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Diagnostic accuracy of the ID-Migraine: a systematic review.

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Diagnostic accuracy of the ID-Migraine: a systematic review and meta-analysis

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3-4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5-6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	NA
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8-9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8-9



PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8-9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	10;27
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10; 22-25
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	11
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	29-30
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	11-13;26
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	11;28
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	12
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	14-15
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	15-16
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	2

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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Diagnostic accuracy of the ID-Migraine: a systematic review and meta-analysis

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Conflict of interest: no conflict

Keywords: ID-Migraine, migraine disorders, sensitivity and specificity

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4
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6
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9 and RCSI Medical School, Dublin.
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16 **Abbreviations**

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19 IHS - International Headache Society
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23 QUADAS- Quality of Diagnostic Accuracy Studies
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27 95% CI – 95% Confidence Interval
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30 ROC curve – Receiver Operating Characteristic curve
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Abstract

Objective: The purpose of this systematic review with meta-analysis is to determine the diagnostic accuracy of the ID Migraine as a decision rule for identifying patients with migraine.

Background: The ID Migraine screening tool is designed to identify patients with migraine in primary care settings. Several studies have validated the ID Migraine across various clinical settings, including primary care, neurology departments, headache clinics, dental clinics, ENT and ophthalmology.

Method: A systematic literature search was conducted to identify all studies validating the ID Migraine, with the International Headache Criteria as the reference standard. The methodological quality of selected studies was assessed using the Quality of Diagnostic Accuracy Studies tool. All selected studies were combined using a bivariate random effects model. A sensitivity analysis was also conducted, pooling only those studies using representative patient groups (primary care; neurology departments; and headache clinics) to determine the potential influence of spectrum bias on the results.

Results: Thirteen studies incorporating 5,866 patients are included. The weighted prior probability of migraine across the thirteen studies is 59%. The ID Migraine is shown to be useful for ruling out rather than ruling in migraine, with a greater pooled sensitivity estimate (0.84, 95% CI 0.75 – 0.90)

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3 than specificity (0.76, 95% CI 0.69 – 0.83). A negative ID Migraine score reduces the probability of
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5 migraine from 59% to 23%. The sensitivity analysis reveals similar results.
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11 **Conclusions:** This systematic review quantifies the diagnostic accuracy of the ID Migraine as a brief,
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13 practical and easy to use diagnostic tool for Migraine. Application of the ID Migraine as a diagnostic
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15 tool is likely to improve appropriate diagnosis and management of Migraine sufferers.
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Background

Migraine is a common disorder affecting approximately 18% of women and 6-8% of men.¹⁻² Despite the prevalence and burden of migraine,³⁻⁵ less than half of current migraineurs have ever received a medical diagnosis of migraine,² with only one-third receiving migraine-specific prescription medications.⁶⁻⁷ Recognizing and diagnosing migraine is challenging for a number of reasons, including low rates of medical consultation specifically for headache. Less than half of migraineurs, even those with highly disabling headaches, consult a doctor for a complaint of headache.² Increasing patient consultation for headache and improving the accuracy of clinical diagnosis is important to improve the quality of life for many individuals who are not diagnosed or treated appropriately for migraine.⁸

Taking a thorough case history is the single most important factor when assessing patients with headache, allowing for the identification of a headache diagnosis and determining the treatment plan. The International Headache Society (IHS) developed a comprehensive headache classification system in 1988 which includes diagnostic categories of migraine with and without aura⁹; this system was updated in 2004.¹⁰ However, this classification system has been criticised for being too cumbersome for primary care or generalist physicians to apply.¹¹ Therefore efforts have been made to develop a more efficient method of diagnosing migraine than the full IHS criteria. A previous review demonstrated the diagnostic utility of various individual symptoms (including nausea, photophobia, phonophobia, exacerbation by physical activity, and aura) in the diagnosis of migraine using the IHS criteria as the reference standard for diagnosis.¹² However, as migraine is a symptom complex, it is unlikely that any one symptom identified in the clinical examination will be sufficient

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3 to rule in or out the condition. US researchers addressed this limitation developing the three item
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5 Identification of Migraine (ID Migraine), a brief, self-administered clinical prediction rule for adults,
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7 which they then validated prospectively.¹³ The three items relate to presence of photophobia,
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9 nausea and disability (inability to work, study or do what you needed to do for at least one day). A
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11 patient scores positive for migraine if they endorse two of the three items on the ID Migraine.
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13 However, as this tool was derived as a screening tool to identify migraine in primary care settings,
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15 two pre-screening items are included to identify eligible patients for the ID Migraine test. Firstly,
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17 patients must report two or more headaches in the previous three months. Secondly, patients must
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19 indicate that they wish to speak to a healthcare professional about their headaches or that they have
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21 experienced a headache that had limited their ability to work, study or enjoy life.¹³ Several studies
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23 have validated the ID Migraine screening tool since its derivation in 2003. The aim of this study is
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25 to perform a comprehensive systematic review and meta-analysis of validation studies of the ID
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27 Migraine to determine its accuracy as a decision rule for identifying patients with migraine.
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Methods

Search strategy

The PRISMA guidelines for the reporting of systematic reviews and meta-analyses were followed to conduct this review.¹⁴ We aimed to identify all studies validating the ID Migraine irrespective of setting. A systematic literature search was conducted in November 2010 and included the following search engines: the Cochrane Library, EMBASE and PubMed. A combination of the following keywords and MeSH terms were used: ‘migraine disorders’, ‘ID Migraine’, ‘sensitivity and specificity’, ‘diagnose/diagnosis/diagnostic/diagnosis, differential’ This search was supplemented by handsearching references of retrieved articles and searching Google Scholar. No restrictions were placed on language.

Study selection and data extraction

Studies were included if they met the following inclusion criteria: 1) validate the ID Migraine using the IHS criteria as the reference standard⁹⁻¹⁰; 2) use a cohort or cross-sectional study design; 3) include sufficient data to allow for the calculation of sensitivity, specificity, negative and positive predictive values and the prevalence of migraine. Studies that included patients with a chronic disease, were excluded from the analysis. Data was extracted on study setting, pre-screening items used, patient characteristics and prevalence of migraine. The number of true positives, false positives, true negatives and false negatives for the ID Migraine were also extracted from each validation study and a 2 x 2 table was constructed. Authors were contacted to provide further information when there was insufficient detail in an article to construct the 2 x 2 table.

Quality assessment

The methodological quality of the selected studies was evaluated independently by two reviewers (GC & SH) using the Quality of Diagnostic Accuracy Studies (QUADAS) tool, a validated tool for the quality assessment of diagnostic accuracy studies.¹⁵⁻¹⁶ This tool was modified to ensure appropriateness for the present study and included 13 of the 14 questions from the QUADAS tool. If no consensus was achieved studies were evaluated by a third independent reviewer (TF).

Data synthesis and analysis

A bivariate random effects model was used to estimate summary estimates of sensitivity and specificity and their corresponding 95% confidence interval. Positive and negative likelihood ratios were also reported. This approach was used as it preserves the two-dimensional nature of the original data and takes into account both study size and heterogeneity beyond chance between studies.¹⁷ Using Bayes theorem the post-test odds of migraine were also estimated by multiplying the pretest odds by the likelihood ratio, where pre-test odds are calculated by dividing the pre-test probability by (1-pre-test probability) and the post-test probability equals post-test odds divided by (1 + post-test odds).¹⁸

We also plotted the individual and summary estimates of sensitivity and specificity for the ID Migraine in a summary receiver operating characteristic (ROC) graph, plotting the mean sensitivity (true positive) on the y-axis against 1- specificity (false negative) on the x axis. We also plotted the 95% confidence region and 95% prediction region around the pooled estimates to illustrate the

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2
3 precision with which the pooled values were estimated (confidence ellipse around the mean value)
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5 and to illustrate the amount of between study variation (prediction ellipse). We assessed
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7 heterogeneity visually using the summary ROC plots and statistically by using the variance of logit
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9 transformed sensitivity and specificity, with smaller values indicating less heterogeneity among
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11 studies.
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15 We used Stata version 10.1 (StataCorp College Station, Tx, USA), particularly the metandi
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17 commands for all statistical analyses.
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Results

Study Identification

A flow diagram of the search strategy is presented in Figure 1. Two researchers (SH, GC) screened all potential articles. The search strategy yielded 4,111 papers of which 4,091 were excluded based on their title or abstract. Eleven of the remaining 20 articles met the inclusion criteria and were selected for analysis.^{13, 19-28} However, one article contained information on three different study groups, thus resulting in thirteen studies for inclusion.

INSERT FIGURE 1 HERE

Study characteristics

Table 1 summarizes the characteristics of the included studies. One study was based in the US¹³, three in Italy^{19, 23-24}, one in Portugal²⁰, four in Turkey^{21, 25-26, 28}, one in Korea²² and one in Singapore²⁷. The mean weighted prior probability is 59.1%. The included studies range in size from 37²⁴ to 1,816²¹ participants. A total of 5,866 participants are included in the analysis.

INSERT TABLE 1 HERE

Study Quality

The summary diagram of the quality assessment is shown in Figure 2. The overall quality of the included studies is moderate to good. However, it is unclear whether test review bias was avoided in twelve of the thirteen studies as it was not explicitly stated that the results from the ID Migraine were interpreted without the knowledge of the reference standard (IHS criteria). It was also unclear whether the IHS criteria was interpreted blind to the results of the ID Migraine in five studies. Furthermore, ten studies did not clearly report the time difference between assessing patients using the ID migraine and the IHS criteria. Finally, spectrum bias is also identified as a potential source of bias in seven studies as they include patients who are not representative of patients who will receive the ID Migraine in primary care, neurology departments or headache clinics. In order to determine the potential influence of spectrum bias on the meta-analysis, a sensitivity analysis was conducted, pooling only those studies using representative patient groups (primary care; neurology departments; and headache clinics i.e. similar to the setting of intended use of ID Migraine).^{13, 19-21, 27-28}

INSERT FIGURE 2 HERE

Diagnostic test accuracy of all included studies

The pooled sensitivity, specificity and the respective variance of the logit-transformed sensitivity and specificity for the thirteen studies are presented in Table 2. The positive and negative likelihood ratios are also presented in Table 2. These results indicate the diagnostic utility of the ID migraine in ruling out rather than ruling in migraine, with a greater sensitivity (0.84, 95% CI 0.75-0.90) than

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3 specificity (0.76, 95% CI 0.69-0.83). Using Bayes theorem a positive score on the ID Migraine
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5 increases the pre-test probability from 59% to 84%, whereas a negative ID Migraine score reduces
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7 the probability of migraine to 23%.
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17 The individual and summary estimates of sensitivity and specificity, the 95% confidence region and
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19 95% prediction region are presented in a ROC graph in figure 3. The 95% confidence region is
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21 narrow thus indicating precision of the pooled estimate. The prediction region (amount of variation
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23 between studies) is wider thus suggesting heterogeneity across studies. The heterogeneity is greater
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25 in relation to sensitivity estimates compared to specificity, with a smaller variance of the logit-
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27 transformed specificity (Table 2).
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32 INSERT FIGURE 3 HERE
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39 *Sensitivity analysis*

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41 The pooled sensitivity, specificity and the respective variance of the logit-transformed sensitivity and
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43 specificity for the sensitivity analysis, which pools data from 6 studies are presented in Table 2. The
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45 positive and negative likelihood ratios are also displayed. The mean weighted prior probability of
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47 migraine for the 6 included studies is 60%. As with the previous analysis, the ID Migraine is found
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49 to be greater at ruling out migraine, with a sensitivity of 0.88 (95% CI 0.75-0.93). Similar to the
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51 previous analysis a positive score on the ID Migraine increases the pre-test probability from 60% to
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53 82%, whereas a negative ID Migraine score reduces the probability of migraine to 21%. The
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variation between studies is greater for sensitivity as in the previous analysis pooling all thirteen studies. The variance of the logit-transformed specificity is also smaller than that of the previous analysis pooling all thirteen studies. (Table 2). The summary ROC graph is displayed in figure 4.

INSERT FIGURE 4 HERE

For Peer Review

Discussion

Principal findings

This systematic review shows that the ID Migraine is a useful tool, particularly for ruling out migraine, in symptomatic patients with headache when assessed against the IHS criteria. A negative ID Migraine score, less than two positive responses, reduces the post-test probability of migraine from 59% to 23%. These results relate to various clinical settings including primary care, neurology, dental clinics, ENT, ophthalmology, workplace and school. The sensitivity analysis which removed those studies with potential to introduce spectrum bias, revealed similar results, supporting the use of the ID Migraine to rule out migraine in symptomatic patients presenting to primary care, neurology departments or headache clinics.

Context of previous studies

Previous reviews have sought to identify a more efficient method of diagnosing migraine than the full IHS criteria. One meta-analysis identified nausea, photophobia, phonophobia, and exacerbation of headache with physical activity as the best individual symptoms for ruling in or out migraine.¹¹ A more recent review examined the diagnostic utility of combinations of clinical features in identifying patients with migraine.¹² In this review only four studies examining combinations of clinical features were identified. In addition, each of the studies represented a different clinical prediction rule thus preventing any pooled analysis. Though ID Migraine was identified in this review, only the derivation study was reported. The present study's focus on the ID migraine allows us to determine the diagnostic accuracy of the ID migraine across a number of clinical settings and countries.

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7 *Strengths and limitations of this study*
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10 Following a systematic search we identified 13 studies validating the ID Migraine. This is the first
11 study to pool the various validation studies to determine the accuracy of the ID Migraine across
12 various clinical settings and countries. We conducted a sensitivity analysis to determine whether there
13 are any differences when restricting pooled analysis to settings similar to the intended use of the ID
14 Migraine (primary care; headache clinics; and neurology departments). Our findings show little
15 difference in the pooled estimates when restricting analysis to these three settings, thus supporting
16 the generalizability of the overall study findings.
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30 The results of this meta-analysis should be interpreted in the context of the study limitations. Firstly,
31 although migraine is more prevalent in women we do not know whether the diagnostic accuracy of
32 the ID Migraine varies as a function of gender. Unfortunately, the data were not available for men
33 and women separately. Secondly, methodological quality of the studies needs to be considered. For
34 example, ten studies did not clearly report the time between assessing patients using the ID Migraine
35 and the neurologists assessment using the IHS criteria. Finally, the pretest probability of patients
36 presenting to primary care or headache clinics with headache as the primary complaint is likely to be
37 lower than the mean weighted prior probability used in this analysis (60%). Ebell estimates a
38 prevalence of 33% to be a reasonable estimate for patients attending primary care with a
39 headache.²⁹ This is similar to the prevalence estimate of 38.2% reported in a study involving
40 patients attending their GP with a primary complaint of headache.²⁷
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3 The higher prevalence in several of the included studies is an artefact of study design as eight of the
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5 thirteen studies used additional pre-screening items (other than experienced a headache in the past
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7 three months), as recommended by Lipton. The most problematic pre-screening item recommended
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9 by Lipton is 'experience headache limiting your ability to work, study or enjoy life', as this exact
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11 item is also one of the three items on the ID Migraine. Therefore if a patient responds positively to
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13 this item at the pre-screening stage, that patient will automatically have a score of one on the ID
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15 Migraine before even taking the test. While pre-screening items are important it is not considered
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17 appropriate to use the same item at both the pre-screening and the screening phase. Furthermore,
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19 we question the appropriateness of the term pre-screening and screening in relation to the ID
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21 Migraine. It may be more useful to consider the ID Migraine as a two step rule, with the pre-
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23 screening items representing the screening phase and the three item ID Migraine representing the
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25 diagnostic phase that would then determine subsequent management (treatment and/or
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27 prophylaxis).
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37 *Implications for practice*

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40 The results of this study confirm the diagnostic utility of the ID Migraine as a brief, easy to use
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42 diagnostic tool. Following a positive score on the ID Migraine, a physician could consider starting
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44 their patient on migraine specific medication and monitor their response to treatment so ensuring
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46 that that symptoms improve or in the case of prophylaxis, migraine headache frequency is reduced.
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48 If a patient does not respond to treatment or prophylaxis it is possible that their result on the ID
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50 Migraine was a false positive and the patient will require further diagnostic assessment. On the other
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3 hand if a patient has a negative result on the ID Migraine, a physician can have greater certainty that
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5 the patient does not have a migraine, and can pursue alternative diagnoses.
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8 9 *Conclusions*

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11 Migraine is underdiagnosed and undertreated, in clinical care. This systematic review quantifies the
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13 diagnostic accuracy of the ID Migraine as a brief, practical and easy to use diagnostic tool for
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15 Migraine. Application of the ID Migraine as a diagnostic tool is likely to improve appropriate
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17 diagnosis and management of Migraine sufferers.
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Table 1: Characteristics of studies included in the review

Authors (country)	Study setting	Pre-screening items used	Participants: n, sex, mean age (range)	Prevalence of migraine †
Lipton et al 2003 (US)	Primary care	1) 2+ headaches in previous 3 months 2) Experienced headache limiting their ability to work, study, enjoy life OR Wish to speak to healthcare professional about their headaches	n=443 110men; 333 women 39.3 years (18-55)	79%
Brighina et al 2007 (Italy)	Headache centre*	1) 2+ headaches in previous 3 months 2) Experienced headache limiting their ability to work, study, enjoy life	n=222 59 men; 163 women 38.7 years (18-65)	67%
Gil-Gouveia et al 2010 (Portugal)	Headache outpatients	1) 2+ headaches in previous 3 months	n=131 21 men; 110 women 39.2 years (18-73)	63.4%
Karli et al 2007 (Turkey)	Neurology outpatients	1) 2+ headaches in previous 3 months 2) Experienced headache limiting their ability to work, study, enjoy life OR Wish to speak to healthcare professional about their headaches	n=1816 45.2 years	50.5%

1 2 3 4 5 6 7 8 9 10 11	Kim et al 2006 (Korea)	TMJ and orofacial pain clinic	1) 2+ headaches in previous 3 months 2) Experienced headache limiting their ability to work, study, enjoy life OR Wish to speak to healthcare professional about their headaches	n=176 33 men; 143 women 30.7 years (18-55)	18.8%
12 13 14 15 16 17 18 19 20	Di Piero et al 2007 (Italy)	Primary care	Sensitisation campaign stressing impact of headache on quality of life. People asked to respond if: 1) Suffered from headaches 2) Wish to speak to healthcare professional about their headaches	n=195 16% men; 84% women 40.5 years	92%
21 22 23 24 25 26 27 28 29	Di Paolo et al 2009 (Italy)	Dental clinic	No pre-screening questions applied	N=37 5 men;32 women 34 years	91.9%
30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49	Siva et al 2008 (Turkey)	Workplace	1) 2+ headaches in previous 3 months 2) Experienced headache limiting their ability to work, study, enjoy life OR Wish to speak to healthcare professional about their headaches	n=227 78 men; 149 women 31.9 years (18-55)	51.5%

1 2 3 4 5 6 7 8 9 10 11	Zarifoglu et al 2007 (Turkey)	School setting	1) 2+ headaches in previous 3 months	n=1014 14.67 years (12-17)	33%
12 13 14 15 16 17 18 19 20	Khu et al 2008 (Singapore)	Primary care	1) Patients consulting Gp with primary complaint of headache	n=584 25% men; 75% women 37 years (8-74)	38.2%
21 22 23 24 25 26 27 28 29	Ertas et al 2008 (Turkey)	Neurology outpatients	1) 2+ headaches in previous 3 months 2) Experienced headache limiting their ability to work, study, enjoy life OR Wish to speak to healthcare professional about their headaches	n=530 36.2 men; 63.8% women 46.5 years	63.8%
30 31 32 33 34 35 36 37 38	Ertas et al 2008 (Turkey)	Ophthalmology outpatients	1) 2+ headaches in previous 3 months 2) Experienced headache limiting their ability to work, study, enjoy life OR Wish to speak to healthcare professional about their headaches	n=228 41.9% men;58.1% women 47.3 years	65.4%
39 40 41 42	Ertas et al 2008	ENT	1) 2+ headaches in previous 3 months 2) Experienced headache limiting their ability to	N=263	54%

(Turkey)	outpatients	work, study, enjoy life OR Wish to speak to healthcare professional about their headaches	47.1% men; 52.9% women 43.3 years	
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*headache centres not requiring the additional pre-screening item as patients are referred to headache centre therefore seeking healthcare advice

† Mean weighted prior probability=59.1%

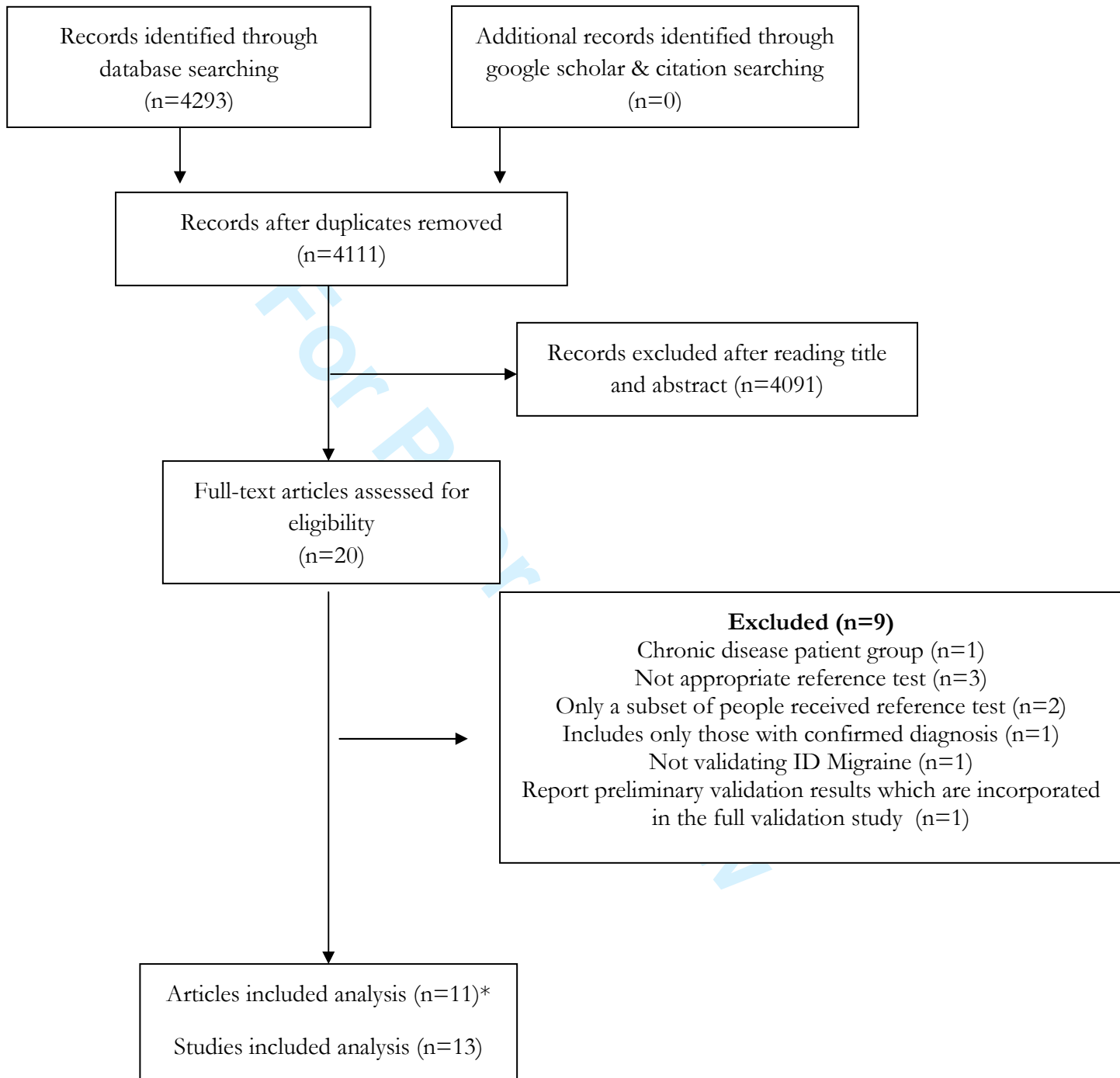
For Peer Review

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Table 2. Summary estimates of sensitivity, specificity and positive and negative likelihood ratio’s for all included studies and for sensitivity analysis

	No. of studies (patients)	Sensitivity (95% CI)	Variance Logit Sensitivity	Specificity 95% CI	Variance Logit Specificity	+ LR (95% CI)	-LR (95% CI)
ID Migraine <i>(All studies)</i>	13 (5,866)	0.84(0.75-0.90)	0.87	0.76(0.69-0.83)	0.39	3.55(2.76-4.57)	0.21(0.14-0.32)
ID migraine <i>(Sensitivity analysis)</i>	6 (3,142)	0.88(0.75-0.93)	0.87	0.71(0.63-0.78)	0.19	2.99(2.45-3.60)	0.17(0.11-0.33)

Figure 1. Search strategy



*One article contained data on 3 different settings

Figure 2. Quality assessment

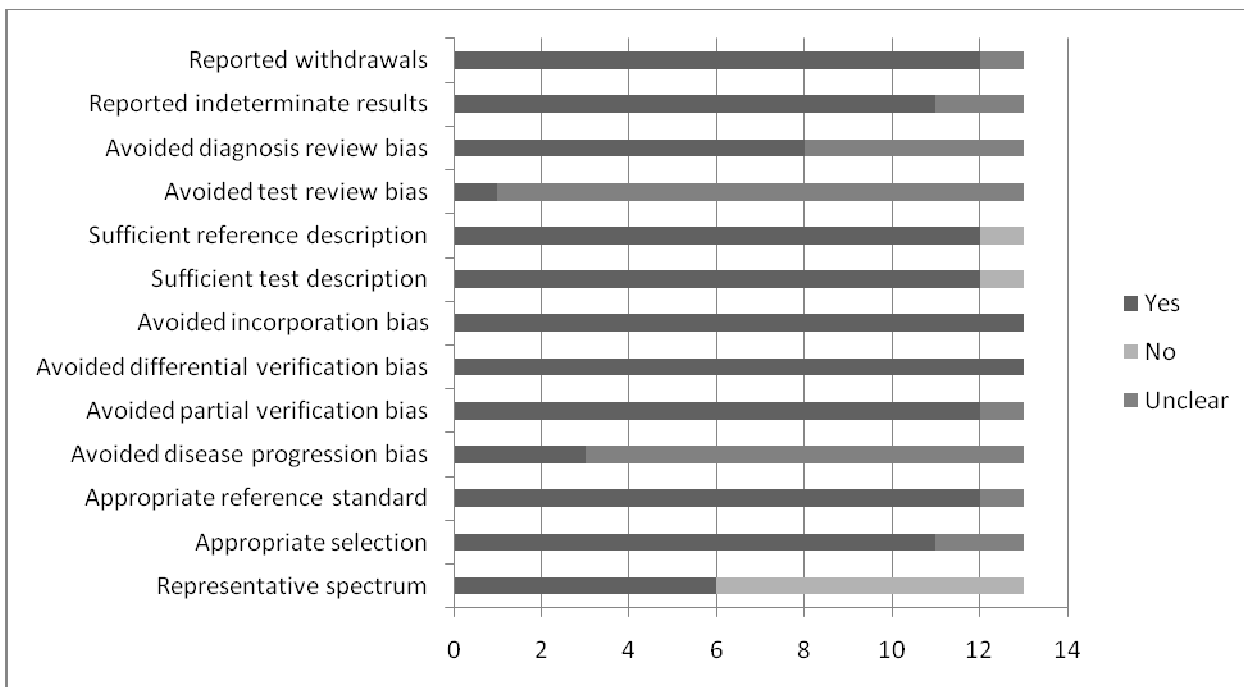
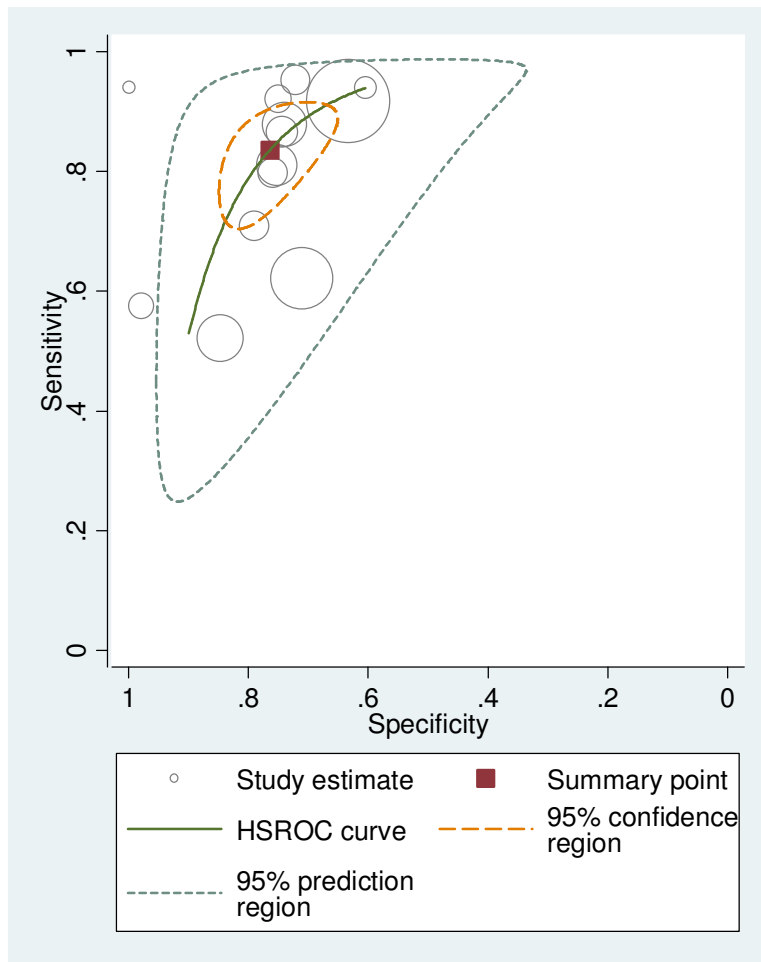


Figure 3. Receiver Operating characteristic graph with 95% confidence region and 95% prediction region for all included studies (n=13)



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Figure 4. Receiver Operating characteristic graph with 95% confidence region and 95% prediction region for sensitivity analysis (primary care; headache clinics; and neurology departments) (n=6)

