



TITLE: The ABCD2 Scoring System for Transient Ischemic Attacks: A Review of the Diagnostic Accuracy and Predictive Value

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CONTEXT AND POLICY ISSUES

Stroke is currently the third leading cause of death or disability in Canada.¹ Between the years of 1999 and 2002 there were 32,448 first time strokes in Canada, which results in an incidence of 14.4 in 10,000 and is 15 times more prevalent in people over the age of 80.¹ The economic burden associated with these conditions has been estimated at \$3.6 billion per year. In the United States studies have shown that approximately 23% of strokes are preceded by a transient-ischemic attack (TIA) and there are 240,000 TIAs diagnosed yearly.²⁻⁴

The classic definition of a TIA has been modified several times over the past 12 years. Initially it was defined as a rapid and recurrent onset of neurologic deficiency that lasts for less than 24 hours.⁵ The currently used definition was instituted in 2009 and is: “a transient episode of neurologic dysfunction caused by focal cerebral, spinal cord, or retinal ischemia, without acute infarction.”^{4,5} Correct diagnosis of TIA from mimic symptoms can be critical as more rapid medical intervention can lessen the risk of ischemic stroke.¹ The most common mimic symptoms are: seizures, migraines, metabolic disturbances, and syncope.⁵

The increased risk for stroke development post-TIA has led health-care providers to develop prediction tools to calculate the risk that a patient may succumb to subsequent ischemic events. Initial investigations resulted in the development of two scoring systems that utilize easily obtainable criteria for patient classification.² These are the California and ABCD scoring systems. Both of these predictive tools were developed to be able to determine the risk of stroke within seven days post-TIA. Considering that the highest risk of stroke occurs within 48 hours post-TIA, and that half of all the post-TIA strokes will occur within this time, experts sought to develop a novel scoring system for use in clinical diagnosis.³ In 2007 this resulted in the incorporation of the California and ABCD into the ABCD² prediction tool.^{2,3,6} The outcomes from this calculation produce scores between 0 and 7 and incorporate the following criteria:

- age >60 years (1 point),
- blood pressure >140/90 mm Hg (1 point),

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- clinical features unilateral weakness (2 points), speech disturbance (1 point), other symptoms (0 points),
- duration of symptoms >60 mins (2 points) 10-59 mins (1 point) <10 mins (0 points),
- diabetes mellitus (1 point).^{2,6}

Unfortunately over the past few years there are conflicting studies and reviews on the accuracy of the predictions that are given by the ABCD² system.^{7,8} Evidence has ranged from conclusions showing a high degree of accuracy to results that are comparable to chance.⁷ Accurately calculating the risk of stroke post-TIA is critical to determine how a patient should be treated and will also reduce the overall costs and stress on the health-care system that result from misdiagnosis.^{4,8}

The purpose of this report is to determine the diagnostic accuracy and predictive value of the ABCD² scoring system for identification of TIA and its capability for estimation of future stroke risk.

RESEARCH QUESTION

1. What is the diagnostic accuracy and predictive value of the ABCD² scoring system for the identification of transient ischemic attacks and estimation of future risk for stroke?

KEY FINDINGS

Evidence from systematic reviews suggests there is some predictive value to ABCD² scoring, but results are dependent on setting and method of scoring, with ABCD² performing more poorly in studies conducted in emergency department settings or when scores are determined by retrospective chart review in place of face-to-face evaluation. This is consistent with individual studies that show low predictive value in emergency department settings and lack of agreement in ABCD² scores between referring physicians and stroke specialists.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 1), University of York Centre for Reviews and Dissemination (CRD) databases. Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between December 01, 2009 and January 29, 2014.

Selection Criteria and Methods

One reviewer screened the titles and abstracts of the retrieved publications and evaluated the full-text publications for final article selection. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adults experiencing stroke-like symptoms/signs of transient ischemic attack
Intervention	ABCD ² scoring tool
Comparator	None
Outcomes	Accuracy for diagnosing a true TIA versus a seizure, migraine, or non-vascular event Predictive value - estimation of future risk of developing stroke Appropriate usage
Study Designs	Health technology assessments, systemic reviews, meta-analysis, randomized-controlled trials and non-randomized studies

Exclusion Criteria

Articles were excluded if they did not meet the criteria outlined in Table 1. Studies must also have been published between December 01, 2009 and January 29, 2014 and be in English. Finally articles were excluded if they were duplications of the same study.

Critical Appraisal of Individual Studies

Systemic reviews were assessed using the Assessment of Multiple Systemic Reviews (AMSTAR) tool.⁹ Randomized controlled trials (RCTs) and non-randomized trials were assessed using the Downs and Black checklist¹⁰ for the adequacy of allocation concealment, blinding of healthcare providers, clinicians, data collectors and outcome assessors, randomization, losses to follow-up, description of intention-to-treat, and early stopping of the trial. Numeric scores were not calculated, instead the strengths and limitations of included studies are described narratively.

SUMMARY OF EVIDENCE

Quantity of Research Available

The initial literature search identified 131 publications for investigation. After review of titles and abstracts 92 articles were rejected as not meeting the selection criteria and 39 publications were retrieved for full-text review. Of these, twelve were found to fulfill all of the required conditions. Two systematic reviews and ten non-randomized studies were included in this report. A PRISMA flow chart for paper selection is provided in Appendix 1.

Summary of Study Characteristics

Details of the characteristics of individual studies are provided in Appendix 2.

Systematic Reviews

There were two systematic reviews found from the literature search for this investigation. The first of these was completed in Ireland in 2011,³ and was conducted on patients >18 years old. The literature search was completed in July 2010 with the goal of determining the predictive value of ABCD² scoring for stroke prediction at seven and 90 days post-TIA. There were a total of 16 studies that met the requirements for paper inclusion representing a total of 8,482 patients. The included studies must have used the ABCD² scoring system and have been published in English.

The second review was published by Giles and Rothwell in 2010.¹¹ This investigation was conducted in the United Kingdom and searched literature published between January 2000 and July 2009. In addition they searched unpublished records from several different conferences and congresses. All studies where ABCD or ABCD² scoring was used were included. Papers were excluded if their outcomes were only available by dichotomized or trichotomized scores as these scores are potentially data dependent. The goal of this investigation was to systematically review both published and unpublished data to determine the predictive value and generalizability to different clinical settings and users. This review included 20 publications.

Non-randomized Studies

There were ten non-randomized studies found during the literature search for this investigation. These publications are made up of prospective or retrospective cohort studies from various regions. Seven of these studies used single-centre patient cohorts from individual hospitals. Of these seven, two were published in the United States of America,^{12,13} two in Iran,^{7,14} one in China,¹⁵ one in the United Kingdom,¹⁶ and the final one in Australia.¹⁷

Three multi-centre non-randomized studies were identified. The study conducted by Ghia et al. 2012¹⁸ was carried out using patient cohorts from two hospitals in an area in the United Kingdom. The final two investigations utilized cohorts from multiple sources. In the study produced in Italy,⁸ patients were found from one university hospital, one private hospital and 128 general practitioners.⁸ The final study conducted in Canada in 2014 and obtained its cohorts from 8 different Canadian emergency room departments.¹⁹

Many of the studies, including the systematic reviews, used receiver operator characteristic (ROC) area under the curve (AUC) as the outcome of interest for predictive value. AUC ranges from 0.5 indicating chance prediction and 1.0 indicating perfect prediction.

Summary of Critical Appraisal

Details of the critical appraisal of individual studies are provided in Appendix 3.

Systematic Reviews

There were two systematic reviews found in the literature search relevant to the research question. Galvin et al.³ included detailed methodology for the inclusion/exclusion criteria for their investigation. This includes a PRISMA flow chart and details of the search criteria and quality assessment for included literature, and an analysis found no evidence of publication bias. Study selection and assessment was performed by two independent reviewers. In addition the statistical analyses utilized represent the most commonly employed calculations for the type

investigations under examination, however both prospective and retrospective studies were pooled together, as were hospital- and population-based studies, which may not have been appropriate. The authors reported the external validity of the included studies to be good, but cited inadequate blinding as a key limitation to their internal validity. The authors were not able to complete an analysis at the two day time-point due to variations in the onset of symptoms, which is the time frame in which ABCD² was intended to be the most useful. Additionally there was high variability in the time between diagnosis and TIA onset in the included literature.

The review by Giles and Rothwell¹¹ performed a comprehensive literature search, included an attempt to identify unpublished studies by searching for abstracts from key conferences. However, their analysis included a wide range of publication types with many methods for study design and different study settings. This degree of heterogeneity in the results and make limit the precision of the findings, though subgroup analyses on key sources of heterogeneity were conducted. It was unclear whether study selection and data extraction was performed by two independent reviewers. The authors also state that at the time of publication, statistical methods for pooling receiver operator characteristic area under the curve (AUCs) were limited. It is therefore unclear whether the methods used were appropriate. Finally none of the identified studies were completed on a prospective cohort where scoring is done in a face-to-face manner with a patient by a non-specialist (whom these scoring systems were developed for). All of the scoring done in a prospective manner was completed by a neurologist.

Non-randomized Studies

There were ten non-randomized studies found in the literature search for this investigation. Six of these publications contained ABCD² scoring that was completed by a stroke specialist not a general practitioner giving more credence to the results.^{7,8,12,14,15,17} Four publications were completed on a restrictively small sample size (between 100 and 178 participants).^{8,14-16} Two studies contained ABCD² scoring results that were diagnosed by emergency room physicians and not stroke specialists.^{18,19} There were also six studies,^{7,12-15,17} that were conducted on limited cohorts from only one hospital unit, which may limit broader generalizability. Finally five papers were found that were conducted on retrospective populations where clinical diagnosis occurred previous to ABCD² analysis.^{7,12,13,15,18} The reviewed literature has indicated that the retrospective scoring of TIA patients results in lower AUCs and may result in bias from limited professional input for scoring calculation.

Summary of Findings

Details of the findings of individual studies are provided in Appendix 4.

Systematic Reviews

The two systematic reviews included in this report had similar findings for the use of ABCD² scoring.

In the study by Galvin et al.³ they found that the ABCD² scoring system accurately predicted the rate of post-TIA stroke across all scoring groups. However they found that there is a tendency towards an under-prediction of risk in the high risk group at seven days but that by 90 days post-TIA there was an overestimation propensity in ABCD² scoring, but neither finding was statistically significant. In a subgroup analysis of population-based studies (including patients

recruited from primary care), the under-prediction of risk at seven days for high risk-patients (ABCD² score of 6 or 7) was statistically significant.

In the review by Giles and Rothwell¹¹ the ABCD² scoring system was found to give accurate prediction except when it is used in a retrospective fashion, suggesting a limitation to validation using retrospective data. In this review a total of 20 cohorts from 20 papers were investigated. The pooled AUC result of 18 studies that included the 7 day time point was 0.72 (95% Confidence Interval [CI] 0.63 to 0.80) indicating that there was good predictive capability. In addition the authors found that the results were highly heterogeneous between each study cohort. This heterogeneity was associated with the high variability in study methodology which accounts for 75% of the variation. In a subgroup analysis of studies that used retrospective data from emergency department records, the AUC was 0.68 (95% CI 0.64 to 0.72), while studies based on face-to-face evaluation or neurology clinic records had a pooled AUC of 0.74 (95% CI 0.64 to 0.84). For stroke risk beyond 7 days (8 to 90 days), the authors found that the pooled AUC was lower than for 0 to 7 days, but the actual value was not reported.

Non-Randomized Studies

Three of the studies^{8,12,16} compared the scoring results completed by trained neurological experts and general practitioners. There is agreement among these studies that a large degree of variation exists between expert and non-expert scoring. Bradley et al.¹⁶ found that there was only agreement in 51% of the cases. The largest discrepancies were found in the scoring of the clinical features (i.e. weakness and speech impairment). This was confirmed in the 2013 study by Ishida et al.¹² which found that the rate of conformity between experts and non-experts ranged between 44% and 58%.

When predictive scoring was examined in the remaining seven papers there is again a high degree of conformity in all but one of the publications. Six of these papers found that there is limited predictive value to the ABCD² scoring system. For example in the emergency department study by Ghia et al.¹⁸ there was no difference in the proportion of strokes among patients receiving a low or moderate-high ABCD² score. A study in adults at eight Canadian emergency departments,¹⁹ also found low predictive value for stroke risk at 7 days when the ABCD² score was calculated by the enrolling physician (AUC 0.56, 95% CI 0.47 to 0.65) or the coordinating centre (AUC 0.65, 95% CI 0.57 to 0.73). Sanders et al.¹⁷ discovered that, for patients referred by the emergency department, at two days post-TIA there is a 20% chance of misclassification and at 90 days there is a 38% chance. Ghandehari et al.⁷ found that for TIA patients, ABCD² had weak predictive value for recurrent stroke at three days (AUC 0.591, 95% CI 0.526 to 0.657) and 30 days (AUC 0.599, 95% CI 0.536 to 0.663). In contrast, a community-based study that examined predictive scoring⁸ found that at two days post-TIA the ABCD² scoring system was highly predictive (AUC 0.85, 95% CI 0.72 to 0.97) but that this was lower at 7 (AUC 0.69, 95% CI 0.56 to 0.82), 30 (AUC 0.69, 95% CI 0.56 to 0.85), and 90 days (AUC 0.76, 95% CI 0.67 to 0.86).

In the study by Zhao et al. (2013),²⁰ the goal was to determine if the ABCD² scoring system was able to distinguish between TIA and minor stroke. Similar to the study by Bradley et al., they found that the most important criteria to distinguish TIA from minor stroke are the clinical features and symptom duration. They also found that there is no statistical difference between TIA and minor stroke patients in ABCD² scores for age, hypertension or diabetes.

Finally in the paper by Stead et al. (2011),¹³ the authors examined whether an emergency department with an existing TIA diagnosis program in use would benefit with the addition of the ABCD² scoring system. They determined that at both 7 days and 90 days post-TIA there was no incremental benefit of with the addition of ABCD² results to standard emergency department central nervous system and carotid artery imaging.

Limitations

The systematic reviews included in this report contain literature searches covering substantial breadth of the topic of interest. Both were of high methodological quality and included detailed criteria for paper inclusion and exclusion. In the review by Galvin et al. (2011)³ the papers that were included had wide variation in symptom onset. This made it impossible for the reviewers to provide any conclusions on the data at the 2 day time point post-TIA when the highest risk of stroke is found. Both reviews pooled studies conducted in different settings, or with different methodologies, which may have been inappropriate, however some of that heterogeneity was explored with subgroup analyses. The studies included in the systematic reviews generally had good external validity, but may have had limited internal validity due to lack of blinding.

The literature review for this investigation found twelve studies in total that met the inclusion criteria. Six of the ten non-randomized studies found were completed on cohorts from single hospitals. This may make it difficult to generalize their findings to the broader health-care system. It limits generalizability due to the limited number of professionals completing ABCD² scoring. In addition, four of these studies were completed on a small sample sizes which may limit the reliability of the conclusions.

The standard procedure for the scoring of ABCD² utilizes three categories for the ranking of patient risk: low (score 0-3), moderate (score 4-5) and high (score 6-7). Two of the studies included here modified this to using only two categories, low (score 0-4) and high (5-7) and little evidence supporting this change is given.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

The systematic reviews included in this report all indicate that the ABCD² scoring system is a valuable tool for clinical use. Though in the publication by Galvin et al. (2011) there was a trend towards overestimation at 90 days and an underestimation at 7 days, with the latter becoming statistically significant in population-based studies. The review by Giles and Rothwell demonstrated that the predictive value drops off if calculated from a retrospective analysis rather than face-to-face assessment. Additionally, one study showed that there was poor agreement in ABCD² scoring when completed by referring physicians versus trained neurological professionals. This is consistent with the findings of the individual non-randomized studies included in this report, many of which demonstrated poor predictive accuracy in emergency department settings. This suggests that application of the ABCD² scoring system is setting dependent. As a result of these investigations only limited support can be shown for the predictive value of ABCD² scoring across clinical settings.

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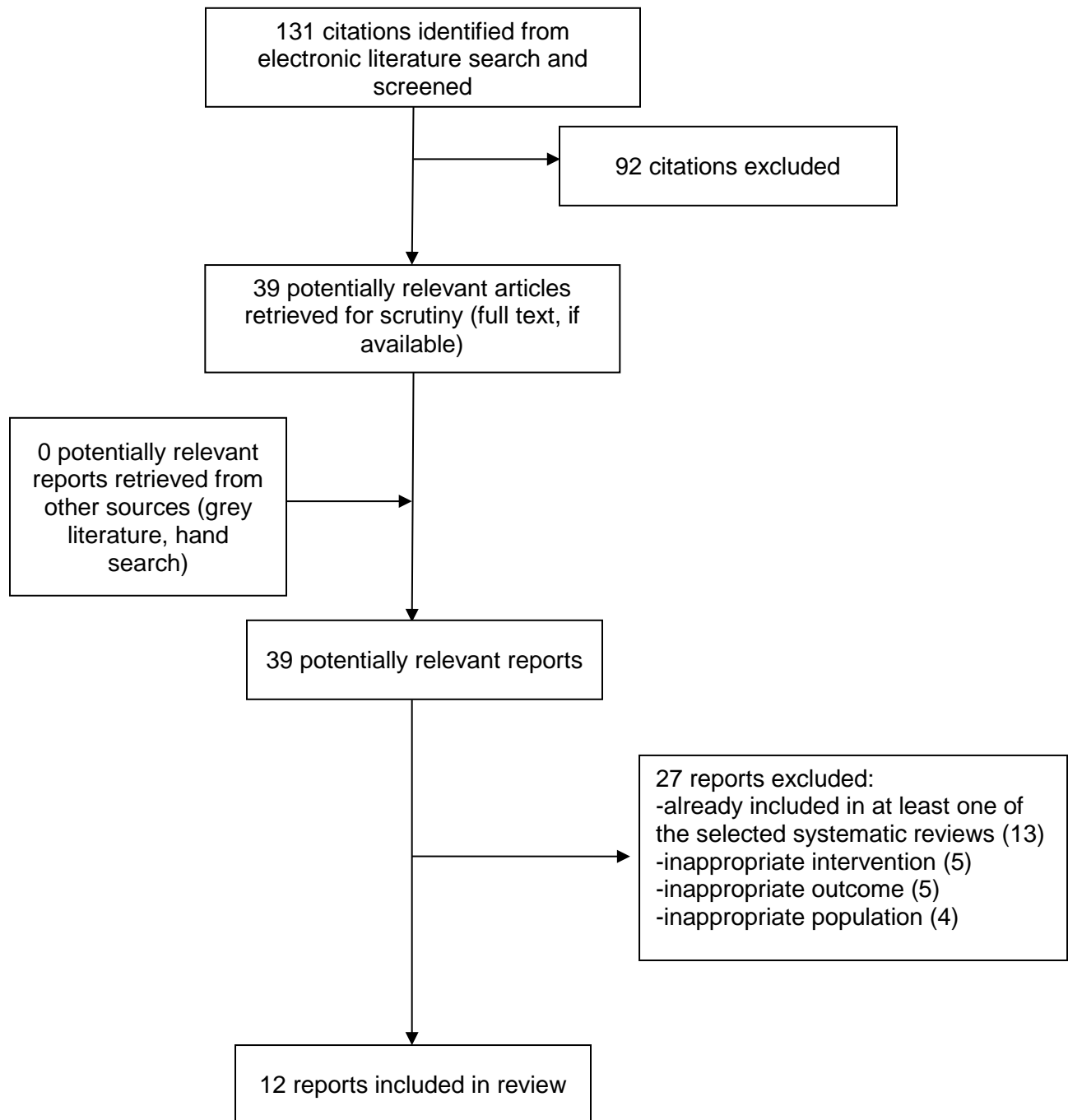
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APPENDIX 1: Selection of Included Studies



APPENDIX 2: Study characteristics

First Author, Publication Year, Country	Eligibility Criteria	Included Study Designs / Overall Goals	Number of Included Studies
Systematic Reviews			
Galvin et al., 2011, Ireland ³	<ul style="list-style-type: none"> • Prospective or retrospective cohort studies • adult patients >18 years old • ABCD² score calculated • care setting is both population and hospital based patients • outcome is subsequent stroke at 7 or 90 days • Search terms included: 'transient ischaemic attack' OR 'TIA' AND 'cerebrovascular accident' OR 'CVA' OR 'stroke' AND score' OR 'prediction' OR 'prognosis' OR 'risk'. 	<ul style="list-style-type: none"> • The literature search took place in July 2010 and included the following search engines: the Cochrane Library, EMBASE, Science Direct and PubMed. • Goal – to determine the predictive value of the ABCD² scoring system at both 7 and 90 days post TIA in three risk strata; low, moderate and high. 	16 publications included
Giles and Rothwell, 2010, United Kingdom ¹¹	<ul style="list-style-type: none"> • prospective or retrospective cohort studies • all studies where ABCD or ABCD² scoring is used are included • excluded if outcomes were only available by dichotomized or trichotomized scores (as these potentially are data dependent) • search terms included: transient isch(a)emic attack OR TIA OR amaurosis fugax AND prognosis OR outcome OR predict OR risk OR ABCD OR ABCD2 • Publication between January 200 to July 2009 	<ul style="list-style-type: none"> • Literature search took place on July 15 2009 in the following search engines: Pubmed, Ovid Medline and EMBASE • Goal – to systematically review published and unpublished data to determine predictive value and generalizability to different clinical settings and users 	20 publications included (14 additional publications included in references)

Non-randomized Studies

First Author, Publication Year, Country	Study Design	Patient Characteristics, Sample Size (n)	Objectives
Non-randomized Studies			
Bradley et al., 2013, United States of America ¹⁶	<ul style="list-style-type: none"> included all patients who had suspected TIA between Feb 2010 and July 2011 and referred to Rapid Access Stroke Prevention (RASP) clinic 	<ul style="list-style-type: none"> N=101, mean age 60 years old included all patients who had suspected TIA between Feb 2010 and July 2011 and referred to Rapid Access Stroke Prevention (RASP) clinic 	To examine patient data from RASP clinic analyzed by a general practitioner or other non-stroke specialist and compare it with results from trained experts.
Cancelli et al., 2011, Italy ⁸	<ul style="list-style-type: none"> N=178 TIA cases, mean age 76.4 years old Utilized hot and cold pursuit: hot – daily review of hospital admissions and referrals from neurological imaging and various wards, cold – monthly review of discharge records/rehabilitation services and death certificates 	<ul style="list-style-type: none"> Cohorts came from 1 university hospital, 1 private hospital and 128 general practitioners Included patients reporting for care with incident/recurrent stroke and TIA between April 1 2007 and March 31 2009 in Udine district of Italy included both incident and recurrent TIA events 	To examine the overall incidence of TIA in Udine district and analyze the predictive capability of ABCD ² for short term stroke risk accuracy
Chardoli et al., 2013, Iran ¹⁴	<ul style="list-style-type: none"> N=100, mean age is 60.79 years old patients with a history of TIA were excluded 	<ul style="list-style-type: none"> patients reporting to the Hazrat Rasoul Akram Hospital and diagnosed with TIA between 2009 and 2010 	To evaluate the ABCD ² system in the emergency department for clinical decision making
Ghandehari et al., 2012, Iran ⁷	<ul style="list-style-type: none"> N=511 (393 TIA and 118 minor ischemic stroke), mean age 68.5 years old retrospective cohort study Symptom onset <24 hours Had premorbid modified 	<ul style="list-style-type: none"> Included upon analysis by hospital if entered hospital from 2000 – 2011 Endpoint if novel ischemic event or 	To appraise the predictive value of ABCD ² scoring in the analysis of TIA and minor ischemic stroke patients

First Author, Publication Year, Country	Study Design	Patient Characteristics, Sample Size (n)	Objectives
	Rankin scale ≤1	vascular death at 3 or 90 days <ul style="list-style-type: none"> • Follow up continued for 3 months if endpoints not reached before 	
Ghia et al., 2012, United Kingdom ¹⁸	<ul style="list-style-type: none"> • N=789, mean age 69.6 years old • Retrospective cohort study • If patient had multiple TIA events then only first is included • Follow up risks investigated at 2, 30, 90 and 365 days post-TIA 	<ul style="list-style-type: none"> • Included TIA diagnosis from 2 hospitals, Liverpool and Bankstown • Cohort selected from patients attended to from Jan 1 2004 to Dec 31 2006 • ABCD² scoring completed by emergency room attending physician 	To assess the scoring accuracy and clinical relevance of ABCD ² scoring in modern TIA cohorts
Ishida et al., 2013, United States of America ¹²	<ul style="list-style-type: none"> • Retrospective cohort study • N=102, mean age 62 years old • Only patients with full set of diagnostic criteria filled out are included 	<ul style="list-style-type: none"> • Included patients first seen at University of Pennsylvania Medical Center between Dec 2010 and March 2012 • Medical records identified and results blacked out then given to 2 neurological experts for independent analysis 	To determine the convergent validity, of accuracy compared with a prospectively assigned score, and inter-rater reliability of retrospective estimation of the ABCD ² score from medical records.
Perry et al., 2011, Canada ¹⁹	<ul style="list-style-type: none"> • N=2056, age ≥18 years old, prospective cohort study • Excluded if confirmed with stroke, symptoms last >24 hours, Glasgow Coma Scale <15, defined other cause for symptoms, presentation >7 days after symptom onset 	<ul style="list-style-type: none"> • Patients >18 years old diagnosed with TIA between 2007 and 2010 presenting at emergency room of 8 Canadian hospitals 	to externally validate the ABCD ² scoring system in the emergency department setting for TIA patients at high risk of stroke at 7 and 90 days post-TIA

First Author, Publication Year, Country	Study Design	Patient Characteristics, Sample Size (n)	Objectives
Sanders et al., 2011, Australia ¹⁷	<ul style="list-style-type: none"> • N=512 age averaged between 61.1 and 74.3 depending on category examined • Rejected if symptom duration lasted >24 hours • Follow up achieved in 96.0% of cases 	<ul style="list-style-type: none"> • Patients referred from emergency department to stroke care unit with suspected TIA at Monash Medical Centre between June 2004 to Nov 2007 • Patients referred from emergency department to stroke care unit with suspected TIA at Monash Medical Centre between June 2004 to Nov 2007 • TIA scoring initially completed by emergency room physician then subsequently confirmed by stroke expert 	To investigate the effectiveness of the ABCD ² scoring system in an Australian tertiary-hospital cohort
Stead et al., 2011, United States of America ¹³	<ul style="list-style-type: none"> • N=637, mean age 73 years old • Retrospective cohort study • Patients ≥18 years old, symptom duration <24 hours, • Patients excluded if symptoms last >24 hours or they have acute ischemic or hemorrhagic stroke 	<ul style="list-style-type: none"> • Consecutive adult patients presenting to clinic with TIA were included • ABCD² scores were calculated retrospectively by professionals blinded to patient outcomes 	To investigate whether the ABCD ² score gave value to the existing institutional protocol for risk stratification at Mayo Clinic in Rochester Minnesota
Zhao et al., 2013, China ¹⁵	<ul style="list-style-type: none"> • N=171, mean age is 59.3 years old • Retrospective cohort study • Patient included if: <ul style="list-style-type: none"> - present with focal neurological signs believed to be cerebrovascular in origin - availability of brain CT in 	<ul style="list-style-type: none"> • Patients reporting to Nanjing Drum Tower Hospital between Jan 2010 and Dec 2012 • Patients separated into TIA and minor ischemic stroke 	To investigate the differences between TIA and minor stroke based on ABCD ² score, digital subtraction angiography and blood lipids, which

First Author, Publication Year, Country	Study Design	Patient Characteristics, Sample Size (n)	Objectives
	emergency department and MRI within 24 hours - initial analysis included ABCD ² , blood lipids/glucose/electrocardiogram • had digital subtraction angiography within first 7 days after MRI screening	based upon MRI imaging within 24 hours of TIA onset	is more accurate when MRI is not available

APPENDIX 3: Summary of critical appraisal

First Author, Publication Year	Strengths	Limitations
Systematic Reviews		
Galvin et al., 2011 ³	<ul style="list-style-type: none"> • Includes PRISMA flow chart and study characteristic search criteria are included • Contained independent quality assessment of paper inclusion • All statistical analyses are detailed and appropriate for examinations being conducted 	<ul style="list-style-type: none"> • Unable to include analysis at 2 days post TIA as the variation in the time of symptom onset in included studies makes it impossible to obtain an accurate scoring • Is high variation in the onset of TIA to clinical diagnosis and this diagnosis is not always performed by a neurological specialist
Giles and Rothwell, 2010 ¹¹	<ul style="list-style-type: none"> • Most comprehensive review of all existing scoring systems included in reviewed papers • Contained most detailed analysis of included/excluded papers • Papers included are classified well according to study design and methodology 	<ul style="list-style-type: none"> • Studies of performance and prediction do not use a standardized set of guidelines for methodological progression in areas such as: inception criteria, clinical setting, score application or treatment • there are very limited protocols for statistical analysis methods for meta-analysis of AUCs • None of the studies identified here were completed on a prospective cohort where scoring is done face-to-face with the patient by a non-specialist (whom these methods were developed for). All of the scoring done in prospective manners was completed by neurologists
Non-randomized studies		
Bradley et al., 2013 ¹⁶	<ul style="list-style-type: none"> • Significant use of standard statistical calculations utilized • Well developed and comprehensive study methodology 	<ul style="list-style-type: none"> • No assessment of inter-observer agreement with experts from various backgrounds are used • Not all patients underwent DWI which puts some of the diagnosis of TIA under question • Cohort obtained from a single hospital • Completed on relatively small study population
Cancelli et al., 2011 ⁸	<ul style="list-style-type: none"> • Well established analysis of statistical methods used • Used distinguishing population based study design and multiple sources for patient recruitment 	<ul style="list-style-type: none"> • Had variability in ABCD² scoring depending on professional completing the diagnosis • Many patients who have TIA do not seek medical help therefore true

First Author, Publication Year	Strengths	Limitations
Systematic Reviews		
Galvin et al., 2011 ³	<ul style="list-style-type: none"> Includes PRISMA flow chart and study characteristic search criteria are included Contained independent quality assessment of paper inclusion All statistical analyses are detailed and appropriate for examinations being conducted 	<ul style="list-style-type: none"> Unable to include analysis at 2 days post TIA as the variation in the time of symptom onset in included studies makes it impossible to obtain an accurate scoring Is high variation in the onset of TIA to clinical diagnosis and this diagnosis is not always performed by a neurological specialist
Giles and Rothwell, 2010 ¹¹	<ul style="list-style-type: none"> Most comprehensive review of all existing scoring systems included in reviewed papers Contained most detailed analysis of included/excluded papers Papers included are classified well according to study design and methodology 	<ul style="list-style-type: none"> Studies of performance and prediction do not use a standardized set of guidelines for methodological progression in areas such as: inception criteria, clinical setting, score application or treatment there are very limited protocols for statistical analysis methods for meta-analysis of AUCs None of the studies identified here were completed on a prospective cohort where scoring is done face-to-face with the patient by a non-specialist (whom these methods were developed for). All of the scoring done in prospective manners was completed by neurologists
Non-randomized studies		
Bradley et al., 2013 ¹⁶	<ul style="list-style-type: none"> Significant use of standard statistical calculations utilized Well developed and comprehensive study methodology 	<ul style="list-style-type: none"> No assessment of inter-observer agreement with experts from various backgrounds are used Not all patients underwent DWI which puts some of the diagnosis of TIA under question Cohort obtained from a single hospital Completed on relatively small study population
	<ul style="list-style-type: none"> All patients included were followed up by a neurologist 	<ul style="list-style-type: none"> results may differ from those given Small sample size of included patients
Chardoli et al., 2013 ¹⁴	<ul style="list-style-type: none"> ABCD² scoring/triage completed by neurologist not general practitioner 	<ul style="list-style-type: none"> Very small sample size of included patients Single hospital used as cohort source

First Author, Publication Year	Strengths	Limitations
Systematic Reviews		
Galvin et al., 2011 ³	<ul style="list-style-type: none"> Includes PRISMA flow chart and study characteristic search criteria are included Contained independent quality assessment of paper inclusion All statistical analyses are detailed and appropriate for examinations being conducted 	<ul style="list-style-type: none"> Unable to include analysis at 2 days post TIA as the variation in the time of symptom onset in included studies makes it impossible to obtain an accurate scoring Is high variation in the onset of TIA to clinical diagnosis and this diagnosis is not always performed by a neurological specialist
Giles and Rothwell, 2010 ¹¹	<ul style="list-style-type: none"> Most comprehensive review of all existing scoring systems included in reviewed papers Contained most detailed analysis of included/excluded papers Papers included are classified well according to study design and methodology 	<ul style="list-style-type: none"> Studies of performance and prediction do not use a standardized set of guidelines for methodological progression in areas such as: inception criteria, clinical setting, score application or treatment there are very limited protocols for statistical analysis methods for meta-analysis of AUCs None of the studies identified here were completed on a prospective cohort where scoring is done face-to-face with the patient by a non-specialist (whom these methods were developed for). All of the scoring done in prospective manners was completed by neurologists
Non-randomized studies		
Bradley et al., 2013 ¹⁶	<ul style="list-style-type: none"> Significant use of standard statistical calculations utilized Well developed and comprehensive study methodology 	<ul style="list-style-type: none"> No assessment of inter-observer agreement with experts from various backgrounds are used Not all patients underwent DWI which puts some of the diagnosis of TIA under question Cohort obtained from a single hospital Completed on relatively small study population
Ghandehari et al., 2012 ⁷	<ul style="list-style-type: none"> Used professional neurological stroke specialist for all ABCD² scoring Good use of accepted statistical analysis for scoring system analysis professional neurological 	<ul style="list-style-type: none"> No description of follow-up given ABCD² score developed for use on TIA not minor ischemic stroke therefore certain aspects not appropriate for use here (such as duration) Discussion included in study does

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Systematic Reviews		
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Non-randomized studies		
Bradley et al., 2013 ¹⁶	<ul style="list-style-type: none"> Significant use of standard statistical calculations utilized Well developed and comprehensive study methodology 	<ul style="list-style-type: none"> No assessment of inter-observer agreement with experts from various backgrounds are used Not all patients underwent DWI which puts some of the diagnosis of TIA under question Cohort obtained from a single hospital Completed on relatively small study population
	stroke specialist for all ABCD ²	<ul style="list-style-type: none"> not focus on results of this investigation but on an analysis of previous literature. No discussion of any limitations or strengths Only a single hospital used to provide patients

First Author, Publication Year	Strengths	Limitations
Systematic Reviews		
Galvin et al., 2011 ³	<ul style="list-style-type: none"> • Includes PRISMA flow chart and study characteristic search criteria are included • Contained independent quality assessment of paper inclusion • All statistical analyses are detailed and appropriate for examinations being conducted 	<ul style="list-style-type: none"> • Unable to include analysis at 2 days post TIA as the variation in the time of symptom onset in included studies makes it impossible to obtain an accurate scoring • Is high variation in the onset of TIA to clinical diagnosis and this diagnosis is not always performed by a neurological specialist
Giles and Rothwell, 2010 ¹¹	<ul style="list-style-type: none"> • Most comprehensive review of all existing scoring systems included in reviewed papers • Contained most detailed analysis of included/excluded papers • Papers included are classified well according to study design and methodology 	<ul style="list-style-type: none"> • Studies of performance and prediction do not use a standardized set of guidelines for methodological progression in areas such as: inception criteria, clinical setting, score application or treatment • there are very limited protocols for statistical analysis methods for meta-analysis of AUCs • None of the studies identified here were completed on a prospective cohort where scoring is done face-to-face with the patient by a non-specialist (whom these methods were developed for). All of the scoring done in prospective manners was completed by neurologists
Non-randomized studies		
Bradley et al., 2013 ¹⁶	<ul style="list-style-type: none"> • Significant use of standard statistical calculations utilized • Well developed and comprehensive study methodology 	<ul style="list-style-type: none"> • No assessment of inter-observer agreement with experts from various backgrounds are used • Not all patients underwent DWI which puts some of the diagnosis of TIA under question • Cohort obtained from a single hospital • Completed on relatively small study population
Ghia et al., 2012 ¹⁸	<ul style="list-style-type: none"> • Reviewers of patient medical records blinded to outcomes which imparts assessment and secondary scoring of ABCD² scores • Used multiple sources for retrospective patient recruitment 	<ul style="list-style-type: none"> • Initial ABCD² scores completed by an emergency department physical not a stroke specialist. • Scoring system for ABCD² results only contained two categories instead of three as is typical. • Goals of study not clearly defined

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Systematic Reviews		
Galvin et al., 2011 ³	<ul style="list-style-type: none"> Includes PRISMA flow chart and study characteristic search criteria are included Contained independent quality assessment of paper inclusion All statistical analyses are detailed and appropriate for examinations being conducted 	<ul style="list-style-type: none"> Unable to include analysis at 2 days post TIA as the variation in the time of symptom onset in included studies makes it impossible to obtain an accurate scoring Is high variation in the onset of TIA to clinical diagnosis and this diagnosis is not always performed by a neurological specialist
Giles and Rothwell, 2010 ¹¹	<ul style="list-style-type: none"> Most comprehensive review of all existing scoring systems included in reviewed papers Contained most detailed analysis of included/excluded papers Papers included are classified well according to study design and methodology 	<ul style="list-style-type: none"> Studies of performance and prediction do not use a standardized set of guidelines for methodological progression in areas such as: inception criteria, clinical setting, score application or treatment there are very limited protocols for statistical analysis methods for meta-analysis of AUCs None of the studies identified here were completed on a prospective cohort where scoring is done face-to-face with the patient by a non-specialist (whom these methods were developed for). All of the scoring done in prospective manners was completed by neurologists
Non-randomized studies		
Bradley et al., 2013 ¹⁶	<ul style="list-style-type: none"> Significant use of standard statistical calculations utilized Well developed and comprehensive study methodology 	<ul style="list-style-type: none"> No assessment of inter-observer agreement with experts from various backgrounds are used Not all patients underwent DWI which puts some of the diagnosis of TIA under question Cohort obtained from a single hospital Completed on relatively small study population
		<ul style="list-style-type: none"> Is a retrospective analysis of patient reports not first-hand prospective analysis
Ishida et al., 2013 ¹²	<ul style="list-style-type: none"> During secondary analysis of ABCD² scores the reviewers were blind to all previous results Secondary scoring utilized 	<ul style="list-style-type: none"> Patients all come from single hospital care unit making the results subject to personal bias for ADABC² scoring

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Systematic Reviews		
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Non-randomized studies		
Bradley et al., 2013 ¹⁶	<ul style="list-style-type: none"> • Significant use of standard statistical calculations utilized • Well developed and comprehensive study methodology 	<ul style="list-style-type: none"> • No assessment of inter-observer agreement with experts from various backgrounds are used • Not all patients underwent DWI which puts some of the diagnosis of TIA under question • Cohort obtained from a single hospital • Completed on relatively small study population
	neurological experts not simply general practitioners	<ul style="list-style-type: none"> • Study did not review the actual clinical validity of the scores only a comparison between specialist and non-specialist
Perry et al., 2011 ¹⁹	<ul style="list-style-type: none"> • Prospective cohort analysis utilized • Follow-up completed on 91.1% of total enrolled patients 	<ul style="list-style-type: none"> • ABCD² scoring completed by emergency doctor not neurological specialist. Misdiagnosis was

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Systematic Reviews		
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Giles and Rothwell, 2010 ¹¹	<ul style="list-style-type: none"> • Most comprehensive review of all existing scoring systems included in reviewed papers • Contained most detailed analysis of included/excluded papers • Papers included are classified well according to study design and methodology 	<ul style="list-style-type: none"> • Studies of performance and prediction do not use a standardized set of guidelines for methodological progression in areas such as: inception criteria, clinical setting, score application or treatment • there are very limited protocols for statistical analysis methods for meta-analysis of AUCs • None of the studies identified here were completed on a prospective cohort where scoring is done face-to-face with the patient by a non-specialist (whom these methods were developed for). All of the scoring done in prospective manners was completed by neurologists
Non-randomized studies		
Bradley et al., 2013 ¹⁶	<ul style="list-style-type: none"> • Significant use of standard statistical calculations utilized • Well developed and comprehensive study methodology 	<ul style="list-style-type: none"> • No assessment of inter-observer agreement with experts from various backgrounds are used • Not all patients underwent DWI which puts some of the diagnosis of TIA under question • Cohort obtained from a single hospital • Completed on relatively small study population
	<ul style="list-style-type: none"> • Doctors completing the scoring blinded to patient diagnosis • ABCD² scoring guidelines given to physicians to have conformity in results • Cohort gathered from 8 different sources 	<ul style="list-style-type: none"> • common problem. • Study only separated ABCD² scores into two categories not the typical three. • The data for the 90 day time point is not shown only mentioned briefly

First Author, Publication Year	Strengths	Limitations
Systematic Reviews		
Galvin et al., 2011 ³	<ul style="list-style-type: none"> Includes PRISMA flow chart and study characteristic search criteria are included Contained independent quality assessment of paper inclusion All statistical analyses are detailed and appropriate for examinations being conducted 	<ul style="list-style-type: none"> Unable to include analysis at 2 days post TIA as the variation in the time of symptom onset in included studies makes it impossible to obtain an accurate scoring Is high variation in the onset of TIA to clinical diagnosis and this diagnosis is not always performed by a neurological specialist
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Non-randomized studies		
Bradley et al., 2013 ¹⁶	<ul style="list-style-type: none"> Significant use of standard statistical calculations utilized Well developed and comprehensive study methodology 	<ul style="list-style-type: none"> No assessment of inter-observer agreement with experts from various backgrounds are used Not all patients underwent DWI which puts some of the diagnosis of TIA under question Cohort obtained from a single hospital Completed on relatively small study population
Sanders et al., 2011 ¹⁷	<ul style="list-style-type: none"> Large sample of consecutive patients included and use of physicians from both emergency room and stroke care unit used for scoring Follow-up completed on 96.0% of enrolled patients 	<ul style="list-style-type: none"> Criteria for risk group classification not clearly given Only used high and low categories instead of high, moderate and low as is typical Patients included were obtained in a tertiary manner from a single

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Systematic Reviews		
Galvin et al., 2011 ³	<ul style="list-style-type: none"> • Includes PRISMA flow chart and study characteristic search criteria are included • Contained independent quality assessment of paper inclusion • All statistical analyses are detailed and appropriate for examinations being conducted 	<ul style="list-style-type: none"> • Unable to include analysis at 2 days post TIA as the variation in the time of symptom onset in included studies makes it impossible to obtain an accurate scoring • Is high variation in the onset of TIA to clinical diagnosis and this diagnosis is not always performed by a neurological specialist
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Non-randomized studies		
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		department therefore application of these findings may be questionable for primary care settings
Stead et al., 2011 ¹³	<ul style="list-style-type: none"> • Individuals conducting ABCD² scoring were not involved in patient care allowing for impartial scoring assessments 	<ul style="list-style-type: none"> • ABCD² score is established from medical records not hands on at the time of evaluation • Expert neurologic specialists only

First Author, Publication Year	Strengths	Limitations
Systematic Reviews		
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Non-randomized studies		
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	<ul style="list-style-type: none"> Individuals conducting ABCD² scoring were blind to the patient outcome Very little loss on follow-up and all those lost had low ABCD² scores indicating that they would not have been contradictory to results found 	<ul style="list-style-type: none"> consulted "as needed" for TIA diagnosis and criteria for requirement not provided. Single hospital used for cohort selection

First Author, Publication Year	Strengths	Limitations
Systematic Reviews		
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Zhao et al., 2013 ¹⁵	<ul style="list-style-type: none"> • Professional stroke physician classified the TIA or stroke results in all cases 	<ul style="list-style-type: none"> • Is a retrospective analysis of patients using medical records not actual hands on analysis at time of triage • Cohort selected from only one hospital with a small patient sample size

First Author, Publication Year	Strengths	Limitations
Systematic Reviews		
Galvin et al., 2011 ³	<ul style="list-style-type: none"> Includes PRISMA flow chart and study characteristic search criteria are included Contained independent quality assessment of paper inclusion All statistical analyses are detailed and appropriate for examinations being conducted 	<ul style="list-style-type: none"> Unable to include analysis at 2 days post TIA as the variation in the time of symptom onset in included studies makes it impossible to obtain an accurate scoring Is high variation in the onset of TIA to clinical diagnosis and this diagnosis is not always performed by a neurological specialist
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Non-randomized studies		
Bradley et al., 2013 ¹⁶	<ul style="list-style-type: none"> Significant use of standard statistical calculations utilized Well developed and comprehensive study methodology 	<ul style="list-style-type: none"> No assessment of inter-observer agreement with experts from various backgrounds are used Not all patients underwent DWI which puts some of the diagnosis of TIA under question Cohort obtained from a single hospital Completed on relatively small study population
		<ul style="list-style-type: none"> The imaging technique used (MRI) is not capable of distinguishing very small lesions therefore making results of stroke questionable

Appendix 4: Summary of findings

First Author, Publication Year	Main Study Findings	Authors' Conclusions
Systematic Reviews		
Galvin et al., 2011 ³	<ul style="list-style-type: none"> • Of 7 day risk studies; <ul style="list-style-type: none"> - ABCD² correctly predicts rate of stroke occurrence, of 357 strokes predicted 388 actually occurred across all scoring groups - Is a tendency towards underestimation in high risk group (RR 0.48, 95% CI 0.27-0.88, I²=0%) - 9.5% of strokes that occur happen in low risk group, 51% in moderate and 39.5% in high • Of 90 day risk studies; <ul style="list-style-type: none"> - ABCD² tends to overestimate as prediction of 626 strokes when only actually 426 occurred - 13.6% of all strokes occur in low, 50% in moderate and 36.4% in high 	<ul style="list-style-type: none"> • The prediction accuracy of ABCD² scoring system is confirmed by this review • System is appropriate for classification of all risk strata groups • Authors state, "In spite of its limitations the ABCD² is easy and quick to administer and it is a useful tool to assist clinicians in management of individuals with TIA."(page 375)
Giles and Rothwell, 2010 ¹¹	<ul style="list-style-type: none"> • A total of 20 cohorts were identified containing 9808 patients <ul style="list-style-type: none"> - Pooled¹AUC prediction rates were 0.72 (0.67 to 0.77) • ABCD² population had 18 cohorts with 9436 patients and 442 strokes at 7 days <ul style="list-style-type: none"> - Pooled AUC prediction rates were 0.72 (0.63 to 0.80) • ABCD population had 18 cohorts with 8470 patients and 351 strokes at 7 days • In 16 cohorts where scores for both ABCD and ABCD² were calculated at 7 days the predictive power (AUC) is 0.72 (0.66 to 0.78) and 0.72 (0.63 to 0.82) respectively and P diff = 0.97 • Early phase stroke risk is highest in patients with unstable vascular pathology though at later stages it is determined by established risk factors therefore indicating that the AUC for 0-90 days is driven by predictive power in the acute phase and implies that the score will over-predict risk in TIA patients who present after delay • Found significant heterogeneity in AUCs with poor performance in cohorts where 	<ul style="list-style-type: none"> • ABCD system is not intended to be a replacement for trained clinical assessment and is expected to preform below average for specific groups (such as normotensive patients with arterial dissection or cerebral vasculitis) • Development of novel versions of these scoring methods that incorporate criteria such as markers of vascular instability (cerebral imaging) will improve the predictive capability for the management of secondary care after initial diagnosis

First Author, Publication Year	Main Study Findings	Authors' Conclusions
	<p>retrospective analysis is used for scoring</p> <ul style="list-style-type: none"> • Found that 75% of this heterogeneity is accounted for when retrospective analysis styles are used indicating that: <ul style="list-style-type: none"> - Direct assessment is more accurate - misdiagnosis is more common in emergency departments - in the United Kingdom high-risk TIA patients typically report to the emergency department which leads to an unrepresentative case mix and potentially reduced predictive power. 	
Non-randomized Studies		
Bradley et al., 2013 ¹⁶	<ul style="list-style-type: none"> • Mean ABCD² scores in confirmed TIA category for general practitioner (GP) were 2.24 (SD=0.98) and for stroke specialist (SS) were 2.69 (AD=1.29) • In entire data set 20 of 29 patients given moderate or high ranking by GP were given low by SS • In only 51% of cases did SS agree with GP scoring • Largest discrepancy occurred in clinical features with failure to diagnose: <ul style="list-style-type: none"> - hemiparesis in 9 of 20 where present and 4 of 14 where not present - speech disturbance in 21 cases GP did not score applicable point 	<ul style="list-style-type: none"> • Authors state: "is only moderate agreement between referring GP's and stroke experts and a very large degree of underestimation in moderate to high risk TIA patients of which subsequent stroke risk is underestimated"(page 34) • These results indicate that ABCD² scoring by non-experts cannot be used by itself to classify patients for risk of stroke. • Recommend that a stroke specialist be consulted in all use of ABCD² scoring
Cancelli et al., 2011 ⁸	<ul style="list-style-type: none"> • N=178 • TIA greater in men, overall incidence per 1000 is 0.56 (vs. women at 0.49) (95% CI 0.45-0.61) • Stroke risk at 2, 7, 30, 90 days is 2.5%, 5.6%, 6.2% and 11.2% respectively. • No patient with recurrent TIA had ABCD² score <4. • AUC for 2 day indicates high predictive value at 0.85 (95% CI 0.72-0.97), for other time points: <ul style="list-style-type: none"> - 7 day AUC – 0.69 (95%CI 0.56-0.82) - 30 day AUC - 0.69 (95%CI 0.56-0.85) - 90 day AUC - 0.76 (95%CI 0.67-0.86) 	<ul style="list-style-type: none"> • ABCD² scoring is highly predictive of the risk of stroke at 2 days post-TIA • At longer time points this predictability drops • No association was found between atrial fibrillation or carotid stenosis and the risk of TIA

First Author, Publication Year	Main Study Findings	Authors' Conclusions
	<ul style="list-style-type: none"> • ABCD² score varied depending on professional completing analysis 	
Chardoli et al., 2013 ¹⁴	<ul style="list-style-type: none"> • N=100 • Of the 50 patients with ABCD² score ≤4 47 did not develop cerebral vascular accident • Positive predictive value in high risk group, ABCD² >4, had 16% occurrence risk • Sensitivity and specificity for ABCD² predicting TIA at cut off of 4 was 72.2% and 52.8 respectively 	<ul style="list-style-type: none"> • Even though patients with ABCD² score >4 are more apt to have TIA or stroke event in the short term than those with lower the lower group are still at significant risk. As a result the ease of discharge of these low scoring patients should be cautioned. • Authors state; "We believe that ABCD² does not have the potential to become a cornerstone in predicting a repeated TIA/CVA after initial TIA" (page 613)
Ghia et al., 2012 ¹⁸	<ul style="list-style-type: none"> • Total population = 798 patients <ul style="list-style-type: none"> - 3 had stroke in 2 days, 7 in 30 days, 15 in 90 days and 19 in 1 year - 255 patients had low ABCD²score and 534 had moderate/high - Percentage of stroke between low and moderate/high group at 30, 90, and 1 year is 1.2 and 0.8, 2.0 and 1.9, and 2.4 and 2.4 - Specificity and sensitivity of ABCD² score in moderate/high group was 57.1% (95% CI 25.0-84.2) and 32.2% respectively at 30 days. At 90 days it was 66.7% (95% CI 38.7-87.0) and 32.3% (95% CI 29.0-35.7) - At 1 year 8 strokes occurred in hospitalized patients (high group) and 11 in discharged (low group) - After 2, 7, and 30 days discharged patients (low score) made up 100% of stroke victims (n=3). After 90 days 9 strokes in discharged vs. 6 in admitted - Predictive value of ABCD² at 30 days was 0.75% (95% CI 0.29-1.91) and at 90 days was 1.87% (95% CI 0.95-3.53). When analyzed for patients in discharged vs. admitted with 	<ul style="list-style-type: none"> • The ABCD² scoring was unable to predict early stroke risk • These scores were associated with steering clinicians to incorrectly delay management strategies which resulted in the occurrences of avoidable strokes. • Is recommended that a wider validation of ABCD² stroke risk score be used before clinical decision making is completed

First Author, Publication Year	Main Study Findings	Authors' Conclusions
	<p>moderate/high score was 0% in admitted and 3.31% in discharged</p>	
<p>Ghandehari et al., 2012 ⁷</p>	<ul style="list-style-type: none"> • 117 strokes, 99 TIA, and 11 vascular deaths occurred within 3 months in total population • ROC AUC values for 3 months is 0.599 (95% CI 0.536-0.663) and at 3 days is 0.591(95% CI 0.526-0.657) • 21.6% of total TIA patients had a low score, 52.9% had intermediate and 24.2% had high • At 3 days 24.2% of low, 36.4% of intermediate and 40.2% of high groups had a novel stroke event • At 3 months 22.7% of low, 36.9% of intermediate and 40.4% of high groups had a novel stroke event 	<ul style="list-style-type: none"> • Distribution of the ABCD² score in the entire group of 511 patients did not significantly relate to stroke recurrence at either 3 days or 3 months. • Clinical diagnosis by a trained neurological expert will always be superior to the ABCD² scoring system. • ABCD² system showed high predictive value for minor ischemic stroke but is not useful for prediction of TIA patients
<p>Ishida al., 2013 ¹²</p>	<ul style="list-style-type: none"> • 33% of patients reviewed in low risk, 58% in moderate risk and 9% in high • The analysis between comparing scoring results from 2 investigating neurologists demonstrated a 72% match for total score and 82% for risk category • When compare neurologist results to retrospective scoring one neurologist had 58% match the other 44% • Retrospective matches for risk category placement was 57% for one neurologist and 71% for the other 	<ul style="list-style-type: none"> • Found that there was a significant degree of homology for the comparison of inter-rater analysis but very limited homology between retrospective analysis and current • The categories that demonstrated the most dissimilar results were the clinical features and duration. Authors attribute this to these aspects relying heavily on patient input and self-reporting • Found that 1/3 of patients were misclassified when using retrospective analysis
<p>Perry et al., 2011 ¹⁹</p>	<ul style="list-style-type: none"> • 38 patients had stroke within 7 days, 27 between 7 and 90 days • Of 38 only 15 had a score of >5, sensitivity 31.6% (95% CI 19.1-47.5) • At 7 days when a cut point of 2 is used was highly sensitive (94.7%, 95% CI 82.7-98.5) but not specific (12.5%, 95% CI 11.2-14.1), 90 days showed similar results • 7 days: 	<ul style="list-style-type: none"> • Authors state: "This prospective study found that the high-risk ABCD² score is not sensitive enough to be the sole guide for assessing risk for patients in emergency departments with transient ischemic attack." (page 1144)

First Author, Publication Year	Main Study Findings	Authors' Conclusions
	<ul style="list-style-type: none"> - AUC 0.65 (95% CI 0.58–0.73) when scored by the coordinating centre - AUC 0.56 (95%CI 0.47–0.65) when scored by the treating physician • 90 days: <ul style="list-style-type: none"> - AUC 0.65 (95% CI 0.59–0.70) (coordinating centre) - AUC 0.60 (95% CI 0.54–0.67) (treating physician) 	
Sanders et al., 2011 ¹⁷	<ul style="list-style-type: none"> • Of 488 patients investigated 301 had confirmed TIA • The portion of patients having stroke at 2 and 7 days was 1.37% (95% CI 0.37-3.47) and at 90 days was 2.42% (95% CI 0.98-4.95) • AUC results are: <ul style="list-style-type: none"> - 2 days - 0.80 (95% CI 0.68-0.91) - 90 days - 0.62 (95% CI 0.40-0.83) • The PPV and PLR was poor when using cut off of ≥ 4, a cut off of ≥ 5 had only modest specificity • Using a cut off of ≤ 4 for low risk resulted in misclassification of 11.6% 	<ul style="list-style-type: none"> • ABCD² scoring if used alone has poor predictive results following TIA in a clinical setting • The use of cut off scoring led to approximately half of patients with ipsilateral carotid stenosis and atrial fibrillation being wrongly categorized
Stead et al., 2011 ¹³	<ul style="list-style-type: none"> • Total of 15 ischemic strokes at 90 days • Incidence of risk: <ul style="list-style-type: none"> - 7 days (original vs. retrospective cohorts) <ul style="list-style-type: none"> - Low – 2.0% and 1.1% (95%CI 0.29-3.78) - Med – 6.0% and 0.3% (95%CI 0.05-1.67) - High – 10.9% and 2.7% (95%CI 0.92-7.60) - 90 days (original vs. retrospective cohorts) <ul style="list-style-type: none"> - Low - 3.7% and 2.1% - Med – 9.9% and 2.1% - High – 17.5% and 3.6% • Results indicate that ABCD² score did not add any value when patients have been diagnosed with existing TIA work-up at 7 and 90 days post-TIA 	<ul style="list-style-type: none"> • An emergency department TIA analysis using brain carotid imaging is an effective initial diagnostic approach if it is completed in conjunction with proper prevention strategies • The addition of ABCD² scores into the emergency department protocol did not significantly aid in risk classification • Authors agree with the study from North Dublin which cautioned that ABCD² may not be an appropriate method for use in an emergency department of an institution that already has the ability to provide full TIA work-up
Zhoa et al.,	<ul style="list-style-type: none"> • 102 patients had TIA and 69 had stroke 	<ul style="list-style-type: none"> • Found that minor stroke

First Author, Publication Year	Main Study Findings	Authors' Conclusions
2013 ¹⁵	<ul style="list-style-type: none"> • Mean ABCD² score for TIA patients 3.28 and for minor stroke was 4.33 • A cut off point of ≥ 4 is optimal with 66.7% sensitivity and 55.9% specificity to discriminate TIA from minor stroke • Score of ≥ 6 had 30.4% sensitivity and 88.2% specificity to discriminate TIA from minor stroke • Most important criteria to distinguish between TIA and minor stroke are the clinical symptoms and symptom duration (longer = minor stroke) • Is almost no difference between TIA and minor stroke for age, hypertension and diabetes • Distinguishing features for duration are more telltale as 53% of TIA patients last under 60 minutes while 72% of minor stroke patients last longer. • Weakness is 2x more prevalent and speech disturbance is 3x more likely in minor stroke 	<p>patients have higher overall scores</p> <ul style="list-style-type: none"> • In scores ≥ 4 more likely to have high percentage of minor stroke • In scores of ≤ 3 more likely to be true TIA • Given a score ≥ 6 the sensitivity suffers • Both sensitivity and specificity suffer when ABCD² used to distinguish both • ABCD² score cannot supersede the judgment of a trained neurologist or the use of neuroimaging

AUC – area under curve, CVA – cerebral vascular accident, ROC – receiver operating characteristic curves, PPV – positive predictive value, PLR – positive likelihood value