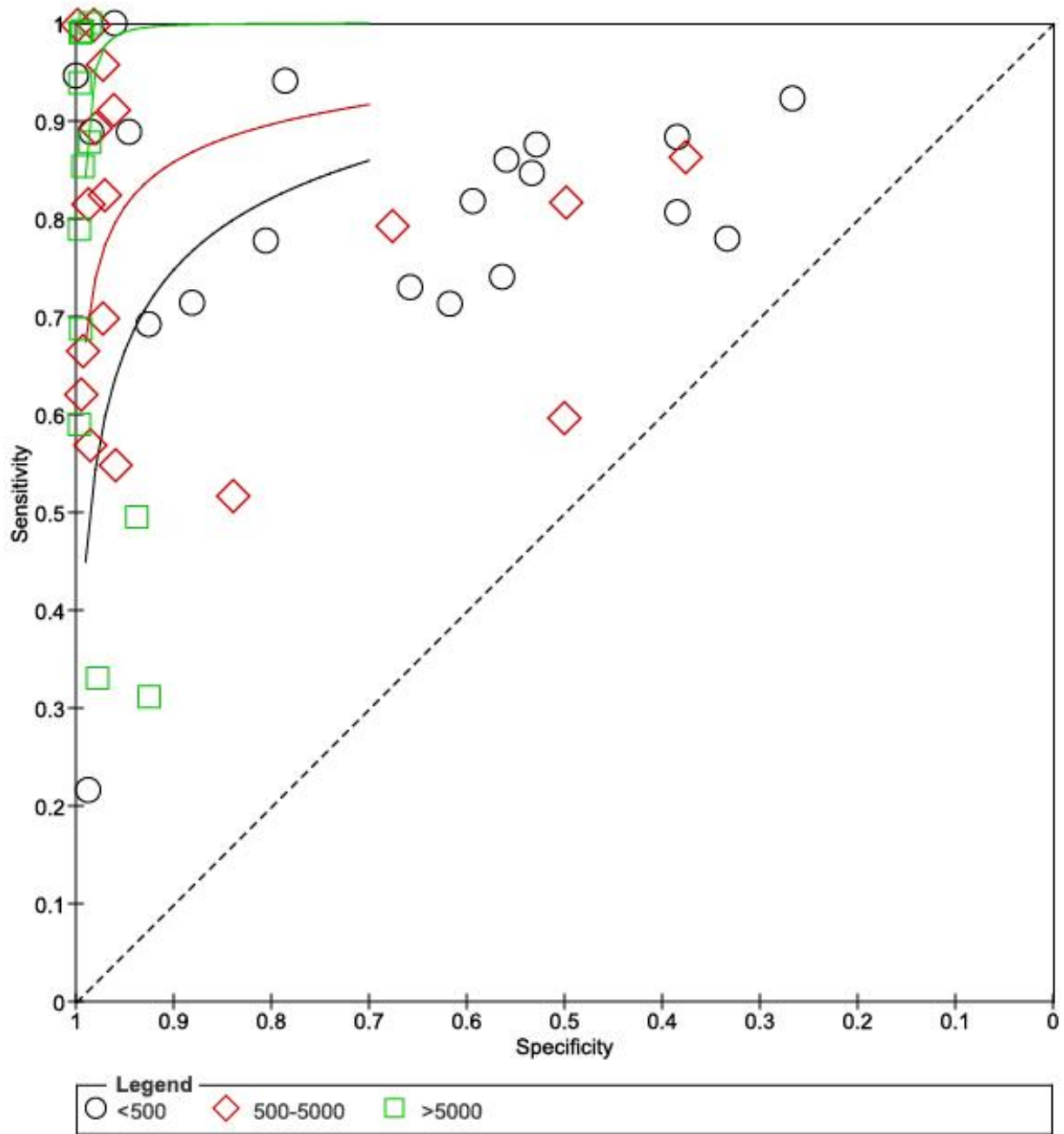
eFigure 4. SROC Plot of M-CHAT(-R/F) by Likelihood Level of Sample (Low Likelihood n = 27, High Likelihood n = 22)



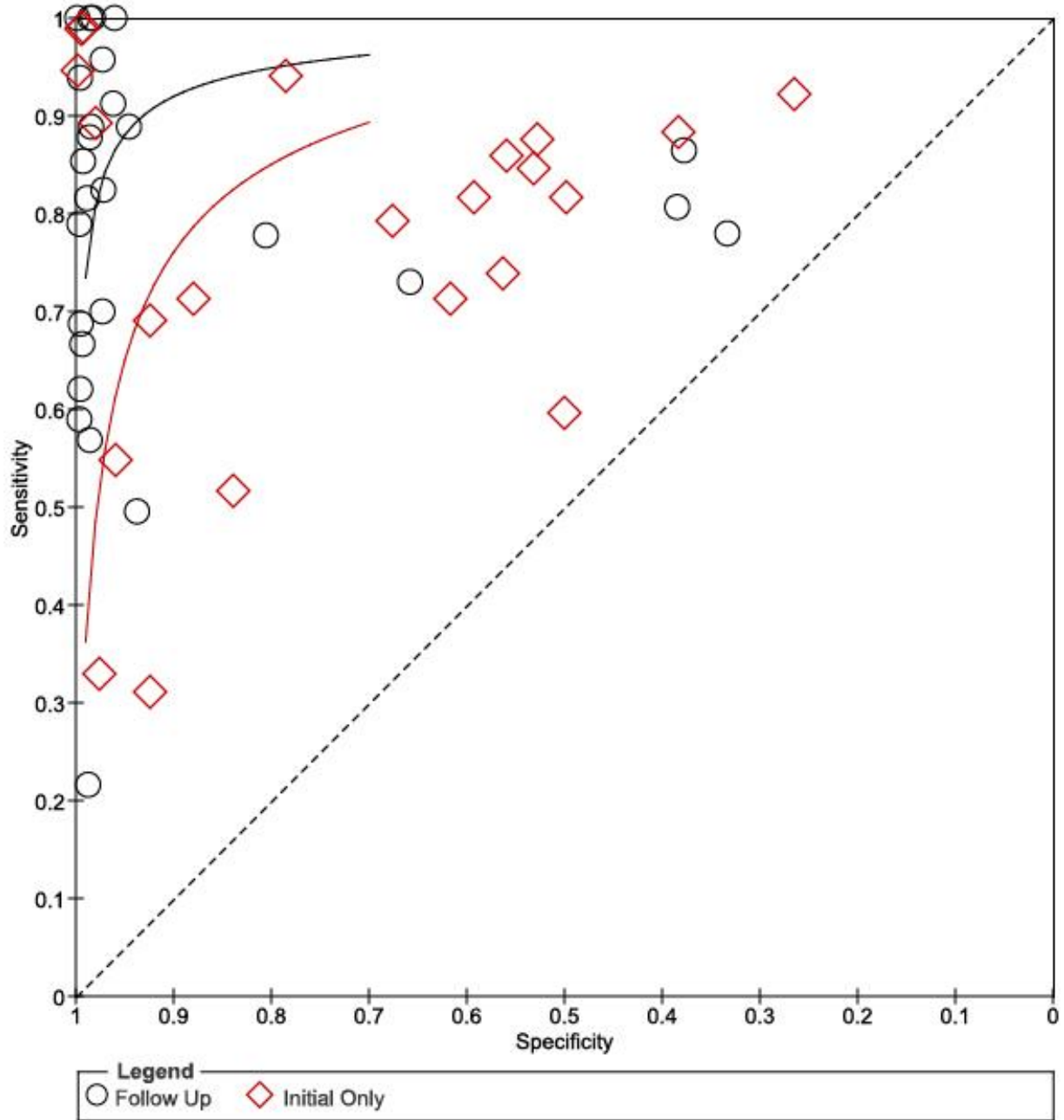
eFigure 5. SROC Plot of M-CHAT(-R/F) by Case Confirmation Strategy (Concurrent n = 40, Prospective n = 9)



eFigure 6. SROC Plot of M-CHAT(-R/F) by Sample Size (Small n = 20, Medium n = 17, Large n = 12)



eFigure 7. SROC Plot of M-CHAT(-R/F) With Follow-up vs Initial Only (Initial n = 22, Follow-up n = 27)



eFigure 8. SROC Plot of M-CHAT(-R/F) by Language (English/Primarily English n = 26, Other Language n = 23)

