REVIEW ARTICLE

Assessment of the diagnostic performance of two new tools versus routine screening instruments for bipolar disorder: a meta-analysis

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Objective: The present meta-analysis was conducted to determine the diagnostic accuracy of the bipolarity index (BI) and Rapid Mode Screener (RMS) as compared with the Bipolar Spectrum Diagnostic Scale (BSDS), the Hypomania Checklist (HCL-32), and the Mood Disorder Questionnaire (MDQ) in people with bipolar disorder (BD).

Methods: We systematically searched five databases using standard search terms, and relevant articles published between May 1990 and November 30, 2021 were collected and reviewed.

Results: Ninety-three original studies were included (n=62,291). At the recommended cutoffs for the BI, HCL-32, BSDS, MDQ, and RMS, the pooled sensitivities were 0.82, 0.75, 0.71, 0.71, and 0.78, respectively, while the corresponding pooled specificities were 0.73, 0.63, 0.73, 0.77, and 0.72, respectively. However, there was evidence that the accuracy of the BI was superior to that of the other tests, with a relative diagnostic odds ratio (RDOR) of 1.22 (0.98-1.52, p < 0.0001). The RMS was significantly more accurate than the other tests, with an RDOR (95%CI) of 0.79 (0.67-0.92, p < 0.0001) for the detection of BD type I (BD-I). However, there was evidence that the accuracy of the MDQ was superior to that of the other tests, with an RDOR of 1.93 (0.89-2.79, p = 0.0019), for the detection of BD type II (BD-II).

Conclusion: The psychometric properties of two new instruments, the BI and RMS, in people with BD were consistent with considerably higher diagnostic accuracy than the HCL-32, BSDS, and MDQ. However, a positive screening should be confirmed by a clinical diagnostic evaluation for BD.

Keywords: Bipolar disorder; screening; accuracy studies; systematic review; meta-analysis

Introduction

The mood disorders encompass a large group of psychiatric diseases, of which major depressive disorders, bipolar disorder (BD), and cyclothymia can be detected on the basis of DSM-IV diagnostic criteria.¹ BDs are often undiagnosed and, thus, often go untreated²; delays in diagnosis will delay treatment accordingly. The lifetime prevalence range for BD is 1.4 to 6.4% globally.³⁻⁵ BD is subdivided into type I (BD-I) and type II (BD-II). According to the DSM-5 criteria, the lifetime prevalence of BD-I is about 1% and that of BD-II is 1.3% in the general population.⁶⁻⁸

According to earlier reports, some individuals who met criteria for BD were never diagnosed with it, but in comparison, more people were misdiagnosed with BD, with correct diagnosis often being delayed by about 10 years.⁹ Accurate and concise tools have since largely improved

Correspondence: Fakher Rahim, Ahvaz Jundishapur University of Medical Sciences, Health Research Institute, Research Center of Thalassemia & Hemoglobinopathies, Ahvaz, Iran. E-mail: Bioinfo2003@gmail.com the diagnosis of BD, including the Mood Disorders Questionnaire (MDQ), a 13-item checklist based on DSM-IV criteria and clinical experience¹⁰; the Hypomania Checklist-32 (HCL-32), a globally validated self-applied questionnaire to facilitate the diagnosis of BD-II¹¹; and the Bipolar Spectrum Diagnostic Scale (BSDS), a self-report questionnaire for BD.¹²

The estimated sensitivity and specificity of the MDQ are in the range of 73-76% and 86-90%, respectively.¹³⁻¹⁶ The HCL-32 was reported to have 48-66% and 59-71% sensitivity and specificity respectively for screening BD.^{17,18} Thus, both the MDQ and HCL-32 tools have relatively acceptable sensitivity and specificity for BD screening. At lower prevalence or low clinical pretest probability, high negative predictive values were confirmed, indicating that available instruments effectively rule out BD; however, the positive predictive value decreases significantly, leading to a greater number of

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"false positives."¹⁹ Recently, two new instruments for the diagnosis of BD have been introduced: the Bipolarity Index (BI)²⁰ and the Rapid Mood Screener (RMS).²¹ BI, a diagnostic aid, is a clinician-rated tool that focuses on five clinical domains, including signs and symptoms, age at onset, disease course, treatment response, and family history. Considering the clinical domains covered by BI, this diagnostic method may be more conducive than the MDQ, BSDS, and HC-32, of which previous studies reported a specificity of 100% in the differential diagnosis of BD.²²

Various studies have shown that about 40-50% of patients with BD are undiagnosed at the time of referral and are often treated as having monopolar depression.^{23,24} Since a large number of individuals with BD suffer substantial complications and consequences due to this lack of proper diagnosis, a diagnostic tool with appropriate psychometric properties is still needed. The present meta-analysis was conducted to determine the diagnostic accuracy of psychometric properties of the BI and RMS as compared to the BSDS, the HCL-32, and the MDQ in people with BD.

Methods

This systematic review with meta-analysis was conducted according to the Meta-analyses of Observational Studies in Epidemiology,²⁵ Preferred Reporting Items for Systematic reviews and Meta-Analyses,²⁶ and Synthesizing Evidence from Diagnostic Accuracy Tests²⁷ guidelines.

Search strategy

We systematically searched databases including Scopus, ISI Web of Sciences (WOS), PubMed/MEDLINE, EMBASE, and PsycINFO using the standard search terms "Bipolarity index"[Text] AND ("Bipolar Disorder" OR "Bipolar and Related Disorders" OR "Mood Disorders" OR "Mania") OR ("Depression" OR "Depressive Disorder") AND ("Hypomania Checklist" OR "HCL" OR "Hypomania/Mania Symptoms Checklist" OR "Hypomania Symptoms Checklist"). Relevant articles published between May 1990 and November 30, 2021 were collected and reviewed.

Inclusion and exclusion criteria

Prospective, national, population-based studies considering individuals with BD and using the BI tool for diagnosis were included. Articles that had incomplete or unidentified data, various designs (conference abstracts, reviews, case reports, letters), and duplicate publications were excluded.

Study selections

After exclusion of duplicates, two authors (MS and FR) independently screened titles and abstracts of potential papers considering predefined inclusion and exclusion criteria. Any disagreements were resolved by either reevaluation of the source article or consulting a third author (ME).

Data extraction

Information, including authors' names, year of publication, country, age, sample size, and study design were extracted for analysis.

Methodological quality assessment

Two reviewers (MS and FR) assessed the methodological quality of the included studies using the Newcastle-Ottawa Scale and the Quality Assessment of Diagnostic Accuracy Studies tools. Disagreements were resolved by either discussion or reevaluation of the original article with a third reviewer (ME).

Statistical analysis

We retrieved odds ratios (ORs) with 95% confidence intervals (95%CIs) from the eligible studies, and calculated summary ORs with the random-effects or fixedeffect models, depending on the level of heterogeneity, to evaluate the diagnostic utility of the BI in the screening and diagnosis of individuals with BD.28 We then measured heterogeneity across studies using Cochran's Q statistic and the l^2 test. When the l^2 values exceeded 50%, indicating high heterogeneity, sensitivity and subgroup analyses were performed to discover the source of the heterogeneity. A hierarchical summary receiver-operating characteristic (HSROC) curve and a summary receiver operating characteristic (SROC) curve were constructed. All experiments were viewed with the HSROC curve as a circle and plotted. The area under the curve (AUC) was computed to determine the diagnostic precision. An AUC approaching 1.0 would mean outstanding results, while one approaching 0.5 would denote poor performance. Among numerous subgroups, the 95%CI of the AUC was compared. When the sensitivity and specificity were directly unavailable, they were calculated according to the following formulas: sensitivity = TP / (TP + FN) and specificity = TN / (FP + TN). Publication bias was measured using Deeks' regression test.²⁹ The analysis was conducted using version 1.4 of the Meta-DiSc software³⁰ and RevMan 5.3.

Ethics statement

As this systematic review with meta-analysis relied exclusively on previously published studies, ethics committee approval and informed consent were waived.

Results

Search results

Overall, 834 records were found through the initial search. Of 679 articles, 292 duplicates were found and 357 were omitted due to irrelevant titles and abstracts. The remaining 185 entered full-text screening; of these, 94 were excluded due to predefined criteria (Figure 1). Ultimately, 93 studies (n=62,291) were included (Table S1, available as online-only supplementary material).^{11-16,20,21-24,31-100}



Figure 1 Flow diagram of the selection process.

Methodological quality of included studies

The methodological quality of the included studies is shown in Figure S1, available as online-only supplementary material. A total of nine studies were at high risk of bias in the participant selection domain.^{13,24,31,40,41,51,63,64,93} Also nine studies were at high risk of bias in the reference standard domain.^{32,39,42,45,46,52,77,86,98} Moreover, a total of two studies were at high risk of bias in the flow and timing domain.^{42,107} Three studies were at high risk of bias for all index tests other than one threshold^{32,42,77} (Figure 2).

Comparison of the BI, HCL-32, BSDS, MDQ, and RMS for the detection of bipolar disorder (indirect comparison)

The pooled sensitivities and specificities for the BI, HCL-32, BSDS, MDQ, and RMS at specific cutoffs were measured for a separate meta-analysis of each instrument at a common cutoff (Table 1). At the recommended cutoffs for the BI, HCL-32, BSDS, MDQ, and RMS, the pooled sensitivities were 0.82 (95%CI 0.81-0.83), 0.75 (95%CI 0.74-0.76), 0.71 (95%CI 0.69-0.73), 0.71 (95%CI 0.70-0.73), and 0.78 (95%CI 0.73-0.82), respectively. The corresponding pooled specificities were 0.73 (95%CI 0.72-0.74), 0.63 (95%CI 0.62-0.63), 0.73 (95%CI 0.71-0.74), 0.77 (95%CI 0.76-0.78), and 0.72 (95%CI 0.68-0.77), respectively. However, there was evidence that the accuracy of the BI was superior to that of the other tests with a relative diagnostic OR (RDOR) (95%CI) of 1.22 (0.98-1.52, p < 0.0001).

We compared the performance of the three existing tools, including the HCL-32 (28 studies), MDQ (55 studies), and BSDS (14 studies), with the two new instruments, BI (nine studies) and RMS (three studies), using all available studies (Figure 3). The pattern of the SROC curves and the accuracy of the screening instruments varied considerably, because accuracy of each tool differed with different cutoffs (Figure 4). Though the



Figure 2 Summary risk of bias and applicability concerns: review authors' judgments regarding each domain of each included study.

number of studies was not comparable, the BI curve was consistently above those of the HCL-32, BSDS, MDQ, and RMS in the region covering maximum observed data at higher values of sensitivity and lower specificity. Both the BSDS and RMS curves were above the HCL-32 and MDQ curves.

Direct comparison

- Comparison of the BI with HCL-32 for the detection of BD: The BI curve was consistently above the HCL-32 curve in the region encompassing most of the observed data (Figure S2).
- Comparison of the BI with BSDS for the detection of BD: The BI curve was consistently above the BSDS curve in the region comprising most of the observed data (Figure S3).
- Comparison of the BI with MDQ for the detection of BD: The BI curve was consistently above the MDQ curve in the region involving most of the observed data (Figure S4).
- Comparison of the RMS with HCL-32 for the detection of BD: The RMS curve was consistently above the HCL-32 curve in the region encompassing most of the observed data (Figure S5).
- Comparison of the RMS with BSDS for the detection of BD: The RMS curve was not consistently above the BSDS curve in the region comprising most of the observed data (Figure S6).
- Comparison of the RMS with MDQ for the detection of BD: The BI curve was consistently above the MDQ curve in the region involving most of the observed data (Figure S7).
- Comparison of the BI with RMS for the detection of BD: The BI curve was consistently above the RMS curve in the region involving most of the observed data (Figure S8).

Detection of BD-I

Overall, 14 studies used various instruments to detect BD-I using the HCL-32 (six studies, 4,799 patients), MDQ (five studies, 4,144 patients), and RMS (three studies, 800 patients) (Figure 5).

Overall, each instrument had acceptable diagnostic accuracy for the detection of BD (Figures S9-12).

At the recommended cutoffs for the HCL-32, MDQ, and RMS, the pooled sensitivities were 0.65 (0.63-0.67), 0.78 (0.76-0.80), and 0.78 (0.73-0.82), respectively. The corresponding pooled specificities were 0.64 (0.62-0.66), 0.67 (0.65-0.69), and 0.72 (0.68-0.77), respectively (Table 2).

Detection of BD-II

Overall, 28 studies used various instruments to detect BD-II: the HCL-32 (10 studies, 6,316 patients), BSDS (five studies, 515 patients), MDQ (14 studies, 3,772 patients), and BI (one study, 800 patients) (Figure 6).

At the recommended cutoffs for the HCL-32, BSDS, and MDQ, the pooled sensitivities were 0.70 (0.68-0.72), 0.78 (0.67-0.87), and 0.52 (0.49-0.56), respectively. The corresponding pooled specificities were 0.65 (0.63-0.66), 0.63 (0.58-0.67), and 0.77 (0.76-0.79), respectively (Table 2).

We compared the test performance and diagnostic accuracies of the BI, HCL-32, BSDS, MDQ, and RMS for detection of BD-I (Figure 7A) vs. BD-II (Figure 7B). The RMS was significantly more accurate than the other tests, with an RDOR (95%CI) of 0.79 (0.67-0.92, p < 0.0001), for the detection of BD-I. However, there was evidence that the accuracy of the BI was superior to that of the other tests, with an RDOR of 1.93 (0.89-2.79, p = 0.0019), for the detection of BD-II (Table 2). More detailed components of diagnostic accuracy, including sensitivity, specificity, positive and negative predictive values, and likelihood ratios for each test, are given in Supplementary Material S13.

Discussion

The present meta-analysis was conducted to determine the diagnostic accuracy of two new instruments, the BI and RMS, in people with BD, comparing these instruments to already available tools such as the HCL-32, BSDS, and MDQ. The findings showed that the utility and diagnostic accuracy of the BI were significantly superior to those of the other tools, especially for BD-II.

BD and other chronic mental disorders such as schizophrenia are different, but their symptoms are sometimes confused. If a good clinical history is lacking or the context of the patient's current life situation is ignored,

			Sei	nsitivity		Sp	ecificity		Diagnos	tic OR	
Test	Papers (n)	Participants (n)	Pooled (95%CI)	P (%)	p-value	Pooled (95%CI)	P (%)	p-value	Pooled (95%CI)	P (%)	p-value
В	6	11,474	0.82 (0.81-0.83)	98.9	< 0.0001	0.73 (0.72-0.74)	99.1	< 0.0001	47.20 (12.01-185.52)	99.2	< 0.0001
HCL-32	28	20,837	0.75 (0.74-0.76)	95.9	< 0.0001	0.63 (0.62-0.63)	97.6	< 0.0001	7.50 (5.65-9.95)	92.1	< 0.0001
BSDS	14	7,256	0.71 (0.69-0.73)	80.0	< 0.0001	0.73 (0.71-0.74)	97.0	< 0.0001	13.49 (8.80-20.69)	80.6	< 0.0001
MDQ	55	21,924	0.71 (0.70-0.73)	95.4	< 0.0001	0.77 (0.76-0.78)	95.6	< 0.0001	9.04 (7.32-11.17)	85.6	< 0.0001
RMS	ю	800	0.78 (0.73-0.82)	91.4	< 0.0001	0.72 (0.68-0.77)	82.1	0.0038	14.24 (3.16-64.1)	93.7	< 0.0001
95%Cl = $6Questionn$)5% confidence aire: OR = odds	interval; BI = Bipola s ratio; RMS = Rapi	rity Index; BSDS = Bil d Mood Screener.	polar Spec	trum Diagnosti	c Scale; DOR = diagn	lostic odds	ratio; HCL-32	= Hypomania Checklist-32;	MDQ = M	ood Disorder

Diagnostic performance of two new tools for Dipolar disorder	
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misdiagnosis may occur. Substantial misdiagnosis rate between BD and other chronic mental disorders, especially mood disorders, may lead to delay in receiving proper and timely treatment and achieving symptom control.

Overall, for the detection of both types of BD, the BI was significantly more accurate than the HCL-32, MDQ, BSDS, and RMS, while to detect BD-I, the RMS was significantly more accurate, and for the detection of BD-II, the MDQ had superior diagnostic accuracy. Differences in the characteristics of the studied instruments can explain these findings. Our meta-analysis showed 0.82 and 0.73 for the BI at recommended cutoff in psychiatric services. respectively. In this context, Carvalho et al.¹⁸ performed a meta-analysis to compare the diagnostic accuracy of the BSDS, the HCL-32, and the MDQ, and reported summary sensitivities of 81, 66, and 69%, as well as specificities of 67, 79, and 86% for the HCL-32, MDQ, and BSDS in psychiatric services, respectively. Thus, the BI could be more accurate than the other available tools for the detection of BD in primary-care or general-population settings. Given that the BSDS, HCL-32, and MDQ were proposed to improve the diagnosis of less exuberant cases of BD,^{12,31} this may explain why the other tools are less accurate than the BI for detection of BD.

Recently, Sun et al.¹¹¹ conducted a meta-analysis to assess the diagnostic accuracy of BI for the detection of BD and found diagnostic superiority of the BI, with significant heterogeneity. The pooled sensitivity, specificity, and accuracy of the BI were 93% (95%CI 93-100), 85% (95%CI 69-96), and 86% (95%CI 77-93), respectively.¹¹² Our meta-analysis of an individual test showed that the pooled sensitivity, specificity, and accuracy of the BI were 82% (95%CI 61-100), 73% (95%CI 52-100), and 93% (95%CI 77-97), respectively. Thus, our meta-analysis also showed a diagnostic superiority of the BI over other instruments, with significant heterogeneity. The Sun et al.¹¹¹ meta-analysis included only five studies that used the Chinese version of the BI, but our analysis encompasses studies from America, Asia, and Europe. Wang et al.¹⁷ performed a meta-analysis of studies that directly compared the HCL-32 and the MDQ in detecting BD, and reported that the HCL-32 showed higher sensitivities (82% [95%CI 72-89] vs. 80% [95%CI 71-86]) and lower specificities (57% [95%CI 48-66] vs. 70% [95%CI 59-71]) compared to the MDQ. Our findings are in line with those of Wang et al.¹⁷ in terms of direct comparison of these two instruments, but they included only nine studies, while our meta-analysis included 28 studies using the HCL-32 and 55 using the MDQ. In another meta-analysis, Carvalho et al.¹⁸ assessed the diagnostic accuracy of 53 original studies, both directly and indirectly, and showed that the HCL-32 is consistently more accurate than the MDQ, especially for BD-II. The present meta-analysis showed that the BI has a higher sensitivity for the diagnosis of BD-II compared to other instruments. Given that around 70% of individuals with BD-I are first misdiagnosed, with an average disease onset-to-diagnosis delay of 5 to 10 years, a group of multidisciplinary professionals developed the RMS (a six-item instrument) to offer a pragmatic method to shed light on the necessity for accurate and timely

Braz J Psychiatry. 2022;44(3)

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Ter Meulen 2020	1,244	FP 891	FN 613	1N 966	30.0	Europe	0.67 (0.65, 0.69)	0.52 (0.50, 0.54)	Sensitivity (95%CI)	
Ma 2016 Aiken 2015	418	141	197	474	40.0	Asia	0.68 (0.64, 0.72)	0.77 (0.74, 0.80)		
Guo 2014	162	12	14	164	50.0	Anierica Asia	0.92 (0.87, 0.96)	0.93 (0.88, 0.96)		
He 2014 Li 2015	112	0 20	8 18	120	50.0 50.0	Asia Asia	0.93 (0.87, 0.97) 0.85 (0.77, 0.91)	1.00 (0.97, 1.00) 0.83 (0.75, 0.90)		
Lin 2011	155	35	21	141	50.0	Asia	0.88 (0.82, 0.92)	0.80 (0.73, 0.86)	· · · · ·	
Zhu 2013	81	35	14	509 60	50.0	Asia	0.85 (0.77, 0.92)	0.63 (0.53, 0.73)	 7	
Hypomania Checklist-3	2 (HCL	-32)							0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1
Study	TP	FP	FN	TN	Cutoff	Continent	Sensitivity (95%CI)	Specificity (95%CI)	Sensitivity (95%CI)	Specificity (95%CI)
Chou 2012	7	28	0	24	8.0	Asia	1.00 (0.59, 1.00)	0.46 (0.32, 0.61)		
Poon 2012	26	82	5	192	11.0	Asia	0.84 (0.66, 0.95)	0.70 (0.64, 0.75)		-
Carta 2006 Angst 2005	20	39 78	4	60 82	12.0	Europe	0.83 (0.63, 0.95)	0.61 (0.50, 0.70)		-
Feng 2017	221	105	130	245	14.0	Asia	0.63 (0.58, 0.68)	0.70 (0.65, 0.75)		
Kim 2018	381	192	133	322	14.0	Asia	0.74 (0.70, 0.78)	0.63 (0.58, 0.67)		-
Leao 2012 Mever 2011	66 123	66 223	7 17	61 125	14.0 14.0	America Europe	0.90 (0.81, 0.96) 0.88 (0.81, 0.93)	0.48 (0.39, 0.57) 0.36 (0.31, 0.41)		-
Meyer 2017	1,335	685	377	1,027	14.0	Europe	0.78 (0.76, 0.80)	0.60 (0.58, 0.62)		
Perugi 2012	485	126	86	445	14.0	Europe	0.85 (0.82, 0.88)	0.78 (0.74, 0.81)		
Wang 2019	201	105	130	186	14.0	Asia	0.85 (0.80, 0.89) 0.63 (0.58, 0.68)	0.79 (0.73, 0.84) 0.70 (0.65, 0.75)		
Wu 2008 Yang 2011	131	13	29	26	14.0	Asia	0.82 (0.75, 0.88)	0.67 (0.50, 0.81)		
Haghighi 2011	74	5	28	56	14.5	Asia	0.73 (0.63, 0.81)	0.92 (0.82, 0.97)	-	
Garcia-Castillo 2012	22	2,022	154	2,661	15.0	Europe Asia	0.83 (0.80, 0.85) 0.71 (0.52, 0.86)	0.57 (0.55, 0.58) 0.48 (0.36, 0.57)		
Sasdelli 2013	60	40	34	54	15.0	Europe	0.64 (0.53, 0.73)	0.57 (0.47, 0.68)		
Mosolov 2021	107	47	44	104	16.0	Europe	0.71 (0.63, 0.78)	0.69 (0.61, 0.76)	-	
Bech 2011	374	299	89	164	17.0	Europe	0.81 (0.77, 0.84) 0.90 (0.79, 0.96)	0.35 (0.31, 0.40) 0.70 (0.57, 0.81)		
Forty 2010 Soares 2010	42	18 18	17	58	18.0	Europe	0.71 (0.58, 0.82)	0.76 (0.65, 0.85)		
Lee 2016	192	96	341	437	19.0	Asia	0.36 (0.32, 0.40)	0.82 (0.78, 0.88)		· · · · · ·
Bipolar Spectrum Diag	nostic	Scale	BSDS	5)					0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1
Study	TP	FP	FN	TN	Cutoff	Continent	Sensitivity (95%CI)	Specificity (95%CI)	Sensitivity (95%CI)	Specificity (95%CI)
Zimmerman 2010	81	427	9	444	8.0	America Asia	0.90 (0.82, 0.95)	0.51 (0.48, 0.54)		· · ·
Castelo 2010	55	10	15	34	11.0	America	0.79 (0.67, 0.87)	0.77 (0.62, 0.89)	-	
Shabani 2019	153	64	54	143	11.0	Asia	0.80 (0.52, 0.96)	0.69 (0.62, 0.75)		
Aiken 2015 Chu 2010	1,314	426 3	537 26	1,425	12.0	America Asia	0.71 (0.69, 0.73) 0.74 (0.64, 0.82)	0.77 (0.75, 0.79) 0.97 (0.91, 0.99)		1 A A A A A A A A A A A A A A A A A A A
Imamura 2015	11	3	17	24	12.0	Asia	0.39 (0.22, 0.59)	0.89 (0.71, 0.98)		
Sanchez de la Cruz 2018	128	6	72	194	12.0	America	0.64 (0.57, 0.71)	0.97 (0.94, 0.99)	-	
Nassir Ghaemi 2005 Vazguez 2010	52 46	4	16 19	23 32	13.0 13.0	America Asia	0.76 (0.65, 0.86) 0.71 (0.58, 0.81)	0.85 (0.66, 0.96) 0.89 (0.74, 0.97)		
Zaratiegui 2011	228	4	113	18	13.0	America	0.67 (0.62, 0.72)	0.82 (0.60, 0.95)		
Shabani 2009	39	14	34	54	14.0	Asia	0.52 (0.45, 0.62)	0.79 (0.08, 0.88)	0 02 04 06 08 1	0 02 04 06 08 1
Mood Disorder Questic	onnaire	(MDQ)							
Study	TD	FD	EN	TN	Cutoff	Continent	Soncitivity (05%CI)	Specificity (05%(CI)	Soncitivity (05%CI)	Specificity (05%(CI)
Study Wang 2009	TP 5	FP 22	FN	TN 25	Cutoff 2.0	Continent Asia	Sensitivity (95%Cl) 0.83 (0.36, 1.00)	Specificity (95%Cl) 0.53 (0.38, 0.68)	Sensitivity (95%CI)	Specificity (95%CI)
Study Wang 2009 Hu 2012 Hughas 2016	5 93	FP 22 94 34	FN 1 216 87	TN 25 1,084 199	2.0 3.0 3.0	Continent Asia Asia Furope	Sensitivity (95%Cl) 0.83 (0.36, 1.00) 0.30 (0.25, 0.36) 0.63 (0.56, 0.69)	Specificity (95%Cl) 0.53 (0.38, 0.68) 0.92 (0.90, 0.94) 0.85 (0.80, 0.90)	Sensitivity (95%CI)	Specificity (95%Cl)
Study Wang 2009 Hu 2012 Hughes 2016 Paterniti 2018	5 93 146 632	FP 22 94 34 219	FN 1 216 87 211	TN 25 1,084 199 624	2.0 3.0 3.0 3.0	Continent Asia Asia Europe America	Sensitivity (95%Cl) 0.83 (0.36, 1.00) 0.30 (0.25, 0.36) 0.63 (0.56, 0.69) 0.75 (0.72, 0.78) 0.71 (0.50, 0.89)	Specificity (95%Cl) 0.53 (0.38, 0.68) 0.92 (0.90, 0.94) 0.85 (0.80, 0.90) 0.74 (0.71, 0.77) 0.72 (0.60, 0.84)	Sensitivity (95%CI)	Specificity (95%Cl)
Study Wang 2009 Hu 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012	5 93 146 632 45 20	FP 22 94 34 219 16 63	FN 1 216 87 211 18 11	TN 25 1,084 199 624 43 211	Cutoff 2.0 3.0 3.0 3.0 4.0 4.0	Continent Asia Europe America Asia Asia	Sensitivity (95%Cl) 0.83 (0.36, 1.00) 0.30 (0.25, 0.36) 0.63 (0.56, 0.69) 0.75 (0.72, 0.78) 0.71 (0.59, 0.82) 0.65 (0.45, 0.81)	Specificity (95%Cl) 0.53 (0.38, 0.68) 0.92 (0.90, 0.94) 0.85 (0.80, 0.90) 0.74 (0.71, 0.77) 0.73 (0.60, 0.84) 0.77 (0.72, 0.82)	Sensitivity (95%CI)	Specificity (95%CI)
Study Wang 2009 Hu 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Nagata 2013 Sasdelli 2013	TP 5 93 146 632 45 20 10 2	FP 22 94 34 219 16 63 20 4	FN 216 87 211 18 11 5 9	TN 25 1,084 199 624 43 211 43 52	Cutoff 2.0 3.0 3.0 4.0 4.0 5.0 5.0	Continent Asia Europe America Asia Asia Asia Europe	Sensitivity (95%Cl) 0.83 (0.36, 1.00) 0.30 (0.25, 0.36) 0.63 (0.56, 0.69) 0.75 (0.72, 0.78) 0.71 (0.59, 0.82) 0.65 (0.45, 0.81) 0.67 (0.38, 0.88) 0.18 (0.02, 0.52)	Specificity (95%Cl) 0.53 (0.38, 0.68) 0.92 (0.90, 0.94) 0.85 (0.80, 0.90) 0.74 (0.71, 0.77) 0.73 (0.60, 0.84) 0.77 (0.72, 0.82) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98)	Sensitivity (95%CI)	Specificity (95%CI)
Study Wang 2009 Hu 2012 Hughes 2016 Paternii 2018 Gan 2012 Poon 2012 Nagata 2013 Sasdelli 2013 Shabani 2009 Shim 2019	TP 5 93 146 632 45 20 10 2 71	FP 22 94 34 219 16 63 20 4 20	FN 1 216 87 211 18 11 5 9 42	TN 25 1,084 199 624 43 211 43 52 48	Cutoff 2.0 3.0 3.0 4.0 4.0 5.0 5.0 5.0	Continent Asia Europe America Asia Asia Asia Europe Asia	Sensitivity (95%Cl) 0.83 (0.36, 1.00) 0.30 (0.25, 0.36) 0.63 (0.25, 0.36) 0.75 (0.72, 0.78) 0.71 (0.59, 0.82) 0.65 (0.45, 0.81) 0.67 (0.38, 0.88) 0.18 (0.02, 0.52) 0.63 (0.53, 0.72) 0.69 (0.55, 0.72)	Specificity (95%Cl) 0.53 (0.38, 0.68) 0.92 (0.90, 0.94) 0.85 (0.80, 0.90) 0.74 (0.71, 0.77) 0.73 (0.60, 0.84) 0.77 (0.72, 0.82) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98) 0.71 (0.58, 0.81) 0.92 (0.87, 0.81)	Sensitivity (95%CI)	Specificity (95%Cl)
Study Wang 2009 Hu 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Nagata 2013 Sasdelli 2013 Shabani 2009 Shim 2018 Thase 2021	TP 5 93 146 632 45 20 10 2 71 187 136	FP 22 94 34 219 16 63 20 4 20 17 70	FN 1 216 87 211 18 11 5 9 42 21 64	TN 25 1,084 199 624 43 211 43 52 48 191 130	Cutoff 2.0 3.0 3.0 4.0 4.0 5.0 5.0 5.0 5.0 5.0	Continent Asia Europe America Asia Asia Asia Europe Asia Asia Asia Asia	Sensitivity (95%Cl) 0.83 (0.36, 1.00) 0.30 (0.25, 0.36) 0.75 (0.72, 0.78) 0.77 (0.59, 0.82) 0.65 (0.45, 0.81) 0.67 (0.38, 0.88) 0.18 (0.02, 0.52) 0.63 (0.53, 0.72) 0.90 (0.85, 0.94) 0.66 (0.61, 0.74)	Specificity (95%Cl) 0.53 (0.38, 0.68) 0.92 (0.90, 0.94) 0.85 (0.80, 0.90) 0.74 (0.71, 0.77) 0.73 (0.60, 0.84) 0.77 (0.72, 0.82) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98) 0.71 (0.58, 0.81) 0.92 (0.87, 0.95) 0.65 (0.58, 0.72)	Sensitivity (95%CI)	Specificity (95%CI)
Study Wang 2009 Hu 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Nagata 2013 Sasdelli 2013 Shabari 2009 Shihar 2018 Thase 2021 Vohringer 2016 Wang 2020	TP 5 93 146 632 45 20 10 2 71 187 136 231 382	FP 22 94 34 219 16 63 20 4 20 17 70 48 235	FN 1 216 87 211 18 11 5 9 42 21 64 29 70	TN 25 1,084 199 624 43 211 43 52 48 191 130 212 217	Cutoff 2.0 3.0 3.0 4.0 4.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0	Continent Asia Asia Europe America Asia Asia Asia Asia Asia America Asia America	Sensitivity (95%CI) 0.83 (0.36, 1.00) 0.30 (0.25, 0.36) 0.63 (0.56, 0.69) 0.75 (0.72, 0.78) 0.77 (0.59, 0.82) 0.65 (0.45, 0.81) 0.67 (0.38, 0.88) 0.18 (0.02, 0.52) 0.63 (0.53, 0.72) 0.90 (0.85, 0.94) 0.68 (0.61, 0.74) 0.88 (0.84, 0.92) 0.88 (0.81, 0.88)	Specificity (95%CI) 0.53 (0.38, 0.68) 0.92 (0.90, 0.94) 0.85 (0.80, 0.90) 0.74 (0.71, 0.77) 0.73 (0.66, 0.84) 0.77 (0.72, 0.82) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98) 0.71 (0.58, 0.81) 0.92 (0.87, 0.95) 0.65 (0.58, 0.72) 0.82 (0.76, 0.86) 0.48 (0.43, 0.53)	Sensitivity (95%CI)	Specificity (95%Cl)
Study Wang 2008 Hu 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Nagata 2013 Sasdelli 2013 Shabari 2008 Shabari 2008 Shabari 2008 Shabari 2008 Zaratiegui 2011 Uwang 2020 Zaratiegui 2011	TP 5 93 146 632 45 20 10 2 71 187 136 231 382 184 81	FP 22 94 34 219 16 63 20 4 20 17 70 48 235 0 10	FN 1 216 87 211 18 11 5 9 42 21 64 29 70 157 14	TN 25 1,084 199 624 43 211 43 52 48 191 130 212 217 135	Cutoff 2.0 3.0 3.0 4.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 5	Continent Asia Asia Europe America Asia Asia Asia Asia Asia Asia Asia America Asia America Asia America	Sensitivity (95%CI) 0.83 (0.36, 1.00) 0.30 (0.25, 0.36) 0.63 (0.56, 0.69) 0.75 (0.72, 0.78) 0.77 (0.72, 0.78) 0.65 (0.45, 0.81) 0.67 (0.38, 0.88) 0.18 (0.02, 0.52) 0.63 (0.45, 0.91) 0.65 (0.45, 0.91) 0.68 (0.61, 0.74) 0.88 (0.84, 0.92) 0.88 (0.81, 0.88) 0.54 (0.49, 0.59) 0.86 (0.61, 0.74) 0.88 (0.81, 0.88) 0.54 (0.49, 0.59) 0.86 (0.77, 0.92)	Specificity (95%CI) 0.53 (0.38, 0.68) 0.92 (0.90, 0.94) 0.85 (0.80, 0.90) 0.74 (0.71, 0.77) 0.73 (0.66, 0.84) 0.77 (0.72, 0.82) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98) 0.71 (0.58, 0.81) 0.92 (0.87, 0.95) 0.65 (0.58, 0.72) 0.82 (0.76, 0.86) 0.48 (0.43, 0.53) 1.00 (0.75, 1.00) 0.87 (0.77, 0.93)	Sensitivity (95%CI)	Specificity (95%CI)
Study Wang 2009 Hu 2012 Hugbes 2016 Paterniti 2018 Gan 2012 Poon 2013 Sasdelli 2013 Shabani 2009 Shim 2018 Thase 2021 Vohringer 2016 Wang 2020 Zaratilegul 2011 Lin 2011 Hardby 2005	TP 5 93 146 632 45 20 10 2 71 187 136 231 382 184 81 35	FP 22 94 34 219 16 63 20 4 20 4 20 17 70 48 235 0 10 19	FN 1 216 87 211 18 11 5 9 42 21 64 29 70 157 14 11	TN 25 1,084 199 624 43 211 43 52 48 191 130 212 217 13 65 89	Cutoff 2.0 3.0 3.0 4.0 4.0 5.0 5.0 5.0 5.0 5.0 5.0 6.0 6.0 6.0	Continent Asia Asia Europe America Asia Asia Asia Europe Asia America America Asia America Asia America Asia Asia Asia Asia Asia Asia Asia Asi	$\begin{array}{l} \textbf{Sensitivity} (95\% CD)\\ 0.83 (0.36, 1.00)\\ 0.83 (0.25, 0.36)\\ 0.63 (0.65, 0.66)\\ 0.75 (0.72, 0.76)\\ 0.71 (0.59, 0.82)\\ 0.65 (0.45, 0.81)\\ 0.67 (0.38, 0.88)\\ 0.18 (0.02, 0.52)\\ 0.63 (0.53, 0.72)\\ 0.90 (0.85, 0.54)\\ 0.68 (0.61, 0.74)\\ 0.88 (0.61, 0.74)\\ 0.88 (0.61, 0.74)\\ 0.88 (0.61, 0.74)\\ 0.88 (0.61, 0.74)\\ 0.88 (0.61, 0.67)\\ 0.76 (0.61, 0.67)\\ 0.76 (0.61, 0.67)\\ 0.76 (0.61, 0.67)\\ 0.76 (0.61, 0.67)\\ 0.76 (0.61, 0.67)\\ 0.76 (0.61, 0.67)\\ 0.76 (0.61, 0.67)\\ 0.76 (0.61, 0.67)\\ 0.76 (0.61, 0.67)\\ 0.76 (0.61, 0.67)\\ 0.76 (0.61, 0.67)\\ 0.76 (0.61, 0.67)\\ 0.85 (0.77, 0.92)\\ 0.76 (0.61, 0.67)\\ 0.76 (0.61, 0.67)\\ 0.76 (0.61, 0.67)\\ 0.85 (0.77, 0.92)\\ 0.76 (0.61, 0.67)\\ 0.85 (0.77, 0.92)\\ 0.76 (0.61, 0.67)\\ 0.85 (0.77, 0.92)\\ $	Specificity (95%cU) 0.53 (0.38) 0.68) 0.53 (0.38) 0.69) 0.85 (0.30) 0.90) 0.74 (0.71, 0.77) 0.73 (0.60) 0.84) 0.77 (0.72, 0.82) 0.68 (0.55, 0.79) 0.33 (0.83, 0.98) 0.71 (0.74, 0.83) 0.85 (0.58, 0.78) 0.85 (0.58, 0.78) 0.85 (0.58, 0.72) 0.85 (0.58, 0.72) 0.85 (0.58, 0.72) 0.82 (0.76, 0.86) 0.48 (0.43, 0.53) 1.00 (0.75, 1.00) 0.87 (0.77, 0.93) 0.82 (0.74, 0.88)	Sensitivity (95%CI)	Specificity (95%CI)
Study Wang 2009 Hug 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Nagata 2013 Sasdelli 2013 Sasdelli 2013 Shabari 2009 Shibari 2009 Shibari 2009 Zaraitegui 2011 Lin 2011 Hardoy 2005 Lee 2013 Carata 2006	TP 5 93 146 632 20 10 2 71 1876 231 382 184 81 35 25 18	FP 22 94 34 219 16 63 20 4 20 17 70 48 235 0 10 19 4 4 14	FN 1 216 87 211 18 11 59 42 21 64 29 70 157 14 11 56 6	TN 25 1,084 199 624 43 211 43 221 48 191 130 212 217 13 65 89 28 85	Cutoff 2.0 3.0 3.0 4.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 6.0 6.0 6.0 6.0	Continent Asia Asia Europe America Asia Asia Europe Asia America America Asia America Asia America Asia America Asia Asia Asia America Asia Asia Asia Asia Asia Asia Asia Asi	Sensitivity (95%Cl) 0.83 (0.36, 1.00) 0.83 (0.36, 1.00) 0.63 (0.56, 0.69) 0.75 (0.72, 0.78) 0.71 (0.59, 0.82) 0.65 (0.45, 0.81) 0.67 (0.38, 0.88) 0.18 (0.02, 0.52) 0.63 (0.53, 0.72) 0.90 (0.85, 0.94) 0.68 (0.81, 0.84) 0.68 (0.84, 0.52) 0.85 (0.77, 0.92) 0.85 (0.77, 0.92) 0.85 (0.74, 0.55) 0.85 (0.77, 0.92) 0.76 (0.61, 0.87) 0.31 (0.21, 0.42) 0.75 (0.53, 0.90)	Specificity (65%CI) 0.53 (0.38, 0.68) 0.92 (0.90, 0.94) 0.85 (0.80, 0.90) 0.74 (0.71, 0.77) 0.73 (0.60, 0.84) 0.77 (0.72, 0.82) 0.68 (0.55, 0.79) 0.33 (0.83, 0.98) 0.71 (0.55, 0.79) 0.53 (0.84, 0.84) 0.52 (0.87, 0.55) 0.64 (0.43, 0.53) 1.00 (0.75, 1.00) 0.87 (0.77, 0.92) 0.88 (0.71, 0.98) 0.88 (0.71, 0.98) 0.88 (0.77, 0.92) 0.88 (0.77,	Sensitivity (95%CI)	Specificity (95%CI)
Study Wang 2009 Hug 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Nagata 2013 Sasdelli 2013 Shabari 2009 Shibari 2009 Shibari 2009 Zaratiegul 2011 Lin 2011 Lin 2011 Lin 2011 Caria 2006 Wale genzkhon 2014 Galdherr 2012	TP 5 93 146 632 45 20 10 2 71 187 136 231 382 184 81 382 184 81 5 25 18 197	FP 22 94 34 219 63 20 4 20 4 20 17 70 48 235 0 10 19 4 4 4 54	FN 1 216 87 211 18 11 5 9 42 21 64 290 700 157 14 11 56 69 26	TN 25 1,084 199 624 43 211 43 52 48 191 130 212 217 13 65 89 28 85 182 59	Cutoff 2.0 3.0 3.0 4.0 4.0 5.0 5.0 5.0 5.0 5.0 5.0 6.0 6.0 6.0 6.0 6.0 6.0 6.0 6.0 6.0 6	Continent Asia Asia Europe America Asia Asia Asia Asia Asia America Asia America Asia America Asia Europe Asia Curope Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia Asia America Asia Asia Asia America Asia Asia America Asia Asia Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Ameri	Sensitivity (95%CI) 0.83 (0.36, 1.00) 0.83 (0.25, 0.36) 0.63 (0.56, 0.69) 0.75 (0.72, 0.78) 0.71 (0.59, 0.82) 0.65 (0.45, 0.81) 0.67 (0.38, 0.88) 0.18 (0.02, 0.52) 0.63 (0.53, 0.72) 0.90 (0.85, 0.94) 0.68 (0.61, 0.74) 0.88 (0.84, 0.92) 0.76 (0.51, 0.57) 0.76 (0.51, 0.57) 0.76 (0.51, 0.57) 0.76 (0.51, 0.57) 0.76 (0.71, 0.82) 0.76 (0.71, 0.82) 0.76 (0.71, 0.82) 0.76 (0.71, 0.82) 0.76 (0.81, 0.84) 0.76 (0.81, 0.84) 0.77 (0.81, 0.84) 0.76 (0.81, 0.84) 0.77 (0.81,	Specificity (65%-C) 0.55 (0.38, 0.68) 0.92 (0.40, 0.94) 0.85 (0.40, 0.90) 0.74 (0.60, 0.84) 0.77 (0.72, 0.82) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98) 0.77 (0.75, 0.82) 0.86 (0.75, 0.79) 0.86 (0.77, 0.83) 0.46 (0.43, 0.53) 1.00 (0.77, 0.93) 0.46 (0.43, 0.53) 1.00 (0.77, 0.93) 0.86 (0.77, 0.89) 0.86 (0.77,	Sensitivity (95%CI)	Specificity (95%CI)
Study Wang 2009 Hug 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Nagata 2013 Sasdelli 2013 Shabani 2009 Shibani 2009 Shibani 2009 Shibani 2009 Zaratiegui 2011 Lin 2011 Lain 2011 Lee 2013 Carta 2006 Waleeprakhon 2014 Golnzalez 2009	TP 5 93 146 632 45 200 2 71 187 136 231 382 184 81 35 25 18 19 87 9	FP 22 94 34 219 16 63 20 4 20 17 70 48 235 0 10 19 4 14 68 54 74 7	FN 1 216 87 211 18 11 5 9 9 42 21 64 9 70 157 14 11 56 6 59 26 0 1	TN 25 1,084 199 624 43 211 43 528 191 130 212 217 130 65 89 28 89 28 85 182 59	Cutoff 2.0 3.0 3.0 4.0 4.0 5.0 5.0 5.0 5.0 5.0 5.0 6.0 6.0 6.0 6.0 6.0 7.0 7.0	Continent Asia Asia Europe America Asia Asia Asia America America Asia America	$\begin{array}{l} \textbf{Sensitivity}(95\%\text{CD})\\ 0.83(0.36,1.00)\\ 0.83(0.25,0.36)\\ 0.63(0.25,0.36)\\ 0.75(0.72,0.76)\\ 0.77(0.59,0.82)\\ 0.65(0.45,0.81)\\ 0.71(0.59,0.82)\\ 0.65(0.35,0.72)\\ 0.90(0.85,0.94)\\ 0.67(0.38,0.88)\\ 0.18(0.02,0.52)\\ 0.63(0.53,0.72)\\ 0.90(0.85,0.94)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.76(0.71,0.92)\\ 0.77(0.62,1,0.42)\\ 0.77(0.68,0.84)\\ 1.00(0.66,1.06)\\ 0.76(0.67,1.0.82)\\ 0.77(0.68,0.64)\\ 1.00(0.66,1.06)\\ 0.66(1.00,0.54)\\ 0.66(0.61,0.67)\\ 0.6$	$\begin{array}{l} \textbf{Specificity} (\textbf{65\%}(0))\\ 0.53 (0.38, 0.68)\\ 0.92 (0.40, 0.94)\\ 0.85 (0.40, 0.90)\\ 0.74 (0.71, 0.77)\\ 0.73 (0.60, 0.84)\\ 0.77 (0.72, 0.82)\\ 0.68 (0.55, 0.79)\\ 0.93 (0.83, 0.98)\\ 0.77 (0.55, 0.81)\\ 0.92 (0.87, 0.95)\\ 0.48 (0.43, 0.53)\\ 1.09 (0.75, 1.00)\\ 0.48 (0.43, 0.53)\\ 1.00 (0.75, 1.00)\\ 0.87 (0.77, 0.93)\\ 0.88 (0.77, 0.93)\\ 0.88 (0.77, 0.93)\\ 0.88 (0.77, 0.93)\\ 0.88 (0.77, 0.93)\\ 0.88 (0.77, 0.93)\\ 0.88 (0.77, 0.93)\\ 0.88 (0.77, 0.93)\\ 0.88 (0.77, 0.93)\\ 0.88 (0.77, 0.93)\\ 0.71 (0.55, 0.63)\\ 0.88 (0.77, 0.93)\\ 0.88 (0.73, 0.93)\\ 0.88 (0.93, 0.93)\\ 0.88 (0.93, 0.93$	Sensitivity (95%CI)	Specificity (95%CI)
Study Wang 2009 Hug 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Nagata 2013 Sasdelli 2013 Shabari 2009 Shibari 2009 Shibari 2009 Shibari 2009 Zaratiegui 2011 Lin 2011 Hardoy 2005 Zaratiegui 2011 Lin 2011 Hardoy 2005 Carta 2006 Goldberg 2012 Gonzalez 2009 Haghighi 2011 Hirschleid 2000	TP 5 933 146 632 45 200 2 71 1876 231 382 184 81 355 255 18 191 87 9 81 80	FP 22 94 219 16 63 20 4 20 17 70 48 235 0 10 19 4 4 14 68 54 74 74 79	FN 1 2166 87 2111 18 111 5 5 9 9 9 9 22 21 644 29 9 70 70 157 144 111 5 6 6 5 59 26 6 0 0 11 29	TN 25 1,084 1999 624 43 211 43 22 48 191 130 212 217 13 65 899 28 855 182 599 116 44 80	Cutoff 2.0 3.0 3.0 4.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 6.0 6.0 6.0 6.0 6.0 6.0 7.0 7.0 7.0 7.0	Continent Asia Asia Europe Asia Asia Asia Europe Asia America Asia America Asia America Asia America Asia America Europe Asia Europe Asia America America America Asia America	$\begin{array}{l} \textbf{Sensitivity}(95\%\text{CD})\\ 0.83(0.36,1.00)\\ 0.33(0.25,0.36)\\ 0.53(0.25,0.36)\\ 0.53(0.25,0.36)\\ 0.57(0.57,0.72,0.76)\\ 0.71(0.59,0.82)\\ 0.56(0.45,0.81)\\ 0.71(0.59,0.82)\\ 0.53(0.53,0.72)\\ 0.90(0.85,0.94)\\ 0.63(0.53,0.72)\\ 0.90(0.85,0.94)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.78(0.66,1.00)\\ 0.79(0.70,0.87)\\ 0.73(0.66,1.00)\\ 0.79(0.70,0.87)\\ 0.73(0.64,0.81) \end{array}$	Specificity (6%-C) 0.53 (0.38, 0.68) 0.92 (0.80, 0.94) 0.85 (0.08, 0.96) 0.74 (0.71, 0.77) 0.73 (0.60, 0.84) 0.77 (0.72, 0.82) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98) 0.66 (0.55, 0.79) 0.93 (0.83, 0.98) 0.66 (0.58, 0.72) 0.82 (0.77, 0.93) 0.62 (0.76, 0.85) 1.00 (0.77, 1.93) 0.82 (0.77, 0.93) 0.82 (0.77, 0.93) 0.82 (0.77, 0.93) 0.82 (0.77, 0.93) 0.86 (0.77, 0.92) 0.86 (0.77, 0.92) 0.73 (0.67, 0.78) 0.73 (0.67,	Sensitivity (95%CI)	Specificity (95%CI)
Study Wang 2009 Hug 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Nagata 2013 Sasdelli 2013 Shabari 2009 Shibari 2009 Shibari 2009 Zaratiegu 2011 Lin 2011 Hardoy 2005 Lee 2013 Gordberg 2012 Gonziez 2009 Harging 202 Carta 2006 Waleperakhon 2014 Goldberg 2012 Gonziez 2009 Harging 2020 State 2013 Gonziez 2009 Harging 2012 Gonziez 2014 Boltoberg 2012 Gonziez 2009 Harging 2000 Imamura 2015 Sometsa 2003	TP 5 933 146 632 450 20 10 2 711 187 136 231 187 1382 184 81 355 255 181 87 91 87 377	FP 22 94 4 219 16 63 30 0 0 0 17 70 48 235 0 0 0 10 19 4 4 68 54 74 74 74 9 9 14 9	FN 1 2166 87 211 18 11 5 5 9 9 42 21 164 29 9 42 21 157 144 111 556 6 6 0 21 29 18 3	TN 25 1,084 199 624 43 211 130 212 217 13 65 89 212 217 13 85 182 85 182 116 44 80 41 88	Cutoff 2.0 3.0 4.0 5.0 5.0 5.0 5.0 5.0 5.0 6.0 6.0 6.0 6.0 6.0 6.0 7.0 7.0 7.0 7.0 7.0 7.0	Continent Asia Asia Europe Asia Asia Asia Europe Asia America Asia America Asia America Asia Curope Asia America Asia Asia America Asia Asia Asia America Asia Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia Americ	Sensitivity (95%Cl) 0.83 (0.36, 1.00) 0.83 (0.36, 1.00) 0.63 (0.56, 0.68) 0.75 (0.72, 0.78) 0.67 (0.59, 0.82) 0.65 (0.45, 0.81) 0.67 (0.38, 0.88) 0.18 (0.02, 0.52) 0.63 (0.58, 0.72) 0.63 (0.58, 0.72) 0.63 (0.58, 0.72) 0.68 (0.61, 0.74) 0.68 (0.61, 0.74) 0.88 (0.61, 0.87) 0.54 (0.49, 0.59) 0.54 (0.49, 0.59) 0.56 (0.48, 0.53) 0.77 (0.68, 0.84) 1.00 (0.66, 1.007) 0.76 (0.64, 0.61) 0.76 (0.53, 0.79) 0.76 (0.64, 0.81) 0.76 (0.53, 0.79) 0.85 (0.62, 0.97) 0.85 (0.62	Specificity (65%-C) 0.55 (0.38, 0.68) 0.92 (0.90, 0.94) 0.55 (0.38, 0.68) 0.92 (0.90, 0.94) 0.55 (0.08, 0.69) 0.74 (0.60, 0.84) 0.77 (0.72, 0.82) 0.68 (0.55, 0.79) 0.53 (0.83, 0.78) 0.56 (0.55, 0.79) 0.56 (0.55, 0.79) 0.82 (0.76, 0.86) 0.48 (0.43, 0.53) 0.82 (0.77, 0.92) 0.82 (0.72,	Sensitivity (95%CI)	Specificity (95%CI)
Study Wang 2009 Hug 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Nagata 2013 Sasdelli 2013 Shabari 2009 Shibari 2009 Shibari 2009 Zarallegia 2011 Lin 2011 Hardoy 2005 Lee 2013 Carta 2006 Waleparaken 2015 Isometaa 2015 Isometaa 2015 Isometaa 2015 Isometaa 2015 Sometaa 2015	TP 5 93 146 632 45 2 2 10 2 2 7 7 136 85 26 1382 184 81 35 25 81 87 9 9 81 80 37 7 7 7 7	FP 22 94 4 219 16 63 20 4 207 170 48 235 0 100 199 4 14 68 54 77 9 9 12 2	FN 1 2166 87 1211 18 11 5 9 42 211 18 111 5 9 42 211 64 42 9 700 1577 14 11 56 6 6 59 60 0 211 29 9 18 3 3 42 2	TN 255 1,084 4 1999 624 4 43 52 2111 130 212 217 133 655 899 8 855 182 599 116 44 800 411 8 8400 411 8 8400 411 8	Cutoff 2.0 3.0 3.0 4.0 4.0 5.0 5.0 5.0 5.0 5.0 6.0 6.0 6.0 6.0 6.0 6.0 7.0 7.0 7.0 7.0 7.0 7.0 7.0 7.0 7.0 7	Continent Asia Asia Europe Europe Europe Europe Europe Europe Europe Europe Europe Asia America America Asia Casta Europe Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia Asia America Asia America Asia Asia America America Asia America Asia America America Asia America Asia America America America America Asia America Amer	$\begin{array}{l} \textbf{Sensitivity}(95\%CI)\\ 0.83(0.38,100)\\ 0.83(0.38,100)\\ 0.63(0.65,0.68)\\ 0.75(0.72,0.78)\\ 0.71(0.59,0.82)\\ 0.65(0.45,0.81)\\ 0.67(0.38,0.88)\\ 0.18(0.02,0.52)\\ 0.63(0.55,0.72)\\ 0.90(0.85,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.77,0.92)\\ 0.58(0.71,0.82,0.71)\\ 0.68(0.61,0.87)\\ 0.31(0.21,0.42)\\ 0.76(0.68,0.84)\\ 1.00(0.68,1.00)\\ 0.77(0.68,0.84)\\ 1.00(0.68,1.00)\\ 0.79(0.63,0.73)\\ 0.73(0.64,0.81)\\ 0.73(0.65,0.73)\\ 0.73(0.65,0.73)\\ 0.73(0.65,0.73)\\ 0.68(0.62,0.57)\\ 0.73(0.64,0.81)\\ 0.68(0.62,0.57)\\ 0.73(0.64,0.81)\\ 0.68(0.62,0.57)\\ 0.73(0.64,0.81)\\ 0.68(0.62,0.57)\\ 0.73(0.64,0.81)\\ 0.68(0.62,0.57)\\ 0.28(0.62,0.57)\\ 0.28(0.62,0.57)\\ 0.28(0.62,0.57)\\ 0.28(0.61,0.84)\\ 0.58(0.62,0.57)\\ 0.28(0.61,0.84)\\ 0.58(0.62,0.57)\\ 0.28(0.61,0.84)\\ 0.58(0.62,0.57)\\ 0.28(0.61,0.84)\\ 0.58(0.62,0.57)\\ 0.28(0.61,0.84)\\ 0.58(0.62,0.57)\\ 0.28(0.61,0.84)\\ 0.58(0.62,0.57)\\ 0.28(0.61,0.84)\\ 0.58(0.62,0.57)\\ 0.28(0.61,0.84)\\ 0.58(0.61,0.84)\\ 0.58(0.61,0.84)\\ 0.58(0.62,0.57)\\ 0.58(0.61,0.84)\\ 0.$	Specificity (65%-C) 0.55 (0.38, 0.68) 0.92 (0.90, 0.94) 0.85 (0.60, 0.90) 0.74 (0.60, 0.84) 0.77 (0.76, 0.82) 0.78 (0.65, 0.79) 0.93 (0.83, 0.98) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98) 0.68 (0.55, 0.79) 0.68 (0.77, 0.92) 0.68 (0.77, 0.92) 0.68 (0.77, 0.92) 0.82 (0.74, 0.89) 0.88 (0.71, 0.96) 0.86 (0.77, 0.92) 0.52 (0.43, 0.62) 0.52 (0.43, 0.62) 0.57 (0.65, 0.58) 0.57 (0.61, 0.85) 0.47 (0.23, 0.72) 0.45 (0.54, 0.68) 0.47 (0.23, 0.72) 0.45 (0.54, 0.68) 0.47 (0.23, 0.72) 0.47 (0.43, 0.42) 0.47 (0.43,	Sensitivity (95%CI)	Specificity (95%CI)
Study Wang 2009 Hug 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Poon 2012 Sasdelli 2013 Ssakelli 2013 Shabari 2009 Shibari 2009 Shibari 2009 Zaratiegul 2011 Lin 2011 Carta 2006 Wale gezota Goraziez 2009 Haghight 2011 Hirschfeld 2000 Imamura 2015 Isometa 2013 Kim 2008 Konuk 2007 Lagologi 2011	TP 5 93 146 632 20 100 2 71 187 136 231 136 231 138 25 188 184 81 191 191 191 177 177 23 100 377 177 177 255 187 187 187 187 186 187 186 187 186 187 186 187 186 187 187 186 187 186 187 186 187 187 186 187 186 187 187 187 187 187 187 187 187	FP 22 94 4219 1663 200 4420 177 700 48235 00 119 44 1688 554 77 99 124 668 654 77 79 912 663 637 77 99 126 637 77 70 149 144 77 70 144 77 70 144 77 70 144 77 70 144 77 70 144 77 70 144 77 70 144 77 70 144 77 70 144 77 70 144 77 70 144 70 140 70 70 70 70 70 70 70 70 70 70 70 70 70	FN 1 2166 87 211 188 111 5 9 9 42 2 121 14 29 9 42 12 14 115 5 6 6 0 211 29 9 26 6 0 0 211 29 9 28 3 3 42 2 3 23	TN 255 1,084 43 290 624 43 2111 139 624 43 2111 130 212 217 217 13 655 899 2165 899 116 44 800 411 8 8400 210 210 210 210 210 210 210 210 210 210	Cutoff 2.0 3.0 3.0 3.0 4.0 4.0 5.0 5.0 5.0 5.0 5.0 5.0 6.0 6.0 6.0 6.0 6.0 6.0 7.0 7.0 7.0 7.0 7.0 7.0 7.0 7.0 7.0 7	Continent Asia Asia Asia Asia Asia Asia Asia Asia	$\begin{array}{l} \textbf{Sensitivity}(95\%CI)\\ 0.83(0.38,1.00)\\ 0.83(0.25,0.36)\\ 0.63(0.25,0.36)\\ 0.63(0.25,0.36)\\ 0.75(0.72,0.76)\\ 0.71(0.59,0.82)\\ 0.65(0.45,0.81)\\ 0.67(0.38,0.88)\\ 0.18(0.02,0.52)\\ 0.63(0.53,0.72)\\ 0.90(0.85,0.94)\\ 0.68(0.61,0.74)\\ 0.88(0.84,0.92)\\ 0.68(0.61,0.74)\\ 0.88(0.84,0.92)\\ 0.63(0.53,0.72)\\ 0.90(0.85,0.94)\\ 0.68(0.61,0.74)\\ 0.88(0.84,0.92)\\ 0.63(0.53,0.72)\\ 0.63(0.53,0.72)\\ 0.63(0.53,0.72)\\ 0.63(0.53,0.72)\\ 0.63(0.53,0.72)\\ 0.63(0.53,0.72)\\ 0.63(0.53,0.92)\\ 0.76(0.68,0.84)\\ 1.00(0.66,1.00)\\ 0.79(0.70,0.87)\\ 0.73(0.64,0.84)\\ 1.00(0.66,1.00)\\ 0.79(0.70,0.87)\\ 0.73(0.64,0.84)\\ 1.00(0.65,1.00)\\ 0.79(0.63,0.79)\\ 0.85(0.62,0.97)\\ 0.85(0.62,0.97)\\ 0.28(0.18,0.42)\\ 0.44(0.46,0.79)\\ 0.68(0.57,0.79) \end{array}$	$\begin{split} & \textbf{Specificity} (\textbf{65}): \textbf{C}) \\ & 0.55 (0.38, 0.68) \\ & 0.52 (0.38, 0.68) \\ & 0.52 (0.30, 0.94) \\ & 0.85 (0.80, 0.90) \\ & 0.74 (0.60, 0.84) \\ & 0.77 (0.72, 0.82) \\ & 0.68 (0.55, 0.79) \\ & 0.93 (0.83, 0.98) \\ & 0.77 (0.75, 0.82) \\ & 0.68 (0.55, 0.79) \\ & 0.93 (0.83, 0.98) \\ & 0.68 (0.55, 0.79) \\ & 0.92 (0.87, 0.95) \\ & 0.68 (0.71, 0.68) \\ & 0.68 (0.71, 0.68) \\ & 0.68 (0.77, 0.98) \\ & 0.68 (0.77, 0.98) \\ & 0.68 (0.77, 0.98) \\ & 0.68 (0.71, 0.96) \\ & 0.68 (0.77, 0.92) \\ & 0.68 (0.77, 0.92) \\ & 0.68 (0.77, 0.92) \\ & 0.68 (0.77, 0.92) \\ & 0.68 (0.77, 0.92) \\ & 0.68 (0.77, 0.92) \\ & 0.68 (0.77, 0.92) \\ & 0.68 (0.77, 0.92) \\ & 0.68 (0.77, 0.92) \\ & 0.67 (0.65, 0.83) \\ & 0.77 (0.65, 0.83) \\ & 0.77 (0.63, 0.87) \\ & 0.77 (0.71, 0.82) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.77 (0.71, 0.82) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.77 (0.71, 0.82) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.77 (0.71, 0.82) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.77 (0.71, 0.82) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.77 (0.71, 0.82) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.77 (0.71, 0.82) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.77 (0.71, 0.82) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.76 (0.54, 0.71) \\ & 0.77 (0.54, 0.72) \\ & 0.76 (0.54, 0.71) \\ & 0.77 (0.54, 0.72) \\ & 0.77 (0.54, 0.72) \\ & 0.77 (0.54, 0.72) \\ & 0.77 (0.54, 0.72) \\ & 0.77 (0.54, 0.72) \\ & 0.77 (0.75, 0.72) \\ & 0.77 (0.75, 0.72) \\ & 0.77 (0.75, 0.72) \\ & 0.77 (0.75, 0.72) \\ & 0.77 (0.75, 0.72) \\ & 0.77 (0.75, 0.72) \\ & 0.77 (0.75, 0.72) \\ & 0.77 (0.75, 0.72) \\ & 0.77 (0.75, 0.72) \\ & 0.77 (0.75, 0.72) \\ & 0.77 (0.75, 0.72) \\ & 0.77 (0.75, 0.72) \\ & 0.77 (0.75, 0.72) \\ & 0.77 (0.75, 0.72) \\ & 0.77 (0.75, 0.72) \\ & 0.77 (0.75, 0.72) \\ & 0.77$	Sensitivity (95%CI)	Specificity (95%CI)
Study Wang 2009 Hug 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Nagata 2013 Sasdelli 2013 Shabani 2009 Shibani 2009 Shibani 2009 Shibani 2009 Zaratlegui 2011 Lin 2011 Lee 2013 Carta 2006 Waleeprakhon 2014 Gonzalez 2011 Hardoy 2005 Lee 2013 Carta 2006 Imaruta 2015 Isometa 2003 Kim 2008 Konuk 2007 Lee 2014 Maduk 2015 Isometa 2003 Kim 2008 Konuk 2007 Leao 2012 Leao 2014 Leao 2014	TP 5 53 33 146 632 20 100 2 71 187 136 231 136 231 1382 25 188 184 81 355 188 184 81 191 87 9 81 80 37 71 177 166 187 186 187 186 187 186 186 187 186 186 187 186 186 186 187 186 186 186 186 186 186 187 186 186 186 186 186 186 186 186	FP 22 94 4219 166 320 420 177 708 420 177 708 4235 00 119 44 168 54 77 9 12 63 63 477 91 12 63 63 677 91 12 63 63 677 91 12 63 63 677 91 12 63 63 677 91 12 63 657 657 657 657 657 657 657 657 657 657	FN 1 216 87 211 18 11 15 9 9 42 1 64 29 9 42 21 64 29 9 70 7 14 11 55 6 6 0 21 1 29 26 20 0 21 1 29 26 20 10 21 1 29 26 20 10 21 1 29 26 20 10 21 1 29 26 20 10 21 1 29 26 20 10 21 1 29 26 20 10 20 1	TN 255 1,084 199 624 43 52 211 43 52 217 130 624 48 191 130 212 217 217 133 689 825 885 182 59 288 55 182 116 44 80 211 928 85 116 85 116 87 119 928 85 110 87 119 94 119 119	Cutoff 2.0 3.0 3.0 3.0 4.0 4.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 6.0 6.0 6.0 6.0 6.0 7.0 7.0 7.0 7.0 7.0 7.0 7.0 7.0 7.0 7	Continent Asia Asia Europe America Asia Asia Asia America Asia	Sensitivity (95%CI) 0.83 (0.36, 1.00) 0.83 (0.25, 0.36) 0.63 (0.56, 0.69) 0.75 (0.72, 0.76) 0.71 (0.59, 0.82) 0.65 (0.45, 0.81) 0.71 (0.59, 0.82) 0.63 (0.53, 0.72) 0.90 (0.85, 0.94) 0.63 (0.53, 0.72) 0.90 (0.85, 0.94) 0.68 (0.61, 0.74) 0.88 (0.84, 0.92) 0.76 (0.61, 0.87) 0.83 (0.81, 0.88) 0.54 (0.49, 0.59) 0.76 (0.51, 0.82) 0.77 (0.56, 1.042) 0.76 (0.51, 0.82) 0.77 (0.56, 1.042) 0.76 (0.51, 0.82) 0.77 (0.56, 1.042) 0.76 (0.51, 0.42) 0.76 (0.51, 0.42) 0.76 (0.51, 0.42) 0.76 (0.51, 0.42) 0.76 (0.71, 0.82) 0.77 (0.54, 0.44) 0.65 (0.63, 0.79) 0.85 (0.82, 0.97) 0.85 (0.82, 0.97) 0.85 (0.82, 0.97) 0.85 (0.82, 0.97) 0.85 (0.82, 0.97) 0.85 (0.82, 0.97) 0.85 (0.76, 70, 70) 0.86 (0.76, 70, 70) 0.76 (0.70, 0.82) 0.86 (0.76, 70, 90) 20 (0.81, 90, 90) 0.86 (0.76, 70) 0.76 (0.70, 0.82) 0.86 (0.76, 70, 90) 0.86 (0.76, 70) 0.85 (0.76, 70) 0.86 (0.7	Specificity (65%-C) 0.55 (0.38, 0.68) 0.92 (0.40, 0.94) 0.85 (0.40, 0.90) 0.74 (0.71, 0.77) 0.73 (0.60, 0.84) 0.77 (0.72, 0.82) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98) 0.48 (0.43, 0.53) 1.00 (0.75, 1.00) 0.48 (0.43, 0.53) 1.00 (0.75, 1.00) 0.87 (0.77, 0.93) 0.87 (0.77, 0.93) 0.88 (0.77, 0.92) 0.86 (0.77, 0.92) 0.86 (0.77, 0.92) 0.73 (0.65, 0.72) 0.73 (0.65, 0.72) 0.73 (0.65, 0.75) 0.75 (0.61, 0.85) 0.77 (0.73, 0.82) 0.77 (0.73, 0.82) 0.77 (0.73, 0.82) 0.77 (0.74, 0.82) 0.77 (0.74, 0.83, 0.87) 0.77 (0.74, 0.84) 0.77 (0.74, 0.84) 0.78 (0.77, 0.74) 0.85 (0.51, 0.55) 0.77 (0.74, 0.84) 0.78 (0.77, 0.74) 0.85 (0.51, 0.55) 0.77 (0.74, 0.84) 0.78 (0.77, 0.84) 0	Sensitivity (95%CI)	Specificity (05%CI)
Study Wang 2009 Hug 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Poon 2012 Poon 2013 Sasdelli 2013 Shabari 2009 Shibari 2009 Shibari 2009 Shibari 2009 Zaratlegui 2011 Lin 2011 Hardoy 2005 Zaratlegui 2011 Lin 2011 Hardoy 2005 Carta 2006 Waleeprakhon 2014 Goldberg 2012 Gonzalez 2009 Hardighiphi 2011 Hirschheid 2000 Imamura 2015 Isometas 2003 Kim 2004 Koruk 2007 Lees 2014 Lee 2012 Lee 2014 Mainty 2014	TP 5 53 33 146 632 20 2 71 136 232 71 137 1382 187 1382 184 181 191 187 9 81 187 197 187 187 187 187 187 187 187 18	FP 22 4 34 219 163 200 177 48 235 20 0 10 10 10 10 10 10 10 10 10 10 10 10	FN 1 2116 87 2111 18 87 211 18 5 9 9 22 11 29 9 700 1157 242 29 700 211 29 9 700 211 29 114 111 56 6 6 0 0 211 29 18 3 3 42 2 13 23 25 29 12 88 6 12 12 19 28 6 12 12 12 12 12 12 12 12 12 12 12 12 12	TN 255 1,084 199 624 43 522 211 1300 212 211 212 217 133 655 899 288 55 182 599 288 55 182 599 288 55 182 212 116 44 44 840 210 82 210 82 116 108 211 119 119 119 119 119 119 119 119 119	Cutoff 2.0 3.0 3.0 4.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 5	Continent Asia Asia Europe America Asia Asia Asia America America Asia America America Asia America Asia America America Asia America Asia America America Asia America America Asia America Asia America America America Asia America A	$\begin{array}{l} \textbf{Sensitivity}(95\%\text{CD})\\ 0.83(0.36,1.00)\\ 0.83(0.36,1.00)\\ 0.63(0.65,0.66)\\ 0.75(0.72,0.76)\\ 0.71(0.59,0.82)\\ 0.65(0.45,0.81)\\ 0.71(0.59,0.82)\\ 0.65(0.45,0.81)\\ 0.67(0.38,0.88)\\ 0.18(0.02,0.52)\\ 0.63(0.53,0.72)\\ 0.90(0.85,0.94)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.78(0.64,0.81)\\ 0.76(0.64,0.81)\\ 0.76(0.64,0.81)\\ 0.76(0.64,0.81)\\ 0.76(0.64,0.81)\\ 0.68(0.57,0.72)\\ 0.28(0.16,0.72)\\ 0.28(0.$	Specificity (65%-C) 0.55 (0.38, 0.68) 0.92 (0.40, 0.94) 0.85 (0.40, 0.90) 0.74 (0.71, 0.77) 0.73 (0.60, 0.84) 0.77 (0.72, 0.82) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98) 0.77 (0.75, 0.82) 0.65 (0.58, 0.71) 0.65 (0.58, 0.71) 0.65 (0.58, 0.72) 0.82 (0.76, 0.85) 0.67 (0.75, 0.30) 0.82 (0.77, 0.93) 0.82 (0.77, 0.93) 0.82 (0.74, 0.89) 0.88 (0.77, 0.92) 0.88 (0.77, 0.93) 0.82 (0.74, 0.89) 0.73 (0.67, 0.76) 0.56 (0.54, 0.76) 0.75 (0.64, 0.85) 0.77 (0.52, 0.75) 0.76 (0.54, 0.68) 0.77 (0.52, 0.75) 0.77 (0.64, 0.68) 0.77 (0.63, 0.67) 0.77 (0.63, 0.67) 0.77 (0.71, 0.82) 0.77 (0.71, 0.82) 0.77 (0.71, 0.82) 0.57 (0.54, 0.68) 0.77 (0.56, 0.68) 0.77 (0.56, 0.68) 0.76 (0.54, 0.71) 0.56 (0.54, 0.71) 0.57 (0.54, 0.57) 0.57 (0.54,	Sensitivity (95%CI)	Specificity (95%CI)
Study Wang 2009 Hug 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Nagata 2013 Sasdelli 2013 Sasdelli 2013 Shabari 2009 Shibari 2009 Shabari 2009 Zaratiegu 2011 Lin 2011 Hardoy 2005 Lee 2013 Gonzalez 2009 Haghigh 2011 Hardoy 2025 Lee 2013 Goldberg 2012 Gonzalez 2009 Haghigh 2011 Hirschield 2001 Hirschield 2003 Kim 2008 Konuk 2007 Lee 2014 McIntyre 2021 Melar 20011 Miller 2004 Maler 2013	TP 5 93 146 6322 20 2 2 71 136 2382 187 136 2382 184 183 184 184 191 191 385 25 25 25 25 25 25 25 25 25 25 20 2 2 2 71 177 136 20 2 2 2 71 177 136 20 2 2 2 7 1 187 7 136 20 2 2 2 7 1187 7 136 20 2 2 2 7 1187 7 136 20 2 2 2 7 1187 7 136 20 2 2 2 7 1187 7 136 20 2 2 2 7 1187 7 136 20 2 2 2 7 1187 7 136 20 2 2 2 7 1187 7 136 20 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	FP 222 944219 2199242 2199242 20024420 420024 20024420 420024 482352 0 0 0 0 0 10 10 10 10 10 10 10 10 10 10	$\begin{array}{c} {\rm FN} \\ 1 \\ 216 \\ 87 \\ 211 \\ 18 \\ 9 \\ 9 \\ 22 \\ 21 \\ 64 \\ 29 \\ 70 \\ 157 \\ 14 \\ 111 \\ 56 \\ 6 \\ 9 \\ 226 \\ 0 \\ 211 \\ 29 \\ 70 \\ 14 \\ 111 \\ 56 \\ 6 \\ 0 \\ 211 \\ 29 \\ 28 \\ 13 \\ 23 \\ 52 \\ 29 \\ 19 \\ 28 \\ 61 \\ 1111 \\ 111 \\ 1111 \\ 111 \\ 111 \\ 111 \\ 111 \\ 111 \\ 111 \\ 111 \\ 11$	TN 255 1,084 199 624 3211 433 522 211 433 522 217 133 52 212 217 133 55 899 288 55 182 212 217 133 65 899 288 55 182 212 217 116 44 44 40 210 82 210 82 210 84 108 82 212 108 108 108 108 108 108 108 108 108 108	Cutoff 2.0 3.0 3.0 4.0 4.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 5	Continent Asia Asia Europe America Asia Asia Asia America Asia America Asia America Europe Asia America Europe Asia Asia America Europe Asia Europe Asia Europe Asia Europe Asia Europe Asia Europe Asia Europe Asia Europe Asia Europe Asia Europe Asia Europe Asia Europe Asia Europe Asia Europe Asia Europe Asia Europe Asia Asia America Europe Asia Asia America Asia Asia America Asia Asia Asia Asia Asia Asia Asia Asi	$\begin{array}{l} \textbf{Sensitivity}(95\%CI)\\ 0.83(0.36,1.00)\\ 0.83(0.36,1.00)\\ 0.63(0.25,0.36)\\ 0.75(0.72,0.76)\\ 0.71(0.59,0.82)\\ 0.65(0.45,0.81)\\ 0.67(0.38,0.88)\\ 0.18(0.02,0.52)\\ 0.63(0.53,0.72)\\ 0.90(0.85,0.72)\\ 0.90(0.85,0.72)\\ 0.90(0.85,0.72)\\ 0.85(0.81,0.84)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.85(0.84,0.92)\\ 0.75(0.65,0.94)\\ 0.75(0.65,0.94)\\ 0.79(0.64,0.92)\\ 0.75(0.65,0.94)\\ 0.79(0.64,0.92)\\ 0.85(0.82,0.97)\\ 0.29(0.18,0.42)\\ 0.85(0.84,0.79,0.92)\\ 0.86(0.77,0.92)\\ 0.86($	$\begin{split} & \textbf{Specificity} (\textbf{GS}). \\ & 0.55 (0.38, 0.68) \\ & 0.52 (0.38, 0.68) \\ & 0.52 (0.30, 0.94) \\ & 0.55 (0.60, 0.54) \\ & 0.57 (0.71, 0.72, 0.52) \\ & 0.57 (0.72, 0.52) \\ & 0.58 (0.55, 0.79) \\ & 0.58 (0.55, 0.79) \\ & 0.58 (0.55, 0.79) \\ & 0.58 (0.55, 0.79) \\ & 0.58 (0.55, 0.79) \\ & 0.58 (0.57, 0.72, 0.52) \\ & 0.58 (0.57, 0.72, 0.52) \\ & 0.58 (0.77, 0.52) \\ & 0.58 (0.77, 0.52) \\ & 0.58 (0.77, 0.52) \\ & 0.58 (0.77, 0.52) \\ & 0.58 (0.77, 0.52) \\ & 0.58 (0.77, 0.52) \\ & 0.58 (0.77, 0.52) \\ & 0.58 (0.77, 0.52) \\ & 0.58 (0.77, 0.52) \\ & 0.57 (0.55, 0.58) \\ & 0.57 (0.55, 0.58) \\ & 0.57 (0.55, 0.58) \\ & 0.57 (0.53, 0.52) \\ & 0.57 (0.53, 0.$	Sensitivity (95%CI)	Specificity (65%CI)
Study Wang 2009 Hug 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Poon 2012 Poon 2013 Sasdelli 2013 Shabari 2009 Shibari 2009 Shibari 2009 Shabari 2009 Carta 2011 Lin 2011 Lin 2012 Carta 2006 Waleperakhon 2014 Goldberg 2012 Gonzalez 2009 Haghighi 2011 Hirschleid 2000 Imamura 2015 Isometas 2003 Kim 2006 Koruk 2007 Leao 2012 Leao 2014 Mahyre 2021 Mayer 2011 Mayer 2011 Mailer 2004 Paimer 2021 Mahyre 2013 Paimer 2013 Paimer 2015	TP 5 5 93 146 632 20 10 2 2 31 187 632 382 231 382 231 382 25 3184 81 187 187 187 187 187 187 187 187 187	FP 222 94 34 219 94 34 219 94 34 219 16 63 22 27 235 0 119 9 4 200 17 70 8 4 235 0 10 19 9 14 468 54 47 44 14 9 9 122 63 37 74 91 11 125 22 77 244 75 37 75 75 75 75 75 75 75 75 75 75 75 75 75	FN 1 6 216 211 8 7 211 8 7 211 8 11 1 5 9 9 42 211 8 11 1 5 9 42 211 64 29 9 7 164 29 9 7 164 29 9 26 6 0 21 29 9 8 13 3 23 25 29 8 13 3 23 25 29 8 13 23 3 5 22 9 8 13 23 3 5 22 9 8 11 1 23 3 12 3 3 5 2 2 1 1 2 2 1 2 1 2 1 2 2 1 2 1 2 2 1 2 1 2 2 1 1 1 2 1 3 1 1 2 1 3 1 1 2 1 3 1 1 2 1 3 1 1 2 1 3 1 1 2 1 3 1 1 2 1 3 1 1 2 1 3 1 1 2 1 3 1 1 2 1 3 1 1 2 1 3 1 1 2 1 3 1 1 2 1 3 1 1 2 1 3 1 1 2 1 3 1 1 2 1 3 1 1 2 1 3 1 1 2 1 3 1 1 1 2 1 3 1 1 1 2 1 3 1 1 1 2 1 3 1 1 1 2 1 3 1 1 1 2 1 3 1 1 1 2 1 3 1 1 1 2 1 3 1 1 1 2 1 3 1 1 1 2 1 3 1 1 1 2 1 3 1 1 1 1	TN 255 1,084 199 624 43 211 43 52 248 8191 130 212 217 217 217 217 217 3 65 89 88 59 288 59 288 59 288 59 116 44 80 41 80 210 212 217 13 212 217 217 217 217 217 217 217 217 217	Cutoff 2.00 3.0 3.0 3.0 3.0 4.0 4.0 5.0 5.0 5.0 5.0 5.0 5.0 6.0 6.0 6.0 6.0 6.0 6.0 6.0 6.0 7.0 7.0 7.0 7.0 7.0 7.0 7.0 7.0 7.0 7	Continent Asia Asia Europe America Asia Asia Asia America Asia America Asia America Asia America Asia America Europe Asia Europe Asia Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Asia America Europe Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Europe Asia America America A	Sensitivity (95%CU) 0.83 (0.36, 1.00) 0.83 (0.25, 0.36) 0.63 (0.56, 0.69) 0.75 (0.72, 0.78) 0.73 (0.59, 0.82) 0.65 (0.45, 0.81) 0.67 (0.38, 0.88) 0.16 (0.02, 0.52) 0.63 (0.55, 0.72) 0.90 (0.85, 0.74) 0.63 (0.53, 0.72) 0.90 (0.85, 0.74) 0.88 (0.81, 0.24) 0.88 (0.81, 0.24) 0.88 (0.71, 0.82) 0.54 (0.49, 0.59) 0.54 (0.49, 0.59) 0.54 (0.49, 0.59) 0.54 (0.49, 0.59) 0.56 (0.53, 0.92) 0.76 (0.68, 0.84) 1.00 (0.66, 1.00) 0.77 (0.85, 0.79) 0.73 (0.64, 0.81) 1.07 (0.53, 0.79) 0.85 (0.62, 0.97) 0.85 (0.72, 0.78) 0.56 (0.73, 0.78) 0.57 (0.39, 0.73) 0.56 (0.73, 0.78) 0.57 (0.39, 0.73) 0.57 (0.39,	$\begin{split} & \textbf{Specificity} (\textbf{65}: \texttt{CO}) \\ & 0.55 (0.38, 0.68) \\ & 0.52 (0.38, 0.68) \\ & 0.52 (0.30, 0.94) \\ & 0.85 (0.80, 0.90) \\ & 0.74 (0.60, 0.84) \\ & 0.77 (0.72, 0.82) \\ & 0.68 (0.55, 0.79) \\ & 0.93 (0.83, 0.98) \\ & 0.77 (0.72, 0.82) \\ & 0.68 (0.55, 0.79) \\ & 0.93 (0.83, 0.98) \\ & 0.68 (0.76, 0.86) \\ & 0.68 (0.76, 0.86) \\ & 0.68 (0.76, 0.86) \\ & 0.68 (0.76, 0.86) \\ & 0.70 (0.76, 0.38) \\ & 0.88 (0.77, 0.96) \\ & 0.88 (0.77, 0.96) \\ & 0.88 (0.77, 0.96) \\ & 0.88 (0.77, 0.96) \\ & 0.88 (0.77, 0.96) \\ & 0.88 (0.77, 0.96) \\ & 0.88 (0.77, 0.96) \\ & 0.88 (0.77, 0.96) \\ & 0.88 (0.77, 0.96) \\ & 0.72 (0.59, 0.83) \\ & 0.90 (0.82, 0.95) \\ & 0.77 (0.63, 0.87) \\ & 0.77 (0.63, 0.87) \\ & 0.77 (0.76, 0.83) \\ & 0.77 (0.76, 0.86) \\ & 0.77 (0.76, 0.86) \\ & 0.77 (0.76, 0.86) \\ & 0.77 (0.76, 0.86) \\ & 0.77 (0.76, 0.86) \\ & 0.77 (0.76, 0.86) \\ & 0.77 (0.76, 0.86) \\ & 0.77 (0.76, 0.86) \\ & 0.77 (0.76, 0.86) \\ & 0.77 (0.76, 0.86) \\ & 0.77 (0.76, 0.86) \\ & 0.77 (0.49, 0.81) \\ & 0.77 (0.49, 0.81) \\ & 0.86 (0.64, 0.77) \\ & 0.77 (0.49, 0.81) \\ & 0.86 (0.64, 0.77) \\ & 0.77 (0.49, 0.81) \\ & 0.77 (0.49, 0.81) \\ & 0.86 (0.64, 0.77) \\ & 0.77 (0.49, 0.81) \\ & 0.86 (0.64, 0.77) \\ & 0.86 (0.64, 0.77) \\ & 0.77 (0.49, 0.81) \\ & 0.86 (0.64, 0.71) \\ & 0.77 (0.49, 0.81) \\ & 0.86 (0.64, 0.71) \\ & 0.77 (0.49, 0.81) \\ & 0.86 (0.64, 0.71) \\ & 0.77 (0.49, 0.81) \\ & 0.86 (0.64, 0.71) \\ & 0.77 (0.49, 0.81) \\ & 0.86 (0.64, 0.71) \\ & 0.87 (0.59, 0.85) \\ & 0.77 (0.49, 0.81) \\ & 0.86 (0.64, 0.71) \\ & 0.86 (0.64, 0.71) \\ & 0.86 (0.64, 0.71) \\ & 0.86 (0.64, 0.71) \\ & 0.86 (0.64, 0.71) \\ & 0.86 (0.64, 0.71) \\ & 0.86 (0.64, 0.71) \\ & 0.86 (0.64, 0.71) \\ & 0.86 (0.64, 0.71) \\ & 0.86 (0.64, 0.71) \\ & 0.86 (0.64, 0.71) \\ & 0.86 (0.64, 0.71) \\ & 0.86 (0.64, 0.71) \\ & 0.86 (0.64, 0.71) \\ & 0.86 (0.64, 0.71) \\ & 0.86 (0.64, 0.71) \\ & 0.86 (0.80, 0.71) \\ & 0.86 (0.80, 0.71) \\ & 0.86 (0.80, 0.71) \\ & 0.86 (0.80, 0.71) \\ & 0.86 (0.80, 0.71) \\ & 0.86 (0.80, 0.71) \\ & 0.86 (0.80, 0.71) \\ & 0.86 (0.80, 0.71) \\ & 0.86 (0.80, 0.71) \\ & 0.86 (0.80, 0.71) \\ & 0.86 (0.80, 0.71) \\ & 0.86$	Sensitivity (95%CI)	Specificity (95%CI)
Study Wang 2009 Hug 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Poon 2012 Sasdelli 2013 Sasdelli 2013 Shabani 2009 Shibani 2009 Shibani 2009 Zaratiegul 2011 Lin 2011 Carta 2006 Wale gezota Gordberg 2012 Gorata 2009 Haghight 2011 Hirschfeld 2000 Imamura 2015 Isometa 2003 Kim 2008 Konuk 2007 Lee 2014 Melrtyre 2021 Mailer 2012 Lee 2014 Melntyre 2021 Mailer 2004 Nailer 2005 Bach 2015 Benazi 2005	TP 5 5 93 3 146 6 632 2 20 0 2 2 7 382 2 31 1 87 6 187 6 187 6 382 2 58 1 87 7 9 9 81 184 8 191 8 7 7 17 12 30 3 9 81 187 7 17 23 30 37 7 17 12 12 2 12 2 12 2 12 2 12 2 12 2	FP 222 94 34 219 94 34 219 94 34 219 16 63 20 20 4 4 20 20 20 20 20 20 20 20 20 20 20 20 20	FN 1 6 211 8 7 211 1 1 216 6 7 211 1 1 5 9 9 42 2 21 1 4 29 9 0 7 157 1 4 4 29 9 0 21 1 56 6 6 59 26 6 0 21 1 29 9 26 6 1 3 3 23 25 2 9 1 8 1 3 3 25 2 9 1 8 1 3 23 3 5 2 2 1 9 1 9 28 8 6 1 1 1 1 23 1 9 28 6 1 1 1 1 23 1 1 1 1	TN 255 1,084 199 624 43 2111 433 52 248 89 191 30 212 217 217 13 65 89 288 599 116 89 288 599 116 89 288 599 116 80 210 212 217 217 217 217 217 217 217 217 217	Cutoff 240 3.00 3.00 3.00 4.00 5.00 5.00 5.00 5.00 5.00 5.00 5	Continent Asia Asia Europe America Asia Asia Asia America Asia America Asia America Asia America Asia America Europe Asia Europe Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Asia America Asia America Asia America Asia America Europe Asia America Asia America Asia America Asia America Asia America Asia America Europe Asia America Asia America Europe Asia America Asia America Europe Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America America Asia America America Asia America Ame	Sensitivity (95%CI) 0.83 (0.36, 1.00) 0.83 (0.36, 1.00) 0.83 (0.36, 0.69) 0.73 (0.72, 0.78) 0.73 (0.78, 0.78) 0.73 (0.74, 0.77) 0.75 (0.71, 0.82) 0.75 (0.71, 0.82) 0.75 (0.73, 0.92) 0.75 (0.73, 0.92) 0.73 (0.78, 0.74) 0.73 (0.78, 0.74) 0.73 (0.78, 0.74) 0.73 (0.78, 0.74) 0.73 (0.78, 0.74) 0.75 (0.73, 0.79) 0.76 (0.71, 0.82) 0.77 (0.78, 0.74) 0.76 (0.73, 0.79) 0.76 (0.70, 0.87) 0.77 (0.78, 0.77) 0.85 (0.82, 0.97) 0.85 (0.82, 0.77) 0.76 (0.70, 0.82) 0.76 (0.74, 0.82) 0.76 (0.72, 0.92) 0.86 (0.77, 0.92) 0.86 (0.77, 0.95) 0.76 (0.55, 0.85) 0.76 (0.55, 0.85) 0.75 (0.55,	Specificity (65%-C) 0.55 (0.38, 0.68) 0.92 (0.90, 0.94) 0.85 (0.80, 0.90) 0.74 (0.71, 0.77) 0.73 (0.60, 0.84) 0.77 (0.72, 0.82) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98) 0.68 (0.71, 0.68) 0.68 (0.77, 0.98) 0.68 (0.77, 0.98) 0.72 (0.55, 0.83) 0.77 (0.63, 0.87) 0.77 (0.75, 0.83) 0.77 (0.76, 0.84) 0.77 (0.68, 0.87) 0.77 (0.68, 0.87) 0.77 (0.68, 0.87) 0.77 (0.68, 0.84) 0.77 (0.68,	Sensitivity (95%CI)	Specificity (05%CI)
Study Wang 2009 Hug 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Poon 2012 Sadelili 2013 Sadelili 2013 Shabani 2009 Shina 2018 Thase 2021 Vohringer 2016 Wang 2020 Zaratiegul 2011 Lin 2011 Hardoy 2005 Lee 2013 Carta 2006 Waleeprakhon 2014 Contaits 2009 Hardoy 2005 Lee 2013 Isometsa 2003 Kim 2006 Konuk 2007 Leao 2012 Lee 2014 McIntyre 2021 Meyer 2011 Miller 2013 Patmer 2021 Aller 2014 Bech 2011 Benazzi 2003	TP 5 93 146 632 45 231 231 187 136 231 136 231 136 231 136 136 231 137 136 136 231 136 231 136 231 136 231 136 231 136 231 231 231 231 231 231 231 231 231 231	FP 222 94 34 2196 44 2196 45 200 16 633 0 10 0 177 7 7 8 82 235 7 44 235 7 44 7 177 91 14 9 9 14 142 633 7 44 7 177 91 14 125 127 244 4537 7 7 8 8 22 27 7 8 8 22 20 10 10 10 10 10 10 10 10 10 10 10 10 10	FN 1 1 6 87 211 18 18 11 5 9 9 42 21 64 4 21 64 9 20 70 0 15 77 0 15 77 0 15 77 0 12 19 28 6 11 11 12 33 35 22 19 28 8 11 11 12 33 52 29 28 6 11 11 12 31 7 7 18 8 2 4	TN 255 2000 2000 2000 2000 2000 2000 2000	Cutoff 240 3.00 3.00 3.00 3.00 5.00 5.00 5.00 5.00	Continent Asia Asia Europe America Asia Asia Asia America America	$\begin{array}{l} \textbf{Sensitivity}(95\%CI)\\ 0.83 (0.36, 1.00)\\ 0.83 (0.36, 1.00)\\ 0.30 (0.25, 0.36)\\ 0.63 (0.56, 0.66)\\ 0.75 (0.72, 0.76)\\ 0.71 (0.59, 0.82)\\ 0.65 (0.45, 0.81)\\ 0.67 (0.38, 0.88)\\ 0.18 (0.02, 0.52)\\ 0.63 (0.53, 0.72)\\ 0.90 (0.85, 0.94)\\ 0.68 (0.61, 0.74)\\ 0.68 (0.61, 0.74)\\ 0.68 (0.61, 0.74)\\ 0.68 (0.61, 0.74)\\ 0.68 (0.61, 0.74)\\ 0.68 (0.61, 0.74)\\ 0.68 (0.61, 0.74)\\ 0.68 (0.61, 0.74)\\ 0.68 (0.61, 0.74)\\ 0.68 (0.61, 0.74)\\ 0.68 (0.61, 0.74)\\ 0.68 (0.61, 0.74)\\ 0.76 (0.61, 0.67)\\ 0.71 (0.52, 0.72)\\ 0.76 (0.61, 0.67)\\ 0.73 (0.64, 0.81)\\ 0.77 (0.74, 0.82)\\ 0.77 (0.74, 0.82)\\ 0.77 (0.74, 0.82)\\ 0.76 (0.70, 0.82)\\ 0.76 (0.70, 0.82)\\ 0.76 (0.70, 0.82)\\ 0.68 (0.67, 0.79)\\ 0.68 (0.67, 0.79)\\ 0.68 (0.67, 0.79)\\ 0.68 (0.67, 0.79)\\ 0.68 (0.67, 0.79)\\ 0.68 (0.67, 0.79)\\ 0.68 (0.67, 0.79)\\ 0.68 (0.67, 0.79)\\ 0.68 (0.77, 0.98)\\ 0.77 (0.24, 0.84)\\ 0.77 (0.24, 0.84)\\ 0.77 (0.24, 0.85)\\ 0.74 (0.27, 0.85)\\ 0.74 (0.27, 0.85)\\ 0.74 (0.27, 0.58)\\ 0.74 (0.27, 0.58)\\ 0.74 (0.27, 0.58)\\ 0.74 (0.25, 0.58)\\ 0.75 (0.25, 0.58)\\ 0.75 (0.25, 0.58)\\ 0.$	Specificity (6%-C) 0.55 (0.38, 0.68) 0.92 (0.40, 0.94) 0.85 (0.40, 0.90) 0.74 (0.71, 0.77) 0.73 (0.60, 0.84) 0.77 (0.72, 0.82) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98) 0.48 (0.43, 0.53) 1.00 (0.77, 102) 0.82 (0.77, 0.93) 0.82 (0.77, 0.93) 0.62 (0.74, 0.89) 0.57 (0.05, 0.63) 0.72 (0.59, 0.83) 0.90 (0.82, 0.55) 0.47 (0.23, 0.72) 0.51 (0.54, 0.68) 0.47 (0.23, 0.72) 0.52 (0.54, 0.71) 0.58 (0.57, 0.54) 0.47 (0.23, 0.72) 0.57 (0.70, 0.84) 0.57 (0.70, 0.84) 0.56 (0.54, 0.71) 0.78 (0.70, 0.84) 0.56 (0.54, 0.71) 0.77 (0.68, 0.87) 0.77 (0.58, 0.87) 0.77 (0.78, 0.85) 0.77 (0.58, 0.77) 0.77 (0.58, 0.77) 0.77 (0.58, 0.77) 0.77 (0.58, 0	Sensitivity (95%CI)	Specificity (05%CI)
Study Wang 2009 Hug 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Nagata 2013 Sasdelli 2013 Sasdelli 2013 Shabari 2009 Simitari 2001 Vohringer 2016 Wang 2020 Zaratiegu 2011 Lin 2011 Hardoy 2005 Lee 2013 Gonzalez 2009 Waleeprakhon 2014 Goldberg 2012 Gonzalez 2001 Imamura 2015 Isometsa 2003 Kim 2006 Konuk 2007 Lee 2014 Melrytre 2024 Meger 2011 Miller 2004 Nailed 2003 Faken 2015 Bech 2011 Benazzi 2003 Chour 2012 Chour 2012 Chung 2008	TP 5 93 146 632 45 245 231 187 137 136 231 138 131 231 231 231 231 231 231 231 231 231	FP 222 94 34 2196 44 2196 45 200 16 633 0 10 0 10 177 7 7 48 235 0 10 0 10 14 4235 0 10 0 10 14 454 74 77 91 14 9 9 14 145 54 77 7 8 12 27 244 557 7 8 8 12 2 25 5	$\begin{array}{c} {\rm FN} \\ 1 \\ 6 \\ 87 \\ 211 \\ 18 \\ 111 \\ 5 \\ 9 \\ 42 \\ 21 \\ 64 \\ 42 \\ 21 \\ 64 \\ 22 \\ 70 \\ 157 \\ 14 \\ 111 \\ 5 \\ 6 \\ 6 \\ 59 \\ 26 \\ 0 \\ 12 \\ 9 \\ 28 \\ 3 \\ 42 \\ 21 \\ 29 \\ 28 \\ 12 \\ 3 \\ 42 \\ 21 \\ 12 \\ 3 \\ 42 \\ 11 \\ 12 \\ 3 \\ 48 \\ 11 \\ 12 \\ 3 \\ 48 \\ 1 \\ 2 \\ 3 \\ 46 \\ 6 \\ 6 \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 \\ 10 $	TN 255 2000 2000 2000 2000 2000 2000 2000	Cutoff 2 2.0 3.0 3.0 4.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 5.0 5	Continent Asia Asia Europe America Asia Asia Asia America Asia America Europe Asia Europe Asia Europe Asia Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe America Europe Asia America Asia America Europe Asia America Europe America Asia America Europe America Europe America Asia Asia America Asia America Europe Asia Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia Asia America Asia Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia Asia Asia Asia Asia Asia Asia Asi	$\begin{array}{l} \textbf{Sensitivity}(95\%CU)\\ 0.83(0.36,1.00)\\ 0.33(0.25,0.36)\\ 0.63(0.56,0.68)\\ 0.75(0.72,0.78)\\ 0.71(0.59,0.82)\\ 0.65(0.45,0.81)\\ 0.67(0.38,0.88)\\ 0.18(0.02,0.52)\\ 0.63(0.56,0.72)\\ 0.63(0.56,0.72)\\ 0.63(0.56,0.72)\\ 0.63(0.56,0.72)\\ 0.63(0.64,0.72)\\ 0.63(0.64,0.72)\\ 0.63(0.64,0.72)\\ 0.63(0.64,0.72)\\ 0.63(0.64,0.52)\\ 0.54(0.46,0.52)\\ 0.54(0.46,0.52)\\ 0.54(0.46,0.52)\\ 0.54(0.46,0.52)\\ 0.54(0.46,0.52)\\ 0.54(0.46,0.52)\\ 0.54(0.46,0.52)\\ 0.54(0.46,0.52)\\ 0.54(0.46,0.52)\\ 0.54(0.46,0.52)\\ 0.54(0.46,0.52)\\ 0.54(0.46,0.52)\\ 0.54(0.46,0.52)\\ 0.54(0.46,0.52)\\ 0.54(0.46,0.72)\\ 0.54(0.46,0.72)\\ 0.54(0.46,0.72)\\ 0.54(0.46,0.72)\\ 0.54(0.52,0.57)\\ 0.52(0.54,0.52)\\ 0.54(0.46,0.72)\\ 0.55(0.54,0.72,0.75)\\ 0.55(0.54,0.72,0.75)\\ 0.57(0.32,0.52)\\ 0.56(0.57,0.73)\\ 0.57(0.52,0.52)\\ 0.56(0.57,0.73)\\ 0.57(0.52,0.52)\\ 0.56(0.57,0.73)\\ 0.57(0.52,0.52)\\ $	Specificity (95%-C) 0.55 (0.38, 0.68) 0.92 (0.90, 0.94) 0.55 (0.38, 0.68) 0.92 (0.90, 0.94) 0.55 (0.38, 0.68) 0.92 (0.90, 0.94) 0.77 (0.60, 0.84) 0.77 (0.72, 0.82) 0.68 (0.55, 0.79) 0.68 (0.55, 0.79) 0.68 (0.55, 0.79) 0.68 (0.71, 0.56) 0.48 (0.43, 0.53) 0.82 (0.74, 0.89) 0.88 (0.77, 0.92) 0.88 (0.77, 0.92) 0.88 (0.77, 0.92) 0.88 (0.77, 0.92) 0.88 (0.77, 0.92) 0.73 (0.67, 0.78) 0.88 (0.77, 0.92) 0.76 (0.61, 0.55) 0.76 (0.61, 0.55) 0.76 (0.61, 0.55) 0.76 (0.61, 0.55) 0.77 (0.63, 0.57) 0.77 (0.63, 0.57) 0.77 (0.63, 0.57) 0.77 (0.64, 0.65) 0.76 (0.64, 0.65) 0.76 (0.64, 0.65) 0.76 (0.64, 0.65) 0.76 (0.64, 0.65) 0.76 (0.64, 0.65) 0.77 (0.63, 0.57) 0.77 (0.63, 0.57) 0.57 (0.63, 0.57) 0.77 (0.63, 0.57) 0.57 (0.53,	Sensitivity (95%CI)	Specificity (65%CI)
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43 2111 43 522 48 1910 133 655 1822 217 217 133 655 1822 217 217 133 655 1822 116 44 40 8203 214 210 212 217 217 133 65 108 214 214 215 212 217 217 217 217 217 217 217 217 217</td> <td>Cutofft 220 300 300 400 500 500 500 500 500 500 500 500 600 6</td> <td>Continent Asia Asia Europe America Asia Asia Asia America Asia America Asia America Europe Asia America Asia America America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America America Asia Asia America Asia America Asia Asia America Asia America Asia Asia America Asia Asia America Asia Asia America Asia America Asia America Asia America Asia America Asia America Asia Asia America Asia America Asia America Asia America Asia America Asia Asia Asia America Asia Asia Asia Asia Asia Asia A Asia A Asia America Asia Asia Asia A Asia A</td> <td>$\begin{array}{l} \textbf{Sensitivity}(95\%CD)\\ 0.83(0.38,1.00)\\ 0.83(0.38,1.00)\\ 0.83(0.25,0.38)\\ 0.63(0.66,0.68)\\ 0.75(0.72,0.78)\\ 0.71(0.59,0.82)\\ 0.65(0.45,0.81)\\ 0.67(0.38,0.88)\\ 0.18(0.02,0.52)\\ 0.63(0.53,0.72)\\ 0.90(0.85,0.72)\\ 0.90(0.85,0.72)\\ 0.90(0.85,0.72)\\ 0.88(0.81,0.84)\\ 0.88(0.84,0.92)\\ 0.88(0.84,0.92)\\ 0.88(0.84,0.92)\\ 0.88(0.84,0.92)\\ 0.88(0.84,0.92)\\ 0.88(0.84,0.92)\\ 0.88(0.84,0.92)\\ 0.88(0.84,0.92)\\ 0.76(0.64,0.59)\\ 0.76(0.64,0.84)\\ 1.00(0.66,1.00)\\ 0.77(0.68,0.84)\\ 1.00(0.66,1.00)\\ 0.79(0.77,0.92)\\ 0.78(0.74,0.82)\\ 0.77(0.64,0.84)\\ 1.00(0.66,1.00)\\ 0.79(0.77,0.92)\\ 0.77(0.64,0.84)\\ 1.00(0.66,1.00)\\ 0.79(0.77,0.92)\\ 0.86(0.27,0.72)\\ 0.86(0.77,0.92)\\ 0.86(0.77,$</td> <td>Specificity (65%-C) 0.55 (0.38, 0.68) 0.92 (0.90, 0.94) 0.55 (0.38, 0.68) 0.92 (0.90, 0.94) 0.55 (0.38, 0.68) 0.92 (0.90, 0.94) 0.77 (0.60, 0.84) 0.77 (0.72, 0.82) 0.68 (0.55, 0.79) 0.93 (0.83, 0.83) 0.82 (0.74, 0.68) 0.48 (0.43, 0.53) 0.48 (0.43, 0.53) 0.48 (0.71, 0.96) 0.48 (0.71, 0.96) 0.48 (0.71, 0.96) 0.48 (0.71, 0.96) 0.48 (0.71, 0.96) 0.52 (0.43, 0.62) 0.52 (0.43, 0.62) 0.52 (0.43, 0.62) 0.53 (0.54, 0.71) 0.52 (0.43, 0.62) 0.54 (0.53, 0.83) 0.52 (0.43, 0.62) 0.57 (0.53, 0.83) 0.57 (0.53, 0.83) 0.57 (0.53, 0.83) 0.57 (0.53, 0.63) 0.77 (0.53, 0.67) 0.77 (0.71, 0.82) 0.77 (0.71, 0.82) 0.57 (0.43, 0.72) 0.77 (0.43, 0.67) 0.78 (0.74, 0.84) 0.57 (0.49, 0.81) 0.57 (0.49, 0.81) 0.57 (0.43, 0.82) 0.77 (0.43, 0.87) 0.77 (0.43,</td> <td>Sensitivity (95%CI)</td> <td>Specificity (65%CI)</td>	FP 224 94 34 219 6 6 300 4 200 1770 48 200 11770 48 200 1170 48 200 1170 48 200 1170 48 200 1170 48 200 119 4 4 4 4 4 4 5 4 7 4 4 9 9 1227 24 24 537 7 8 8 22 25 18 8 122 2 25 18 18 16 10 19 19 19 19 19 19 19 19 19 19 19 19 19	FN 1 1687 2116 877 2118 111 5 9 42 21 649 700 211 559 266 0 211 157 144 1559 266 0 211 157 168 10 216 216 216 216 216 216 216 216	TN 521,084 1999 624 43 2111 43 522 48 1910 133 655 1822 217 217 133 655 1822 217 217 133 655 1822 116 44 40 8203 214 210 212 217 217 133 65 108 214 214 215 212 217 217 217 217 217 217 217 217 217	Cutofft 220 300 300 400 500 500 500 500 500 500 500 500 600 6	Continent Asia Asia Europe America Asia Asia Asia America Asia America Asia America Europe Asia America Asia America America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America America Asia Asia America Asia America Asia Asia America Asia America Asia Asia America Asia Asia America Asia Asia America Asia America Asia America Asia America Asia America Asia America Asia Asia America Asia America Asia America Asia America Asia America Asia Asia Asia America Asia Asia Asia Asia Asia Asia A Asia A Asia America Asia Asia Asia A Asia A	$\begin{array}{l} \textbf{Sensitivity}(95\%CD)\\ 0.83(0.38,1.00)\\ 0.83(0.38,1.00)\\ 0.83(0.25,0.38)\\ 0.63(0.66,0.68)\\ 0.75(0.72,0.78)\\ 0.71(0.59,0.82)\\ 0.65(0.45,0.81)\\ 0.67(0.38,0.88)\\ 0.18(0.02,0.52)\\ 0.63(0.53,0.72)\\ 0.90(0.85,0.72)\\ 0.90(0.85,0.72)\\ 0.90(0.85,0.72)\\ 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Study Wang 2009 Hug 2012 Hughes 2016 Paterniti 2018 Gan 2012 Poon 2012 Poon 2012 Poon 2013 Sasdelli 2013 Sasdelli 2013 Sasdelli 2013 Shabari 2009 Shima 2018 Thase 2021 Vohringer 2016 Wareliso20011 Lin 2011 Hardy 2005 Lee 2013 Carta 2006 Waleeprakhon 2014 Goldberg 2012 Gonzalez 2009 Haghighi 2011 Hirschfeld 2000 Imamura 2015 Isometas 2003 Kim 2006 Konuk 2012 Lee 2014 Molntyre 2021 Mayer 2011 Miler 2004 Paimer 2021 Maler 2013 Paimer 2021 Miler 2004 Chung 2008 Chung 2008 Chung 2008 Chung 2008 Chung 2008	TP 5 93 146 632 45 2 71 136 231 382 184 81 352 184 81 352 184 350 9 81 87 9 81 87 9 81 87 9 81 87 9 81 87 9 81 87 9 81 87 9 81 83 83 84 81 82 83 84 84 81 82	FP 224 94 34 2196 630 4 40 119 4 44 530 7 7 8 12 2 5 18 11 455 12 7 7 8 12 2 5 18 11 455 12 12 12 12 12 12 12 12 12 12 12 12 12	FN 1 1687 2118 877 2118 111 5 9 42 211 6499 700 211 157 144 159 266 6 9 202 157 144 159 202 157 144 159 202 202 202 202 202 202 202 20	TN 25 21,084 1999 624 43 2011 43 52 48 43 59 212 217 13 365 59 28 88 88 88 88 89 2012 217 217 217 13 365 182 218 219 218 219 218 219 218 219 218 219 218 219 218 219 218 219 218 219 218 219 219 218 219 219 218 219 218 219 219 218 219 219 218 219 219 218 219 219 218 219 219 218 219 219 218 219 218 219 218 219 218 219 218 219 218 219 218 219 218 219 218 219 218 219 218 219 218 219 218 219 218 219 218 219 218 219 218 219 218 219 219 218 218 218 218 218 218 218 218 218 218	Cutofft 2003 300 300 300 300 500 500 500 500 500	Continent Asia Asia Europe America Asia Asia Asia America Asia America Asia America Asia America Asia America Europe Asia Europe Asia Europe Asia America Burope Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Asia America Europe Asia America America America America America America America Europe America Europe America Europe America Europe America Europe Asia America Asia America Europe Asia America Europe Asia Asia America Europe Asia Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America Asia America America Asia America America Asia America America America America Asia America America America America America America America Asia America America America America America Asia America Ameri	$\begin{array}{l} \textbf{Sensitivity}(95\%CU)\\ 0.83(0.38,1.00)\\ 0.83(0.38,1.00)\\ 0.83(0.25,0.38)\\ 0.63(0.65,0.68)\\ 0.75(0.72,0.78)\\ 0.71(0.59,0.82)\\ 0.65(0.45,0.81)\\ 0.67(0.38,0.88)\\ 0.18(0.02,0.52)\\ 0.63(0.55,0.72)\\ 0.90(0.85,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.68(0.61,0.74)\\ 0.58(0.47,0.92)\\ 0.76(0.68,0.84)\\ 1.00(0.68,0.84)\\ 1.00(0.68,0.84)\\ 1.00(0.68,0.84)\\ 1.00(0.68,0.84)\\ 1.00(0.68,0.16,0.77)\\ 0.73(0.68,0.84)\\ 1.00(0.68,0.16,0.87)\\ 0.73(0.68,0.84)\\ 1.00(0.68,0.16,0.87)\\ 0.73(0.68,0.84)\\ 1.00(0.68,0.16,0.87)\\ 0.73(0.68,0.84)\\ 1.00(0.68,0.16,0.87)\\ 0.73(0.68,0.74,0.87)\\ 0.73(0.68,0.74,0.87)\\ 0.73(0.68,0.74,0.87)\\ 0.73(0.68,0.74,0.87)\\ 0.73(0.68,0.77,0.95)\\ 0.67(0.48,0.82)\\ 0.68(0.77,0.95)\\ 0.77(0.28,0.16,0.82)\\ 0.68(0.77,0.95)\\ 0.77(0.28,0.16,0.82)\\ 0.68(0.77,0.95)\\ 0.77(0.28,0.16,0.82)\\ 0.68(0.77,0.95)\\ 0.77(0.28,0.16,0.82)\\ 0.68(0.77,0.95)\\ 0.77(0.28,0.16,0.82)\\ 0.74(0.28,0.28,0.58)\\ 0.77(0.28,0.58)\\ 0.77(0.28,0.58)\\ 0.77(0.28,0.58)\\ 0.77(0.28,0.58)\\ 0.77(0.28,0.58)\\ 0.77(0.28,0.58)\\ 0.77(0.28,0.58)\\ 0.77(0.28,0.58)\\ 0.77(0.28,0.58)\\ 0.77(0.28,0.58)\\ 0.77(0.28,0.58)\\ 0.77(0.28,0.58)\\ 0.77(0.28,0.58)\\ 0.77(0.58,0.58)\\ 0.77(0.28,0.58)\\ 0.77(0.58,0.58)\\ 0.77(0.28,0.58)\\ 0.77(0.28,0.58)\\ 0.77(0.28,0.58)\\ 0.77(0.28,0.58)\\ 0.78(0.28,0.58)$	Specificity (65%-C) 0.55 (0.38, 0.68) 0.92 (0.90, 0.94) 0.55 (0.38, 0.68) 0.92 (0.90, 0.94) 0.55 (0.38, 0.68) 0.97 (0.71, 0.72, 0.82) 0.73 (0.60, 0.84) 0.77 (0.72, 0.82) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98) 0.68 (0.55, 0.79) 0.93 (0.83, 0.98) 0.68 (0.57, 0.98) 0.68 (0.77, 0.92) 0.68 (0.77, 0.92) 0.82 (0.74, 0.89) 0.82 (0.74, 0.89) 0.88 (0.71, 0.96) 0.86 (0.77, 0.92) 0.73 (0.67, 0.79) 0.73 (0.67, 0.79) 0.73 (0.67, 0.78) 0.74 (0.55, 0.88) 0.77 (0.58, 0.87) 0.77 (0.58, 0.87) 0.77 (0.58, 0.87) 0.77 (0.63, 0.87) 0.77 (0.63, 0.87) 0.77 (0.68, 0.84) 0.77 (0.68, 0.68) 0.77 (0.78, 0.78) 0.75 (0.78, 0.78) 0.75 (0.78, 0.78) 0.75	Sensitivity (95%CI)	Specificity (65%CI)
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0$</td><td>$\begin{array}{c} \textbf{FN} \\ 1 \\ 216 \\ 877 \\ 211 \\ 181 \\ 159 \\ 942 \\ 221 \\ 44 \\ 299 \\ 422 \\ 211 \\ 116 \\ 299 \\ 422 \\ 211 \\ 116 \\ 299 \\ 226 \\ 291 \\ 298 \\ 122 \\ 129 \\ 281 \\ 113 \\ 234 \\ 424 \\ 201 \\ 424 \\ 201 \\ 102 \\ 241 \\ 102 \\$</td><td>TN 25 1,084 199 624 43 211 43 211 43 211 43 221 217 130 212 217 31 65 89 28 8 8 29 5 182 21 216 44 8 0 4 1 5 10 8 8 21 2 2 5 13 2 2 4 8 8 8 3 10 7 7 8 5 1 5 5 5 5 1 8 8 8 10 7 7 8 5 1 5 5 5 5 1 8 8 8 1 0 7 7 8 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5</td><td>Cutoff 2 2.0 2.0 3.0 3.0 3.0 3.0 3.0 3.0 3.0 3</td><td>Continent Asia Asia Europe America Asia Asia Asia Asia America Asia America Europe Asia Curope Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Asia America Europe Asia America Europe Asia America Europe Asia America Europe America Europe Asia America Asia America Asia America Asia America Asia America Asia 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\\ 291 \\ 298 \\ 122 \\ 129 \\ 281 \\ 113 \\ 234 \\ 424 \\ 201 \\ 424 \\ 201 \\ 102 \\ 241 \\ 102 \\ $	TN 25 1,084 199 624 43 211 43 211 43 211 43 221 217 130 212 217 31 65 89 28 8 8 29 5 182 21 216 44 8 0 4 1 5 10 8 8 21 2 2 5 13 2 2 4 8 8 8 3 10 7 7 8 5 1 5 5 5 5 1 8 8 8 10 7 7 8 5 1 5 5 5 5 1 8 8 8 1 0 7 7 8 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	Cutoff 2 2.0 2.0 3.0 3.0 3.0 3.0 3.0 3.0 3.0 3	Continent Asia Asia Europe America Asia Asia Asia Asia America Asia America Europe Asia Curope Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Europe Asia America Asia America Europe Asia America Europe Asia America Europe Asia America Europe America Europe Asia America Asia America Asia America Asia America Asia America Asia America Europe Asia America Europe Asia America Asia America America America Asia America Ame	Sensitivity (95%CU) 0.83 (0.38, 1.00) 0.83 (0.38, 1.00) 0.83 (0.25, 0.36) 0.63 (0.66, 0.69) 0.75 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\textbf{2350} \\ \textbf{0109} \\ \textbf{44} \\ \textbf{2350} \\ \textbf{0109} \\ \textbf{44} \\ \textbf{468} \\ \textbf{4777} \\ \textbf{912} \\ \textbf{262} \\ \textbf{2778} \\ \textbf{2778} \\ \textbf{225} \\ \textbf{281611} \\ \textbf{458} \\ \textbf{4773} \\ \textbf{23564} \\ \textbf{1913} \\ \textbf{66191} \\ \textbf{6614} \\ \textbf{1913} \\ \textbf{664} \\ \textbf{1913} \\ \textbf{6614} \\ \textbf{1913} \\ \textbf{1913}$</td> <td>$\begin{array}{c} \textbf{FN} 1 \\ 216 \\ 87 \\ 111 \\ 181 \\ 159 \\ 942 \\ 220 \\ 707 \\ 111 \\ 156 \\ 659 \\ 226 \\ 01 \\ 229 \\ 183 \\ 423 \\ 225 \\ 198 \\ 211 \\ 123 \\ 123 \\ 232 \\ 216 \\ 111 \\ 123 \\ 141 \\ 123 \\ 123 \\ 234 \\ 64 \\ 244 \\ 234 \\ 64 \\ 244 \\ 234 \\ 102 \\ 241 \\ 192 \\ 93 \\ 151 \\ 141 \\ 123 \\ 151 \\ 123 \\$</td> <td>TN 25 1,084 199 624 199 624 43 211 43 22 217 130 212 217 130 212 217 130 212 217 130 212 217 130 212 217 130 212 217 130 212 217 217 20 217 20 217 20 217 20 21 20 21 20 21 20 21 20 21 20 21 20 21 20 21 20 21 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\\ \textbf{44} \\ \textbf{2350} \\ \textbf{0109} \\ \textbf{44} \\ \textbf{468} \\ \textbf{4777} \\ \textbf{912} \\ \textbf{262} \\ \textbf{2778} \\ \textbf{2778} \\ \textbf{225} \\ \textbf{281611} \\ \textbf{458} \\ \textbf{4773} \\ \textbf{23564} \\ \textbf{1913} \\ \textbf{66191} \\ \textbf{6614} \\ \textbf{1913} \\ \textbf{664} \\ \textbf{1913} \\ \textbf{6614} \\ \textbf{1913} \\ \textbf{1913}$	$\begin{array}{c} \textbf{FN} 1 \\ 216 \\ 87 \\ 111 \\ 181 \\ 159 \\ 942 \\ 220 \\ 707 \\ 111 \\ 156 \\ 659 \\ 226 \\ 01 \\ 229 \\ 183 \\ 423 \\ 225 \\ 198 \\ 211 \\ 123 \\ 123 \\ 232 \\ 216 \\ 111 \\ 123 \\ 141 \\ 123 \\ 123 \\ 234 \\ 64 \\ 244 \\ 234 \\ 64 \\ 244 \\ 234 \\ 102 \\ 241 \\ 192 \\ 93 \\ 151 \\ 141 \\ 123 \\ 151 \\ 123 \\ $	TN 25 1,084 199 624 199 624 43 211 43 22 217 130 212 217 130 212 217 130 212 217 130 212 217 130 212 217 130 212 217 130 212 217 217 20 217 20 217 20 217 20 21 20 21 20 21 20 21 20 21 20 21 20 21 20 21 20 21 20 21 20 21 20 21 20 21 20 21 20 21 20 21 20 21 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Figure 3 Forest plot of BI, HCL-32, BSDS, MDQ, and RMS, including sensitivity and specificity of included studies. 95%CI = 95% confidence interval; BI = bipolarity index; BSDS = Bipolar Spectrum Diagnostic Scale; FN = false negative; FP = false positive; HCL-32 = Hypomania Checklist-32; MDQ = Mood Disorder Questionnaire; RMS = Rapid Mood Screener; TN = true negative; TP = true positive.



Figure 4 Summary estimates and 95% confidence region of the meta-analyses showing diagnostic test accuracies of BI, HCL-32, BSDS, MDQ, and RMS for detection of any type of bipolar disorder (BD). BI = bipolarity index; BSDS = Bipolar Spectrum Diagnostic Scale; FN = false negative; FP = false positive; HCL-32 = Hypomania Checklist-32; MDQ = Mood Disorder Questionnaire; RMS = Rapid Mood Screener; TN = true negative; TP = true positive.

detection of BD.^{21,113,114} In line with our findings, the RMS provided high accuracy for detection of BD-I, with a sensitivity, specificity, and accuracy of 88, 80, and 84%, respectively.⁷⁶

Although this meta-analysis involved a large number of studies and participants, there were some limitations. Comparing the accuracy and diagnostic value of the two new instruments with the three existing ones was prone to confounding due to differences in study characteristics and population.¹¹⁵ The main limitation of the BI is that the observer is not blind to the results of the Mini International Neuropsychiatric Interview (MINI), which, as a structured diagnostic interview, has become an integral part of psychiatry, not only being considered the diagnostic gold standard in psychiatric research but also increasingly being used to help ensure diagnostic precision in clinical practice.¹¹⁶ Because several parts of the BI are derived from structured interviews, it is difficult to completely ignore the influence of MINI results. This may limit the generalizations of the findings, but is consistent with how the scale is used in clinical practice. Another limitation is relying on a sole interviewer in a practice environment and the absence of longitudinal follow-up.

The present meta-analysis shows that the diagnostic value and accuracy of a new instrument, the BI, exceeded those of existing instruments including the BSDS, HCL-32, and MDQ. However, it should be noted that these tools should not be considered as a means of definitive diagnosis, because a significant proportion of patients diagnosed with BD do not actually have the disorder.¹¹⁰ Therefore, it is recommended that a confirmatory diagnostic interview and clinical observation be performed simultaneously. Moreover, cost-benefit analysis to assess the cost of false positives with the use of screening tools not only is important, but failure to account for real cases of BD may lead to erroneous results and suboptimal decision making. Finally, well-designed clinical studies, especially randomized controlled trials (RCT), of BD screening instruments should offer evidence of their impact on patient outcomes.

In conclusion, a large number of patients with BD continue to experience complications and consequences due to a lack of proper diagnosis. To diagnose these disorders accurately, in addition to a clinical interview, a diagnostic tool with appropriate psychometric properties is still needed. Though available BD screening tools have

Table 2 S general cc	ummary diagr mmunity popu	nostic characteristi Ilations	ics of BI, HCL-32, B	SDS, MD0	α, and RMS I	or detection of any	/ type of b	ipolar disorde	r in mental health ce	nter, prim	ary care, or
			Sei	nsitivity		Sp	ecificity		Diagn	ostic OR	
Test	Papers (n)	Participants (n)	Pooled (95%CI)	P (%)	p-value	Pooled (95%CI)	P (%)	p-value	Pooled (95%CI)	P (%)	p-value
HCL-32 BD-I BD-II	6 10	4,799 6,316	0.65 (0.63-0.67) 0.70 (0.68-0.72)	98.3 97.7	< 0.0001< 0.0001	0.64 (0.62-0.66) 0.65 (0.63-0.66)	93.8 95.5	< 0.0001< 0.0001	3.48 (2.50-4.85) 5.53 (4.21-7.79)	84.2 78.6	< 0.0001< 0.0001
BSDS BD-II	4	515	0.78 (0.67-0.87)	0.0	0.9659	0.63 (0.58-0.67)	84.9	0.0002	6.85 (3.72-12.6)	0.0	0.7693
MDQ BD-I BD-II	- 14 14	4,144 3,772	0.78 (0.76-0.80) 0.52 (0.49-0.56)	96.0 92.6	< 0.0001< 0.0001	0.67 (0.65-0.69) 0.77 (0.76-0.79)	91.1 97.0	< 0.0001< 0.0001	8.67 (4.44-16.93) 3.93 (4.21-7.79)	91.6 60.2	< 0.0001 0.0019
RMS BD-I	ო	800	0.78 (0.73-0.82)	91.4	< 0.0001	0.72 (0.68-0.77)	82.1	0.0038	14.24 (3.16-64.1)	93.7	< 0.0001
95%CI = 9 HCL-32 =	5% confidence i Hypomania Che	nterval; BD-I = bipolɛ icklist-32; MDQ = Mo	ar disorder type I; BD-I ood Disorder Questior	l = bipolar o naire; OR	lisorder type II; = odds ratio; R	BI = bipolarity index; MS = Rapid Mood So	BSDS = Bij creener.	polar Spectrum	Diagnostic Scale; DOR	l = diagnost	ic odds ratio;

356 M Sayyah et al.

HCL-32-Bipolar I										
Study	TP	FP	FN	TN	Cutoff	Continent	Sensitivity (95%CI)	Specificity (95%CI)	Sensitivity (95%CI)	Specificity (95%CI)
Angst 2005	248	121	78	205	14.0	Europe	0.76 (0.71, 0.81)	0.63 (0.57, 0.68)		
Feng 2017	235	109	116	242	14.0	Asia	0.67 (0.62, 0.72)	0.69 (0.64, 0.74)	-	
Mever 2011	122	85	26	55	14.0	Europe	0.88 (0.75, 0.88)	0.39 (0.31, 0.48)		
Meyer 2017	632	324	270	486	14.0	Europe	0.70 (0.67, 0.73)	0.60 (0.57, 0.63)	-	-
Yang 2011	315	150	141	306	14.0	Asia	0.69 (0.65, 0.73)	0.67 (0.63, 0.71)		
Lee 2016	70	40	243	180	19.0	Asia	0.22 (0.18, 0.27)	0.82 (0.76, 0.87)	-	-
MDQ-Bipolar I							. , ,	, , , ,	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1
Study	TP	FP	FN	TN	Cutoff	Continent	Sensitivity (95%CI)	Specificity (95%CI)	Sensitivity (95%CI)	Specificity (95%CI)
Hu 2012	1,204	550	283	937	3.0	Asia	0.81 (0.79, 0.83)	0.63 (0.61, 0.65)	-	
McIntyre 2021	50	14	8	50	7.0	America	0.86 (0.75, 0.94)	0.78 (0.66, 0.87)		
Mever 2011	118	43	30	97	7.0	Europe	0.80 (0.72, 0.86)	0.69 (0.61, 0.77)		
Chung 2008	85	50	100	135	7.0	Asia	0.46 (0.39, 0.53)	0.73 (0.66, 0.79)		
Cyprien 2014	155	32	40	163	7.0	Europe	0.79 (0.73, 0.85)	0.84 (0.78, 0.88)		
51							,	,		
RMS-Bipolar I									0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1
Study	TP	FP	FN	TN	Cutoff	Continent	Sensitivity (95%CI)	Specificity (95%CI)	Sensitivity (95%CI)	Specificity (95%CI)
Montano 2021	122	28	17	111	4.0	America	0.88 (0.81, 0.93)	0.80 (0.72, 0.86)		
Thase 2021	136	70	64	130	4.0	America	0.68 (0.61, 0.74)	0.65 (0.58, 0.72)		
McIntvre 2021	51	13	7	51	6.0	America	0.88 (0.77, 0.95)	0.80 (0.68, 0.89)		
									0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Figure 5 Forest plot of BI, HCL-32, MDQ, and RMS including sensitivity and specificity of included studies on patients with BD-I. 95%CI = 95% confidence interval; BI = Bipolarity Index; FN = false negative; FP = false positive; HCL-32-Bipolar I = Hypomania Checklist-32 (HCL-32)-Bipolar disorder type I; MDQ-Bipolar I = Mood Disorder Questionnaire (MDQ)-Bipolar disorder type I; RMS-Bipolar I = Rapid Mood Screener (RMS)-Bipolar disorder type I; TN = true negative; TP = true positive.



Figure 6 Forest plot of HCL-32, BSDS, MDQ, and BI including sensitivity and specificity of included studies on patients with BD-II. 95%CI = 95% confidence interval; BI = Bipolarity Index; FN = false negative; FP = false positive; HCL-32-Bipolar I = Hypomania Checklist-32 (HCL-32)-Bipolar disorder type I; MDQ-Bipolar II = Mood Disorder Questionnaire (MDQ)-Bipolar disorder type II; RMS-Bipolar I = Rapid Mood Screener (RMS)-Bipolar disorder type I; TN = true negative; TP = true positive.



Figure 7 Summary estimates and 95% confidence region of the meta-analyses showing diagnostic test accuracies of BI, HCL-32, BSDS, MDQ, and RMS for detection of any type of BD-I (A) vs. BD-II (B). BD-1 = bipolar disorder type I; BD-II = bipolar disorder type II; HCL-32-Bipolar I = Hypomania Checklist-32 (HCL-32)-Bipolar disorder type I; HCL-32-Bipolar II = Hypomania Checklist-32 (HCL-32)-Bipolar disorder type II; MDQ-Bipolar I = Mood Disorder Questionnaire (MDQ)-Bipolar disorder type I; MDQ-Bipolar II = Mood Disorder Questionnaire (MDQ)-Bipolar disorder type II; RMS-Bipolar I = Rapid Mood Screener (RMS)-Bipolar disorder type I.

acceptable diagnostic accuracy, as shown in previous studies, the results are still not entirely satisfactory because only a limited number of parameters are considered. The present study showed that the diagnostic accuracy of two new instruments, the BI and RMS, is considerably higher than that of available tools such as the HCL-32, BSDS, and MDQ. Nevertheless, a positive screening result should still be confirmed by a clinical diagnostic evaluation for BD.

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