The Study of Diagnostic Value of Bipolarity Index for Bipolar Disorder in China: Meta-analysis of Sensitivity and Specificity

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Abstract

Background

The diagnosis of bipolar disorder is still one of the key problems in psychiatric clinic. Although DSM-5 has made some important changes, it has not completely changed the missed diagnosis and misdiagnosis of bipolar disorder.It was very important that diagnostic scale was used in clinic.But the study results of assist diagnostic scale for bipolar disorder should been concluded and analyzed.Bipolarity index was one of assist diagnostic scale,which should be analyzed comprehensively.

Methods

We searched CBM, CNKI , WANFANG and CSSCI in Chinese to find literature from Julyr 31 2004 to July 31 2020 related to Bipolarity Index in diagnosis for bipolar disorder ,among which results such as comments, letters, reviews and case reports were excluded. The rate of sensitivity,specificity,accuracy,positive predictive value and negative predictive value in diagnosis was synthesized and discussed.

Results

A total of 1237 subjects were included in 5 studies. Random effect model is used to account for the data by Revman 5.2. The results showed that the sensitivity of BI in diagnostic was 0.93 (95% CI: 0.93–1.00), the specificity was 85% (95% CI: 0.69–0.96). the positive predict value was 74% (95% CI: 0.53–0.91).the negative predict value was 95% (95% CI: 0.81–1.00).and accuracy was 86% (95% CI: 0.77–0.93). Significant heterogeneity was detected across studies regarding these incidence estimates.

Conclusion

The idea diagnostic value of BI was found. although the significant heterogeneity detected in studies.We must interpret the results with caution and also put attention to this result,which include comparison to other diagnostic scale,perfecting sue of BI in clinical psychiatry.

Background

Although DSM-5 has made some important changes, it has not completely changed the missed diagnosis and misdiagnosis of bipolar disorder [1,2]. There were two pattern and five themes were identified from the interviews. The first pattern, living with undiagnosed bipolar disorder, demonstrated common experiences of distinguishing impulsive moods and behavior, suffering life challenges, and seeking relief. The second pattern, acclimating to a new diagnosis of bipolar disorder, demonstrated participants' ways of understanding the diagnosis and reconciling the diagnosis[1]. At same times,first episode was often depression that always product disdiagnosis as major depressive episode(MDD), the diagnosis of bipolar disorder (BD) is often preceded by an initial diagnosis of depression, creating a delay in the accurate diagnosis and treatment of BD,and the findings from the study suggested that an earlier diagnosis of depression is related to experiencing a longer delay in conversion to BD [2].Therefore, combined or increased use of diagnostic scales, such as HCL-32, MDQ and so on, has become an important clinical auxiliary diagnostic means. In order to change or improve the accuracy of diagnosis of bipolar disorder[3,4]. Both HCL-32 scales and the MDQ had higher sensitivity and higher specificity in screening for BD,although their had some slight differences in diagnostic value. At the same time, the bipolar index scale is also one of the auxiliary diagnostic methods [5,6], its application may be more conducive to the diagnosis of bipolar disorder [7,8].

Different from HCL-32 and MDQ, the bipolar index scale not only focuses on clinical symptoms or manifestations, but also involves family history, course of illness characteristics and treatment response[9,10], which is similar to soft bipolar diagnostic criteria that involves clinical manifestation,first onset age,family history, personality characteristics and treatment response[11, 12].The diagnostic criteria of soft bipolar had been established in China and also been revised after DSM-5 and relation to bipolarity index [13]. But bipolarity index seems to have more diagnostic specificity than HCl-32 [14,], mainly because it collects more relevant information than HCL-32 and MDQ that are more closely related to the diagnosis of bipolar disorder. The result showed that bipolarity index had 100% specificity in diagnosis of bipolar disorder, which indicates that bipolar index scale may have more specific significance in the diagnosis of bipolar disorder [14].Their finding indicates good reliability and validity for the Chinese version of the BPx, which encourages its use as a measure of diagnostic confidence for bipolar spectrum disorders. Further prospective study is necessary to determine if the BPx is useful in identifying subgroups among MDD subjects at high risk for conversion to BPD[6,14].

Chinese scholars have made special research on different items of bipolar index scale, and also put forward its diagnostic value [10,15] They found the Chinese version of bipolarity index scale had high reliability and validity. With defined cut-off score,it can help early recognition of bipolar disorder and provide a new evaluation tool for clinical psychiatry[15]. Since Chinese scholars translated and introduced bipolar disorder into China, many clinical studies have been carried out to evaluate the clinical value of bipolar index scale [16,17,18]. These studies all indicated that there was a higher sensitivity and specificity in screening bipolar by bipolar index, and the patients with positive family history,more episodes and first episode with younger age tend to getting higher bipolarity index score.But these studies also different in diagnostic value,such as sensitivity , specificity,accuracy,positive predictive value(PPV) and negative predictive value(NPV)[14,15,16,17,18].

Bipolar disorders (BDs) are often not recognized with potentially drastic consequences for the individuals and their families. It was very important that diagnostic scale was used in clinic.But the study results of diagnostic scale for bipolar disorder should been concluded and analyzed.Despite some limitations, using the HCL-32 as a first screening in patients seeking help for depression can be recommended, but should never be used on its own for diagnosing by meta-analysis[19]. They also suggested future research should examine whether screening properties can be improved by developing an algorithm incorporating the negative consequences reported for different areas in the HCL-32.A systematic review and meta-analysis of accuracy studies for

the bipolar spectrum diagnostic scale (BSDS), the hypomania checklist (HCL-32) and the mood disorder questionnaire (MDQ) were also performed[20].Although accuracy properties of the three screening instruments did not consistently differ in mental health care services, the HCL-32 was more accurate than the MDQ for the detection of type II BD. It means that meta-analysis of diagnostic scales may found some new results.This study just is meta-analysis about the data of clinical studies in China in the past, and analyzes the diagnostic value of bipolar index scale again.

Methods

1. Literature retrieval methods:

1.1This study was performed according to the recommendations of the Moose [20]. Two reviewers independently searched the database.The database includes all Chinese databases: Chinese Biomedical Database (CBM), China National Knowledge Infrastructure (CNKI), WANFANG and Chinese Social Sciences Citation Index (VIP) databases .

1.2 Search key words: Bipolar index ; bipolar disorder (mood disorder ,mania,bipolar depression,depression).

1.3 The search strategy:The search strategy was based on combinations. To retrieved all articles,we search papers by “Bipolar index and bipolar disorder(or mood disorder or mania or bipolar depression or depression”, And then further screen the papers related.Last query was updated on July 31 2004 to July 31 2020.References of retrieved articles were cross-searched to identify any studies missed by the electronic search strategies.see figure 1.

1.4 Inclusion and Exclusion Criteria

The two researchers reviewed the initial retrieved publications independently. The discrepancy was resolved through discussion by all reviewers. Studies that met the following criteria were included: (1) study about bipolar index in use for diagnosis of bipolar disorder or (2) study about bipolar index in screen for diagnosis of bipolar disorder in clinical study or . (3)study about bipolar index in use for diagnosis of bipolar disorder in patients with depression or ; (4) study about bipolar index in use for diagnosis of bipolar disorder in other affection patients; and(5)study paper is written in Chinese.However, articles had incomplete or unidentified data were excluded, as well as abstracts, reviews, case reports, letters and duplicate publications.

1.5 Two psychiatrists reviewed each included article independently, using the 11-item checklist that was recommended by the Agency for Healthcare Research and Quality (AHRQ) [21]. An item would be scored ‘0’ if it was answered ‘NO’ or ‘UNCLEAR’ whereas ‘1’ will be given to the answer ‘YES’. Article quality was assessed as follows: low quality = 0–3; moderate quality = 4–7; high quality = 8–11. Differences in article quality were discussed to reach an agreeable final score. The following information was extracted: first author, publication time, the sample size, study population, assessment tools, and the number related to number about sensitivity,specificity,accuracy,PPV and NPV.See table 1.

1.6 Statistic analysis:All statistical analyses were performed using Statistical Analysis System software (Revman 5.2), and the P value for the overall effect <0.05 with two-tailed was considered statistically significant. The heterogeneity of all involved studies was assessed by I2. When it was lower than 50%, the studies with an acceptable heterogeneity were considered, and then the fixed-effects model with Mantel-Haenszel method was used; otherwise, a random effect model with the Der Simonian and Laird (DL) method was adopted.

1.7Assessment of publication bias was investigated for each of the pooled study groups mainly by the Egger’s linear regression test. As supplement approach, the Begg’s rank correlation also was applied to assess the potential publication bias.

Results

5 studies, with 1237 subjects, met the inclusion criteria and were included for the final meta-analysis. The 1237 subjects all were studied as samples diagnosed bipolar disorder or no bipolar disorder. The sample size of the studies ranged from 75 to 727. Assessment tools used in the studies are the revision of the Chinese version BI[6] The main features of the 5 articles were summarized in Table1. AHRQ scores suggested that all 5 studies scored at eight as high quality.

A total of 1237 subjects were included in 5 studies. Random effect model is used to account for the data by Revman 5.2. The results showed that the sensitivity of BI in diagnosis for BD was 0.93 (95% CI: 0.93–1.00), see figure2. The specificity was 0.85 (95% CI: 0.69–0.96),see figure 3. The accuracy was 0.86 (95% CI: 0.77–0.93),see figure 4.The positive predict value was 0.74(95% CI: 0.53–0.91),see figure 5.The negative predict value was 0.95 (95% CI: 0.81–1.00), See figure 6.

Significant heterogeneity was detected across studies regarding these incidence estimates,which all were higher than 90%.

Assessment of publication bias for each of the pooled study groups mainly by the Egger’s linear regression test and the Begg’s rank correlation was not investigated because of smaller sample size than 9.

Discussion

Rates of misdiagnosis between major depressive disorder and bipolar disorder have been reported to be substantial, and the consequence of such misdiagnosis is likely to be a delay in achieving effective control of symptoms, in some cases spanning many years. Particularly in the midst of a depressive episode, or early in the illness course, it may be challenging to distinguish the 2 mood disorders purely on the basis of cross-sectional features. To date, no useful biological markers have been reliably shown to distinguish between bipolar disorder and major depressive disorder[23]. So,It maybe feasible to

nomenology,which include age of onset, symptoms,response to treating drug,such as mood stabilizer,atypical

antipsychotics,or antidepressant.Inspired by clinical experience and driven by an intent to assign a “bipolar profile” to the individual treatment-seeking patient with a probable mood disorder, experienced investigators in the field of BD created the bipolarity index (BI) in 2004 [24]. The BI is a 0–100 continuous scale that covers five illness dimensions with a maximum of 20 points per domain: I. signs and symptoms; II. age of onset; III. course of illness; IV. response to treatment, and V. family history. “Classic” BD according to the authors of the BI would be characterized by: I. at least one euphoric manic episode; II. early age of onset; III. recurrent and fully remitting illness course; IV. positive response to a mood stabilizer; and V. having a first-degree family member with BD. The five dimensions of the BI highlight that the conceptualization of “bipolarity” that underlies the BI goes beyond the mere symptomatic assessment of lifetime affective symptoms, as the DSM-IV categorization requires. Instead, the authors of the BI added additional state and trait variables, based on their clinical experience and on the earlier theories of Kraepelin[7]. By doing so, the BI represents a broader view of mood disorders that is now termed “bipolarity”, that represents a more conservative view of the classic conceptualization of mood disorders, which Kraepelin considered to include risk for shifts to elevated mood states. Hence, it is well possible that the BI estimates a latent trait of bipolarity that may become apparent as bipolar conversion at a later stage in those with a lifetime UD. Studies into the concurrent validity of the BI against a lifetime DSM-IV classification of BD, although potentially flawed by observer bias[25] as the diagnosis of BD and BI answers are often provided by the same clinician, found good to excellent metrics [5, 6, 26].So comprehensive analysis of BI for diagnosis is needed,which also was original intention of this study,although it was just in China.

In China, many psychiatrists are interested in the application of BI in the diagnosis of bipolar disorder, and have carried out a series of related studies. The most studies support the important diagnostic function of BI,although these studies have some different conclusions. Therefore, it is meaningful to evaluate the results comprehensively, which is the original intention of our study[14-18].

This studies, with 1237 subjects, met the inclusion criteria and were included for the final meta-analysis. The sample size of the studies ranged from 75 to 727. Assessment tools used in the studies are the revision of the Chinese version BI[6]The result in this study found that the sensitivity of BI for diagnosis of BD was 0.93 (95% CI: 0.93–1.00), the specificity was 0.85 (95% CI: 0.69–0.96). the positive predict value was 0.74 (95% CI: 0.53–0.91).the negative predict value was 0.95 (95% CI: 0.81–1.00).and accuracy was 0.86 (95% CI: 0.77–0.93). Just according to the data of study, BI was ideal tool of diagnosis for BD.In fact,same result also showed in other study outside of China[5, 7,26] This also was found that significant heterogeneity was higher across studies regarding these incidence estimates,which means that we must interpret the results with caution and also put attention to this result.

Compared to other assist diagnostic scale for diagnosis of BD,such as, HCL-32, MDQ, BSDS,BI include age of onset,family history,response to treatment and course of illness .Mosolov
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s study found that at a cut-off of ≧50, the Bipolarity Index had a high sensitivity (0.91) and specificity (0.90)[5].Ma`s study found that the cut-off score between the MDD and BPD groups was 42.0, with a sensitivity of 0.957 and specificity of 0.881 (Z = 63.064, P < 0.001); the cut-off score between the MDD and BPD II groups was 34.0, with a sensitivity of 0.810 and specificity of 0.855 (Z = 20.174, P < .001); and the cut-off score between the BPD II and BPD I groups was 57.0, with a sensitivity of 0.680 and specificity of 0.772 (Z = 9.636, P < 0.001)[6].Wendela G. ter Meulen and their colleagues found each point increase in BI score significantly predicted incident BD (HR [95%CI]= 1.047[1.018–1.076], p = 0.001). At the optimal cut-off of 30, sensitivity was 67%, specificity 52%, PPV 3% and NPV 98%[7].These indicated that BI had special role in diagnosis of BD and maybe more useful than HCL-32,MDQ[5,6,7,26]

The age of onset was paid attention in BI,in which younger is years old of first onset, higher is scale,such as score is 20 when age of first onset was 15-19 years old[24].It also means younger is years old of first onset,higher possibility of BD is it.The current many studies discussed the diagnosis of bipolar disorder in children throughout the years as it has evolved, focusing on very early-onset and early-onset bipolar disorder. Proper care of children with bipolar disorder requires a thorough understanding of the subtleties in symptoms at different developmental ages, as well as a shift in diagnostic thinking, which grew to include disruptive mood dysregulation disorder (DMDD)[27].This also means age of onset maybe have a etiological value.In fact,in clinical practice,early age of onset was found to be associated with longer delay to treatment (Hedges' g=0.39, P=.001), greater severity of depression (Hedges' g=0.42, P<.001), and higher levels of comorbid anxiety (OR=2.34, P<.001) and substance use (OR=1.80, P<.001)[28]. So attention about age of onset be not only needed in BI, but also be needed in clinical psychiatry.

Recurrent distinct manic episodes separated by periods of full recovery was described in BI with 20 score,which was a special course of illness, and comorbid substance abuse was given 10 score,Recurrent unipolar MDD with three or more major depressive episode was given 5 score[24].A study found that among patients with a current diagnosis of RDD, 40.8% had a diagnosis of bipolar disorder (bipolar I disorder: 4.9%; BD-II: 35.9%)[26].Certain risk factors such as the young age of onset and greater episode frequency are useful predictors of bipolar diatheses. Substance use disorder comorbidity is more prevalent in males whereas depression and suicidal behaviours are more frequent in females with BD. Comorbid anxiety and personality disorders also encumber the illness course[29].It means that attention of illness course will not only help diagnosis of BD,but also understand the traits of BD.

Worsening dysphoria or mixed symptoms during antidepressant treatment subthreshold for mania was given 10 score in BI[24],which was actually about sue of antidepressant in bipolar depression and mixed episode.It is very controversial issues in psychopharmacology.The study found the rate of manic switch in AD-m (Antidepressant monotherapy) was significantly higher than the AD-c(Antidepressant combination) AD-c group[30]. It suggests that the risk of manic switch is especially prominent in the first months of AD use. Antidepressants use in combining it with a mood stabilizers (MS) may not be adequate in preventing switches in shorter terms. However, in longer term uses addition of MS to ADs may decrease the risk of switches.The correct selecting adjunctive second-generation antidepressant therapy with a mood stabiliser or an atypical antipsychotic in treatment for bipolar depression[31].The key point is switching to mania in the treatment of unipolar depression,which had been solved in DSM-5 that can be diagnosed as BD[32]. Antidepressant-induced mania or hypomania in first edition of soft bipolar criteria was very important item[11],but was revised out of second criteria of soft bipolar because of publication DSM-5[13].

The 20 score was assessed in item of “at least one first-degree relative with documented bipolar illness”in BI and 10 score was assesses in item of “first-degree relative with documented recurrent unipolar MDD or schizoaffective disorder or any relative with documented bipolar illness of any relative with documented recurrent unipolar MDD and behavioural evidence suggesting bipolar illness”[24]. It suggest that bipolar disorder had heavier genetic load. More and more evidence support the fact that a significant relationship exists between the degree of kinship and the heritability of bipolar disorder.In fact,positive family history have higher diagnostic specificity for BD[13,32],A dimensional definition based on 3 or more hypomanic symptoms during depression was the most supported by using bipolar family history as validator[32]. At same time, Patients reporting family history of a mood disorder had an earlier age at onset of depression/mania, more phases, rapid cycling and more suicide attempts. Across different assessments, patients with family history showed consistently elevated depressive symptoms, such as lower concentration and energy, higher suicidal ideation, as well as increased racing thoughts and distractibility within the manic spectrum of symptoms[33].

This study was first analysis about BI in diagnosis for bipolar disorder,which maybe indicate that BI was a important assist diagnostic scale for diagnosis of BD,although a comprehensive meta-analysis of accuracy studies about MDQ,HCL-32,BSDS had been finished to screen bipolar spectrum disorders[20].It maybe BI include more information compared to MDQ,HCL-32,BSDS

This study had several limitations. Firstly, the sample size of this meta-analysis was relatively small. Only 5 studies and 1237 subjects were involved. It is difficult to reflect the BI value in clinical psychiatry in China. Secondly, collecting data style may influence the result of investigation, for example,different cut-off can get different detection rate of sensitivity,specificity,PPV,NPV and accuracy . so it was very import to establish a same cut-off or sub-analysis according different cut-off.Thirdly, not all the studies had same diagnostic criteria of BD, which maybe a very important factor affecting sensitivity,specificity,PPV,NPV and accuracy. Fourthly, it is notable that studies included in this meta-analysis had high heterogeneity and also had certain bias in data,which can not been reflected by Egger’s linear regression test and Begg’s rank correlation because of smaller sample size.These factors are partly responsible for the prospective heterogeneity source of sensitivity,specificity,PPV,NPV and accuracy. also affect us to see the real significance of BI in clinical psychiatry and difference with other assist diagnostic scale.

Conclusions

A total of 1237 subjects were included in 5 studies. Random effect model is used to account for the data by Renvman 5.2. The results showed that the sensitivity of BI in diagnostic was 0.93 (95% CI: 0.93–1.00), the specificity was 85% (95% CI: 0.69–0.96). the positive predict value was 74% (95% CI: 0.53–0.91).the negative predict value was 95% (95% CI: 0.81–1.00).and accuracy was 86% (95% CI: 0.77–0.93). Significant heterogeneity was detected across studies regarding these incidence estimates. The idea diagnostic value of BI was found. although the significant heterogeneity detected in studies.We must interpret the results with caution and also put attention to this result,which include comparison to other diagnostic scale,perfecting sue of BI in clinical psychiatry,for example,personality and temperament also maybe a important factor that not involved in BI.

Abbreviations

BD=bipolar disorder

MDD=major depression disorder

MDQ=Mood Disorder Questionnaire

DSM-5=Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition

HCL-32=**hypomania checklist-32**

PPV=positive predictive value

NPV=negative predictive value

BSDS=bipolar spectrum diagnostic scale

CBM=Chinese Biomedical Database

CNKI=China National Knowledge Infrastructure

CSSCI=Chinese Social Sciences Citation Index (VIP)

RDD=recurrent depressive disorder

DMDD=disruptive mood dysregulation disorder

Declarations

Ethics approval and consent to participate

Not Available

Consent to publication

All authors agree to publish our paper and no conflict in any interests.

Availability of data and material.

See Table1

Competing interests

There were not any financial and non-financial competing interests.

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Authou's contribution

Our authors have different contributions to this article. Dr SFL participated in collection of data and the writing of the article, Dr SFL and Dr ZJF assessed the quality of researched papers. Dr ZJF complete most statistic analysis.All authors reviewed all researched paper. Prof.JWD participated in the design , statistical processing and the final revision of the article.

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Tables

Table1 Characteristics of studies included in the meta-analysis

Author	Cases	participants	BI	Diagnostic criteria and other assist tool	Index	Quality score
Ma[16]	727	BD,BD-II,MDE	BI(Chinese version)	DSM-IV-TR	Sensitivity Specificity Accuracy	8
Zhu[14]	95	BD,MDE	BI(Chinese version)	DSM-IV HCL-32	Sensitivity Specificity Accuracy	8
Guo[15]	176	BD,MDE	BI(Chinese version)	MINI,ADE	Sensitivity Specificity Accuracy PPV NPV	8
Li[17]	120	BD,MDE	BI(Chinese version)	DSM-5 ICD-10	Sensitivity Specificity Accuracy PPV NPV	8
He[18]	120	BD,RMDD	BI(Chinese version)	DSM-IV,MINI	Sensitivity Specificity Accuracy	8

BD=Bipolar Disorder;MDE=Major Depression Episode;BI=Bipolarity Index;MINI=Mini-international neuropsychitric interview;

DSM-IV=American diagnostic and statistic manual of mental disorders,4th edition;RMDD=Recurrent major depressive disorder;

ADE=Affective disorder evaluation.

Figures

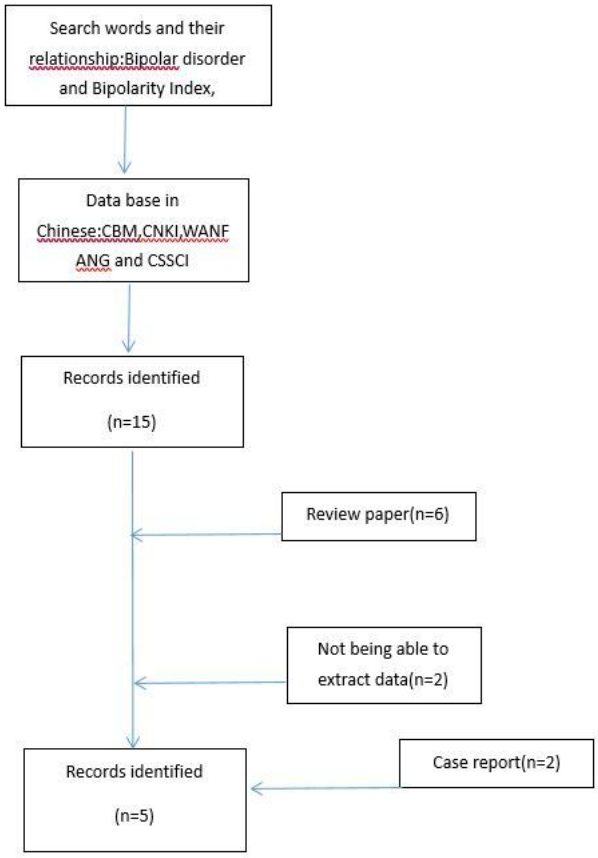

Figure 1

Flowchart of selection of studies for inclusion in meta-analysis

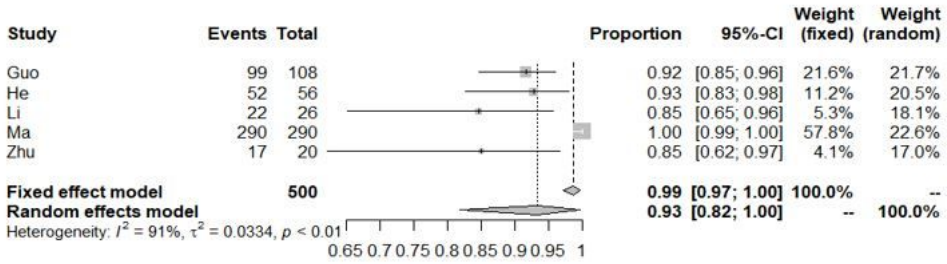

Figure 2

pooled sensitivity of meta-analysis in 5 studies

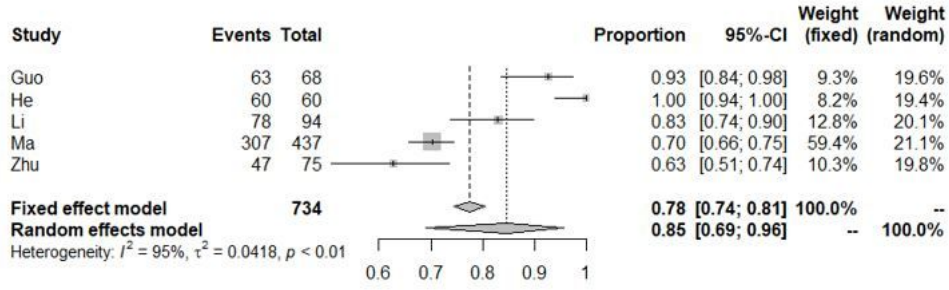

Figure 3

pooled specificity of meta-analysis in 5 studies

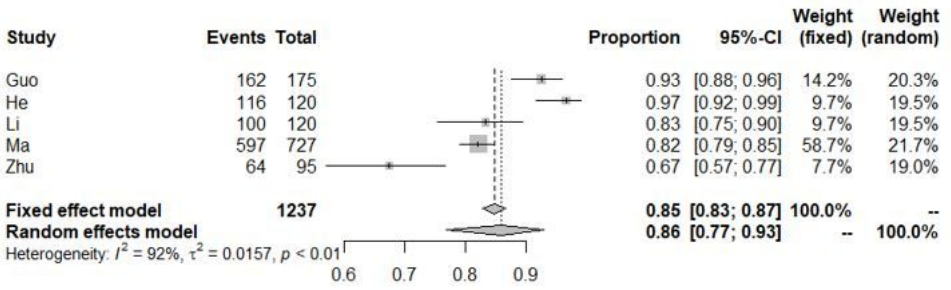

Figure 4

pooled accuracy of meta-analysis in 5 studies

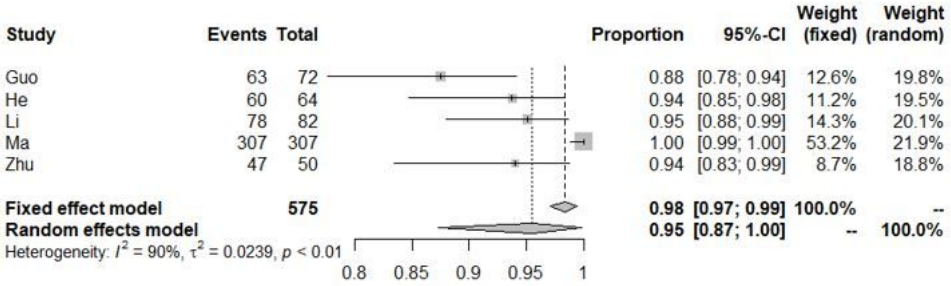

Figure 5

pooled PPV of meta-analysis in 5 studies

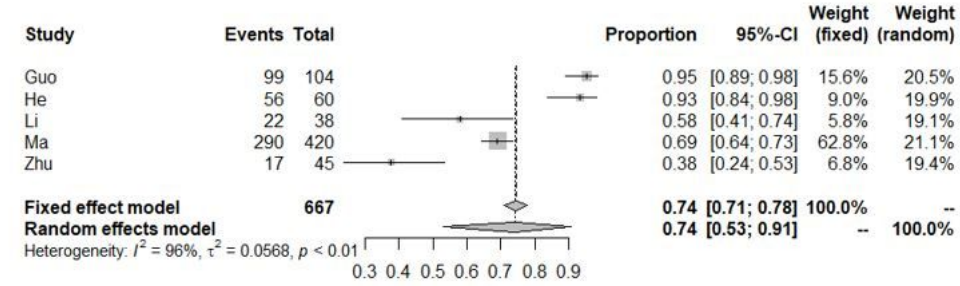

Figure 6

pooled NPV of meta-analysis in 5 studies