Diagnosis and Management of Transient Ischaemic Attack in Primary Care

Thesis submitted for the degree of Doctor of Philosophy at the University of Leicester

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Thesis abstract

Background

Most patients with Transient Ischaemic Attack (TIA) present to their general practitioner (GP). Early identification and specialist assessment reduces the risk of subsequent stroke and mortality.

Aim

To examine the diagnosis and immediate management of suspected TIA in primary care, and to evaluate the performance of a diagnostic tool (Dawson score) for TIA to guide GPs' referral decisions and to triage clinic referrals.

Design and setting

A mixed methods approach was taken, incorporating three inter-related studies. Firstly, a systematic review on the diagnosis and management of TIA. Secondly, an external validation of the Dawson score at a TIA clinic in the midlands of England. Thirdly, a qualitative study, involving 10 GP telephone interviews to explore their views of TIA, and the potential of a diagnostic tool. A further exploratory study looked into alternative cut-offs for the Dawson score in response to GPs' suggestions, and derived a logistic regression model to estimate risk of TIA.

Results

The review found limitations in GPs' ability to diagnose TIAs and demonstrated the potential for a diagnostic tool to enhance referral patterns. The external validation study concluded that the diagnostic tool could be used alongside GPs' clinical judgement to reduce the number of non-cerebrovascular referrals to the TIA clinic. GPs reported that TIA was likely to be suspected in obvious TIA candidates, and referrals were a strategy to eliminate uncertainty whilst seeking reassurance. A diagnostic tool for TIA could improve the decision-making process and enhance GP confidence. Further analyses concluded that GPs' desired risk percentages combined with clinical judgement may be more useful than cut-offs.

Conclusions

The thesis demonstrated the complexity of GPs' TIA diagnostic and referral decisions, and supported the value of a diagnostic tool. Further work directed towards using primary care data to further develop and implement a diagnostic tool is recommended.

Acknowledgement

Firstly, I would like to acknowledge the team of very supportive supervisors who have guided me throughout this course of work. I would like to thank Professor Andrew Wilson, Dr Amit Mistri, Dr Nicholas Taub and Professor Carolyn Tarrant for providing excellent supervision, insight, advice and practical support without which, this thesis would have been extremely difficult to complete.

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Authorship and contribution statement

All the chapters within this thesis are entirely the product of my own work. This work has been consistently supported particularly in reference to the concept, design, analysis, interpretation and write up of the individual studies which, contribute to the thesis as a whole by my supervisors: Professor Andrew Wilson (AW), Dr Amit Mistri (AM), Professor Carolyn Tarrant (CT) and Dr Nicolous Taub (NT).

AW and AM provided Priyanka Bose (PB) with guidance on the design of the systematic review (Chapter 2). The search strategy was developed by all authors (PB, AW and AM). Keith Nockels, the academic librarian and Selina Lock, the research services consultant guided PB with the different search engines (Medline, Embase, Web of Science and Scopus); and the search was conducted by PB. PB and AW independently read full papers for inclusion and extracted data from included papers. AW and PB further reviewed the data to assess the methodological quality of the papers identified from the systematic review. AW and AM further supported PB with the synthesis of the findings. PB interpreted the findings with the help of AW and AM, and PB further wrote the manuscript with support from AW and AM. All authors discussed the feedback on the manuscript and contributed to the final publication.

AW, AM and NT aided PB with the design in both the feasibility and external validation study outlined in Chapter 3. PB participated in observational consultations prior to the feasibility study and collected the data for a period of 3 months in the external validation study. PB collated the data in preparation for statistical analyses, and AM helped obtain the data from the clinic database. NT provided guidance on the statistical analyses and PB carried out the experiments with support on the write up of this chapter from AW and NT. Their guidance were further extended for the exploratory Chapter 5 which enabled further analyses and interpretation of the findings.

PB, AW, AM and CT designed and directed Chapter 4. PB led the ethics application (University of Leicester Sponsor green light process, University of Leicester ethics committee, research and governance and HRA approval); and AM helped PB with the recruitment of participants for this study. All authors helped develop the invitation letter,

consent form and information sheet that were sent to GPs via the practice managers. Their guidance was extended through to developing a topic guide based on the findings from the systematic review (Chapter 2). AW particularly advised on setting up pilot interviews with GPs and amending the topic guide accordingly before the main interviews with GPs.

CT aided with qualitative methods through coding and identifying themes. AW, AM and CT all supported the write up of this chapter. PB wrote the manuscript with direction from CT and AW, which led to the publication of this study.

All supervisors guided the final discussion chapter (Chapter 6) and provided their individual expert thinking.

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Chapter 1: Introduction

This chapter introduces the topic of Transient Ischaemic Attack (TIA) with particular focus on the diagnosis of the condition in primary care. The chapter also provides a context to the programme of work outlined in this thesis by highlighting:

1. The association between TIA and stroke
2. The importance of early TIA diagnosis in primary care and efficient referral to secondary care
3. The difficulties of the diagnosis and management of TIA in primary care

Subsequently, the research objectives for this thesis will be described, and an overview of the chapters will be detailed.

1.1. Defining TIA, stroke and minor stroke

Stroke, minor stroke and transient ischaemic attack (TIA) are conditions caused by restricted blood supply to the brain (1-3). Definitions of stroke, minor stroke and TIA are summarised in Table 1.1, followed by a more detailed description of the definitions cited within the literature.

Table 1.1: Definition of stroke, minor stoke and TIA

Diagnosis	Definition	Symptoms	Evidence of infarction
TIA	Traditionally defined as temporary episodes of focal brain dysfunction of presumed vascular aetiology (4)	Short lasting, usually less than 24 hours	No
Stroke	Rapidly developing clinical signs of focal or global disruption of cerebral function, lasting 24 hours or longer and can lead to disability or death of the patient (5)	Long-lasting and disabling, symptoms lasting longer than 24 hours	Yes
Minor stroke	An episode of neurological dysfunction whereby symptoms are mild and non-disabling. In clinical practice, both minor	Lasting longer than 24 hours	Yes

	stroke and TIA patients experience similar diagnostic evaluations, as both groups have relatively high early risk of stroke recurrence (6)

Symptoms of both TIA and stroke are weakness, numbness or paralysis (either on the left or right side of the body); loss of coordination, speech and visual disturbances (2). TIAs and minor strokes (TIAMS) are considered to be manifestations of the same disease as they have the same aetiology and a similar prognosis (7).

In 1975, the first internationally accepted clinical classification for cerebrovascular disorders was formulated, which included the diagnostic criteria for transient attacks of neurological dysfunction (8). Transient neurological attacks (TNAs) are attacks with temporary (<24hours) neurological symptoms and without a clear cause, and can present with focal symptoms (TIA), non-focal symptoms that can include non-localising cerebral symptoms or mixed TNA, if the symptoms presented are a mix of focal and non-focal symptoms. In comparison to focal TNA (defined as a TIA), non-focal TNA symptoms include blurred vision, unsteadiness, confusional states, transient global amnesia and paraesthesia and unlike a TIA, the prognostic significance of TNA with non-focal or mixed symptoms has not been established (4).

The standard definition of TIA has been questioned (9, 10). In 2002, it was proposed that TIA should be defined as a brief episode of neurological dysfunction due to a focal disturbance of the brain or retinal ischemia, with clinical symptoms usually lasting less than one hour, and without evidence of infarction (1).

More recently, the American Heart Association/American Stroke Association (AHA/ASA) updated the definition of TIA to remove the reference to time (symptoms typically lasting less than one hour) and defined TIA as a transient episode of neurological dysfunction caused by focal brain, spinal cord or retinal ischemia, without acute infarction (2). However, this diagnostic definition relies on the use of early magnetic resonance imaging (MRI) and/or computed tomography (CT) scan which is not always available in UK hospitals (2).

The new definition has not been universally adopted and organisations such as the National Institute for Health and Care Excellence (NICE) (11) and World Health Organisation (WHO) (12) still use the 24-hour criteria.

During the past 25 years, imaging the brain and its blood supplying vessels safely and efficiently has become a reality, and over the past 10 years modern brain and vascular imaging has become more available (13). Therefore, as knowledge and technology keep evolving, the nature, causes, clinical and imaging findings in patients with cerebrovascular diseases will continue to be researched and understood. Furthermore, the definitions will most likely continue to change.

1.2. Incidence/prevalence of TIA

TIA is common, with annual incidence of 15–83 patients per 100,000 population recorded across the world and in the UK. However, estimates of incidence and prevalence need to be considered with caution (14). The prevalence and incidence of TIA are frequently underestimated due to a lack of recognition of symptoms (2). For example, it has been reported that a considerable proportion (3.2% in a population survey of over 10,000) of adult's experience TIA symptoms but do not seek medical advice. Thus, not receiving a physician-diagnosis (15). Estimating the incidence and prevalence of TIA is also complicated by the change in definition of TIA (time vs tissue-based definition) and variable adoption of the new proposed classification.

1.3. The burden of TIAMS

A multicentre Spanish study of 1,255 patients reported that 2.6% of patients experienced a stroke in the first week after a TIA event and 3.0% had a stroke 8–365 days later (16). Furthermore, a large population-based cohort study in US, consisting of 16,409 participants reported that 15% of ischaemic strokes were preceded by a TIA (17). Another study found 23% of patients with ischaemic stroke have had a prior TIA, usually between hours to days before a stroke (18).

Two prospective observation studies evaluated the risk of stroke after a TIA or minor stroke at 1 year and at 5-years (19)(20). The study evaluating the 1-year risk included a total of 4,789 patients at 61 sites in 21 countries. The results highlighted that the stroke rate at days 2, 7, 30, 90 and 365 were 1.5%, 2.1%, 2.8%, 3.7% and 5.1%, respectively. The 5-year follow up study included 3,847 patients. Of the 61 sites, 42 had follow-up data on more than 50% of their patients at 5 years (3,847), which represented 80.3% of the initial cohort. Stroke

occurred in a total of 9% (345 patients) during the 5-year period. A primary outcome event of fatal stroke occurred in 13% (44 patients), with 149 of the 345 patients (43.2%) experiencing a stroke during years 2–5.

A study using data from a rapid access clinic for patients with suspected TIAMS and follow up data from four overlapping data sources estimated the 5-year risk of ischaemic stroke, myocardial infarction (MI), major haemorrhage or death. Of the 5,997 patients who were seen at the rapid access clinic, 60% (n=3,604) were diagnosed as TIAMS or with other diagnoses (40%, n=2,392). By 5 years, 19% (95% CI: 12–15%) of the patients with a clinical diagnosis of TIAMS had a subsequent ischaemic stroke or MI compared with 10% (95%CI: 9-12%) in patients with other diagnosis, with an overall higher hazard of stroke or MI compared to patients with other diagnoses (21).

There is evidence to suggest that the burden of TIAMS may extend beyond the risk of stroke. Fatigue was found to be common in TIAMS patients (22). Similarly, a study looking into ongoing impairments following a TIA which included a total of 9419 TIA patients and 46,511 controls found that TIA was associated with significantly increasing subsequent consultations for fatigue, psychological impairment which included depression, anxiety and post-traumatic stress disorder as well as cognitive impairment. The findings from this paper highlights that impairments exist after initial symptoms of TIA have resolved which should be considered by clinicians when treating TIA patients (23). Additionally, another study found that 15% of patients who experienced a TIA or minor stroke and were previously not disabled had at least slight disability at days 90 post-TIA (24).

1.4. Benefits of early management

Diagnosis and treatment of TIA are often delayed by the lack of immediate access to a TIA clinic (25). The SOS-TIA study on the feasibility and effects of a hospital clinic with 24hr access included 1,085 patients with suspected TIA of which 574 (53%) were seen within 24hr of symptom onset. The study found that the early identification and specialist treatment of TIAMS reduces the risk of subsequent stroke and consequent disability and mortality (25).

In an observational study, the early assessment and management of TIA and minor stroke resulted in an 80% reduction of recurrent stroke at 3 months from initial TIA. The early use of Existing Preventive Strategies for Stroke study (EXPRESS) established comparable results

(26). Urgent initiation of stroke prevention drugs such as aspirin, statins or antihypertensive agents reduced the risk of stroke within 90 days in patients with TIA, and minor stroke by 80% (26). Also, in the NORTHSTAR study, set in five TIA clinics where patients were seen within the first day, the risk of stroke observed within 90 days was less than half of what was expected (27).

1.5. Rapid access TIA clinic

If a TIA is suspected either in primary care by the GP or in the emergency department by a hospital doctor, the patient will be referred to the rapid access TIA clinic. At the rapid access TIA clinic, a stroke consultant will ask about the patients' history and undertake examination(s) (that may be appropriate for the patient) to determine a diagnosis (11).

Patients with a TIA are at very high risk of imminent stroke (highlighted in section 1.3). This risk could be decreased by 80% if patients are promptly investigated and treated by stroke specialists (25, 26). Rapid access TIA clinics are now widespread across the UK (28), Wales (29), as well as Australia (30), New Zealand (31) and many other countries. Most TIA clinics in England are run from Monday to Sunday and include an assessment from a stroke specialist, and a wide range of investigations such as brain, arterial imaging to enable a diagnosis of stroke/TIA and also alternate diagnoses. Rapid access clinics are also useful in identifying new and potentially treatable risk factors. These include hypertension, diabetes mellitus, hypercholesterolaemia and ensuring patients are on optimal antiplatelet therapy. Additionally, specialists are able to discuss the diagnosis, benefits of therapeutic interventions and lifestyle changes following on from the diagnosis. These include diet, exercise, smoking cessation, driving and in some cases, surgery (29).

The introduction of rapid access TIA clinics has generated an awareness among general practitioner's that patients with symptoms suspected of TIA should be treated immediately and referred urgently (32). The TIA clinic provides a safe alternative to hospital admission (11). Despite this however, TIA clinics struggle to achieve timely assessments which was less than 7 days for low-risk patients and within 24 hours for high-risk patients at the time of conducting this study (33). The average waiting time for a clinic appointment in 2016 was 9 days with patients waiting a maximum wait up to 23 days. Although this seemed to improve in Wales in 2018, when the average waiting time was 2.5 days with all patients seen in less

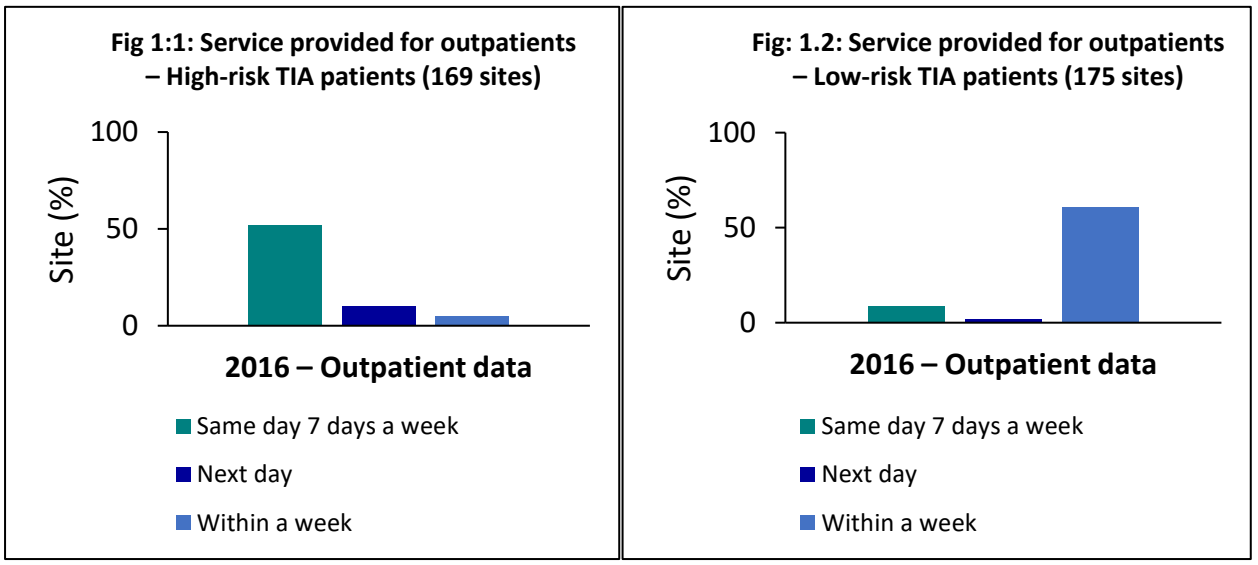
than 7 days. The TIA mimic referrals to the service have been around 60% which has remained relatively unchanged (29).

Access to prompt assessment and TIA clinic varies considerably between Australian hospitals. It was reported that nineteen sites (26%) reported access to a specialist outpatient clinic for TIA management. In this survey, only 5% of sites involved a stroke specialist for an initial assessment of the suspected TIA patient. Additionally, over 60% of the sites outlined a wait of more than a week and 30% more than a month. Given that the benefits of early assessment and intervention of TIA has been consistently outlined (25, 26), these delays are concerning (34). Similarly, a study reported that there is room for improvement of the Dutch system of TIA management due to the delay from symptom onset to review in the rapid access TIA service. The guidelines' recommendation of an assessment by a neurologist at the TIA clinic the same or next day was not met, resulting in inadequate prevention of an early stroke (35).

It is difficult to estimate the exact proportion of TIA patients who are seen in clinic within the 24hr–7day timeframe. However, a small study in Leicestershire reported that approximately 10% of high-risk patients were seen within 24 hours and 40% of low risk referrals were seen within 7 days (36). Figure 1.1 and 1.2 shown below from the 2016 Sentinel Stroke National Audit Programme (SSNAP) refers to the data collected from NHS hospital Trusts in England, Wales and Northern Ireland. Just over 50% of sites cannot offer a same day 7-days a week service for high-risk patients (Fig 1.1) and just over 60% of low-risk patients are seen within a week (Fig 1.2) (37). Aside from the SSNAP data, there is limited evidence in the UK and other countries on providing an outpatient service within 24-hour and 7 days to suspected TIA patients. However, a study looking into 134 Australian hospitals reported that over 60% of sites reported a wait of more than a week, and 30% more than a month (38). Additionally, another study in New Zealand found that two district health boards stated that most patients were assessed in outpatient clinics with a usual waiting time of 1 week or more (39). Although the evidence on the number of patients seen within the recommended timeframe and how many TIA clinics are able to provide services to suspected TIA patients is limited, the failure to rapidly assess patients with TIA represents a missed opportunity for stroke prevention. Additionally, given the benefits of early assessment after TIA, the delays reported are concerning.

Referrals without increase in resources, lack of clinic support staff or dedicated clinic space, and clinic cancellations that contribute to clinic delays have been some of the issues that have been identified (29). With the high number of referrals that do not have a diagnosis of TIA nor stroke, the TIA clinic capacity has become an issue. As highlighted above, clinics are already struggling to see suspected TIA patients according to the recommended NICE timeframes. This is currently only achieved in 35% of UK centres and the nationwide median delay from referral to specialist TIA clinic is approximately 12 days (40). A significant proportion of suspected TIA patients (30–50%) referred to the clinics are assessed as not having a TIA (NICE, 2019) (41)[1]. This ultimately leads to delays in seeing patients who truly do have a TIA. Therefore, failing to meet guidelines on next day assessment, and potentially reducing effectiveness of TIA clinics at preventing subsequent stroke.

Figure 1.1 and 1.2: Provision of services for high-risk and low-risk suspected TIA patients



1.6. Risk stratification

Risk scores have been used to assess patients to prioritise them for urgency of referral. In order to predict early risk of stroke after a TIA, various risk scores have been developed. The original ABCD score (42) was derived from the Oxfordshire community stroke project. The score consisted of four components which were: age, blood pressure, clinical features of TIA and the duration of symptoms. The clinical features found to be a predictive factor of stroke

[1] https://www.nice.org.uk/guidance/ng128/chapter/Rationale-and-impact

after a TIA were then tested in a derivation cohort of 209 TIA patients recruited from the Oxford Community Stroke Project classification (OCSP) (43).

Johnson et al (7) proposed a modified risk score (ABCD2), with the additional element of diabetes. In a later and larger validation study (7) it was confirmed that within 4,800 TIA cases the ABCD2 score was highly predictive of subsequent early stroke risk.

Risk categories were assigned 0–3 low-risk, 4–5 moderate risk, 6–7 high-risk (7), the details of which are provided in Table 1.2.

Table 1.2. Risk categories of stroke according to the ABCD2 score

	Score	*2 days*	*7 days*	***90 days***
High-risk	6–7	8%	12%	18%
Moderate risk	4–5	4%	6%	10%
Low-risk	0–3	1%	1.2%	3.1%

An ABCD2 score (≥4) have substantially higher early 7-day risk of stroke which ranges between 5.6 and 23.8% (44-48). One study showed that 80% of strokes were in the high ABCD2 >4 category (49), and in another study, all subsequent strokes (n= 4, 8.3%) were within the first 7 days after a TIA and had an ABCD score >4. Similarly, another study (46) showed that 5 out of 57 patients (8.8%) with score 5 and 6 on ABCD had strokes within 7 days. These studies consistently indicate that patients classified with ABCD or ABCD2 scores 4–5 (labelled as moderate risk) and higher have a substantially higher risk of early stroke. This has led in the ABCD2 scores to be divided into two categories: low risk 0–3 and high-risk ≥4, and these are the categories that are consistently used.

The ABCD2 score falls under the terminology of a clinical prediction rule (section 1.10) as it classifies an individual into a risk group (high risk or low risk). The score will be referred to as a risk stratification score in the following chapters in consistency within existing literature (50). The ABCD2 scoring criteria is outlined in Table 1.3.

Table 1.3: ABCD2 scoring criteria for the estimation of stroke risk in TIA patients

ABCD2		
A	Age ≥60 years	Y (1 point)
B	Blood pressure >140/90 mmHG	Y (1 point)
C	Clinical features: Unilateral weakness	Y (2 points)
	Speech disturbance without weakness	Y (1 point)

	Other	Y (0 points)
D	Duration >60 minutes	Y (2 points)
	10–60 minutes	Y (1 point)
	<10 minutes	Y (0 points)
D	Diabetes	Y (1 point)

1.7. Prioritisation of referrals

In practice, most TIA patients are not assessed at specialist TIA clinics within the timeframe previously recommended by NICE guidelines (33); high-risk within 24 hours of symptom onset and low-risk within 7 days.

The ABCD2 score was used to prioritise assessment at TIA clinics. However, studies have reported that the ABCD2 score has a low sensitivity and specificity when used by non-specialists in the community or emergency department (51, 52). It has been reported that nearly two thirds of patients who do not develop a subsequent stroke are falsely classified as high-risk. This suggests that the utility of the ABCD2 score in prioritising referrals is limited (53).

The score is frequently inaccurate, with a tendency to underestimate stroke risk (51, 54), with the neurologist agreeing with the referring physician's total ABCD score in only 42% cases (54). These findings emphasise the importance of urgent specialist assessment of suspected TIA patients, and that ABCD2 scores by non-stroke specialists cannot be relied upon in isolation to risk-stratify patients. Furthermore, The ABCD2 does not identify patients with carotid stenosis or atrial fibrillation (AF) as one in five patients with an ABCD2 score less than 4 have symptomatic carotid stenosis of >50% or AF, which underscores benefit from rapid diagnostic evaluation regardless of risk score (55).

Although studies have reported that the stroke risk is higher for high-risk patients according to the ABCD2 score than low-risk, the short-term stroke risk from studies evaluating the ABCD2 score ranged between 1.2%–5.9% within 7 days for low-risk patients with an ABCD2 score of 3 or less (56). This suggests that the risk is still high for low-risk patients and these patients should still be seen within 24-hours.

The ABCD2 score was found not to reliably discriminate between low-risk or high-risk patients (57). 1 patient in 5 with an ABCD2 score of less than 4 had a 90-day stroke risk

similar to patients with an ABCD2 score higher than 4. The authors concluded that low-risk patients should be evaluated without delay regardless of ABCD2 score as these patients have treatable causes associated with highest short-term risk of stroke (58).

Over the last few years, there has been an alteration from solely using the ABCD2 score to reliably discriminate between high-risk and low-risk TIAs (59). The 2017 Australian and New Zealand guidelines outline that the ABCD2 score should not be used in isolation to decide the urgency of assessment for suspected TIA patients. This may delay the recognition of AF and carotid stenosis (55, 59). The UK stroke guidelines from 2017 however, abandon the use of the ABCD2 score which is no longer recommended to be used as a risk stratification tool to prioritise referrals (11, 41, 60). Based on the limited predictive performance of risk score, the NICE committee agreed that all cases of suspected TIA should be considered as potentially high risk of stroke. Also due to the fact that the risk stratification tool is not a diagnostic test, it is important to urgently confirm or refute the diagnosis of a suspected TIA with specialist opinion. This is particularly important because of the significant proportion of suspected TIA (30–50%) who have an alternative diagnosis, that is TIA mimics. Therefore, it was agreed that all suspected TIA patients should have specialist assessment and investigation within 24 hours of the onset of symptoms. Furthermore, an original cost utility analysis was undertaken in 2008. Based on the results, the immediate assessment had both better health outcomes and lower costs compared with assessment within a week for the population of suspected TIA, without the use of a risk stratification tool (NICE, 2019) (41).

It can be proposed that the updated NICE guidelines that abandon the use of the ABCD2 score will therefore, increase the burden of TIA clinics to assess these patients within 24-hours. Single stroke services based on Airedale and Bradford sites report that the sites currently offer a 5-day TIA clinic provision, but do not have a weekend TIA clinic provision. Patients referred over the weekend are often seen on a Monday morning which is non-compliant with the updated 24-hour specialist assessment requirement. Many of the clinics in the UK may have similar 5-day TIA clinic services, and the others which offer a 7-day service are expected to experience challenges in assessing patients within the 24-hour timeframe[2].

[2] http://www.airedale-trust.nhs.uk/wp/wp-content/uploads/2018/11/item-8i-CE-Report-App-1-Stroke-Service.pdf

Based on the updated NICE recommendation, the ABCD2 score is no longer used as a risk stratification tool. Therefore, the problem is not only about assessing patients in terms of urgency, but is a more fundamental issue for GPs on deciding how likely it is that a patient has had a TIA, and is therefore a candidate for referral, based on their symptoms. It can be suggested that there is value for a diagnostic tool that can support GPs' decision-making process in primary care, to help reduce unnecessary referrals.

1.8. Management of TIA and stroke according to NICE guidelines

1.8.1. Rapid recognition of symptoms

Tools have been developed to support patients and healthcare professionals in identifying symptoms of stroke. The Face, Arm, Speech, Time (FAST) was adopted as a tool to improve symptom recognition after stroke and has been formed on the basis of a public education in many countries such as UK, Ireland, USA, Australia and New Zealand. In the UK, FAST was used as an ongoing television public awareness campaign from 2009 onward and recommended for use outside hospital to screen for a diagnosis of stroke or TIA (61).

A study looking into the medical attention after TIAMS before and after UK FAST education campaign among 2243 patients with TIA or stroke in a population-based study reported that after the FAST campaign, patients with major stroke more often sought medical attention within 3 hours. However, for TIAMS there was no improvement in the use of emergency medical services (EMS) or time to seeking medical attention within 24 hours (61).

Studies have indicated a moderate influence of FAST in identifying stroke warning signs. There was an increase in individuals arriving at secondary care, due to fewer individuals contacting GPs as the first response to stroke symptoms, and greater numbers of appropriate patients with stroke symptoms attending specialist centres within the stroke onset time (62-64). However, in this study, no positive association of the FAST television campaign with presentation via EMS after TIAMS were observed. This was also the case when patients attributed their symptoms to stroke, only 23% (130 of 458) contacted EMS. Additionally, patients were unlikely to act according to the FAST campaign when their symptoms did not match the more severe symptoms described in the education advertisements, and patients still delayed in seeking medical attention and presented to

primary care clinicians (65). This correlated to a study in 2013 which found that although 70% of the public surveyed were aware of the FAST campaign, poor recognition of symptoms included leg weakness in 57% and visual loss in 44%. Higher awareness was observed for the FAST symptoms which included facial weakness in 89%, arm weakness, 83% and speech problems 91%. A recent 2019 study found that more than a third of patients experiencing a TIA delays medical attention for more than a day. Thus, critically extending the initiation of stroke preventive treatment. The study reported that there is still insufficient awareness among lay people that symptoms suggestive of TIA should be considered as an emergency (32). The results overall emphasise the need for campaigns that are tailored to transient and less severe symptoms as this may lead to delays in presentation, specialist assessment and secondary prevention.

A recent systematic review examined the effectiveness of FAST campaign based on 11 published articles between 2010 and 2017 using various mass media interventions designed to increase public recognition and emergency response to stroke symptoms. According to the six studies examining the effectiveness of using the FAST method, one study in England reported that approximately 70% of the survey respondents had heard of the campaign previously and over 90% of respondent reported the intention to call EMS when suspecting a stroke. However, most of studies concluded that although the FAST method might make individual's aware of the symptoms, it has limited impact on behaviour as the campaign still does not significantly impact in promoting prompt response for EMS (66).

The campaign is intended for both public and professionals, but it may have more impact on professionals than the public. Accurate recognition of stroke by ambulance or emergency medical services, emergency room departments and primary care doctors are necessary to ensure rapid management to acute stroke units and treatment of these patients. It has been highlighted that pre-hospital ambulance paramedics are in a unique position to reduce delays in presentation and treatment in acute stroke (67).

Two studies evaluated the diagnostic accuracy of FAST by paramedics compared with those of primary care doctors and ER doctors (67, 68). The percentage of correctly identifying cases with a positive diagnosis of stroke/TIA (PPV) for the ambulance staff was 78%. There were no significant differences on the number of non-stroke cases referred to the stroke service between the paramedics, primary care doctors and ER doctors. Additionally, the

ambulance paramedic diagnosis of stroke was as accurate as primary care doctors or ER doctors. Although it was highlighted that the strokes that were admitted were more severe and therefore, may have been easier to diagnose (67). The other study looking into the diagnostic accuracy of FAST by paramedics reported an acceptable inter-observer agreement between neurological signs recorded in the FAST by paramedics and also by stroke physicians after admission (68).

The use of FAST to identify stroke in emergency calls versus paramedics has also been reported. A FAST symptom was present in 56% of the patients with stroke/TIA in emergency medical communication centre, but also in 44% of the patients with a stroke mimic. Alternatively, the FAST was positive in 80% of the stroke/TIA patients included by the ambulance, but not identified by the emergency medical communication centre which highlights a concern of emergency calls not capturing stroke patients, risking a delay of treatment. Additionally, FAST used in the ambulance had a high chance of correctly identifying stroke patients, with a positive predictive value of (74%) (69). This was similar to the positive predictive value reported in the study comparing the diagnostic accuracy of FAST by paramedics versus primary care doctors and by ER doctors (67).

The ROSIER (Recognition of Stroke in the Emergency Room) is a validated tool to discriminate between acute stroke and stroke mimics in individuals presented to the emergency room (70). It is more detailed than the FAST assessment as it includes blood sugar, visual field assessment, leg weakness and documentation of a history of seizures or loss of consciousness. The early use of ROSIER has been shown to have promising results which are more accurate than the FAST (33, 68). However, an alternative study proposed that ROSIER was not better than FAST for pre-hospital recognition of stroke and a revised version of FAST incorporating the assessment of seizure activity may improve stroke identification as well as decision making by ambulance clinicians (71). See Table 1.4 on the test criteria for FAST and ROSIER.

Table 1.4: Test criteria for FAST and ROSIER

	Recognition of symptoms of stroke and TIA	
FAST	Face: The face may have dropped on one side	
	Arms: May not be able to lost both arms and keep them there due to arm weakness or numbness	
	Speech: Slurred speech or may not be able to talk at all, despite appearing awake	
	Time: Call 999 immediately if any of the above symptoms occur	
ROSIER	Has there been loss of consciousness or syncope?	Y (-1 point)
	Has there been seizure activity?	Y (-1 point)
	Asymmetric facial weakness	Y (1 point)
	Asymmetric leg weakness	Y (1 point)
	Speech disturbance	Y (1 point)
	Visual disturbance	Y (1 point)
	Visual field defect	Y (1 point)

1.8.2. Stroke severity test and degree of disability post-stroke scale

A test for stroke severity is usually estimated by the NIHSS which quantifies the severity of neurological deficit through scoring consciousness, eye movement, vision, facial paralysis, leg and arm motor drift, coordination, sensory loss, language, speech and attention (72). Additionally, the modified Rankin Scale is a commonly used scale for measuring the degree of disability or categorise the level of functional independence in daily activities in those who have suffered a stroke. The modified version differs from Rankin's original scale with the addition of grade 0 which, indicates a lack of symptoms (73) (Table 1.5).

Table 1.5: National Institutes of Health Stroke Scale (NIHSS) for stroke severity and modified Rankin scale

	Stroke severity
NIHSS	Level of Consciousness
	Ask month and age
	'Blink eyes' and 'squeeze hands'
	Test horizontal extraocular movements
	Test visual fields
	Test facial palsy
	Test left arm motor drift
	Test right arm motor drift
	Test left leg motor drift
	Test right leg motor drift

	Test limb ataxia
	Test sensation
	Test language/aphasia
	Test dysarthria
	Test extinction/inattention

	Degree of disability or level of independence on daily activities post-stroke
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Dead

1.8.3. Treatment and specialist assessment

Initial management of suspected TIA comprises of the administration of aspirin (300mg daily) and/or clopidogrel to prevent occlusive vascular events; blood tests, including blood glucose, lipids, platelets and an ECG test to exclude AF. Patients should be advised not to drive until they have been seen by a specialist as this is when definitive guidance will be provided. Specialist assessment should confirm a diagnosis of TIA, assess risk factors, manage initial pharmacotherapy and lifestyle advice and if appropriate, refer the patient for brain and carotid imaging (11, 60).

Brain imaging would only be necessary when the vascular territory or pathology is uncertain or a haemorrhage needs to be excluded (33). Carotid imaging however, should be completed if carotid endarterectomy is considered and should be completed within a week from specialist assessment. Individuals with a confirmed diagnosis of TIA are offered a follow-up appointment at one month in primary or secondary care and then annually in primary care. The purpose of the follow-up appointments is to review the patients' drug, risk factor control therapy and lifestyle advice in order to minimise risk of future stroke (33).

1.9. Diagnosis in primary care

GPs do not currently have a diagnostic tool that they can use to assess the likelihood of a TIA. Tools for stroke recognition such as the ROSIER (70) and FAST (67) exist (Table 1.4), but these are based on the demonstration of physical deficits, which are usually absent in TIA, particularly when presentation is delayed (74). TIA symptoms are often under-recognised due to their transient nature (75) and some symptoms such as non-focal symptoms are not incorporated in the FAST acronym (74, 76).

Over 150,000 suspected TIA cases each year are referred to outpatient clinics in England (77). The majority of referrals are made by GPs as they are usually the first contact for most patients who experience symptom(s) of TIA. The GP therefore plays a central role in ensuring that people receive a timely and accurate diagnosis, either in primary care, or from an appropriate specialist as a consequence of a GP referral. The diagnosis however, is not common in general practice, making it difficult for GPs to diagnose TIA with high specificity (78).

There are several conditions which may mimic a TIA, including migraine, partial seizure, vestibular disorders, intracranial lesions, syncope or psychogenic illness, making the diagnosis of TIA difficult (79). Diagnosing a TIA in primary care is based on clinical history and is often challenging due to the lack of residual signs at the time of the assessment. Symptoms of TIA resolve within an hour in 60% of cases and within 2 hours in 71% (18). TIA symptoms continuing if the patient is seen within 24 hours on onset cannot differentiate between TIA and stroke.

As well as missed opportunities for stroke prevention, there are other consequences such as: misdiagnosis/inaccurate diagnosis, including inappropriate investigation, incorrect treatment and the delay in the recognition of a mimic.

1.10. Clinical prediction models

A clinicians' ability to diagnose accurately is central in determining an individuals' prognosis and providing timely and appropriate treatment for that individual. However, the diagnosis can often be challenging. Clinical prediction models are developed to aid clinicians' clinical decision making (80).

A clinical prediction model is a combination of clinical findings that have statistically demonstrated predictability in determining the presence of a condition (diagnosis) or further occurrence of a condition (prognosis) (80, 81). In the diagnostic setting, the probability that a disease is present can be used to inform the referral of patients for further testing, initiate treatment directly or reassure individuals that a serious cause for the symptoms are not likely. On the other hand, in the prognostic setting, predictions can be used to advise patients on lifestyle and therapeutic options based on the risk of developing a particular outcome or event in the future (82, 83). The estimated risk can also be used as a risk stratification to triage urgency of treatment for those who are high or low risk of the condition. Clinical prediction models however, are referred to by an array of terms which include, prognostic models, risk scores or prediction rules (84). Additionally, there is no agreement among developers and researchers in the literature on the established term for clinical prediction tools (85, 86).

Well known diagnostic models include the Wells score, which is used for the diagnosis of deep vein thrombosis (87). Alvarado score which is a clinical scoring system used in the diagnosis of appendicitis (88) and Ottawa Ankle Rules which aide clinicians to decide if a patient with foot or ankle pain should be offered X-rays to diagnose a possible bone fracture (89). Additionally, a well-known prediction model derived and validated in secondary care as a prognostic score is the ABCD2 score which predict the risk of stroke in suspected TIA patients (section 1.6). Although the score has been designed for prognosis, rather than diagnostic, the score has been used for both in clinical practice. However, relatively few data exist on the potential diagnostic usefulness of the score (90, 91) and evidence exist that suggest that the ABCD2 score should not be used to influence diagnostic testing (92). Furthermore, prediction models used for different conditions include the cardiovascular disease risk score (QRISK) which calculates an individual's risk of developing a heart attack or stroke over the next 10 years (93). The Nottingham Prognostic Index is used to determine prognosis following surgery for breast cancer (94) and the Simplified Acute Physiology score used to estimate mortality in the intensive care unit patients (95).

1.11. Dawson score- Diagnostic tool for TIA

Dawson et al (96) derived a diagnostic score for TIA, and at the time of when this thesis was conducted, this was the only specific diagnostic tool for TIA within the literature which was based on the reported symptoms obtained from patients. Dawson et al hypothesised that a diagnostic score could be developed to aid with the diagnosis of TIAMS. Furthermore, its use would reduce non-cerebrovascular referrals, and that this would reduce the overall clinic waiting times and facilitate rapid assessment.

The Dawson score was derived using multivariable logistic regression from routinely recorded secondary care clinical notes. The authors used a derivation and validation method, where a risk score was developed using data contained in the West Glasgow Stroke Registry and was tested on an independent prospective data set from the same source. The impact of the projected reduction in non-cerebrovascular referral rate was then assessed using real data on referral rates and clinic availability during the prospective validation study.

In regards to the model derivation process, the variables that showed discriminatory power were considered for inclusion in a clinical scoring system. Non-weighted (where explanatory variables were assigned a value of 1) and weighted scoring systems (based upon the regression coefficient and rounded to one decimal place) were then developed.

The score includes nine variables, seven of which relate to the clinical event such as headache, loss of consciousness, seizure, diplopia, speech disturbance, unilateral facial and limb weakness. To calculate the Dawson score each variable is given a value if present/absent and all values summed. Table 1.6 below is the score calculation depending on the presence or absence of each variable and the patients' age multiplied by 0.04. Higher values of the score correspond to higher probabilities of the condition.

Table 1.6: Dawson score variables and score calculation

Dawson score		
Variable	Score if yes	Score if no
History of stroke or TIA	0.5	0
Headache	0	0.5
Diplopia	1.2	0
Loss of consciousness	0	1.1
Seizure	0	1.6
Speech abnormalities	1.3	0

Unilateral limb weakness	1.7	0
Unilateral facial weakness	0.6	0
Age	Multiply by 0.04	

The study conducted by Dawson reported a sensitivity of 93% and specificity of 34%, and concluded that the score could be utilised to reduce the number of non-cerebrovascular referrals to the TIA service (96). However, the clinical utility of the score once patients have been referred to a TIA clinic and for triaging patients in secondary care has not been tested in practice. A more detailed discussion on the Dawson score study is provided in section 3.1.2.

1.12. TIA referrals and the potential role of the Dawson score

The GP's objective is not to always reach a definitive diagnosis in primary care. It is also a process which acts as a gateway to specialist diagnosis and further management. If GPs can confidently exclude TIA cases in primary care, then this would reduce the high number of referrals at the clinic, over half of which are not diagnosed as a TIA or stroke (97). There is consensus that diagnosed TIA should not be managed in primary care, rather, it needs specialist investigation.

There is a case for decision support tools to be established in general practice to enable better differentiation of TIA from other transient neurological attacks (TNA), and thereby enable more appropriate use of limited TIA clinic resources. Additionally, there may be a case for clinics triaging patients who are unlikely to have had a TIA to reduce the burden of non-TIA cases. The Dawson score (section 1.11), could help with the diagnosis and management of suspected TIA patients in primary care, and could also help in optimising use of TIA clinics by helping with triage in secondary care (via supporting GP diagnosis/and or triage by clinic staff).

1.13. Rationale for programme of work and aim of the thesis

The literature cited above outlines that TIA patients are at risk of having a stroke, with some patients being at higher risk than others. The literature demonstrates the importance of accurate and early diagnosis of TIA in primary care, immediate management (i.e. when the patient first presents to the GP) including prompt referral for specialist assessment.

Whilst the ABCD2 score was designed as a prognostic tool, it was often perceived as a tool to aid with the diagnosis of TIA. Nevertheless, the diagnostic utility of the score has been studied and shown to be inadequate to guide decisions on referral (98). In addition, recent guidance in the UK excludes risk stratification using this tool, (updated in 2017) (41, 60). Therefore, if referrals are not prioritised by ABCD2, then it is more important to reduce the number of clinic referrals so that high-risk patients are seen promptly, and a validated diagnostic tool would help with this.

Overall thesis aim

To examine the diagnosis and immediate management of suspected TIA in primary care, and to evaluate the performance of a diagnostic tool (Dawson score) for TIA which could be used to guide GPs' referral decisions and to triage clinic referrals.

This thesis used both quantitative and qualitative methods to focus on four aspects:

1. The systematic review: Searched the literature in a structured way and synthesised findings to obtain a comprehensive account of current knowledge on the diagnosis and management of TIA in primary care
2. Study 1: Assessed the utility of the Dawson score in predicting the diagnosis of TIAMS and determined its potential to triage referrals and/or reduce GP referrals at the TIA clinic
3. Study 2: Involved telephone interviews with GPs which:
    - Explored GPs' experiences and views on TIAs (including the diagnosis and immediate management of suspected TIA patients)
    - Investigated the potential utility and practicality of a diagnostic/management tool used in primary care setting
4. Study 3: Explored alternative cut-offs for the Dawson score based on suggestions by GPs in the interviews and derived a logistic regression model to present GPs with the risk of TIAMS using the Dawson score

1.14. Organisation of the thesis

Chapter 1: Outlined the rationale for the thesis and the overall work included. The subsequent chapters cover the following aspects of the thesis:

Chapter 2: Describes a systematic review synthesising the evidence on the diagnosis and immediate management of TIA in primary care.

Chapter 3. Introduces relevant literature on suspected TIA referrals, with details of the pre-clinic and clinic procedure at the TIA clinic in Leicester and the rationale for the clinical utility of the Dawson score study (section 3.1). A feasibility study was carried out to test the most practical way of collecting the data for the clinical utility study exploring three choices (TIA clinic nurse, clinic clerk, clinic aide). This feasibility study additionally assessed whether collecting the Dawson data before the patient attended the clinic was practical, and whether the Dawson score can be calculated and compared to clinic data (section 3.2). Also, the aims and objectives of the clinical utility study of the Dawson score are described (section 3.3), followed by the method, results and discussion of the study (sections 3.4–3.6).

Chapter 4: Begins with an overview of the research on the diagnosis and management of TIA (found from the systematic review), with details of the rationale for the qualitative study which explored GPs' views on the topic (section 4.1). The aims, methods, results, discussion and conclusion are also detailed in sections 4.2–4.6.

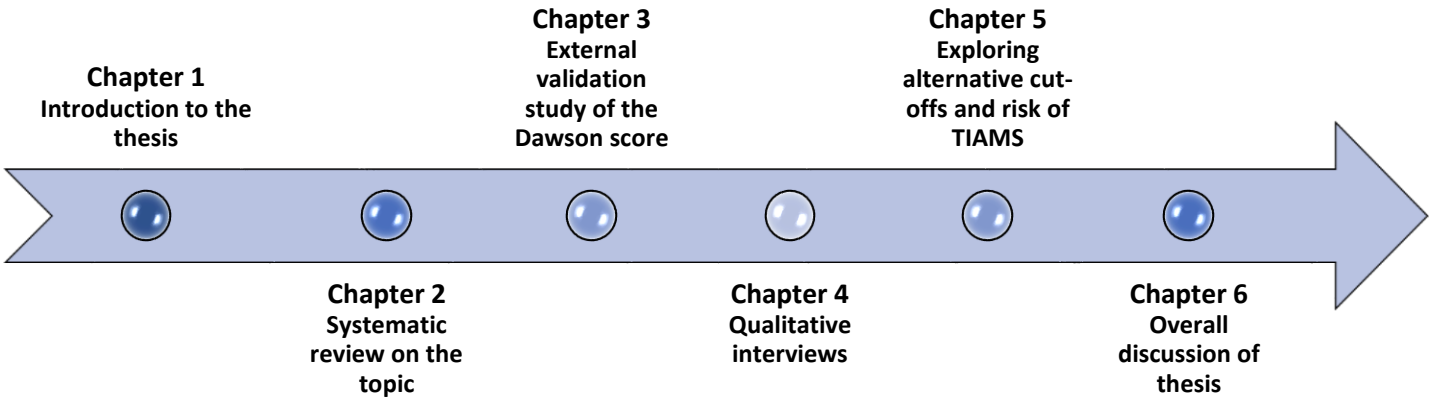
Chapter 5: Describes the aims, method, results and discussion of exploring an alternative cut-off and risk calculation for the Dawson score and estimated risk of TIAMS based on GPs' preferences presented in Chapter 4 (sections 5.1–5.5).

Chapter 6: Summarises the key findings from this thesis, followed by a detailed discussion of each study. The strengths and limitations of the whole thesis are discussed, with recommendations for future work (sections 6.1–6.6).

The focus of this thesis is the diagnosis and management of TIAs, although it is recognised that this condition and minor stroke (TIAMS) are part of the same clinical continuum. Since TIAMS is a relatively new term it was not used in the literature search (Chapter 2). The utility of a potential diagnostic score for TIAMS was assessed because TIA and minor stroke are managed in the same way in TIA clinics, (discussed in Chapter 3). Qualitative interviews with

GPs, (Chapter 4) focused on TIA rather than TIAMS as GPs may not be familiar with the term. A diagram outlining the components of the thesis has been highlighted in Figure 1.3.

Figure 1.3: Diagram of the components of the thesis



Chapter 2: Systematic review

The recognition of TIA in primary care is an important area of clinical concern both in terms of the significance of TIA for the individual with increased risk of stroke and also the considerable burden on healthcare professionals to efficiently diagnose and manage this challenging condition. Chapter 1 described TIA and interventions to assist GPs in the diagnosis and management of this condition. This led to a systematic review which was a necessary step for this research to understand the existing studies on the topic of the diagnosis and management of TIA in primary care to obtain comprehensive account of current knowledge of TIA. The purpose of this systematic review was to understand the challenges associated with the diagnosis and management of TIA, and therefore look at ways to improve GP diagnosis and management of TIA, which depended on synthesising the current evidence on the topic.

Systematic reviews are generally considered a key element of evidence based practice and the gold standard to synthesise existing evidence (99) (100). The purpose of a systematic review is to identify relevant studies, appraise their quality and summarise their results through scientific methodology. This process allows health care providers and researchers to efficiently search a wide range of relevant studies as opposed to searching individual articles, and effectively integrate the existing information (101). The purpose of this systematic review was to understand and therefore look at ways to improve GP diagnosis and management of TIA which depended on synthesising the current evidence on the topic.

Prior to the systematic review, a search was completed to identify whether a systematic review on the topic of the diagnosis and management of TIA in primary care has been previously completed. Cochrane Database of systematic reviews (CDSR) (The Cochrane library, latest issue), Google Scholar, Medline and PROSPERO were searched. PROSPERO is an international prospective register for systematic review protocols which are currently being undertaken. Researchers are encouraged to register their review to help avoid duplication (102). This search was completed to determine if there were any existing reviews related to the topic. To obtain an insight into the extent and quality of existing literature and to inform the search strategy and inclusion criteria for this systematic review.

The results from the search confirmed that no published systematic review on the topic had been conducted. However, there were studies that looked into TIA but focused on the impact of TIA on the patient as well as improving the patients' psychological state through stress/anxiety reduction intervention.

The review was submitted for publication in the Journal of Primary Health Care and was accepted on 1st May 2017 for which the researcher of this thesis was the first author. The final draft of the publication has been attached as an appendix, (Appendix 1).

2.1. Aims

1. To summarise evidence on the diagnosis of TIA in primary care
2. To summarise evidence on the immediate management of TIA in primary care, including prescription and referrals
3. To describe interventions to improve diagnosis and/or management of TIA in primary care

2.2. Methods

The systematic review has been written in accordance with PROSPERO protocol guidance. The protocol for this systematic review was registered on PROSPERO on 08 January 2016 (registration number: CRD42016032995) (Appendix 2).

2.2.1. Defining the research question and determining the types of studies

Defining the research question forms the foundation of systematic reviews as the search strategy is built upon the review question. Therefore, formulating the review question is critical to the overall quality of the systematic review (103).

This study aimed to review the available evidence about primary care physicians' (general practitioner/family doctor) accuracy in diagnosing TIA and immediate management of the condition.

When devising a search strategy, a search tool is used as an organising framework to list terms by the main concepts in the search question. Various tools exist, such as sample, phenomenon of interest design, evaluation, research type (SPIDER) (104) and setting, perspective, intervention, comparison, evaluation (SPICE) (105). The PICO tool focuses on the Population, Intervention, Comparison and Outcomes of a (usually quantitative) review and is recommended by the Cochrane Collaboration (106) to ensure relevant components of the question are well defined.

The PICO tool is the most widely used model for formulating clinical questions to research prognosis, diagnosis and therapies and mostly used in health services research. SPIDER is an alternative to PICO that has a special focus on qualitative research and in social sciences research, SPICE may be more appropriate for formulating research questions. The objective of this study was to look into diagnosis of TIA, particularly attempting to look to improve diagnosis and management through some form of diagnostic tool/guideline, hence PICO was thought to be the best tool to formulate the review question.

The PICO tool does not currently accommodate terms relating to qualitative research or specific qualitative designs, e.g. 'control group' and 'intervention' and may not appropriately locate qualitative research. Therefore, it has often been modified in practice to PICOS where

the ‘S’ refers to study design (107). The study design was included in PICOS to account for qualitative research. The purpose of using PICOS is three-fold (108). Firstly, it directs the focus to the most important issue and outcome. Second, it facilitates the next step in the process which will be the search by prompting thoughts around the language and key terms to be used. Third, it directs the questioner to clearly identify the problem, intervention and outcome. The use of every aspect of PICOS in the literature search question will not always be necessary. For example, the “intervention” and “comparator/control” in PICOS will not apply to qualitative studies. Additionally, the “intervention” can be amended to “Exposure” in non-intervention studies.

This study included both GPs and patients with TIA. GP diagnosis included diagnostic accuracy, GP management and referral included referral rates, urgency and medications. Furthermore, interventions included guidelines, diagnostic aids or education to help improve GP diagnosis and management of TIA. The PICOS tool used to structure the question for this review: P: participation/population, I: intervention/E: exposure, C: comparator/control, O: outcome) S (study design) question formulation are specified in Appendix 3.

2.2.2. Search strategy

Medline, Embase, Web of Science and Scopus databases were searched in September 2015. The four databases were used as Medline focuses on biomedicine and health and Embase includes broad biomedical scope with in-depth coverage of drugs and pharmacology and includes content from journal articles, mostly from peer-reviewed journals. Scopus not only includes the records from Medline and Embase databases, but also include journal titles that go beyond the strictly biomedical disciplines, including health sciences, life sciences, social sciences and humanities. The broad range of content coverage included in Scopus is also similar for Web of Science. Additionally, Web of Science and Scopus outline if the reference has been cited in another paper which is useful in terms of cross referencing and finding secondary sources. The use of four databases were included to ensure comprehensive coverage and to ensure relevant papers were not missed. These databases were searched based on the objectives of the study. For example, if the interest of this study was to look into the psychological impact of TIA rather than the diagnosis and

management of TIA then different database such as PsycINFO would have been searched for literature on behavioural and social sciences. For the databases the application of the terms used in this study differed (Table 2.2.1).

The researcher collaborated with the University of Leicester academic librarian to develop the search terms. The initial step was to think of the key terms which will be used to search across the databases such as 'TIA' 'general practitioner' and 'primary care'. The terms were then searched in Medline and the search results were checked for other terms. The medical subject headings (MeSH) terms were searched in the database[3]. This provided a list of terms which was used to identify different entry terms. Google was also searched along with reading systematic reviews conducted on the topic of primary care to identify the authors search strategy. Some terms varied in different countries; therefore, different terms were used which included the alternative terms to ensure that the search was sufficiently sensitive. The search terms used when carrying out the search are highlighted below.

- attack
- attack*
- care
- diagnos*
- diagnosis
- diagnostic errors
- doctor*
- family
- family doctor*
- family practice
- general
- general practice
- general practioner*
- general practitioners
- gp
- health
- isch?emic
- ischemic
- ischemic attack
- ischemic attack, transient
- misdiagnos*
- patient*
- physicians, family
- practice
- practioner*
- primary
- primary care
- primary health care

[3] https://www.ncbi.nlm.nih.gov/mesh

- tia
- transient
- transient isch?emic attack*

Both medical subject headings (MeSH) and text words were used as search terms to identify the relevant papers. The differences in the application of terms according to each database are highlighted in Table 2.2.1.

Table 2.2.1: Differences in the application of terms according to each database

Databases	Application of terms
Medline and Embase	Medline and Embase both have different indexing techniques. Medline uses MeSH and the terms are signified by a '/' whereas Embase has its own thesaurus and each subject heading needed to be typed in and then selected according to which ones were most relevant. In Medline and Embase various symbols which were used remained the same, e.g. 'transient isch?emic attack' (to cover British and American spellings - ischaemic/ischemic). Thus, the symbol was added in order to include papers which used either term. Also scope note was used in order to look up the definition of each of the subject headings to make sure each heading was correct. When attempting to add 'patients with TIA' as a search term the word 'with' did not identify any relevant articles, the word had to be replaced with 'Adj2' which was the correct term in both databases.
Scopus	The Scopus database does not use subject headings; therefore, the titles and abstracts were searched to take into account all the subject headings of TIA/diagnosis/primary care which were previously used in both Medline and Embase. Double quotation was used to inform Scopus to look for that specific term e.g. ("Transient isch?emic attack*"). Again the '?' looks for alternative spellings and '*' symbol truncates the term. When searching for the terms 'patients with TIA' unlike Medline and Embase the term was different in Scopus. This was researched in the help files within Scopus and it was found that 'NEAR2' replaced 'with' whilst the '2' represented looking at terms which was also included in the title/abstract e.g. 'TIA patients with, patients with TIA' etc.
Web of Science (WOS)	In this database each term had to be typed in manually. Once all the search terms were included it would then have to manually be selected and combined with either a AND/OR. When '.mp.' was added at the end of each term it searches all the titles, abstracts and topics. This process had to manually be typed in within WOS. Whereas, in Medline and Embase it was included within each search.

The search was not limited by language or study design. However, the search was limited to the past 20 years (1995–2015) to exclude out of date practices and acknowledge rapid advances in TIA management (Appendix 3 for database searches). Details of inclusion and exclusion criteria are provided below.

2.2.3. Inclusion criteria

- Types of participants: GP (general practitioner) family doctor, family physician, patients with TIA
- Empirical data (qualitative and/or quantitative)
- Transient ischaemic attack only or stroke and TIA
- No restriction on study design
- Published full text peer reviewed journal articles, systematic reviews including structured abstracts
- Diagnosis and/or management at time of presentation
- All languages

2.2.4. Exclusion criteria

- Emergency department, paramedics, neurologists
- Papers restricted to stroke
- Reviews, editorial/letters, opinion pieces, conference abstracts, case reports and non-systematic reviews
- Studies of long-term management/secondary prevention

2.2.5. Data selection

The titles and abstracts of retrieved citations were read by one reviewer (PB) and were excluded if the inclusion and exclusion criteria were clearly not met based on a review of the title and abstract. Full papers were ordered via the University of Leicester Library for all potentially relevant abstracts and also if the titles and abstracts had insufficient evidence to apply the criteria. These papers were reviewed by two researchers (PB, AW). Any disagreements were resolved through discussion and if necessary, were resolved by a third

reviewer (AM). The selection process was illustrated using a PRISMA flow diagram (Fig 2.3.1).

2.2.6. Strategy for data synthesis

Two reviewers (PB and AW) read the included studies and independently listed the main findings from each one. Data from the included papers were extracted using a standardised data extraction form (Appendix 4). Data extracted were structured around participant characteristics, intervention (if applicable), and outcomes and the three questions were analysed separately. Three questions were analysed and categorised separately (Table 2.3.1).

2.2.7. Risk of bias (quality assessment)

Methodological quality relates to the design and conduct of the research which is fundamental to understanding the results and the level of confidence in the findings as well as whether the studies are valid and reliable (109). As a systematic review is a synthesised summary of the available evidence, assessing the quality of the included studies is a vital part of interpreting the evidence (110).

Various quality assessment tools exist in the literature[4] for the quality assessment of controlled intervention studies, observational and cross-sectional studies and case series studies included in a systematic review. This systematic review included studies that used both qualitative and quantitative study designs. Due to this, it can be difficult to assess the quality of the included studies using quality assessment tools because many of these tools are useful only for a limited number of research designs. It is common for reviewers to select a different assessment tool for each type of study design included in their review. This process can be time consuming to search and also to learn about the different selection of new tools used for each study design. Additionally, since the evidence will use two or more research designs, the results cannot be directly compared (111).

[4] https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools

At the time of the systematic review, the only validated tool for appraising the methodological quality of both qualitative and quantitative study designs as well as mixed methods studies was the mixed methods appraisal tool (MMAT) (112) (Appendix 5).

The MMAT provides the methodological quality criteria for different study designs within a single tool. Additionally, the tool focuses on a limited number of core criteria which can be time efficient when assessing the quality of the papers and includes a specific criteria for mixed methods studies which is not often found in other tools (113).

The MMAT has been pilot tested using 32 evaluation studies for efficiency and reliability, the agreement was moderate to perfect between reviewers regarding the overall quality score of appraised studies (112). Additionally, it is regarded to be unique in terms of appraising the common types of study designs (112).

The tool contains two screening questions and a further 19 relating to five types of studies; (a) qualitative, (b) randomised controlled trials (c) non-randomised studies (d) quantitative descriptive and (e) mixed methods studies. These specific designs were chosen as they are the most common designs included in the mixed studies reviews. For each category, there are five core criteria, i.e., criteria that are the most relevant to appraise the methodological quality of studies. Each criterion is rated on a scale of yes, no and can't tell.

The MMAT score was applied to a qualitative study by using section 1, quantitative study by using section 2, 3 or 4 for randomised controlled, non-randomised and descriptive studies for a mixed methods study (referring to section 1 for qualitative and the appropriate section for the quantitative component, e.g. 2,3 or 4) and using section 5 (Appendix 5).

The MMAT quality assessment process involves questions around the study design regarding recruitment, randomisation (if applicable), appropriateness of outcome measures and completeness of data. Studies were scored as (0% of quality criteria met); (25% of quality criteria met); (50% of quality criteria met); (75% of quality criteria met) or (100% of quality criteria met) and details of the MMAT applied to the included studies have been provided in Appendix 5.

Two review authors assessed the methodological quality independently and resolved all disagreements through discussion or with the arbitration by a third review author (AM).

When reviewing included papers, most of them used quantitative methods. However, a few papers used qualitative and mixed methods designs.

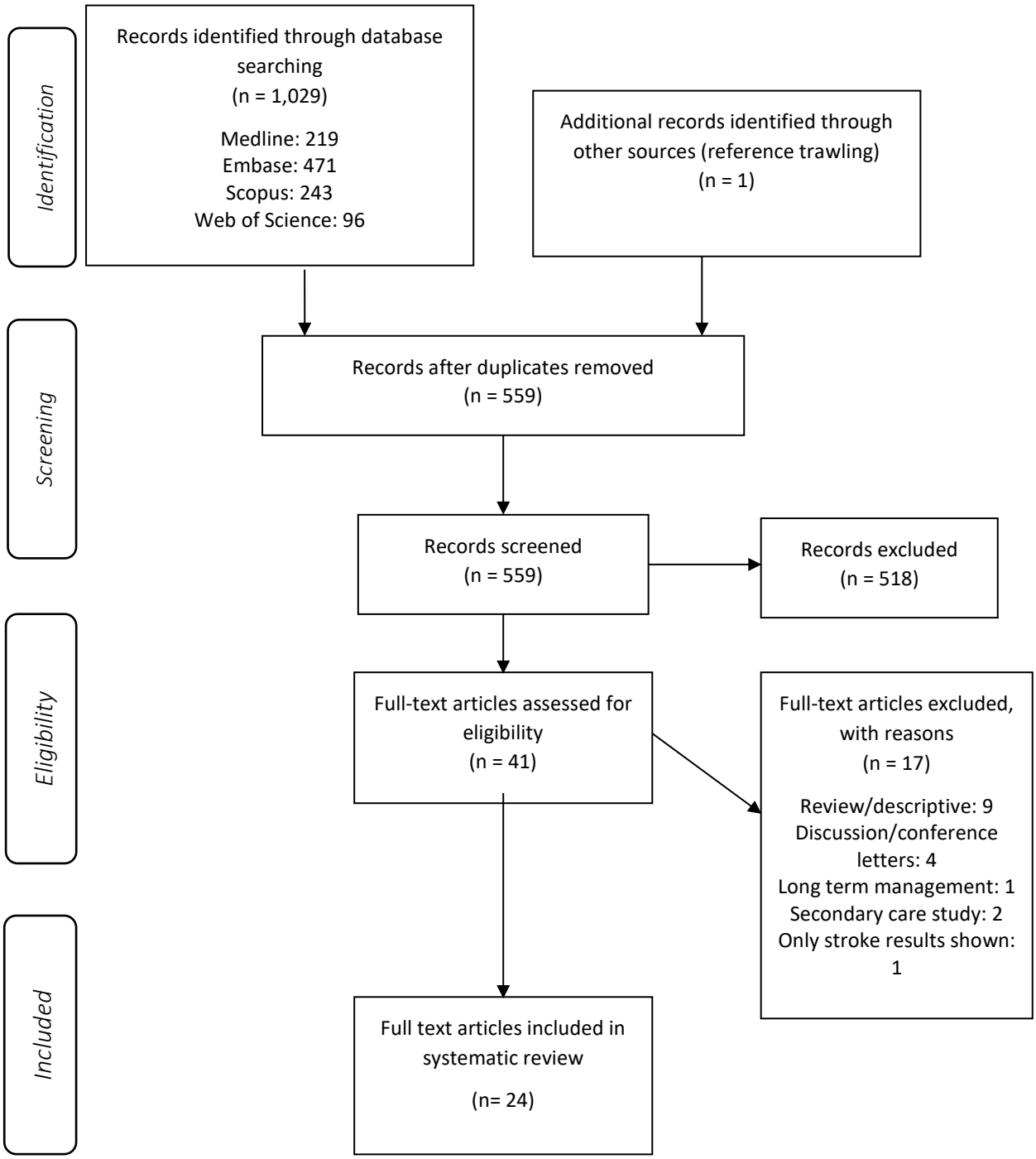
MMAT enables structured exclusion of low-quality studies as well as a description of the quality of included studies (114). Also, the findings from the quality assessment may inform additional sensitivity analysis, and exploration of bias by including or excluding lower quality studies, or a similar number of studies could be grouped and compared (lower versus higher score studies). Sensitivity analyses however, are a common approach when conducting a meta-analysis (115). For this study, the assessment of study quality was not used to exclude studies that otherwise met the inclusion criteria, but provided useful insight into the methods used for data collection and analysis. The aim of the systematic review was to gain an understanding of the broad overview across the topic and to draw attention to the low or high-quality papers, the results of which were discussed narratively.

Provided the data were similar, a meta-analysis would have been feasible. The focus would have been to explore GP diagnostic accuracy in studies which used similar methods that when combined in a meta-analysis the results will be a meaningful description of the set of studies (116). The rationale for a meta-analysis is that, by combining the studies, the overall generalisability is increased as well as the statistical power of the analysis (from the increased sample size), resulting in increased precision of the estimates of treatment effects.

2.3. Results

This review identified 1,029 papers and included a total of 24 papers. See Fig 2.3.1 for the process of including the appropriate papers.

Figure 2.3.1: Flow chart documenting the results of the systematic review selection



The studies are categorised as the following:

1. Knowledge and reported practice based on case vignettes and surveys
2. Actual practice of diagnosis/recognition of emergency and/or prescription
3. Intervention studies

Table 2.3.1 highlights knowledge (based on case vignettes/surveys), actual practice and intervention studies. Indicating contribution to the subcategories (diagnosis, recognition of urgency and/or prescription) and for intervention studies (diagnosis, referral and/or management) (Appendix 6). Each study contributed to one or more of the subcategories.

Table 2.3.1: Studies according to categories and sub-categories

Results		**Knowledge / reported practice**		
Author	**Type of study**	**Diagnosis & prognosis**	**Recognition of urgency**	**Prescription**
Mead et al (1996) (117)	Questionnaire		X	X
Wiszniewska et al (2000) (118)	Questionnaire		X	X
Middleton et al (2003) (119)	Questionnaire	X		X
Nguyen-Huynh Mai et al (2003) (120)	Telephone interview	X	X	
Tomasik et al (2003) (121)	Case vignette	X	X	X
Roebers et al (2007) (122)	Questionnaire		X	
Jagadesham et al (2008) (123)	Questionnaire	X	X	X
Purroy et al (2011) (124)	Questionnaire	X	X	
Edwards et al (2012) (125)	Face to face interview		X	
Jackel et al (2012) (126)	Telephone interview	X	X	X
Leung et al (2012) (127)	Questionnaire	X	X	X
Ismail, Negm (2013) (128)	Questionnaire	X	X	X
Ranta, Cariga (2013) (129)	Case vignettes	X	X	X
Total 13		9	12	9

Results		Actual Practice		
Author	**Type of study**	**Diagnosis**	**Recognition of urgency**	**Prescription**
Otten et al (1995) (130)	Questionnaire examining actual cases		X	X
Goldstein et al (2000) (131)	Retrospective cohort	X	X	X
Gibbs et al (2001) (132)	Retrospective cohort	X	X	X
McNeill (2008) (133)	Audit (referral letters)	X	X	
Magin et al (2013) (134)	Retrospective cohort	X	X	
Clarey et al (2014) (135)	Prospective cohort	X	X	
Total 6		5	6	3

Results		Intervention		
Author	**Type of study**	**Diagnosis**	**Referral**	**Management**
Wright et al (2006 & 2007) (136, 137)	Cluster-randomised trial Diagnostic guidelines		X	X
Lavin & Ranta (2014) (138)	Cohort study of Diagnostic tool (Electronic Decision Score) (EDS)	X		
Ranta et al (2014) (139)	Uncontrolled (before and after) (EDS)	X	X	X
Lasserson et al (2015) (98)	Cross -sectional (clinical and research records/referral letters)	X Testing of tool, potential intervention		
Ranta et al (2015) (140)	Randomized controlled trial (EDS)Diagnostic tool	X	X	X
Total 5		4	3	3

Knowledge/reported practice studies

The studies described in this section used different data collection methods to assess GPs' knowledge of TIA and the management of this condition. Structured postal questionnaires, case scenario based postal questionnaires, emailed case vignette based on hypothetical patient cases with potential TIA, semi-structured telephone interviews and semi-structured face to face interview were used.

2.2.8. Diagnosis and prognosis

A total of nine studies explored GPs knowledge of TIA. Studies were sub-categorised into those that explored the definition of TIA/diagnosis of TIA, symptoms of TIA, and knowledge of risk of stroke.

Definition and diagnosis of TIA

A survey conducted in Leeds, United Kingdom which included 40 GPs (66% response rate) found that all 40 of the GPs correctly identified that TIA was an abbreviation of a transient ischaemic attack and symptoms lasted <24 hours (123).

Purroy et al (124) conducted a cross sectional survey with 138 GPs (53% response rate) from 24 primary care centres in Spain found that 124 (90%) of Primary Care Physicians (PCPs) correctly identified the short duration of TIA symptoms, 43, (31%) answered less than one hour and 81, (59%) answered less than 24 hours.

In the United States Nguyen-Huynh et al (120) conducted structured telephone interviews of 200 PCPs (43% response rate) from 40 different states to assess GPs knowledge of TIA. The study reported that 44, (22%) recognised that TIA symptoms should resolve within 24 hours. The remainder thought that longer symptom duration was associated with TIA diagnosis, as 44% thought duration of 25–48 hrs was consistent with TIA, 4% thought 3–7 days and 9% thought more than 7 days.

Ismail & Negm (128) in Egypt found that of the 95 primary health care physicians who responded to the questionnaire (73% response rate), 37% did not know the duration of TIA, 21% identified duration of symptoms of TIA (within 1 hr) and 42% defined duration

according to the older definition (within 24 hr). The authors suggested that GPs responding within 24 hours were 'wrong', but this is still a definition that is widely used.

In New Zealand Ranta & Cariga (129) used case vignettes to compare GP and general physicians' diagnosis with stroke specialists (deemed as the 'gold standard'). The study included 10 GPs, 12 physicians and 12 stroke specialists. The study reported that GPs achieved a diagnostic accuracy of 76% (range 45–100%), nearly the same as general physicians 79% (33–100%).

Symptoms and risk factors

Jagadesham et al.'s, reported results from postal questionnaires which included 40 GPs (66% response rate) from Leeds Royal Infirmary, United Kingdom (123). The study outlined that GPs incorrectly considered non-specific symptoms of vertigo (75%) and confusion (70%) to typically represent a TIA. Similarly, in the United States, Nguyen-Huynh et al (120) found that out of 200 PCP's, 47% incorrectly identified vertigo as a typical TIA symptom. This study also found that 98–100% of PCPs were aware of the risk factors associated with TIA and 27% correctly identified 5 TIA symptoms. Additionally, Ismail & Negm (128) found that out of 95 primary health care physicians in Egypt (73% response rate), 35% of symptoms chosen by primary health care physicians were not consistent with TIA.

In Spain, Purroy et al (124) found of the 138 GPs included in the study, 20% provided a correct answer of the symptoms of TIA. They also found that 68% of the GPs had awareness of visual symptoms and isolated vertigo was incorrectly listed as a typical TIA symptom by 34%.

A study conducting telephone interviews with 24 physicians across France, Spain, Italy, UK, US and Germany attempted to identify global trends in the current clinical pathways underlying the management of patients with TIA. In this study, Jäkel et al (126) found that across all countries 69% of GP respondents highlighted the need for GP awareness on knowledge of symptom and risk recognition.

A case-vignette based questionnaire on transient monocular blindness and symptoms of hemispheral ischaemia included 89 GPs from one healthcare district of Warsaw, Poland (89% response rate) (121). In regards to monocular blindness, 63 (71%) GPs achieved a correct /probably correct diagnosis, and a correct/probably correct diagnosis was made by

52, (58%) GPs on hemispheral ischaemia. A correct diagnosis for hemispheric ischaemia was more likely if patients were aged over 65 years (86, 97%) than younger (74, 87%). Patients with no non-specific symptoms and with a first attack were given a higher percentage of correct diagnoses than patients with recurrent attacks and with non-specific symptoms.

Stroke risk following TIA

Middleton et al (119) conducted a study in Australia with 296 GPs (60% response rate). The results from this study showed that only 12% of 296 GPs correctly identified the risk of stroke following a TIA. Although the GPs knowledge of risk of stroke was poor, most GPs (94%) correctly identified modifiable stroke risk factors. Also, Purroy et al (124) reported that of the 138 GPs included in the study, 43% recognised the risk of stroke recurrence; 47% proposed the correct answer which was that the risk should be identified the same as for an established stroke, 43% proposed that the risk was higher than that of stroke and 10% suggested the risk was lower than that of stroke.

A survey was conducted in Australia, to determine the level of knowledge amongst GPs relating to stroke risk following TIA. This study by Leung et al (127) found all 32 GPs (16% response rate) correctly identified early risk of stroke but it was underestimated by 23% of GPs. Also, out of 296 GPs, 251 (85%) of GPs overestimated the risk of stroke in another study conducted in Australia (119). Similarly, Jäkel et al (126) in a study across 6 countries (France, Germany, Italy, Spain, UK and US) found that out of the 24 GPs included in the study, the percentage of GPs who classified their patients with TIA according to risk level were as follows: Spain 0%, Germany 25%, France 75%, Italy, UK and US 100%.

Please refer to Appendix 6 for a more condensed summary of the individual studies on diagnosis for the knowledge-based studies

Conclusion

Most studies demonstrated significant knowledge gaps for TIA. There was general recognition of the transient nature of TIA symptoms. Whilst the duration of symptoms used to define TIA has not been agreed internationally, the 24-hour definition in Egypt was considered the ‘old definition’, whereas the 24-hour definition is still the standard definition in the UK, Spain and United States.

It is evident that many GPs do not fully appreciate stroke risk following a TIA. It was demonstrated in some studies doctors overestimated the subsequent risk, whilst other doctors underestimated the risk. Most importantly, it was apparent in several studies that GPs gave undue prominence to some symptoms not typical of TIA.

The two qualitative studies identified knowledge gaps for TIA as many GPs thought that longer symptom duration was consistent with TIA diagnosis. Consistent evidence of GPs incorrectly identifying vertigo as a typical TIA symptom was reported. Although GPs were aware of the risk factors associated with TIA, only a small proportion of GPs were able to correctly identify symptoms of TIA. Furthermore, the use of risk stratification for identifying TIA patients was found to be low in countries other than the UK and US e.g. Spain and Germany.

Overall the studies highlighted a need for more education on the symptoms of TIA, as it would potentially improve the reliability of the diagnosis of TIA and reduce unnecessary referrals to secondary care.

2.2.9. Recognition of urgency

A total of 12 studies investigated the recognition of TIA as an emergency, investigation and immediate management. Four aspects were explored which were, recognition as medical emergency, decision to admit to hospital, referral and investigation rates and referral routes.

Recognition as medical emergency

In Germany, Roebers et al (122) examined PCPs' early management of patients with suspected stroke/TIA using case vignettes. The study explored 395 PCPs' perception of TIA from 4 regions of North Rhine-Westphalia, Germany (55% response rate). The study reported that the majority, (84%) of PCPs agreed that TIAs were medical emergencies. Additionally, 39% reported that they were more likely to treat TIA patients as outpatients compared to stroke patients. PCPs in this study were aware that patients should be managed as a medical emergency, but only a minority, 33% would admit TIA patients. Contrasting results were found by Ismail and Negm (2013) in Egypt. In this study consisting of 95 primary health care physicians, only 34% of PCPs referred patients with TIA as an

emergency and only 27% referred for hospital admission. In Spain, Purroy et al found that of the 138 GPs included in the study, 108 (78%) managed patients suffering from TIA by sending them to an emergency service of a hospital centre.

Using case vignettes in Germany Roebers et al (122) reported that of the 395 PCPs included in this study, 51% agreed that outpatient referral was preferred in TIA cases. Additionally, 33% of PCPs identified that lack of therapeutic benefits of hospital admission was the reason behind this. A study in Australia explored barriers which could influence GPs' decision to admit stroke/TIA patients in 32 GPs (127). The study highlighted that the barriers to effectively manage potential TIA cases were due to the lack of knowledge by GPs (19%), and the lack of time in general practice consultations (16%).

Referral and investigation rates

Wiszniewska, et al (118) included 159 practising GPs in 4 cities in Poland to assess GPs management of TIA/stroke (53% response rate). The study reported GPs would refer 50% of patients with TIA. 64% of the GPs referred patients with motor impairments and 54% doctors referred patients with vision impairments. Furthermore, 11% of GPs did not refer patients who already had a history of previous TIA.

In a United Kingdom survey of 294 GPs' in Greater Manchester, the referral rates varied considerably (117), with some GPs reporting they referred no patients, whilst others referred all patients. In terms of the 24% of GPs who did not arrange investigations themselves, the median percentage of patients referred to a specialist was 50%, which was also the same for GPs who did arrange some form of investigation.

A survey in the United Kingdom by Jagadesham et al (123) included 40 GPs sampled from a trust database from the General Royal Infirmary in Leeds. The study found that referral varied among doctors and depended on the presenting symptoms. GPs were not referring 22–40% of TIA patients for further investigation and management. Low rates of referral were also reported in United States (120) which included 200 PCPs, of which, only 37% PCPs would refer to a neurologist. Additionally, Tomasik et al (121) study which included 89 GPs (89% response rate) reported that patients with known risk factors and the elderly were more likely to receive a TIA diagnosis by GPs.

Referral routes

In a qualitative study, using telephone interviews Jäkel et al (126) reported that the extent to which patients with TIA present to medical services varied between countries. The study identified 24 GPs who reported that approximately half of patients with TIA in France, Germany, Spain and the UK sought initial medical assistance from their GP/PCP. On the other hand, in Italy and the US approximately 70% presented to the emergency room (ER).

Ranta & Cariaga (56) in New Zealand used case vignettes to explore referral decisions in 10 GPs, 12 physicians and 12 stroke specialists. In a study consisting of 294 GPs in Greater Manchester, United Kingdom, Mead et al (1996) (117) found that median reported referral rate to the TIA clinic was 50%, with substantial variation between GPs. However, since the study was published in 1996, there has been a drive to develop TIA clinics in all UK hospitals and practice is likely to have altered significantly.

The ABCD2 score is a tool which is used to estimate the risk of stroke in TIA patients, and has been used to prioritise assessment at TIA clinics (section 1.6). A qualitative study in the UK consisting of interviews with 9 GPs (6 of whom used the ABCD2 score) found that the ABCD2 scoring system was generally liked and most complied with its use, as it offered a 'substantial means to navigate the referral system'(125). The scoring system served as a tool to facilitate communication between GPs and hospitals as it ensured a swift referral to secondary care.

In this study, the scoring system was also used in multiple ways beyond its original remit, such as a diagnostic and prognostic tool as well as an education tool for GPs and patients. Despite the advantages of the ABCD2 score, the interviews also found that GPs or emergency doctors may use the TIA clinics as a place to send patients they are unsure about. Furthermore, a minority of GPs were unaware of the score and/or thought it was an unnecessary tool.

Please refer to Appendix 6 for a more condensed summary of the studies that looked into TIA as a recognition of urgency for the knowledge-based studies

Conclusion

Referral rates among GPs were variable, but there was consistent evidence of under referral, variation in use of ED and type of specialist referred to. Referral practices varied according to time; it was not until publication of the OXVASC studies in 2002 that the high early risk of stroke after a TIA was known (141).

The qualitative study in the UK found the ABCD2 score to be a useful tool to facilitate referrals to secondary care. The score was not only used as a prognostic and diagnostic tool, but was also seen as an education tool for GPs and patients. GP interviews from this study also highlighted that GPs may use the TIA clinics as a place to send patients they are unsure about to either confirm/exclude a diagnosis.

Despite the majority of GPs perceiving TIA as an emergency, there was variable practice in admitting patients with TIA. In Spain, the majority of GPs admitted suspected TIA patients to hospital, whilst low rates of admission were found in Germany and Egypt. The results were dependent on local policy and guidelines/recommendations.

2.2.10. Prescription

A total of nine studies investigated prescribing. Two aspects were examined: treatment and influence of symptoms.

Treatment

An Australian survey suggested that GPs were uncertain in selecting treatment for TIA. Out of the 32 GPs included, 15 correctly responded to questions about anti-hypertensive treatment and slightly more (20/32) about managing hyperlipidaemia (127).

In Egypt, of the 95 physicians, antiplatelet were reportedly prescribed for TIA by 57% and anticoagulants by 22%. 2% did not prescribe any treatment and 26% prescribed inappropriate treatment (brain stimulants/anti-oxidants) (128).

In Poland, a minority of GPs (16%) of the 159 included in the study prescribed antiplatelet, 20% prescribed vitamin B and 55% prescribed sedative drugs (118). In the United Kingdom, Mead et al (1996) (117) found that of the 294 GPs included, 290 (99%) of GPs routinely initiated aspirin for patients with TIA. In a UK study based in Leeds General Royal Infirmary

that included 40 GPs, the percentage was higher at 50–70% doctors prescribing antiplatelet (123) than in Tomasik et al (121) study where it was reported that in the event of a TIA, less than 22% of the 89 included GPs would prescribe an antiplatelet drug.
In an Australian survey which asked 296 GPs about prescribing aspirin for TIA patients, 54% responded this was highly likely and 32% somewhat likely (119).
Another study in New Zealand examined the rate of initiation of best medical treatment in 10 GPs, 12 physicians and 12 stroke specialists. The study found that 27% of GPs prescribed antiplatelet, statin and an antihypertensive, in comparison to 31% of general physicians and 92% of stroke specialists (129).

Jäkel et al's (126) study across 6 countries (France, Germany, Italy, Spain, UK and US) found that in the US different medications were prescribed according to risk level, unlike UK, France and Germany.

Symptoms

In Leeds, United Kingdom Jagadesham et al reported results from postal questionnaires from 40 GPs. Doctors were more likely to prescribe anti-platelets in TIA with monocular visual loss than any other symptoms (123). In another study in Poland including 159 GPs, antiplatelet were used by 20% of GPs in patients with motor impairments and 12% for patients with visual impairments (118).

Please refer to Appendix 6 for a summary of the studies that explored GP initiating prescription for the knowledge-based studies

Conclusion

Consistent evidence was found for the under use of effective medication, especially aspirin and variable use of ineffective medication, such as sedatives. Initiation of medication also differed according to country. The qualitative study on GP interviews suggested that different medications were prescribed according to risk level in the US, but this was not the case in UK, France and Germany. The differences could be due to variance in guidelines on prescription in different countries, and policy differences in whether drugs should be initiated in primary or secondary care.

An important methodological consideration in surveys is response rate as it has been widely regarded as a key indicator of data quality (142). The assumption is that the higher the

response rate, the greater the likelihood that the sample will represent the population and therefore, accurately reflect results that would have been derived from the entire population (143). Furthermore, higher response rates may mean that it is more likely that all participants who may differ with regards to the attitudes, opinions or other information being measured will be included.

In the quality assessment tool that was used (MMAT), an adequate rate was defined as 60% or above, which was achieved in 5 of 24 included studies (Table 2.3.2). Studies have reported that response rates have been declining to the point where many cross-sectional surveys now have response rates below 50% (144-146). This was evident from the studies included in this review where the response rate was between 16–60% and two studies achieved a response rate of 73% and 89%. Dillman et al (147) outlines that responding to surveys has changed from being an obligation to being a matter of respondent choice and convenience. Studies have demonstrated that across countries there appears to be variation in response rates. There is a wide variation in the components of non-response such as non-contact, refusal and unable to participate i.e. due to illness or language difficulty. The variation in response rates are also apparent in the studies included in this systematic review. Response rates from Australia varied between 16–60%, Poland 89%, Germany 55%, UK 66%, Spain 53% and Egypt 73% (Table 2.3.2). The table below only outlines the studies that reported the response rates. For the full list of studies please see Appendix 6.

Table 2.3.2: Individual study response rates

Study author	Country	Response rate
Mead et al (1996) (117)	United Kingdom	294/640 (46%)
Wiszniewska et al (2000) (118)	Poland	159/300 (53%)
Middleton et al (2003) (119)	Australia	296/490 (60%)
Nguyen-Huynh Mai et al (2003) (120)	United States	1,289/2,978 (Quota sample 200)
Tomasik et al (2003) (121)	Poland	89/100 (89%)
Roebers et al (2007) (122)	Germany	395/714 (55%)
Jagadesham et al (2008) (123)	United Kingdom	40/60 GPs (66%)
Purroy et al (2011) (124)	Spain	138/258 (53%)
Leung et al (2012) (127)	Australia	32/202 (16%)
Ismail, Negm (2013) (128)	Egypt	95/130 (73%)
Otten et al (1995) (130)	Netherlands	308/464 (66%)

Actual practice studies

Similar to the knowledge-based studies described above, this section on actual practice studies also used different methods to assess GPs' diagnostic accuracy and management of TIA. The methods were retrospective cohort identifying new cases of TIA presenting to GPs using a general practice research database; data were retrieved using various diagnostic codes, prospective audit of referrals from GP and hospital emergency department first seen at the TIA clinic. Data were extracted from the referral letters and from clinical notes of stroke physicians. Practice audit based on retrospective, structured medical record abstraction from medical practices, audited GP referral letters for presumed acute stroke or TIA and a prospective cohort study in which patients with possible TIAMS are followed for 12 months post event.

2.2.11. Diagnosis

A total of five retrospective cohort and surveys explored GP management of suspected TIA, specifically with regards to diagnostic accuracy and symptoms related to diagnosis. These are based on real cases rather than vignettes covered in the previous section.

Diagnostic accuracy

McNeill (133) conducted a study in 1 TIA clinic in the UK in which referral letters of patients of presumed acute stroke or TIA were assessed. The sample included a total of 72 participants, including 68 with stroke and 4 with TIA. The study reported that in 17 cases, (24%), the examination differed between GP and admission examination and admitting doctors did not detect some signs documented by GPs. This highlighted a high rate of discrepancy in examination findings between the GP and admission examination. 27% of the presumed diagnosis of stroke was correct and overall, of 4 patients with suspected TIA, 2 were diagnosed with a TIA.

In a retrospective cohort study in Australia Magin et al assessed referrals from GPs and EDs first seen at the clinic within the Hunter New England area Health service and the John Hunter TIA/minor stroke acute access clinic (134). There was a total of 344 referrals of which 231 attended and were seen at the clinic (127 referred by GP and 104 referred by

ED). The results outlined that overall, 121 (52%) of the patients referred to a TIA clinic were diagnosed as having had a TIA or stroke. Of the 127 patients referred by a GP, 23% were diagnosed as TIA, 10% unclassified and 50% was not stroke. A higher ABCD2 score was significantly associated with having a final diagnosis of TIA, and being on antiplatelet or anticoagulant medication at the clinic attendance.

A study by Gibbs et al (132) in the UK which included 27 TIA and 25 stroke cases examined a GP database between 1992–1996 to determine whether initial GP management of TIA/stroke was uniform across the UK and the validity of GP diagnosis. The study found that of the GP diagnostic code for TIA in 27 cases, specialists agreed with a cerebrovascular diagnosis in 18 (66%) cases and confirmed as either a TIA or stroke. Of the 25 stroke cases, 20 (80%) were confirmed by a specialist as either a TIA or stroke.

Symptoms related to diagnosis

In a prospective cohort analysis including patients of 17 Australian general practices in the regions of New South Wales, Australia, Clarey et al (135) examined a total of 179 patients presenting as possible TIAMS (87 TIAMS and 92 TIAMS-mimics). A total of the 120 patients presenting with TIA symptoms to the GP, 49 (41%) were confirmed as TIAMS. Of unconfirmed cases, migraine was the most common TIAMS-mimic (29%) followed by vestibular dysfunction (17%), seizure and syncope/presyncope (8%).

A retrospective study by Goldstein et al (131) included primary care physicians from 27 primary care practices in two separate communities in Eastern US and 95 patients with first ever TIA. The study found that limb weakness was the most common deficit in the TIA patients (46%) followed by facial weakness (21%) and speech/ language disturbances (dysarthria: 16%, aphasia: 13%).

Please refer to Appendix 6 for a summary of the studies that explored diagnosis for practice based studies.

Conclusion

Results from several settings suggest that a specialist diagnosis of TIA is confirmed in around 50% of people suspected to have a TIA by their GP/PCP. Cases referred from ED were more likely to be true TIA than those referred to clinics by GPs, which may be influenced by GPs referring high risk/definite cases to ED or more severe cases presenting directly to ED.

2.2.12. Recognition of urgency

A total of six retrospective cohort and survey studies explored urgent referral to clinic or ED. Overall three aspects were examined, referral to ED, ABCD2 scoring system and aspects of patient history influencing referral.

Referral to ED/hospital admission or TIA clinic

In an Australian cohort study Clarey et al (60) examined a total of 120 patients presenting with symptoms the GP thought to be due to TIA. Of these, 12% were referred to the ED.

In the US Goldstein et al (131) included 95 patients in a retrospective study. The results highlighted that 2% of TIA patients diagnosed in primary care were admitted to hospital. 14% were referred to a neurologist, 13% to a cardiologist and 6% to a vascular surgeon. A study examining actual cases to determine the rate of referral to a specialist in the Netherlands, included 287 GPs in the area around the academic medical centre in Amsterdam (130). This study similarly found that cardiology referral was made by 15%.

A study by Gibbs et al (132) in the UK included 27 TIA and 25 stroke cases and examined GP database to determine referral of patients in practices across different regions in the UK. The mean rate of referral for TIA within 7 days of diagnosis was 19% and the range between regions was 14–26%.

ABCD2 scoring system

Magin et al (134) in a retrospective cohort within the Hunter New England area in Australia explored paths to care which included 231 attendees to the TIA clinic of which 127 were referred by a GP. This study found that the mean time from onset of TIA to referral was 9.2 days. The mean time of referral to being seen in clinic was 13.6 days. Also, the mean time from the event to being seen in clinic was 17.2 days. Of these 156, (37%) were seen at the clinic within 7 days. 39% patients with an ABCD2 score of less than 3 (low-risk) were seen within 7 days. 37% with an ABCD2 score of 4–7 (high-risk) were seen within a day. Thus, the score helped GPs with high-risk patients to be seen more promptly.

Aspect of patient history influencing referral

McNeill's (2008) audit examined referral letters and the information a total of 72 primary care doctors provided. The study found that 91% of letters provided a past medical history. Other factors were also noted such as 88% drug history, social history e.g. smoking and alcohol usage by 88% and any examinations by 58% (133). In the Netherlands, a cross-sectional survey by Otten et al in 287 GPs also noted the completion of a physical examination of 91% of patients. Also, younger patients and those independent in daily activities were more likely to be referred, than elderly and patients who were physically disabled (130).

Please refer to Appendix 6 for a summary of the studies that explored referral in the practice based studies.

Conclusion

Studies from Australia, US, New Zealand, Netherlands and UK showed a high proportion of cases of TIA were not referred. The low referral rate in Australian studies can be explained by GPs having access to imaging. The guidelines in the US, New Zealand and Netherlands may also differ from the UK guidelines which could explain lower referral rates. But, the low rate in referral in the UK suggests GPs are not following the guidelines which states all suspected TIA patients should be referred for specialist assessment; however, some studies were old and pre-dated the guidelines.

The Australian study on the ABCD2 score showed that a quarter or similar of TIA patients being seen in clinic within the seven-day of the event was similar to in the United Kingdom. However, the waiting time was higher within the Australian study (Australia: 37%, 17.2 days, UK: 35%, 12 days).

2.2.13. Prescription

Three studies examined antiplatelet (dipyridamole and aspirin), statins and antihypertensive prescribed by GPs.

Treatment

A US based study by Goldstein et al (131) included GPs from 27 primary care practices in two separate communities in Eastern US and also 95 patients. The study reported that GPs began a new antiplatelet in 47% of patients with TIA and in 63% in those who were not hospitalised. Additionally, in Amsterdam, Netherlands, Otten et al (130) study consisting of 287 GPs reported that 74% of TIA patients received aspirin, whilst 2% received both aspirin and dipyridamole.

A UK based study by Gibbs et al (132) investigated prescription rates in 27 TIA cases within 7 days of diagnosis. It was found that 38% of patients were prescribed antiplatelet, and 1% prescribed anticoagulants.

Please see Appendix 6 for a condensed summary of the studies that looked into prescription in the practice based studies.

Conclusion

The results showed variable rates of prescriptions by GPs at the time of presentation, with as expected, higher rates in those not referred. Overall, there was evidence of under-prescribing, which could be addressed through education and guidelines.

Intervention studies

As shown in Table 2.3.1, intervention studies were placed into three categories (diagnosis/referral/management). The table provided in Appendix 6 shows which studies contributed to these. One study was based on a diagnostic tool (the Dawson score) developed in secondary care that could potentially be used in primary care.

Three studies explored the use of an electronic decision tool for TIA/stroke and one study examined the impact of guidelines. Four studies aimed to improve diagnosis, three studies explored referral and a total of three studies aimed to improve aspects of management.

2.2.14. Diagnosis

Lasserson, Mant, Hobbs & Rothwell (98) study looked into clinical and research records from TIA clinics and consultation and referral letters from primary care to physicians were used to examine the potential utility of the Dawson score in primary care (96).
In the original paper the development of the tool was in secondary care. The Dawson score, based on the reported symptoms from patients, is the only diagnostic tool within the literature and includes nine variables, seven of which relate to the clinical event (headache, loss of consciousness, seizure, diplopia, speech disturbance, unilateral facial and limb weakness). The other variables are history of TIA/stroke and age.
In this study, the potential of the Dawson score for use in primary care was tested using data from 92,000 patients registered at nine general practices in Oxfordshire. The results were based on patients referred to a TIA clinic which compared the score derived from primary care data with the score derived from hospital clinic data.

The study found that 209 out of 513 patients (40.7%) had a final diagnosis of TIA. Patients with TIA had a higher Dawson score than those with other diagnoses using data from both primary care (7.21 versus 6.34) and secondary care (7.48 versus 6.01) (98). At the recommended diagnostic cut-off of 5.4, both primary care and secondary care derived scores had similar sensitivity (92.3% vs 93.4% respectively) but specificity was poor in both; 29.3% vs 18.1% respectively. The authors concluded that the differences in the recording of clinical features between primary and secondary care explained the differential performance of the Dawson score. They proposed that a tool for TIA diagnosis in primary care should be derived and validated in a primary care setting to improve applicability.

Differences in the results obtained using primary and secondary care data were due to differences in the recording of clinical features. Absence of documentation of a symptom in the primary care record in the study was interpreted as absence of the symptom. This may have been due to incomplete histories being taken in primary care or incomplete recording of absent symptoms. The study did not include patients with suspected TIA that were not referred, or cases referred to the emergency department.

The electronic decision tool (EDS)

Three studies examined an electronic decision support tool that aid GPs to accurately diagnose and manage TIA and stroke patients in accordance with the New Zealand guidelines (138-140). The EDS is a computer algorithm which incorporates diagnostic criteria and risk stratification according to the New Zealand guideline. The tool aims to improve GPs' diagnostic accuracy by providing GPs with definitions for neurological symptoms, guiding them in obtaining a focussed history and examination and providing immediate diagnostic feedback, 'TIA likely or unlikely'. However, these patients must all be referred to be seen by a specialist.

A prospective study of the effect on process of care following the implementation of electronic decision support (EDS) included 139 patients after EDS and referred to New Zealand's district's TIA clinic or inpatient care with the diagnosis of TIA. The study reported significant increases in the rate of initiating best medical therapy and behavioural counselling; for example, smoking cessation, diet, exercise and driving (139).

A 14-month safety audit reviewed 79 patients managed with the help of the TIA/stroke EDS tool to assess the safety of the tool in the primary care setting. The study reported that the decision support tool improved guideline adherence and reduced risk of a subsequent stroke (relative risk 0.27, 95% confidence intervals 0.05, 1.41, p = 0.098, or TIA (relative risk 0.26, confidence intervals 0.70, 0.97, p = 0.045). Furthermore, no safety issues were found with the use of the EDS (138). Similar results were observed from a randomised controlled trial that included 172 patients in the intervention group and 119 in the control group from four health districts in New Zealand. The tool achieved the guideline recommended urgent referral. Ninety-day TIA or stroke occurrence was lower in the intervention group, with 4/172 (2.3%) compared to 10/119 (8.5%) in the control: relative risk 0.26 (confidence intervals 0.70, 0.97, p = 0.045). The use of the tool reduced 90-day stroke risk, which did not reach statistical significance because of an unexpectedly low proportion of participants with 90-day stroke. The proportion of patients in the intervention group with a 90-day stroke was 1.2%, the same as that achieved in the SOS-TIA study (25) with rapid <6 hours specialist assessment for all suspected TIA patients (148). This suggests that GP initiated management with the aid of the TIA/stroke decision support tool may achieve a similar effect to more

intensive rapid access specialist clinics. Fewer vascular events or deaths occurred in the intervention group: relative risk 0.27 (confidence intervals 0.009, 0.78, p = 0.016) (140).

2.2.15. Referral

The prospective study of the effect on process of care following the implementation of the EDS tool which included 130 patients before EDS and 139 patients after EDS reported that the median time to the specialist review for the intervention group was 3 days and the control was 4 days, hazard ratio 1.45 (confidence intervals 1.13, 1.86) (139).

A randomised controlled trial in the UK included 76 general practices in three Bradford primary care trusts examining the effect of guidelines to manage TIAs. 43 practices were included in the intervention group and the control group included 33 practices. The study found that guidelines led to a non-statistically significant increase in referrals of patients with confirmed TIA. Additionally, time to carotid imaging for the intervention group was 7 days and control group was 24 days (136, 137).

In a randomised controlled trial of the EDS which included 56 practices from four health districts of New Zealand, 172 patients were included in the intervention group and 119 in the control group. The study reported that more intervention patients received guideline-adherent care for TIA; 76.2% in the intervention group and 41.2%, 95% CI; 2.39–8.71, p = 0.001. This included urgent referral for high-risk patients, immediate start of medication and comprehensive management for low-risk with or without referral within 7 days (140).

2.2.16. Management

Ranta et al's trial of EDS included implementation of the combination of antiplatelet, statin, and anti-hypertensive medications. The implementation of this the EDS tool was associated with a significant improvement in the rate of best medical therapy within 24 hours: relative risk, 1.33 (95% confidence intervals; 1.02, 1.71) p = 0.04 and behavioural counselling: relative risk, 1.68 (95% confidence intervals; 1.31, 2.16) p<0.0001 (139). Documentation of behavioural counselling including smoking cessation, diet/exercise and driving advice was noted in 66% of patients in the intervention group compared with the control group in a study that included practices in three Bradford primary care trusts in the UK. Additionally,

the implementation of guidelines for the management of TIA improved the treatment of TIA (odds ratio of complying with guidelines 1.8; 95% CI 1.1 to 2.8) (137).

Studies on the EDS conducted by Ranta et al (2014) reported that the tool can improve the initiation of best medical TIA therapy and reduced the time delays to specialist assessments. However, Ranta et al (2015) could not demonstrate an association with 90-day stroke risk to the small sample size. The results from this study and Ranta et al (2014) suggested that the tool improved guideline adherence and no evidence of safety issues with the use of the tool was found.

An additional study by Lavin & Ranta looking into the safety of the EDS tool in clinical practice found no evidence to indicate any serious associated risk. While no patients diagnosed by the EDS as 'non TIAs' had symptom recurrence, three patients diagnosed by EDS as TIA but triaged as 'low-risk' suffered a subsequent TIA. This suggests that the tool may be better suited to diagnosis rather than triaging TIA patients. The triaging of the three patients was made according to the New Zealand TIA guidelines. Thus, suggesting further refinement of current guideline endorsed risk stratification may be required.

Please see Appendix 6 for a condensed summary of the studies that looked into diagnosis, referral and management/prescription for the intervention studies.

Conclusion

The use/performance of the Dawson score to assist diagnosis in patients presenting to primary care is still uncertain and further work on an external validation study using data derived from primary care would be helpful. The studies looking into the EDS reported that the tool improved the use of medication and timely referrals, with no adverse effects and may have some utility in the diagnosis of TIA rather than to triage. The EDS was reported to improve guideline adherence and reduced subsequent stroke and death and no safety issues were found. Significant improvement in the rate of rapid initiation of best medical therapy was highlighted for example, smoking cessation, diet, exercise and driving and reduced time delays to specialist assessment. Although the EDS tool showed some promising results, the authors proposed that further refinement may be required along with larger studies in order to draw definite conclusions on the utility of the tool in preventing strokes and improving clinical outcomes.

Studies showed that the use of guidelines increased referrals, however, the increased referral of true cases of TIA was not significant (136, 137). Thus, further research may be important to explore if this approach is beneficial in improving performance in primary care.

2.4. Discussion

This was the first systematic review to be conducted on the topic of the diagnosis and management of TIA in primary care. This review summarised evidence on three aspects of TIAs in general practice which were: diagnosis, management and interventions to improve diagnosis and/or management. Studies of diagnosis and management were of two types. Firstly, knowledge and reported practice (based on case vignettes or surveys) and secondly observational studies in which actual practice was reported.

2.4.1. Diagnosis

The majority of knowledge and reported practice studies found limitations in GPs' knowledge and abilities to diagnose TIA, the extent of which varied between countries and over time.

The duration of symptoms used to define TIA varied across counties, but it is important to note that the definition of TIA has not been agreed internationally. The 24-hour definition in Egypt was considered the 'old definition', whereas in the UK, the 24-hour definition is still the standard definition, as it is in Spain and United States. It is interesting to point out that even though the 24-hour definition is still the standard definition in Spain, just over half of the GPs included in the study answered less than 24-hours when asked to define TIA. Similarly, in the US, the majority of GPs thought that longer symptom durations were compatible with TIA. This is concerning considering that it has been consistently cited in the literature that symptoms lasting more than 24-hours are associated with stroke, including the widely used World Health Organisation diagnostic criteria for stroke (149).

One reason for over-diagnosis, suggested by questionnaires and case vignette studies, is that GPs tended to put overemphasis on non-specific symptoms such as isolated vertigo. The inconsistency in clinical diagnosis is mainly due to the uncertainty about the nature of several transient isolated brainstem symptoms. Most clinical guidelines do not specify which of these symptoms should be deemed as TIA. The National Institute of Neurological Disorders and Stroke (NINDS) criteria state that most transient isolated brainstem symptoms such as vertigo, dizziness, focal symptoms suggestive of migraine and confusion should not be defined as TIA. Some TIA symptoms may also overlap with non-specific TIA

symptoms for example, headache with the addition of other symptoms (speech disturbance or visual disturbances) has been frequently diagnosed as migraine. Additionally, studies have reported that patients admitted to hospital with isolated vertigo have a three-fold increase in stroke risk (150) and that isolated vertigo can be the only manifestation of vertebrobasilar ischaemia (151, 152) Therefore, a high index of suspicion is particularly important given the short-time window available for prevention of stroke. It can be said that in patients with isolated vertigo plus vascular risk factors, referral for specialist opinion would appear to be reasonable.

The lack of understanding regarding TIA symptoms and risk associated with TIA was evident in this review. It has been reported in studies from Japan and France that GPs are under-educated about the risk of stroke after TIA, and many GPs find it difficult to manage these patients (153-155). This evidence supports the findings from this review that the lack of understanding in GPs are consistent across different countries. Furthermore, it was not only GPs who lacked knowledge; neurologists had the same problem (153).

The findings from this review outlined variation in the over estimation of subsequent stroke risk and underestimation of the risk after a TIA. Underestimating stroke risk after TIA can largely account for failure to refer patients for emergency evaluation, which can prevent subsequent strokes in patients of all ages, even if they are comorbid (156). Over estimating the risk of stroke after TIA could be explained because of the increase in efforts to raise awareness of stroke risk in recent years but may lead to over referral due to misdiagnosis of patients. It is uncertain how urgently patients must be seen and there is great variation in practice (153). However, it is important that both high risk and low risk patients are still referred and seen at the clinic due the risk of stroke.

GPs may benefit from guidelines to assist their practice. With training and introducing appropriate knowledge and recent guidelines of TIA to all primary care physicians, this could lead to better performance in the assessment and management of TIA (127). Furthermore, guidelines might be more effective if they emphasise the importance of emergency management of all TIA patients, regardless of age or comorbidity.

Only one study attempted to validate all TIA diagnoses made by GPs, and this suggested the diagnosis was correct in approximately two-thirds of cases (134). The level of disagreement between GP and TIA clinic diagnosis should be tempered with the knowledge that there is a

high rate of disagreement amongst stroke specialists with regards to the diagnosis (129, 157). Additionally, it is difficult to infer much about diagnostic accuracy from studies examining patients referred to TIA clinics due to selection bias (inclusion of patients with higher clinical suspicion of TIA, and exclusion of patients not referred).

Despite the benefits of prompt referral, data from TIA clinics internationally consistently showed that about 50% of referrals were not confirmed as TIA. These findings may reflect lack of knowledge amongst GPs and the difficulties experienced to accurately diagnose suspected TIA patients. It is concerning because GPs usually represent the first medical contact for most TIA patients (158).

A recent systematic review published after the completion of this review in 2017 (78) aimed to identify how many patients referred to a TIA clinic actually have a TIA (through the calculation of the positive predictive value) of first contact healthcare referral (GPs and ED doctors). The results showed that the proportion of referred patients with a final diagnosis of TIA and/or minor stroke ranged from 22.0% and 77.9% and from 12.9% to 72.5% of patients with a final diagnosis of TIA. The positive predictive value differed according to the reference standard i.e. 13 out of 18 studies had a positive predictive value of more than or equal to 50% for a combined TIAMS outcome, but only 4 out of 18 studies had a positive predicative value of more than or equal to 50% when the reference standard was just TIA. Of the patients not diagnosed as TIA, half of the final diagnosis were neurological or cardiovascular conditions.

The main diagnostic challenge of TIA is that the symptoms and signs have usually resolved by the time of assessment (159). Additionally, the diagnosis in consultations relies heavily on the patient's history making the diagnosis difficult (160). There is also no test for TIA and the gold standard remains assessment by a clinical expert. It is well documented that any cause of transient neurological symptoms is a potential TIA, opening up to a huge range of alternative diagnoses. Frequent causes of transient neurological symptoms that can mimic a TIA are: migraine aura, seizure and low blood sugar. This contributes to the difficulties of accurately diagnosing this challenging condition (159).

2.4.2. Management

As outlined above, accurate diagnosis is vital for suspected TIA patients. However, the immediate management of these patients is also necessary to evaluate the patient's symptoms to diagnose as TIA or as other causes. Additionally, advice on lifestyle choices can be made to prevent a future stroke.

Unsurprisingly, reported referral behaviour varied between countries, with no consistency in management strategies; some favour admission of high-risk cases and others advocate outpatient management. It was also reported that despite the majority of GPs perceiving TIA as a medical emergency, there was variable practice in admitting patients with TIA. In Spain, suspected TIA patients were admitted to hospital, whilst low rates of admission were found in Germany and Egypt. Firstly, it is important to note that while most studies agree on the need for urgent evaluation for TIA patients, there are no clear guidelines on hospitalisation.

There are limited data regarding the ideal care pathway for TIA patients once a decision to admit the patient to hospital has been made (161-163). Evidence from 15 hospitals contributing to a German registry highlighted that management in a stroke unit was associated with reduced risk of stroke, or death at 90-days. However, this was only in men with TIA (162). Similarly, declining trends in the 90-day risk of stroke in Australia were observed in patients with an incident TIA if managed in hospitals with a stroke unit (163). On the other hand, a study examined hospitalisation compared to same-day clinic and concluded that hospitalisation may not be cost-effective or globally beneficial based on limited hospital resources (164).

In the US, referral to the rapid access clinic is an uncommon management route (165). Most patients in the US present to the ED, which was also outlined in Jakel et al's., study where approximately 70% of suspected TIA patients presented to the ED (126). Patients will be managed by completing a diagnostic workup in the ED, discharging patients to have workup performed by their primary physician or admitted to the hospital (165). Similarly, in Australia, access to TIA clinics/specialists are not widely available, especially outside major cities. This leads to a high risk of potentially avoidable mortality and morbidity (166).

It can be proposed that the variable referral patterns highlighted in this review could be because patients presenting to general practice may be advised by GPs to be referred to a TIA clinic or be admitted but may not consent to this. Alternatively, patients may put pressure on the GP to refer or admit them to hospital even if they are labelled as low-risk.

The low admissions rate can be explained if the patients have been managed by the GP or as an outpatient if they were low-risk patients. The stratification of stroke risk using tools such as the ABCD2 score (section 1.6) recommends specialist assessment is needed for all suspected TIA patients. The ABCD2 was found to categorise four of every five patients as high risk, which may limit the utility in triaging, and indicating that the score is unlikely to have great impact on reducing the workload at the TIA clinic (56). The limitations have specific clinical implications such as, the risk stratification based on </≥4 does not reliably distinguish patients who need the most urgent intervention from those with mimics, and does not significantly reduce the workload on the limited capacity of the TIA clinic. Guidelines that recommend urgent treatment based on the ABCD2 score ≥4 while patients with low scores wait for up to a week risk missing patients with risk factors that require specific prompt treatment (55). Patients with suspected TIA/minor stroke require urgent expert assessment to identify those with true TIA/minor stroke, identify key risk factors, and implement appropriate secondary prevention as fast as possible.

It was evident that referral rates among GPs were variable, but there was consistent evidence of under referral for reported and actual practice in Australia, United States, New Zealand, Netherlands and the UK. These results may signify a missed opportunity to identify and prevent a stroke. Considering the mounting evidence that specialised clinics for managing patients with TIA are associated with a reduced risk of stroke such as the EXPRESS and SOS-TIA studies (25, 156), it is of concern that only 50% of patients with TIA were being referred by GPs. Only two studies examined actual referral rates. In the UK, this was found to be only 19%, but the study was conducted in the 1990s when the benefits of specialist intervention were not well recognised. Referral practices varied according to time; it was not until publication of the OXVASC studies in 2002 that the high early risk of stroke after a TIA was known (141). Since the UK study examining referral rates was published in 1996, there has been a drive to develop TIA clinics in all UK hospitals and practice is likely to have altered significantly. In a smaller Australian study, 36% of TIA suspects were referred. In

part, this apparently low rate could be because GPs have direct access to imaging, so management can be optimised without specialist assessment. Alternatively, a study looking into the management of TIA in Adelaide, Australia outlined that there are currently no formal pathways for TIA care in this city (167). Additionally, the relevance to the practice in Australia, particularly rural practice is uncertain. The organisation of care, access to imaging and access to specialists are different from that in the UK (166). Therefore, the lack of access to urgent expert stroke care may dictate that GPs practise contrary to the guideline advice reflected in the Australian National Stroke Foundation guidelines (NSF-guidelines) (166).

Some of the studies as mentioned above were small scale including small number of GPs limited to a specific part of the UK, Spain, Egypt as well as Australia, and may not be representative of other areas to those represented. Furthermore, some studies were fairly old and predated current guidelines, so may not reflect current levels of knowledge and practice. More research is therefore needed to investigate whether under-referral remains a problem in current practice.

Consistent evidence was found for the under-use of effective medication for knowledge based and also for observation practice studies. In the UK, the majority of the GPs included in the studies routinely initiated aspirin for patients with TIA. The high rate of initiation of effective medication in the UK could be justified by the clear guidelines that GPs adhere to in the management of these patients e.g. NICE guidelines. Initial management according to the guidelines comprises of the administration of aspirin (300mg daily) and/or clopidogrel to prevent occlusive vascular events (11, 60). As discussed earlier, in Australia evidence suggests that patients presenting to primary care are managed very differently to those in the UK (166). Brief guidelines on the appropriate drug initiation after a TIA could explain under-use of treatment (both internationally and across regions) (167).

2.4.3. Interventions

There is currently no diagnostic tool for TIA and the results from this study supports the need for a decision support tool to aid GPs with the diagnosis and management of these patients. Although there are several validated diagnostic support tools for stroke recognition such as the FAST and ROSIER, this is not the case for TIA. The ABCD2 score (7) has been assessed for its utility as a diagnostic tool for TIA (168, 169). However, the score's

primary role remains as a risk stratification tool for low and high-risk patients and to prioritise these patients at the TIA clinic once the decision to refer has been made.

The Dawson score was the only published tool at the time of this review which aimed to improve diagnosis of TIA (96). It is important to highlight that the Dawson diagnostic tool for TIA was derived using patients who had been referred to clinics. This highlights that the implementation of the diagnostic score may not improve recognition of missed TIA.

In the Dawson paper, the clinic diagnosis was used rather than the final diagnosis which would have been supported by brain imaging. Therefore, Dawson et al assessed whether the scoring system can distinguish those who the specialist believes require further investigation for cerebrovascular disease from those who do not. In addition to this, given that the score was developed using data generated during assessment by stroke specialists, it is not certain that GPs would come to the same conclusions, and already there are disagreement amongst specialists regarding TIA diagnosis (129).

Lasserson et al conducted an external validation of the Dawson score. The study looked into clinical and research records from TIA clinics, consultations and referral letters from primary care to physicians to examine the potential utility of the Dawson score in primary care. The score was derived from primary care data in patients referred to the TIA clinic and compared with the score derived from hospital clinic data.

Lasserson et al reported differences in the recording of clinical features between primary care and subsequent secondary care review, which resulted in differential performance of the Dawson score in these settings. There has been evidence to suggest that histories elicited from patients with TIA in primary care may differ from assessments completed in secondary care (98). This difference has been noted before particularly for stroke onset times (170). This evidence was also noted from observation of small differences in ABCD and ABCD2 score from retrospective calculation in clinical notes between primary and secondary care (54, 171).

It is important to note that in both the Dawson et al and Lasserson et al studies, GPs may not have referred all patients with transient neurological symptoms to the TIA clinic, by either managing them in primary care or sending them to ED. Thus, the performance of the Dawson score to detect TIA among all patients presenting to primary care with transient symptoms is still unknown (98).

The Diagnosis of TIA (DOT) score was published in 2017 after this systematic review had been completed. It is a new tool to aid non-specialists with the diagnosis of TIA and is an internally validated web and mobile app based diagnostic tool which encompasses both brain and retinal TIA. The sensitivities were very similar in the DOTS and Dawson score; but other measures such as positive and negative predictive values and AUC were superior for DOTS. The score attempts to cover the entire spectrum of TIA/stroke that would be expected in a TIA clinic which include anterior and posterior circulation and retinal events. Overall, the DOT score shows promise as a diagnostic tool for TIA and could potentially improve the triage of patients assessed for suspected TIA (193).

Guidelines are currently being used in the UK to manage suspected TIA patients (NICE) and the need for clearer guidelines in Australia has been highlighted above (127). Previous research has demonstrated that clinicians are more likely to comply with guidance if they are compatible with their own values (172). Although, the studies looking into the use of guidelines in this study reported that the use of guidelines increased TIA referrals, the increased referral of true cases of TIA was not significant (136, 137). It can be suggested based on the results of this review that GPs are aware that managing TIA is difficult. GPs wish to refer all true cases of TIA, however, a dilemma in TIA management is the fact that GPs are also handling patients presenting with symptoms that could be due to TIA and TIA mimics. Therefore, it poses a dilemma to manage these patients even with the use of guidelines. Additionally, the risk associated with missing a patient with a true TIA affects GPs referral decisions despite what it may say in guidelines (173). Without the referrals overburdening the TIA clinic, it is vital that true TIA cases are referred. The study concluded that healthcare professions are more likely to comply with clinical guidelines following a tailored intervention. However, this will depend on various components as highlighted by previous reviews (174, 175) and also by the NICE guidance in the UK (176). Some of these components of effective implementation strategy included: strong professional support, clear recommendations about the clinical content, robust research evidence base demonstrating effectiveness of guidance and guidance that it is not too complex or expensive to adopt.

The use of new technologies such as computerised decision support tools may provide generalists with additional support that goes beyond referencing a guideline (139, 140). In

New Zealand, the electronic decision support (EDS) tool aimed to improve care settings by supporting GPs with the diagnosis and management of TIA.

The proportion of patients in the intervention group with a 90-day stroke was 1.2%, the same as that achieved in the SOS-TIA study (25) with rapid <6 hours specialist assessment for all suspected TIA patients (148). This suggests that GP initiated management with the aid of the TIA/stroke decision support tool may achieve a similar effect to more intensive rapid access specialist clinics. Furthermore, the recent and widespread use of secondary preventive medications to reduce cardiovascular risk may have had a significant impact on current stroke rates (177).

Although the electronic decision support tool improved management e.g. the tool improved use of medication, timely referrals with no adverse effects and reduced subsequent stroke, its impact on diagnosis has not been reported. The author concluded that the study results are intended to be widely applicable nationally and internationally. However, guidelines on TIA have shown to differ in Australia and in the UK (166) and since the EDS tool was based on New Zealand guidelines, the implementation of the tool may need refinement. Additionally, larger studies are needed to draw definite conclusions on the utility of the tool in improving clinical outcomes.

2.4.4. Methodological issues

It is important to point out some methodological issues with the included studies. Although it is known that response rates have been declining to the point where many cross-sectional surveys now have response rates below 50% (144-146). It can be suggested that a response rate of 70% is an adequate threshold when assessing the quality of studies. The MMAT quality assessment tool that was used in this study included a fairly liberal threshold of 60%. Despite this it is important to highlight that even with this low threshold, only 5 of the 24 included studies achieved this response rate. Non-response leads to a smaller final sample size, which was definitely the case with some of the studies included in this review which were small scale including small number of GPs limited to a specific part of UK, Spain, Egypt as well as Australia. Therefore, it could be proposed that this led to a loss of accuracy in population estimates and may not be representative of those areas to those represented in the small-scale studies.

Previous studies have shown that in GP surveys, non-responders are more likely to be older, more experienced, solo practitioners and less qualified than responders (178). It is likely that responders to surveys on TIA are more interested and have a high awareness of the topic, which would mean results overestimate GP knowledge and good practice. This has been demonstrated by a previous study that showed that questionnaires designed to be of more interest to participants were more likely to be returned (179).

The overall response rates were higher in studies conducting case vignettes than structured questionnaires and telephone interviews, suggesting that this approach is more acceptable than 'exam style' questions. The reason for the particularly low GP participation in studies conducting interviews (125, 126) may be due to the fact that interviews require a great amount of time to collect information usually more than 30 minutes to 1 hour. This makes the method time-consuming in comparison to postal questionnaires and may lead to the reduction in the number of participants (180).

The included studies using non-validated questionnaires with little or no mention on how the validity issues were addressed. These raises concerns on reliability and validity of the studies. It can also be proposed that researchers could use a previously validated questionnaire to potentially avoid any issues with validity that may come from developing a new questionnaire. Moreover, using a previously validated and published questionnaire will save time and resources; the researcher will also be able to compare their findings with those from other studies. However, despite the advantages of this, there is little existing literature relating to the management of TIA in general practice and in general, there is a lack of validated questionnaires for assessing knowledge (181). Therefore, there may be limited previously validated questionnaires that can be used to assess GPs knowledge on the diagnosis and management of TIA in primary care. Additionally, the studies reported results from various aspects such as definition of TIA, stroke risk, symptoms, referral routes, TIA as a medical urgency and prescription, with a couple of these studies also using case scenarios (122, 127). Therefore, it may have been easier for researchers looking into this topic to develop and validate a questionnaire, rather than using a previously validated one.

Using a questionnaire may help highlight issues of importance which may have not been previously mentioned within the literature. However, a limitation of surveys is that responses to questions about awareness/management may not reflect actual practice. This

could relate to some of the studies included in this review. For example, GPs may provide similar responses to their colleagues on how patients are managed due to the fear of being judged, despite differences in their management for suspected TIA patients in practice. This methodological limitation may influence the interpretation of results because actual behaviour is typically over-reported (119, 182). Nevertheless, this would not be uncommon as the lack of knowledge regarding the diagnosis and management of TIA was prominent amongst the majority of GPs in this study, which extended both nationally and internationally. Also, each GP/PCP will differ in terms of their medical training and their own beliefs on diagnosing/managing TIA.

It has been highlighted that the vignette methodology does not fully capture the elements of reality under study. The method does not give full context for a case/referral in which decisions are made under high pressure as typically experienced in clinical practice (183). This applies to many of the case vignettes used in this study to analyse the diagnosis and management of TIA in practice. Additionally, participants may give reactions to vignettes based on what they think others would give rather than risk providing their own view (183).

A cohort study is an observational study used to estimate how often disease or life events happen in a certain population. A prospective cohort study takes a group of similar people (a cohort) and studies them over time. A retrospective cohort study (also known as a historic study or longitudinal study) is a study where the participants already have a known disease or outcome. Cohort studies are often susceptible to selection bias (184). In the case of this study, this would relate to the inclusion of patients with higher clinical suspicion of TIA and exclusion of patients not referred. It would therefore be difficult to infer much about the diagnostic accuracy in studies examining patients referred to TIA clinics. In terms of the retrospective cohort studies using medical records and GP databases in this review, researchers cannot control exposure or outcome assessment and must rely on others for accurate recordkeeping. Existing data may be incomplete, inaccurate and therefore questioning the accuracy of the results.

Interventional studies are a type of clinical study in which participants are assigned to groups that receive an intervention/treatment (or no intervention). This is so that researchers can evaluate the effects of the intervention (185). In health research many outcomes of interests are far in the future and some interventions require long-term

implementation before an effect can be measured. This may explain why the studies looking into the EDS 90-day stroke risk may find it difficult to detect intervention effects at follow up periods which only span between 1 to 3 years (186). Furthermore, results may not always mimic real-life treatment situation (e.g. inclusion / exclusion criteria; highly controlled setting) (186).

2.4.5. Strengths and limitations of the systematic review

This is the first time the literature on GP diagnosis and management of TIA has been synthesised. A comprehensive search strategy including all languages and countries was applied. Papers from several countries were included which provided insight from diverse types of health care systems. Additionally, both qualitative and quantitative study designs were included (usually a systematic review considers one or the other) and a quality tool applicable to all study designs was used.

Whilst the search for studies used a formal search strategy and citation searching, it may be possible that potentially relevant studies were missed because authors have used terms that were not included in this study. The search terms focused on diagnosis because at the time of the review, the primary interest was in diagnosis. However, the papers revealed some useful information about management. Therefore, some papers on management that did not include diagnosis may have been missed. Similarly, the screening of titles and abstracts was not double checked by a second reviewer which may have led to an error in excluding potential eligible studies.

Like most quality appraisal tools, there are limitations with the MMAT (section 2.2.7). The tool has been advised to be used by experts or those who have frequently used the tool before. This does not take into account that researchers who have previously not used the tool may wish to use this. Although advise can be sought by emailing the authors, researchers who are new to using the tool may find it difficult to interpret the score and understand the findings. Although the percentages gave a brief idea of the quality of the papers, the in-depth understanding may be lacking (187).

Within the literature, it is encouraged not to calculate an overall score as it does not provide information on what parts of the studies are problematic. Rather, it provides an equal weight to all criteria. It is necessary that the score provides information on what part of the

study are problematic to ensure that relevant and high-quality papers are not excluded (188).

Despite the limitations highlighted above, most of the tools cited within the literature are specific to a particular research design or method as highlighted in section 2.2.7. The MMAT can critically appraise the methodological quality criteria for different study designs included in a systematic review and is one of the widely used tools (188). Furthermore, there is now an updated 2018 version of the MMAT cited within the literature (188).

Although synthesis was difficult because this review used different non-validated questionnaires to explore knowledge and different methods to assess practice, a strength was that this review was able to narratively synthesise the results on this important topic; however, a meta-analysis was not conducted due to the different sources of heterogeneity (variability) across the included papers which may bias the results. A common criticism of meta-analyses is that they often combine apples with oranges (189). Meta-analysis should only be considered when a group of studies is sufficiently homogeneous in terms of participants, interventions and outcomes to provide a meaningful summary. If the studies are clinically diverse then a meta-analysis may be meaningless, and genuine differences in effects may be obscured. Often a combination of all included studies in a single meta-analysis is not appropriate. This is due to a mix of comparisons of different treatments with different comparators, each combination of which may need to be considered separately, and it is important not to combine outcomes that are too diverse (189).

The possibility of meta-analysis was considered in this study, particularly the diagnostic accuracy by GPs which would have subsequent implications for prognosis, investigation and therapy. This review highlighted some interesting findings on the limitations of GPs ability to diagnose a TIA. Thus, it was of interest to explore diagnostic accuracy in GP management which may provide further evidence for techniques that may be successful in promoting the quality of diagnosis e.g. education and training and/or decision support tools. If the studies included in this review used similar methods then studies could have been combined using meta-analysis. In general, different methods had been used to assess practice and different non-validated questionnaires were used to assess knowledge. In studies that looked into diagnostic accuracy, different sampling was used along with different study designs such as cohort retrospective, cross sectional survey etc. Therefore, there was various different

sources of heterogeneity which may bias the results such as different case mix from different countries, different methods and different study designs. Furthermore, the different variables and/or measures used in different studies would make it difficult to combine in a meta-analysis (190). The exclusion criteria for any meta-analysis would be strict due to the reasons above, resulting with one or two studies at most to meta-analyse. Therefore, meta-analysis was inappropriate. The decision to not conduct a meta-analysis due to heterogeneity across studies was similar to the recent systematic review looking into predictive values of referrals for TIA (78).

2.4.6. Future research

Overall the EDS which has shown promising results on the management of TIA, but further research looking into the diagnostic utility of the EDS would be useful to not only educate GPs but to support GPs with their decision-making process. This may increase referrals, optimise referral patterns and timely management. This research could build on initial work undertaken in New Zealand, and would be useful to include larger sample sizes and potential adaptation for use in other health systems.

There is a need for clear guidelines on the management of these patients in order for GPs to improve knowledge and practice with respect to diagnosis, management and referral pathways.

There is a need to examine bigger and more representative samples, which are now possible using routine GP databases. Possible studies could explore what proportion of TIA cases were referred and diagnosed as TIA or the immediate management looking at how many GPs prescribed guideline recommended treatments. Since it would be using routine GP databases, the results would be based on more representative practices.

At the time of the study, the Dawson score was the only validated diagnostic score for TIA. The review highlighted a need for an external validation study to draw conclusions beyond the results of the original Dawson study. There remains significant potential for the development of diagnostic tools for primary care, which should be derived and validated in the primary care setting. A first step could be further work to assess the performance of the Dawson score using data collected for this purpose in primary care.

An external validation study that assesses the performance of the score using data collected from patients referred to the TIA clinic i.e. not primary care, and using data collected for the specific purpose of calculating the Dawson score would be useful to further determine the use of the score. The study could be used to determine whether applying the score before clinic attendance could reduce unnecessary clinic consultations, and be used by clinic staff to triage referrals at the TIA clinic (Chapter 3).

Lastly, the review outlined a need for more qualitative studies particularly looking into under-referral and GPs rationale behind this. Additionally, looking into the particular challenges to do with diagnosis and management from a GP perspective to obtain a better understanding of the nature of the condition along with the difficulties experienced by GPs. It would be useful to understand GPs thoughts on a potential diagnostic tool, particularly exploring practicalities which need to be considered for a diagnostic tool to be used in primary care (Chapter 4).

2.5. Conclusion

Overall, this review outlined that there is consistent evidence that approximately half of patients who are referred to TIA clinics have a cerebrovascular diagnosis confirmed, and that in some countries this militates against services assessing patients promptly. This is a problem of over-referral, meaning that demand on the TIA clinics are excessively high. GPs may refer some patients to exclude rather than confirm a putative diagnosis which may explain over-referrals. But this finding, together with evidence of under referral of patients who do have a TIA emphasises the need for education and decision support tools to optimise referral patterns and support diagnosis of this challenging condition. There was only one diagnostic tool for TIA at the time of this review which was the Dawson score. Although the EDS is a comprehensive tool to improve diagnosis and management, it is not recognised as a diagnostic tool within the literature. Rather, it is more of a management tool that could aid with diagnosis. In addition to this, the symptom checklist to aid with diagnosis was based on clinical judgement, rather than analysis of a dataset. Overall, the EDS tool has shown promising results on the management of TIA, but further research looking into the diagnostic utility of the EDS would be useful to not only educate GPs but to support GPs with their decision-making process.

This thesis aimed to fill certain gaps highlighted by the review. Firstly, the systematic review highlighted that the only diagnostic tool for TIA was the Dawson score, which has potential for clinical application in the diagnosis of TIA. However, in order to assess the performance of the score, there is a need for an external validation study using data collected for this purpose using data from primary care. By exploring the performance of the score, its value for GP diagnosis, initial management and referral practice can be assessed, as well as its potential role in refining referral to minimise overall burden at the TIA clinic. Therefore, this important aspect was explored in Chapter 3.

Secondly, the three qualitative studies included in the systematic review identified knowledge gaps in GPs' knowledge of TIA. GPs were aware of their lack of knowledge of TIA, and identified the need for further awareness of symptoms. Although the ABCD2 score was not developed to aid with diagnosis, GPs found the ABCD2 score to be helpful to aid with their decision-making process as it ensured swift referral to secondary care. Given that the

ABCD2 score is no longer recommended to be used by the NICE guidelines for risk stratification, and is not recommended as a diagnostic tool, GPs may benefit from a tool to help with the diagnosis and management of these patients.

The review identified limited qualitative studies on the diagnosis and management of TIA. Thus, it would be useful to not only get GPs views on TIA to better understand the nature of the initial assessment process, but to also understand their views on the potential utility of a diagnostic tool for TIA in primary care. GPs views on the considerations for implementing it in practice would also be useful, adding to the limited evidence base within the literature. A qualitative study was therefore conducted on this topic in Chapter 4 focusing on the diagnosis, management and potential utility of a TIA diagnostic tool in primary care.

Chapter 3: Clinical utility of the Dawson score: External validation

3.1. Background

Following various secondary prevention studies (25, 156), rapid assessment TIA clinics have been established to investigate and manage this challenging condition. The diagnosis of a TIA however can be difficult. Approximately 50–60% of TIA referrals by non-specialists are diagnosed as non-cerebrovascular mimics (2-4). Inappropriate referrals to TIA clinics can lead to delays for patients with TIA who are at high risk of early stroke and adverse outcomes (191, 192). Additionally, misdiagnosis of non-cerebrovascular conditions labelled as TIA leads to unnecessary anxiety and inappropriate management of these patients.

For GPs, the challenge is to accurately identify low prevalent but serious disease (in this case, TIA) from a background that includes a range of presentations overlapping with those of the serious conditions. Furthermore, GPs need to be mindful of the need to use resources appropriately and not expose patients to unnecessary harms of over investigation and treatment (193).

Stroke diagnostic tools such as FAST (67) and ROSIER (68) have been developed for the use by pre-hospital individuals and emergency room clinicians. The ABCD2 score has also often been used a diagnostic aid for TIA (91). The ability of the score to reliably discriminate between the two groups (low versus high risk after TIA) has been questioned, as a third of mimics were categorised to have an ABCD2 score ≥ 4 (55).

The use of a diagnostic tool for TIA in primary care could improve TIA clinic triage by eliminating some of the mimics and informing appropriate referral from primary care patients for secondary prevention, particularly as the majority of patients with symptoms of TIA attend primary care (194). Given that there is a risk of stroke after a TIA (section 1.3), the total burden of disease will be reduced by optimal secondary prevention after TIA (195). It has been estimated that management strategies for TIA patients, which include risk factor

modification, the use of antithrombotic or anticoagulant drugs and if necessary, carotid surgery could reduce stroke incidence by as much as 50–80% (196). However, this requires prompt assessment and treatment after TIA.

The absence of physical signs in TIA, contributes to the difficulty in deriving simple diagnostic tools. At the time of the start of the thesis, the only known published diagnostic tool for TIA, highlighted by the systematic review in Chapter 2, was the Dawson score (96) (section 2.2.14). Although the score has shown to have some diagnostic ability for TIA, there is a need for an external validation of the score to determine its performance beyond the results outlined in the development paper (96).

3.1.1. Clinical prediction

Highlighted in section 1.10, clinical prediction models are a combination of clinical findings that have statistically demonstrated the predictability in determining the presence of disease (diagnosis) or a future disease outcome (prognosis) for individual patients. These clinical prediction models are developed to aid clinicians' clinical decision making (197).

The probability that the disease is present can be used to refer patients for further testing and/or initiate immediate treatment. Alternatively, in a prognostic setting, predictions can be used to advise patients on lifestyle and therapeutic options based on the risk of developing a particular event in the future (82, 83). The estimated risk can also be used as a risk stratification, such as the ABCD2 score, to triage urgency of treatment for those who are high or low risk of the condition.

Clinical prediction models however, are referred as various terms which include, prognostic models, risk scores or prediction rules (84). Additionally, there is no agreement among developers and researchers in the literature on the established term for clinical prediction tools (85, 86).

There are many well-known diagnostic models which have been outlined in section 1.10, such as the Wells score (87), Ottawa Ankle Rules (89) and a diagnostic score for TIA (Dawson score) (96), which this chapter will look into. In contrast, prediction models for various conditions include the cardiovascular risk score (QRISK) (93) as well as the Nottingham Prognostic Index (94. Additionally, the ABCD2 score (7) predicts the risk of stroke in

suspected TIA patients (section 1.6), and is referred as a risk stratification score within existing literature. Although the score has been designed for prognosis, rather than diagnosis, the score has been used for both in clinical practice. However, relatively few data exist on the potential diagnostic usefulness of the score (90, 91) and existing evidence suggests that the ABCD2 score should not be used to influence diagnostic testing (92).

From 2017, the ABCD2 score according to NICE and Intercollegiate Stroke Working Party (ISWP) no longer recommend the use of the ABCD2 scoring in relation to initial assessment and management of TIA. Nevertheless, at the time of this study: between 3rd October 2016 – 31st January 2017, the ABCD2 score was still being used in practice (by TIA clinic staff to provide appointments within 7 days for low-risk patients, and within 24-hours, including weekend appointments for high-risk patients). Therefore, the performance of the ABCD2 score was also explored in this study.

Model development studies aim to derive a prediction model by confirming the relationship between predictor variables (symptoms, signs or diagnostic tests) and the presence or absence of the condition of interest. Logistic regression is commonly used for diagnostic and short-term e.g. 30-day mortality prognostic outcomes and Cox regression is used for long-term e.g. 10-year risk prognostic outcomes (80).

Calculating the predictive ability of a model on the same data from which the model was developed can provide an estimate of the performance. Some form of validation (e.g. calibration or discrimination) to account for overfitting is also required. This is when the model estimates too many parameters from a sample that is too small. The internal validation uses the original study sample and is a necessary part of model development (80). An ideal but probably unrealistic model will correctly identify every patient who will develop an event versus those who will not, and will not misclassify any patient. The extent to which any model comes close to achieving this goal can be characterised by two related properties of discrimination and calibration. Discrimination refers to how well the model distinguishes those with the disease from those without the disease. Calibration refers to the accuracy of absolute risk estimates (198).

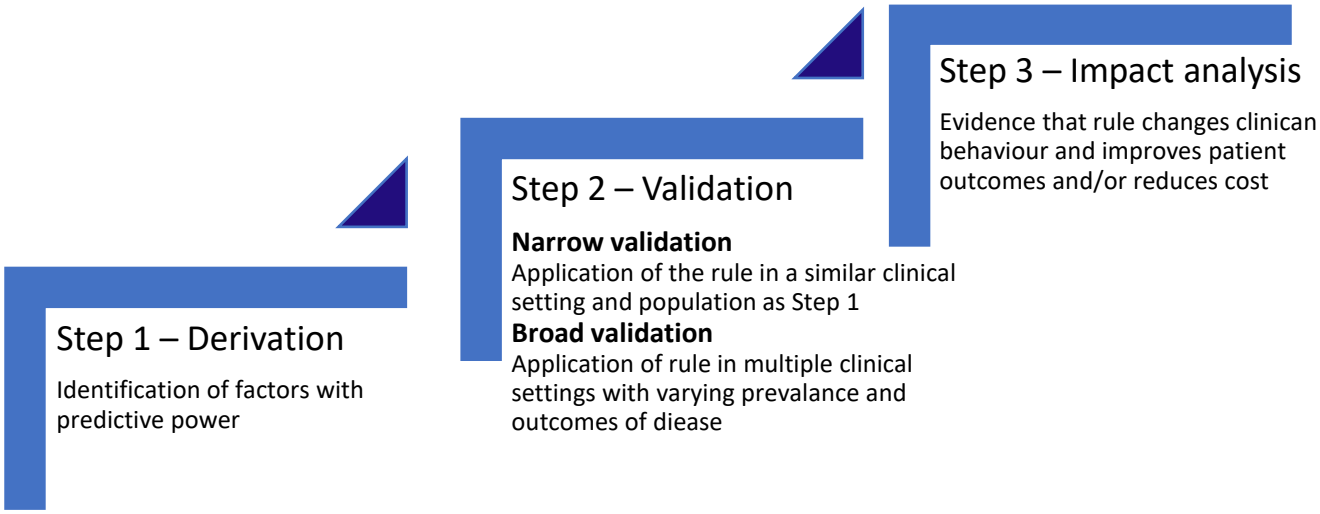
It is strongly recommended that the performance of a model should be evaluated in other participants' data than that originally used for model development. This is referred to as

external validation. External validation may include participants from the same institution in a different usually later time period (temporal validation). Temporal validation refers to when the model performs well across different but related sample populations. Temporal validation cannot examine the transportability and generalisability of the predictive performance of the model to other institutes or countries because the individuals in the development and validation set remain rather similar. Transportability and generalisability are assessed through a geographical validation where the model is validated in another centre or country that was not involved in the original development study. Additionally, domain or setting validation refers to using very different individuals than that used in the development study i.e. model developed in adults and assessed in children (199).

To assess the impact of clinical prediction models a comparative study is necessary. In this stage the study outcomes are measured in a control group exposed to management without the use of information from the prediction model and an experimental group exposed to management with a prediction model (80). This may direct the extent to which a clinical prediction model can be used and the effects on health outcomes is quantified.

Conventionally, multivariable clinical prediction models are developed in a multistep process involving the 3 stages; (derivation, validation and analysis of impact), and can be applied to both prognostic and diagnostic models. A brief description of the development of a clinical prediction model (81) is outlined below in Figure 3.1 adapted from Moons et al (2009)(82).

Figure 3.1: Stages in the development of a clinical prediction model



Prediction tools developed for the use in diagnostic setting has been focused on in this thesis. Such tools provide an estimate of the presence of an outcome e.g. TIAMS diagnosis or non-TIAMS diagnosis and aid with the clinical course of action for these patients. Whether a clinical prediction model in the diagnostic setting is clinically useful in confirming or refuting a diagnosis is determined through the number of cases it correctly identifies as having the disease (sensitivity) and the number it correctly identifies as not having the disease (specificity) (section 3.4.12). A test with 100% specificity correctly identifies all patients without the disease. A test with 80% specificity correctly reports 80% of patients without the disease as true negatives. However, 20% of the patients without the disease are incorrectly identified as false positives. The assessment of the positive predictive value (PPV) and the negative predictive value (NPV) are also key considerations in determining the accuracy of such tools. The PPV of a test is a proportion that is useful to clinicians since it answers the question of how likely is it that the patient has the disease given that the test result is positive. Similarly, the NPV of a test answers the clinical question of how likely is it that the patient does not have the disease given that the test result is negative (200) (section 3.4.12).

3.1.2. Dawson score

Based on the high risk of stroke after TIA (section 1.3) guidelines recommend that patients are assessed as soon as possible and at least within 1 week (11, 201). Fast track TIA clinics can significantly reduce the early risk of stroke (156); however immediate or same day assessment of those with suspected TIA are difficult to achieve nationwide and the importance of measures to optimise efficiency of assessment have been highlighted (156). While diagnostic algorithms are employed in clinical trials (202, 203), they are not widely used in clinical practice. Therefore, this prompted Dawson et al to develop their work on the recognition of a diagnostic tool for TIA. Dawson et al hypothesised that a diagnostic algorithm and clinical scoring system could be developed to aid with the diagnosis of TIAMS. Furthermore, its use would reduce non-cerebrovascular referrals and that this would reduce the overall clinic waiting times and facilitate rapid assessment.

Dawson et al developed and validated a clinical scoring system for identification of TIA patients. The Dawson score was derived using multivariable logistic regression from routinely recorded secondary care clinical notes. Given that by definition a patient with TIA has non-persisting symptoms, the tool is based on the clinical history. A score weighted using the coefficients of the regression model consisted of negative points for headache, loss of consciousness/syncope and ictal features, positive points for diplopia, past history of stroke/TIA, unilateral face/limb weakness, speech disturbance and increasing age. Internal validation performed with a 2:1 cost ratio used for misclassifying a TIA as non-TIA was used to derive an optimal cut point (5.4) for clinical usage.

The authors used a derivation and validation method, where a risk score was developed using data contained in the West Glasgow Stroke Registry and was tested on an independent prospective data set from the same source. The impact of the projected reduction in non-cerebrovascular referral rate was then assessed using real data on referral rates and clinic availability during the prospective validation study.

In regards to the model derivation process, the variables that showed discriminatory power were considered for inclusion in a clinical scoring system. Non-weighted (where explanatory variables were assigned a value of 1) and weighted scoring systems (based upon the regression coefficient and rounded to one decimal place) were then developed.

The score incorporates age which is measured in years, history of stroke and seven variables which relate to the clinical event (headache, loss of consciousness, seizure, diplopia, speech disturbance, unilateral facial and limb weakness) (96). To calculate the Dawson score each variable is given a value if present/absent and all values summed. Table 3.1 below is the score calculation depending on the presence or absence of each variable and the patients' age multiplied by 0.04. Higher values of the score correspond to higher probabilities of the condition. Table 3.1 below is a replica of Table 1.6 (see section 1.11) as a reminder of the Dawson score variables and calculation of the score.

Table 3.1: Dawson score variables and score calculation

Variable	Score if yes	Score if no
History of stroke or TIA	0.5	0
Headache	0	0.5
Diplopia	1.2	0
Loss of consciousness	0	1.1
Seizure	0	1.6
Speech abnormalities	1.3	0
Unilateral limb weakness	1.7	0
Unilateral facial weakness	0.6	0
Age (years)	Multiply by 0.04	

The cut-off selection procedure is an informed decision that takes into account the epidemiologic situation (e.g. prevalence in the target population) as well as the consequences of false negative and false positive results, which may differ according to different decision-making situation. For example, a disease of low prevalence and high cost of false positive diagnoses, it may be recommended to choose a cut-off at the lower part of the receiver operating characteristic (ROC) curve to maximise specificity (section 3.4.12). Alternatively, if the disease prevalence is high and missing any disease individuals has serious consequences, a cut-off value towards the upper part of the curve would be selected to maximised sensitivity (204).

Dawson et al used the (ROC) curve to determine the statistically optimal cut-off score and the sensitivity, specificity, positive and negative predictive values were calculated. ROC

compares sensitivity and specificity at all cut-off points of the diagnostic score to assess its overall performance. The method to determine the cut-off for interpreting a diagnostic score was the cost ratio approach. A cut-off was chosen to minimise the overall cost which accounts for the prevalence of the event and the costs of misclassification in either direction (205). Two 'costs of misclassification models' were developed "when it is presumed that the cost of misclassifying a cerebrovascular patient as a non-cerebrovascular is twice as much as misclassifying in the opposite direction" (96) (p.45) (section 3.4.12). For example, if the cost is considered a 2:1 then it is assumed that misclassifying a cerebrovascular patient as a non-cerebrovascular is twice as much as the cost of misclassifying a non-cerebrovascular as a cerebrovascular (section 3.4.12). With adjustment to reflect the greater seriousness of missing true cerebrovascular patients at 2:1 cost ratio, an optimal cut-off score of >5.4 was used.

The validation study reported a sensitivity and specificity of 93% and 34% in the diagnosis of TIA and minor stroke (TIAMS) when, the score was calculated retrospectively using data entered at the time of hospital appointment. Therefore, a high proportion of patients with TIA were correctly diagnosed with TIA (93%) but a high proportion of patients that did not have TIA were incorrectly identified with TIA (66%). The 3:1 cost model improved sensitivity to 99%, but was abandoned due to poor specificity (12%). The unweighted scoring system was also abandoned due to low performance (sensitivity of 82% and specificity of 60%). Please refer to Appendix 7 for the full Dawson paper.

The study discussion highlighted that a reduction in the rate of referral of non-cerebrovascular diagnoses could significantly improve performance of TIA services and that a clinical scoring system could be used to achieve this. Also, that an independent external validation and comparison to the ABCD2 score would be of use.

The following section highlights the main limitations of the Dawson score based on the derivation data in the original Dawson paper, and also the external validation of the score in Lasserson et al's paper (briefly outlined in section 2.4.3), and will further justify the rationale for this study.

Limitations of the Dawson derivation data set

1. Clinic referred and assessed patients

The Dawson diagnostic tool for TIA was derived using patients who have been referred to clinics. As such, GPs and ED clinicians have been concerned about the underlying diagnosis in these patients to the extent that they chose to refer for a specialist opinion. Derivation datasets comprising of clinic diagnosed TIA patients exclude the correctly recognised and very high risk who have a stroke after referral but before assessment, and those that are missed by GPs but are high risk and present with recurrent stroke. Ideally, the highest risk patients should be identified by a diagnostic tool but they did not appear in the Dawson derivation set. Dawson et al did not systematically search for these patients and therefore, only clinic seen patients were included. Furthermore, this highlights that the implementation of the diagnostic score may not improve the recognition of missed TIA. Given that a TIA diagnostic tool should be applied to all patients with transient symptoms in order to be effective, it should not be derived only from patients where GPs have already considered the diagnosis and referred. Nevertheless, a study looking into all TIAs presenting to primary care is challenging to conduct for various reasons. For example, because of the time required to collect data at the initial consultation in primary care, this will reduce recruitment and population capture of all the phenomena that could predict TIA diagnosis. Patients in primary care also commonly present with multiple problems and the transient event may be discussed at the end of a list of the issues, and GPs may not think of recruitment due to the complexity of this sort of consultation. Additionally, presentation can also occur out of hours from primary care, which is unlikely to result in recruitment and data capture unless arrangement has been made with the practices out of hours service. Also, the clinician may not frequently be from the patient's own practice.

2. Dawson score developed using data generated by stroke specialists

As the score was developed using data generated during assessment by stroke specialists, it is not certain that the score based on data collected by GPs would have the same characteristics.

3. Clinic diagnosis as opposed to final diagnosis

The clinic specialist diagnosis was used to determine the number of patients who had a TIAMS rather than final diagnosis which would have been supported by brain imaging as the reference standard. Therefore, Dawson et al essentially assessed whether the scoring system can distinguish those who the specialists believe require investigation for cerebrovascular disease from those who do not.

External validation study of the Dawson score – Lasserson et al study

An external validation study evaluates the performance of a model in a sample independent to those used for model development. It is to examine whether the model's prediction is reliable in individuals from an alternative population(s) (206). This leads on to the discussion of the Lasserson et al 2015 external validation study (98). The study looked into clinical and research records from TIA clinics, consultations and referral letters from primary care to physicians to examine the potential utility of the Dawson score in primary care (section 2.2.14). In this study, the potential of the Dawson score for use in primary care was based on 92,000 patients registered at nine general practices in Oxfordshire. The score was derived from primary care data in patients referred to the TIA clinic with the score derived from hospital clinic data. At the recommended cut off of 5.4, the sensitivity was similar for both primary and secondary care derived scores (92.3% vs 93.4% respectively) but specificity was poor in both; 29.3% vs 18.1% respectively (98).

1. Differences in history taking

There has been evidence to suggest that histories elicited from patients with TIA in primary care may differ from assessments completed in secondary care (98). This difference has been noted before particularly for stroke onset times (170). This evidence was also noted from observation of small differences in ABCD and ABCD2 score from retrospective calculation in clinical notes between primary and secondary care (54, 171). The Dawson

score comprises of nine variables, seven of which relate to the clinical event. This suggests that that the performance of the tool may be influenced by the differences in history taking. Additionally, in primary care, where the delay of presentation have been reported (148), a TIA recognition tool is likely to rely on accurate history taking. Lasserson et al reported differences in the recording of clinical features between primary care and subsequent secondary care review resulted in differential performance of the Dawson score in these settings.

2. Documentation of symptoms

Primary care data reviewing GP record was limited by the fact that absence of documentation of a symptom was interpreted as it not being present. It could be argued that incomplete histories were taken in primary care if the GP had already decided to urgently refer the patient. Thus, providing additional information would not have altered the GP's management in consultation.

Non-referral of TIAMS patients – Dawson and Lasserson et al study

It is important to note that in both the Dawson et al and Lasserson et al studies GPs may not have referred all patients with transient neurological symptoms to the TIA clinic, by either managing them in primary care or sending them to ED. Thus, the performance of the Dawson score to detect TIA among all patients presenting to primary care with transient symptoms is still unknown (98). Lasserson et al concluded that further work using data derived from primary care would be helpful to improve applicability and account for the risk of stroke after initial presentation to primary care. However, such study is challenging to conduct due to a couple of reasons: the length of time required to collect data at the initial consultation, and patients presenting with multiple problems for which GPs may not think of recruitment due to the complexity of this sort of consultation.

3.1.3. Rationale for the current study

Despite the limitations outlined above, the Dawson score was the only diagnostic score for TIA available at the start of this study. Additionally, the authors argue that the diagnostic tool in particular can be used to aid the clinical diagnosis of TIA by facilitating urgent assessment of those with TIA, and reduce the clinic burden by reducing non-cerebrovascular referrals (96).

The prospective validation set in the Dawson paper reported a sensitivity of 85% for the weighted scoring system, representing failure to detect a TIA and questioning the safe use of the score in clinical practice. However, the 2:1 misclassification scoring system yielded a sensitivity of 97% and specificity of 24% during the development phase, and 93% and 34%, respectively, during the prospective validation phase. The authors concluded that the reduction in non-cerebrovascular referrals would be clinical meaningful as it would reduce delay to assessment in the TIA clinic, and could also help in optimising use of TIA clinics through helping with triage in secondary care. Furthermore, the use of the score would improve knowledge of presentation of stroke and TIA, and therefore may increase detection of TIA.

Due to the complexities of collecting the data in primary care highlighted above, an additional external validation study of the Dawson score was thought to be necessary to assess the performance of the score using data collected from patients referred to the TIA clinic. The purpose of this research was to determine whether applying the Dawson score before clinic attendance could reduce unnecessary clinic consultations. If so, the score could potentially be used by clinic staff to triage referrals. Telephone interviews soon after the referral came through to the TIA clinic were thought to be the best method to ensure that accurate accounts of patients' symptom(s) were captured. This study was necessary to determine the two ways the Dawson score could be used: by the TIA clinic to triage referrals and by GPs to aid with diagnosis. The main validation study addressed the former in this chapter, the latter was explored in the qualitative study and the further analysis study in Chapters 4 and 5.

There are differences between this study and that undertaken by Lasserson et al.

Firstly, the Dawson score has not been externally validated using data collected for the specific purpose of calculating the score. Secondly, a diagnostic tool is of less value at the point at which a patient sees a specialist in a TIA clinic. Specialists use skills and knowledge from training to derive a diagnosis. Whereas, decision tools are more likely to be used by generalists as they support the initial decision-making process. This was the aim of the derivation of the Dawson score, as well as stroke recognition tools for paramedics and generalist clinicians (61, 70). Thus, a pre-clinic validation tool will be more helpful to judge the potential effect of implementation. This was undertaken by deriving the score at the point in which patients were referred by GPs and attended the TIA clinic. The Dawson data

were also collected from internal referrals (ED and in-wards at the local hospital). Prospective population-based cohort data of patients presenting to general practices and EDs has similarly shown a high early risk of recurrent stroke after TIA and minor stroke (207, 208). It was therefore decided to include patient referrals from ED, which is an aspect Lasserson et al did not include in their study. Another justification for including internal referrals which included ED referrals was because this study aimed to look at the Dawson score as a triaging tool at the TIA clinic. Therefore, internal referrals were just as important as GP referrals. Furthermore, Dawson and Lasserson et al did not look into the performance of the Dawson score according to different subgroups. This is an aspect that was explored in this study to further highlight any obvious differences that may impact the management of these patients.

Thirdly, in this study, the performance of the score was examined in a different population and at a different time relative to presentation (section 3.4.1). This prospective study explored whether applying the Dawson score before clinic attendance could potentially reduce unnecessary clinic consultations by those at low-risk of TIAMS. This involved interviewing patients by telephone to collect the Dawson score data soon after the referral to the clinic had been received, and before the patient attended the clinic. The method of systematically collecting the Dawson score soon after referral is also different to the method used by both Lasserson and Dawson et al who highlighted that by using clinical records there is no guarantee of systematic history taking (98).

Lastly, although highlighted in Chapter 1 (section 1.7) that the ABCD2 score from 2017 is no longer recommended for use by the NICE guideline (60) and ISWP (11), at the start of this study the ABCD2 was still being used in primary care. Dawson et al concluded that a comparison of the Dawson score to the ABCD2 score would be of value, and this comparison had not been undertaken.

The patient's ABCD2 score (section 1.6; Table 1.3) (209) is currently used at the participating TIA clinic to allocate the patient the most appropriate appointment date to be seen by a specialist. Although developed as a prognostic tool, evidence suggests that the ABCD2 score is currently used by some GPs as a diagnostic tool (125). Therefore, this study will compare the Dawson score to the ABCD2 score to establish if the score is more useful tool than the ABCD2 score to prioritise low-risk patients.

3.2. Observation and feasibility study at the TIA clinic

The researcher conducted a 3-day observation at the TIA clinic, which outlined an organised and structured procedure in the way the clinic was run. However, the clinic was short staffed with between 1–2 nurses usually attending to 6–10 patients a day. The clinic clerk at the TIA clinic initially arranged the phone appointments and was the focal point for all patients. However, occasionally the nurses and clinic aide also arranged the phone appointments.

Before embarking on the clinical utility of the Dawson score study, a feasibility study was conducted. The feasibility study determined the most appropriate way of collecting patient data to calculate the Dawson score for the main study. The study compared the Dawson components with data on the clinic database recorded prior to the clinic visit (from GP referral letters).

This feasibility study evaluated the practicalities of data collection from two staff members (nurses and clinic aide). The study was conducted in a structured manner and provided an opportunity for each staff member to collect the data.

A few options were initially considered on who should collect the data, which included: GPs, stroke specialists, patients, nursing staff and clinic aide. There were limitations associated with these options. If the Dawson score was to be adopted in clinical practice it would be used by GPs; therefore, the initial consideration for data collection was GPs. However, the data collection process would need approvals by various bodies which include, the clinical commissioning group (CCG) and the NHS. This would involve a lengthy process, and would have not been feasible within the 3-year PhD timeframe. Additionally, there is strong evidence on the pressure and lack of time in GP consultations. Therefore, asking GPs to fill out the Dawson score was felt to be beyond the remit of this project, and it was thought reasonable not to include GPs to collect this data. The main disadvantage with using stroke consultants was their lack of time as they have to deal with the high number of referrals. Sending the Dawson score form before their appointment and requesting patients to self-complete and bring the form on the day of their appointment was also considered. Like any questionnaire based study, the risk of non-response is likely (144-146). This was also

outlined in the studies included in the systematic review (Chapter 2). Additionally, most often the patients would have been seen within a day or two of their referrals. Logistically, these patients would not have received the form on time and therefore, heightening the risk of non-response. For these reasons it was thought best not to request the patients to fill out the Dawson score. Although there are also disadvantages with using nursing staff and clinic aide (mainly issues with being under-staffed), using clinic staff (nurse or clinic aide) replicated real world clinic procedure. The Dawson score may not only be suitable for use in primary care, but could also be used in secondary care to triage patients (section 3.1.3). Therefore, replicating real world clinic procedure provides an understanding of the process and flexibility of using the score in a TIA clinic, as well as the potential challenges. Furthermore, it was the closest point (after referral and at the time of making the clinic appointment) to collect the responses to the Dawson score from the patients. It was felt the closer the point of contact after consultation in primary care, the more likely it will be for patients to recall their symptoms. This method was therefore thought to be the most appropriate for collecting the data.

Initial study design

A standardised questionnaire was used to enable a calculation of the score and clinical features by clinic staff (Appendix 8). The feasibility study was carried out for 2 weeks by the nurse and a further 2 weeks by the clinic aide. This study did not need ethics approval as it was classified as a service evaluation study by the Head of Research Operations (Appendix 9).

Initially, the staff member requested to speak with the patient by telephone before clinic attendance. However, if the patient was unable to speak (e.g. if the patient was partially deaf or had cognitive impairments), then verbal consent from the patient was sought so that the carer/relative/guardian could speak on the patient's behalf. The staff member further recorded who the respondent was (patient/carer/relative). If it was not the patient, the reason for this (lack of cognitive function or other reasons) was also reported.

Other information was also recorded;

- Time taken to collect the data
- Any difficulties encountered in the telephone process

- The date the interview took place

Results

The results from the feasibility study suggested that the nurses were not collecting the expected data sample which was set to a minimum of 40–50 patient data. Rather, they collected 2 over a 2-week period due to high referral rate at the clinic, nurses on leave and/or simply forgetting to collect the data. The feasibility study was extended for another 2 weeks to explore if the data collected by a TIA clinic aide would be more appropriate. The results from this showed that a total of 12 data forms were collected. Although the data was larger than that collected by clinic nurses, the minimum expected sample of 40–50 was not achieved. The researcher was interested to understand the reasons for the limited number of completed forms and had an informal conversation with the staff members. The main barriers of the data collection reported by the clinic staff were lack of time and staff members forgetting to fill out the forms, resulting in very low numbers of patients being included. A further 30-minute semi-structured interview with the clinic aide confirmed these difficulties and highlighted points to consider for the main study and improvements for the future (Appendix 10).

In order to test the level of agreement between the feasibility study Dawson score results collected by the clinic aide and the database Dawson score (this included all the clinical variables of the Dawson score stored on the clinic database) (section 3.4.2) each clinical feature collected in the pilot was compared with the same clinical feature retrieved from the database using STATA 14.0. The level of agreement between clinic and interview data was fairly good. Additionally, there were no obvious difficulties in estimating both the score from the clinic database and from interviews (Appendix 11).

Based on the results from the feasibility study it was thought best for the researcher to collect the data in the main external validation study. In order to gain permission to do this, the researcher had to apply for letter of access by the research and developments office, which was provided for the research until 31st March 2019 (Appendix 12).

3.3. Aims and objectives

To assess the utility of the Dawson score in predicting the diagnosis of TIAMS and determine its use to triage referrals and/or reduce GP referrals to a TIA clinic.

Primary Objective:

To assess the performance of the Dawson score derived from a pre-clinic telephone interview carried out after referral to the TIA clinic, but before clinic attendance in predicting a specialist diagnosis of TIAMS.

Secondary Objectives:

1. To examine differences in the Dawson score derived from interview and from routine clinic data
2. To compare the interview Dawson score with the ABCD2 score for prioritising low-risk patients
3. To assess the performance of interview and clinic Dawson scores in predicting the diagnosis of the following broader cerebrovascular diagnostic categories:
    - TIAMS, transient monocular blindness and retinal artery occlusion
    - TIAMS, transient monocular blindness, retinal artery occlusion, transient global amnesia and intracerebral haemorrhage
4. To explore the performance of the interview Dawson score in sub-groups (diabetes, previous history of hypertension, younger groups versus older groups, sex, ethnicity, Index of Multiple Deprivation (IMD) (least deprived versus most deprived), ABCD2 score (high-risk versus low-risk) and GP versus internal referrals

3.4. Methods

Although the Dawson score has been subject to an external validation, the study used routinely collected data rather than calculation of the score from a pre-clinic interview. This has implications for whether the current existing score could be used appropriately in primary care to identify TIA patients at high risk of stroke for urgent clinic appointments, and whether the score could be used to triage low-risk patients at the TIA clinic to potentially reduce the burden at the TIA clinic.

The results of the feasibility study (section 3.2) confirmed that the study could be carried out in the Leicester TIA clinic collecting data from both internal and GP referred patients, in addition to comparing the interview and clinic Dawson score.

This section focuses on three areas: 1. A detailed overview of external validation studies, which in turn justifies the rationale for the design. 2. Details on the study outlining the design, participant details, study procedure, ethical issues, data entry, missing and duplicate data. 3. A statistical analysis plan, including the statistical methods used and how they were applied.

3.4.1. Research design: External validation

The purpose of clinical prediction models is to facilitate diagnosis and the prognostic probability of having the condition or event of interest. They are often used with a cut-off point to identify individuals at high-risk, who are then given treatment or further tests. For more details on diagnostic and clinical prediction models, including differences see section 3.1.1. Before considering whether to use a diagnostic model, it is essential that its performance is evaluated using data that was not used to develop the model, i.e. external validation (210). This is to examine whether the model's predictions are replicable in individuals from an alternative population(s) for clinical use (206). The issue is whether the results of the original study (Dawson, 2009) can be generalised beyond the specific research context of that study i.e. the Glasgow TIA clinic (211). External validation aims to explore differences in characteristics of the cohort (between the development and validation

cohorts) and to determine how well the model performs. Therefore, a clearly reported external validation study is essential to judge the model's performance (210).

Validation studies range from temporal (samples are from the same hospital or primary care practice only later in time), geographical (sample from different hospital, region or country) and validations across various medical settings (from secondary to primary care setting or vice versa). The validation studies can include different target populations with different study samples (212-214).

Model reproducibility refers to when a model performs accurately across new samples from the same target population. On the other hand, transportability refers to when the model performs well across different but related sample populations which can only be assessed when conducting external validation studies (212, 215).

A lack of external validation studies is often related to the shortage of data available besides the data used for model development (211). A major problem with external validation studies is that they are often based on small and local datasets. Due to this, most external validation studies can usually assess the performance of the model in that specific setting or population (216). Nevertheless, within the literature, it is recognised that the performance of a model tends to differ according to settings and populations (217-219), and multiple external validation studies are needed to fully understand the generalisability of the model (220).

The Dawson score has been externally validated only using routinely collected primary and secondary care data (98), rather than prospectively collected data for this purpose. In this study, transportability was assessed by exploring the score's performance in a different population and in a different TIA clinic setting.

3.4.2. Current TIA clinic set up at the Leicester Royal Infirmary TIA clinic

Patient data are routinely collected data which are added to the Leicester Royal Infirmary (LRI) computer database by either the clinic aide or nurse prior to patient clinic attendance. These data are used to provide a suitable date of appointment based on high or low risk of stroke. For GP referrals, the data provided on the GP referral letters are added to the database. Whereas, for internal referrals, the internal staff from the emergency department

(ED) and hospital in-wards will add the data straight to the Leicester Royal Infirmary computer database.

For the GP referral, data from the referral forms are obtained by clinic nurses at the TIA clinic. The information provided on GP referral forms were a combination of information retrieved from patients in GP consultations and GP records e.g. history of stroke, current/past medications, diabetes. Whereas, the information provided by internal staff at emergency departments and in-wards at the Leicester Royal Infirmary were from patient consultations with hospital doctors, and hospital records (if any).

The data are added to the database on the day the GP referral letters are received at the TIA clinic, and for internal referrals, the day the patient visits the emergency department/in-wards. The following data are added to the database by both TIA clinic staff and ED and/or in-ward staff:

- Symptoms: limb weakness, facial weakness, dysphasia/speech abnormalities, bilateral hemianopia (partial blindness or loss of sight), diplopia (double vision), headache, fainting, tingling/numbness, seizure
- When the symptom/s occurred
- History of TIA/stroke (including crescendo TIA)
- History of hypertension
- History of migraine
- Anticoagulants and antiplatelet agents
- ABCD2 score (low risk ≤3 and high risk ≥4)

If some of the details were missing from the referral letters such as elements of the ABCD2 score, and the nurses/clinic aide felt this information was needed to generate the most appropriate appointment date for that patient, then the TIA clinic staff would attempt to retrieve this information by contacting the GP practice directly. However, if this method was unsuccessful, then this information was updated on the database at the time of clinic consultation. On the other hand, if some of the symptoms that also included the Dawson score elements were not mentioned in the referral letters, then it would be presumed that

the symptom/s were absent in the patient, and would be recorded on the database as 'no', rather than contacting the GP to retrieve this information. This information would be updated at the time of clinic consultation if the symptoms were incorrectly recorded on the database. If any information was missing on the database, then this would also be updated at clinic consultations.

Although the Dawson score elements are part of the routinely collected data at the TIA clinic, the TIA clinic staff and ED and in-ward staff rely on the database template to record all the symptoms listed on the database template, rather than primarily recording the Dawson score data. Furthermore, the collection of the Dawson score data is not for the purposes of calculating the Dawson score. In addition to this, the data are recorded on the database by various members of staff at the clinic (hospital staff: ED and in-ward), nurse or clinic aide and stroke consultants at clinic consultations).

A detailed description of the pre-clinic and clinic processes at the Leicester Royal Infirmary (LRI) TIA clinic are provided below:

Pre-clinic referral process

For internal referrals (from ED and hospital in-wards) appointments are automatically updated onto the computer system and a letter is printed and provided to the patient to confirm the appointment. The referrer (internal staff) have to log onto the computer system and provide the ABCD2 score elements and answer a series of yes/no questions at the point of referral, which included components of the Dawson score.

GP referrals are faxed to the TIA clinic and the information on the faxed GP referrals are recorded on to the computer system by either a nurse or the clinic aide. The referrer (GP) provided the ABCD2 score elements and the Dawson score were collected from the referral letter. This information, although uncertain how frequently would be updated at the time of clinic consultation if the symptoms were incorrectly recorded on the database.

Once the data are provided on the clinic system, an appointment is generated, and the clinic clerk or clinic aide phones the patient to arrange the appointment. All the internal and GP referrals on the computer system are colour coded (red: high-risk patients – ABCD2 score ≥4, green: low risk patients – ABCD2 score ≤ 3).

The ABCD2 high and low-risk score are the standard categories widely reported within the literature and used in other studies such as Johnson et al (7). Low-risk patients are given a weekday appointment and high-risk patients are prioritised for a weekend appointment if necessary.

TIA clinic process

Patients are advised to attend the clinic on the day of their appointment at 8.30am and to bring a copy of their medication history. Five tests are available on the day of the appointment as determined by the doctors and nurses. The potential tests are as follows:

- Brain MRI
- Carotid Duplex ultrasound
- ECG
- Routine bloods
- Routine observations (included lying down and standing up blood pressure, BMI, temperature and pulse)

There are approximately 10 stroke specialists who work at the clinic who are responsible for the final diagnosis of a suspected TIA patient. The final diagnoses include; ischaemic stroke, transient ischaemic attack, other cerebrovascular diagnoses (retinal artery occlusion, transient monocular blindness), other (migraine, vertigo, syncope, transient global amnesia, intracerebral haemorrhage) and no formal diagnosis.

Based on TIA clinic consultation observations at the Leicester Royal Infirmary (Appendix 13), the stroke consultants at the TIA clinic explained that stroke and TIA is a clinical syndrome and there is no gold standard test for specialists to make a diagnosis. A specialist diagnosis at the TIA clinic are based on clinical grounds (description of symptoms, history, risk factors) as well as supporting information (investigations at the TIA clinic). These include BP measurement, ECG, blood test, MRI (which enhances the decision making). LRI has frequent access to MRI which is not usually the case for other TIA clinics.

At present there is little consensus on the optimal imaging strategies after TIA and minor stroke, or if imaging is required at all in some cases (221). The role of imaging differs from that in major stroke; firstly, in patients with TIA and minor stroke, the likelihood of an alternative diagnosis is higher than in patients with major stroke and imaging can identify

these mimics. Also, minor stroke is less likely to be caused by haemorrhage than major stroke and the risk is still lower in TIA, therefore brain imaging can be used to identify an ischaemic and haemorrhagic event. Lastly, brain imaging can be used to identify patients with high risk of early recurrent stroke in order to target suitable treatment (221). Despite the investigations and clinical grounds used to make a diagnosis, it is still difficult for stroke specialists to conclude a diagnosis in some patients who do not fit the 'normal definition' of TIA. These patients could present with no risk factors, with an unclear history and do not fit the risk benefit profile of TIA. Additionally, in some cases where clinicians believe it is a typical TIA, MRI may not show tissue damage and necessary additional investigations may not suggest a TIA.

The challenge stroke consultants are presented with have been observed by the researcher at the TIA clinic at the beginning of this study (Thursday 7th May 2015). The researcher was able to observe and make clinical notes based on 7 patients that were seen at the TIA clinic that day. The clinic observation notes confirmed that the only gold standard diagnosis for TIA is based on the specialist assessment. Furthermore, each consultation with the patient highlighted the difficulty of diagnosing a TIA due to the often vague symptoms e.g. patient blanked out for 2 hours, pain in the neck, and light headedness. Other conditions as well as risk factors contributed to the difficulty of diagnosis such as high cholesterol may have been due to the patient's cancer spreading, and high BP in most of the patients. Consultants consistently attempted to provide the optimal management for the patients by prescribing the most appropriate medications to bring down the patient's cholesterol and/or BP, refer to the optician and setting up urgent/non-urgent MRI as well as heart scans (if necessary) (Appendix 13).

3.4.3. Study design

This was a model transportability study to assess the external validity of the Dawson score. Once suspected TIAMS patients were referred to the TIA clinic, the researcher (author of this thesis) followed a script to collect the data from the patients (or a representative if they were unable to answer) by phone when making an appointment for the patients to attend the clinic. The researcher's script also included the nine variables of the Dawson score i.e., clinical features (headache, diplopia, loss of consciousness/presyncope, seizure, speech

disturbance, unilateral facial weakness, unilateral limb weakness), history of TIA/stroke and age (Appendix 14).

Sample size calculation

Collins et al investigated the impact of sample size on the performance of prognostic models (222). The simulation study suggests that an external validation of a prognostic model requires a minimum of 100 and ideally more than 200 events (in this case positive diagnosis of TIAMS). Based on historic clinic data where 40% of referrals were confirmed TIAMS, it was therefore thought that a sample of 500 (with 200 positive cases expected) would have sufficient power.

The proportion of positive cases was calculated half way through the study, in order to review the composition of the sample. This suggested that 39% of the sample had a positive TIAMS diagnosis which agreed well with the historic clinic data. Additionally, the study would be extended if the target was not achieved within the 3-month recruitment period.

Study participants

All patients attending LRI TIA clinic during the duration of the study (3 months) who agreed to a pre-clinic interview were included. Referrals were made by GPs and hospital doctors (ED and in-patient wards).

Specialists at the TIA clinic

The final diagnosis of TIAMS or other diagnostic categories are made by 10 stroke specialists and based on patients' clinical symptoms, presentations and if required investigations at the clinic (section 3.4.2).

Inclusion Criteria

1. Referred and attended the TIA clinic for suspected TIAMS

Exclusion Criteria

1. Declined verbal consent for telephone interview
2. Follow up patients
3. Repeat attendances during study; first attendance at the clinic was included

4. Patients who were unable to speak English or Hindi
5. Patients below the age of 18

3.4.4. Study procedures

Clinic Dawson score

The Dawson score elements were collected from the referral forms by clinic nurses or clinic aide. The information provided in GP referrals were a combination of information retrieved from patients in GP consultations plus GP records. The information provided by internal staff (for internal patients) at the LRI were from patient consultations with hospital doctors, plus hospital records (if any).

The Dawson score elements were recorded in the clinic database by the TIA clinic staff before the appointment was provided to the patient. There was no structured template for the Dawson score elements in the referral form, so if any symptom(s) such as headache, loss of consciousness were not mentioned they were assumed to be absent.
The Dawson score data along with additional data for each patient were retrieved from the clinic database by a stroke consultant at the TIA clinic which were:

- Referral ABCD2 score
- Demographic data (age, gender, and ethnicity)
- Co-morbidities (smoker, hypertension, diabetes, atrial fibrillation, previous stroke or TIA, other vascular disease)
- Source of referral
- Postcode of the patients' current place of residence from which deprivation was estimated using postcode/IMD linkage calculated using the online NPEU Oxford University IMD tool[5]

These data were obtained from either the GPs, GP referral letters, hospital doctors (ED and in-wards) or stroke specialists at clinic consultations who recorded these data on the clinic database. The specified data was added to an excel sheet by the stroke consultant. This way the Dawson data from the clinic and the Dawson data collected at the interview stage by the researcher were in the same format (in excel), and the Dawson score could be calculated

[5] https://tools.npeu.ox.ac.uk/imd/

efficiently by the researcher and compared for both data sources in STATA 14:0. However, it is important to point out for the clinic score, it is uncertain how much of the data was truly based on GP recorded information as some details, although uncertain how frequently, may have been updated at clinic consultations.

Interview Dawson score

As a novice researcher, it was felt that some qualitative training would be beneficial prior to this study which required collecting responses to the Dawson score directly from suspected TIA patients. The researcher enrolled in a workshop led by two qualitative research experts in order to understand qualitative research approaches (Appendix 15). Through a combination of presentations and individual group exercises, the workshop highlighted the key challenges for qualitative research on health and offer plausible solutions. The workshop also highlighted working across languages and cultural influences on health. For this study, this workshop helped the researcher design the interviewing text which was particularly beneficial for the researcher's script and recording of the interview (Appendix 14) in order to consider patient confidentiality, consent process, providing clear explanations etc. Furthermore, based on the interview with the clinic aide from the feasibility study (section 3.2, Appendix 10) and conversations with the clinic nurses, the researcher's scrip was developed for both internal and GP referrals. These statements included information of their appointment and directions to the clinic before collecting the Dawson score components. A section was also added on the researcher's script to obtain verbal consent from a carer, relative or guardian to respond to the questions on behalf of the patient if needs be. Please see Appendix 14 for the researcher's script.

The researcher collected responses to derive the Dawson score directly from GP and internal clinic referred patients at the time they were called to arrange an appointment at the TIA clinic. The phone call was made as part of the booking process for the clinic and involved asking the Dawson score questions. The phone call was made by one individual (the researcher). The researcher collected the data which included answers to the individual items of the score. The Dawson score data collected from the patients at the time of the appointment was therefore conducted in a more structured way than the routine data collected from the clinic. The data from the interview were added to an excel sheet by the

researcher in preparation for the Dawson score for individual patients to be calculated and compared to the clinic Dawson score data in STATA 14.0.

The primary analysis was to compare the specialist diagnosis of TIAMS to the interview Dawson classification of TIAMS. The interview derived Dawson score rather than the clinic derived score for comparison was the primary aim because the interview score components were collected in a structured way by one individual, rather than relying on clinic or GP data that was not collected for the purposes of calculating the score. Additionally, given the uncertainty of how the clinic score was derived from GP or hospital collected data, it was thought best to use the interview derived Dawson score for comparison with specialist diagnosis. The secondary analysis was to compare the interview Dawson to the clinic Dawson with the specialist diagnosis on the clinic database classified into TIAMS and non-TIAMS categories. Additional secondary analyses included comparing results from the interview Dawson according to the ABCD2 score and to assess the performance of the interview and clinic Dawson score in predicting broader cerebrovascular categories (including TIAMS and major stroke) and cerebrovascular plus transient global amnesia. Further analyses were conducted to explore the performance of the Dawson score in sub-groups (section 3.4.8), and also to explore an alternative and novel cut-off (Chapter 5).

3.4.5. Ethical issues

Informed Consent

Although the study involved collecting additional data at the time the appointment was made, it was considered service evaluation (Appendix 9). On the advice of the head of research operations, University of Leicester and consequently, written patient consent was not necessary. Verbal consent was acquired from the patient or relative/guardian before the telephone interview to answer the Dawson score questions.

Patient confidentiality

Data was pseudonymised by removing the patients' identifiers e.g. hospital number and a study serial number was assigned to each record. Data was stored in a password protected secure flash drive and will be destroyed after three years.

3.4.6. Data

Data entry in Excel

Data obtained at the telephone interview were collected on paper rather than recording the data into excel immediately, due to security reasons (patients' data had to be stored on a password protected computer) that the researcher can easily access.

To avoid errors when inputting patients' responses, a drop-down list (from the data validation option) in Excel was used. Values were 0 if the response to the questions were 'no', 1 if 'yes' and 'missing' for data not available. This prevented any values other than those stated (0, 1 and missing) to be entered in the rows. This was also done for the patients' referral details (whether they were GP or internal). This was applied for all the Dawson data, apart from age, which was typed in a tab at the end of each row, again from the data validation option. However, this time 'allow whole number' was selected.

The researcher was able to conduct interviews in English or Hindi and thus, a field with these two options was added. Lastly, a column for the duration of interview (in minutes) and the date of the interview was added and typed in manually. All the patients in the interview dataset provided a 'yes' or 'no' answer to every question about the symptoms.

Data entry validation

The data were entered in Excel by hand for the 536 interview patients. To confirm correct data entry, data re-entry was performed for 10% of the sample. This was thought to be large enough to indicate a warning of any data entry errors.

The 10% sample was selected at random by an independent person and was re-entered to test for data transcribing errors. This was accepted as good quality control procedures, before the statistical analysis were carried out. The data were entered again independently in a separate file, which were then compared in order to identify any discrepancies (223).

Acceptable error rate

The data contained 12 fields (history of TIA/stroke, headache, diplopia, loss of consciousness, seizure, speech abnormality, unilateral limb weakness, unilateral facial

weakness, age, source of referral, language spoken (English or Hindi) and time taken to complete form.

In total, there was approximately 6,000 items of data and 10% of the sample would total 600. Before the 10% sample calculation was carried out, a reasonable acceptable error rate was thought to be 1% or less.

Results of data entry validation

53 study IDs of the total interview sample of 536 were selected at random. The 'set seed' command was used at the end in STATA in order to save the place that the computer uses to generate the random sample. To generate exactly the same random number, the same set seed number needs to be applied. For example, if the set seed initially was 1826070217, then this exact number needs to be specified in order to obtain the same random sample on a different computer. This is done to enable reproducibility (224).

Results showed that one discrepancy was found for age and one on type of referral, which totals to two errors. The following calculation was completed to check the error rate; 53 (total number of the random sample) x 12 (number of variables) provided a total of 636 data points. 2 /636 produced an error rate of 0.31% (95% CI: 0.04%, 1.13%).

Procedure for accounting for missing data

Interview Dawson score data

The interview data set was checked for missing data. Overall, 5 missing data items were reported (3 patients' data for age and 2 patients' data for type of referral). Nevertheless, when referred back to the paper charts collected during the interview stage, a value for each of the 5 missing field had been recorded and this data was entered into excel.

TIA clinic data

The clinic database included internal validation that ensures completion of yes/no fields, validates numerical entries, and mandates entry of essential clinical information. Thus, it was anticipated that the rate of missing data would be low. However, no missing data were reported.

In terms of mistyping in the clinic database, the required variables were coded, 0, 1 and NULL, thus, mistyping was unlikely to occur. NULL was stated if there was no clear answer, but for this study it was represented as 'no' rather than missing, 0 meant categorically stated 'no' and 1 meant 'yes'. Imputation of missing values were considered at the start of the study. However, since both the interview and clinic datasets showed no missing data, imputation was not needed.

Duplicates

Any duplicate cases were removed and all the data were the same (except the date), thus, the earliest date was chosen. For the interview data, the aim of this study was to attempt to get patient data as close to the time of when the symptoms occurred. Therefore, keeping the earliest date was the closest to the date to when the patient was initially referred.

A reason for duplicates occurring at the interview stage could be due to the researcher accidently interviewing the same patient twice. Some patients' appointments have to be re-arranged, due to patient reasons. Therefore, it was likely that the researcher interviewed the patient when the details went on the system on the first occasion and then re-interviewed the same patient once the patient was provided an alternative appointment date. Given that any repeat attendance diagnosis would be influenced by diagnosis from last attendance, all repeat attendances were excluded from clinic and interview data and first attendance were used. This also avoided the need for statistical allowance for data-clustering when analysing data from non-independent data records.

3.4.7. Comparing participants and non-participants

Participants were patients who were both interviewed and attended the clinic and non-participants were those who were not interviewed but attended the clinic.

It was necessary to use the clinic data when comparing the representativeness of the study (including history of TIA/stroke) due to the dataset including the details for those who were not interviewed but attended the clinic (non-participants). However, in the analysis of participants, the interview history of TIA/stroke variable was used to calculate the Dawson score. Also, age from both the clinic and interview database was compared to check for any discrepancies.

The only baseline characteristic described in the Dawson study that was unavailable in this study was hypercholesterolemia. The clinic database did not consistently record hypercholesterolemia and to extract the data, two continuous variables (total cholesterol and low-density lipoprotein) would need to be retrieved. Due to the large volume of missing data for both, hypercholesterolemia was not used for analyses and this was accepted as a limitation. The analyses described in this section were conducted using STATA 14.0.

Table 3.4.1: Data included in the sample for analyses

<table>
<tr><th>Dawson score clinical features (collected at the time of telephone interview)</th><th>Type of variable</th><th>Baseline characteristics (extracted from clinic records)</th><th>Type of variable</th></tr>
<tr><td>Age</td><td>Continuous</td><td>Age (from date of birth)</td><td>Continuous</td></tr>
<tr><td>Headache</td><td rowspan="8">Categorical</td><td>Sex (male/female)</td><td rowspan="11">Categorical</td></tr>
<tr><td>Diplopia</td><td>Ethnicity (white, south Asian, Black, other)</td></tr>
<tr><td>Loss of consciousness</td><td rowspan="2">Hypertension</td></tr>
<tr><td>Seizure</td></tr>
<tr><td>Speech abnormalities</td><td>History of diabetes</td></tr>
<tr><td>Unilateral limb weakness</td><td>Atrial fibrillation</td></tr>
<tr><td>Unilateral facial weakness</td><td>Cerebrovascular diagnosis</td></tr>
<tr><td>History of stroke/TIA</td><td>Previous history of stroke/TIA</td></tr>
<tr><td rowspan="5"></td><td rowspan="5"></td><td>Final specialist diagnoses (ischaemic stroke, transient ischaemic attack, no formal diagnosis, migraine, other)</td></tr>
<tr><td>Source of referral (GP/internal) (ED and inpatient was combined together – labelled as internal)</td></tr>
<tr><td>History of smoking</td></tr>
<tr><td>ABCD2 score</td><td>Ordinal</td></tr>
<tr><td>IMD (based on postcode)</td><td>Ordinal</td></tr>
</table>

3.4.8. Statistical analysis plan

Testing representativeness of the data

The data items included in the sample for analyses (Table 3.4.1) describe the Dawson clinical features and the baseline characteristics of study participants. Analyses of baseline characteristics compared participants with non-participant clinic attenders to test the representativeness of the sample. Analyses were also carried out with the Dawson score clinical features for the different comparisons (described below).

Primary analysis:

The original cut-off (TIAMS or not TIAMS) for the Dawson score was 5.4 (96). This cut-off was also used in the Lasserson et al study comparing primary and secondary care data (98). In this study the analyses used this cut-off for prediction of a TIAMS diagnosis. 5.4 cut off score may not be replicable or translatable across all populations. Therefore, the primary and secondary analysis will use the 5.4 cut-off to establish whether this is the case or not. Subsequent secondary and exploratory analysis of different cut-off points was reported using ROC/AUC (section 3.4.12), sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) (section 3.4.12).

Secondary and exploratory analyses

1. The same methods of analysis were used to compare specialist diagnosis to the ABCD2 score
2. Bland-Altman plots with 95% limits of agreement (225) were used to compare the agreement between:
    - Interview Dawson score versus clinic Dawson score
3. Scatter plot with the 5.4 cut-off to give a visual representation of:
    - Dawson score above and below the 5.4 who were high-risk or low-risk according to the ABCD2 score
4. ROC comparison of the specialist diagnosis of TIAMS to the clinic Dawson diagnosis of TIAMS

5. ROC curves compared the interview Dawson score to the vascular diagnostic categories which included:
    - TIAMS, transient monocular blindness and retinal artery occlusion
    - TIAMS, transient monocular blindness, retinal artery occlusion, transient global amnesia (TGA) and intracerebral haemorrhage

Exploratory analysis aimed to:

1. Determine the performance of the Dawson score in pre-specified sub-groups which included:
    - Age (the median age was used to split the groups in two: > 68.40 – older, <68.40 – younger)
    - Sex: male versus females
    - History of diabetes versus those without
    - History of hypertension versus those without
    - Ethnicity: White versus Asian
    - IMD (least deprived score of ≤ 8.49 versus most deprived score of ≥ 34.18)
    - ABCD2 score (high-risk patients ≥ 4, low-risk patients < 3)
    - Primary versus secondary care referrals (GP versus internal)
2. Apply the cost ratio method (based on 2:1/3:1 originally used in Dawson study) (section 3.1.2)

3.4.9. Statistical methods

Descriptive statistics

Tables were used to present the results when testing the representativeness of the sample. A table on the difference of age between the interview and clinic data was presented. Along with a table of the proportion of participants missed Monday-Sunday. Similarly, tables were also presented for the baseline characteristics which included comparing non-participants and participants with the percentages and test results given for each.

The baseline characteristics included age, gender, ethnicity, past history of cerebrovascular event, past history of diabetes, cerebrovascular diagnosis, history of hypertension, history of

atrial fibrillation, individual diagnoses, history of smoking, source of referral, IMD interquartile ranges and ABCD2 score.

A table presented Kappa scores for each Dawson clinical feature, along with the total proportion of agreement (between interview and clinic data), the expected agreement, confidence interval and the overall proportion in interview and clinic.

Tables were presented when conducting the comparative analyses for the Dawson data, also when the different sub-groups were examined and when exploring cut-offs. The tables presented the results in number and percentage format to give a clearer understanding of the data and results.

A scatter plot was produced to give a visual representation of how many of those that were high-risk and low-risk according to the ABCD2 score were under and above the 5.4 cut-off of the Dawson score.

General hypothesis testing

To check whether there were any differences between the non-participants and participants for the baseline characteristics, significance testing was conducted. Results from the following tests were all presented with p value using t-test, Pearson's chi-squared for trend, and the Mann-U-Whitney test (discussed later). Additionally, the p values were also presented when the performance of the interview Dawson score in subgroups was explored.

Multiple testing

The Bonferroni correction is frequently used to adjust p values when carrying out multiple statistical tests (226). The method is widely used in various experimental contexts such as; comparing different groups at baseline, studying the relationship between variables and examining more than one endpoint in clinical trials. The Bonferroni method is a simple technique for controlling the overall probability of a false significant result when multiple comparisons are being carried out. This is because the numbers are dependent on the significance threshold and number of tests, e.g. if a significance threshold is p=0.05, then it would be expected that 5% of the test would be statistically significant by chance. Bonferroni correction is often used to account for this by dividing the significance threshold by the number of tests in order to produce an adjusted significance threshold. For example,

if the significance level is p=0.05 and 20 statistical tests are being carried out then the calculation would be 0.05/20 = 0.0025 which would be the adjusted significance level.

When comparing the areas under the ROC (receiver operator curve) (commonly known as the c-statistic) between multiple subgroups, the Bonferroni method was thought to be appropriate. As the number of tests increases, so does the likelihood of a type 1 error i.e. when a significant difference is present when it is not (false positive). Thus, it was important to correct for this by adjusting the significance level. The following calculation was used:

$$\alpha_B = 1 - \frac{(1 - \alpha)}{T}$$

The formula is interpreted where 'α_B' is the Bonferonni adjusted significance level and '*T*' is the number of tests performed (227). For the subgroups, the p value was divided by the number of tests performed, which in this case was 8 (0.05/8 = 0.00625). The Bonferroni adjusted p value was used for the following subgroup analyses:

- Age (older versus younger)
- Sex: (male versus females)
- Patients with diabetes versus those without
- History of hypertension versus those without
- Ethnicity: White versus Asian
- IMD (least deprived versus most deprived)
- ABCD2 score (high-risk patients versus low-risk)
- GP versus internal referrals

95% confidence interval

The confidence intervals (CI) are constructed at a level of 95% which is the standard level reported within the literature. For example, the 95% confidence interval was used when evaluating whether the odds of a TIAMS diagnosis was the same for the high-risk (those with an ABCD2 score of 4 or higher) and low risk group (those with an ABCD2 score of 3 or lower).

For the rest of the results, the CI for the quantity or difference being estimated indicated the margin for random error that should be considered, including ranges of values both above and below the estimated number itself. When conducting the primary, secondary and

exploratory analyses (discussed later under ROC curve section 3.4.12) the CI was given to indicate a range of values that the true value of the AUC (commonly known as the c-statistic) of the ROC reasonably take, allowing a margin for random error.

Statistical tests for continuous data

Independent sample t-test

An independent samples t-test compares the means for two independent groups to determine whether there is statistical evidence that the associated population means are significantly different. A t-test assumes the dependent variable is measured on a continuous scale and when the data is normally distributed (228).

A histogram comparing age from both data sources (interview and clinic) was examined visually to check whether the distributions were at least approximately normal before an independent sample t-test could safely be carried out. If the data were approximately normally distributed, the t-test was used to determine whether there was statistical difference in means between the patients missed and those included in the study.

Bland Altman analysis of agreement

The purpose of the Bland Altman (BA) method is to determine the level of agreement between two different measures that are measuring the same outcome. The BA method is used for continuous and ordinal data. The BA plot shows the level of agreement between two variables of comparison (229).

The standard deviation was used to calculate the BA 95% limits of agreement which was used to compare the two versions of the Dawson score (interview and clinic) to see how closely they agree with one another. Calculating the limits of agreement and plotting the differences against the means was the method for achieving this. The calculation was as follows:

- Lower limit = mean - 2SD
- Upper limit = mean + 2SD

BA suggested these values for the limits of agreement to ensure that on average and if the within-individual differences are normally distributed, then 95% of the data points should lie

within ± 2SD of the mean difference (230). Once the limits were calculated the plot was used to test how close the average of the difference was from zero. In terms of this study, if the regression line is close to zero the results indicate close to perfect agreement (229). The mean difference is a measure of the estimated bias therefore a mean of 0 indicates no systematic bias between the measures.

The BA plot were visually checked to see that there is no pattern between the two measures on the BA plot (231). If there is, it would suggest that there are cases between certain values of the score that there is not much agreement due to differences in the magnitude of measurements (i.e. if the two scores are scaled differently). If the variation in the differences are larger i.e. for smaller mean values and decreases as the mean values become larger then this would be evident on inspecting the BA diagram for a funnel effect (231).

Probability density function

A probability density function (PDF) of a continuous variable is a function that describes the relative likelihood of the measure to take on a given value. From the PDF the probability of an event can be calculated (232). For this study, the PDF was to compare the shape and position of the distribution to observe whether the probability distribution for the interview and clinic scores were similar according to the Dawson score.

3.4.10. Statistical tests for ordinal data

Chi-squared test for trend

Unlike the Pearson's chi-squared test that was used for categorical unordered data (see below), the chi-squared test for trend is used when the variable being compared has ordered categories. The ordering needs to be considered to assess for any differences.

Socioeconomic groupings are an example in this study of an ordered categorical variable. The IMD score for each patient based on their postcode was calculated using the online NPEU Oxford University IMD tool. The results of which were imported into STATA and were categorised to order the data according to the quintiles below:

- 1st ≤ 8.49 (least deprived)
- 2nd 8.5 - 13.79
- 3rd 13.8 - 21.35
- 4th 21.36 - 34.17
- 5th ≥ 34.18 (most deprived)

Mann-Whitney U test

The Mann-Whitney U test is a non-parametric test that allows two groups, conditions or treatments to be compared without assuming that the values are normally distributed (233). Rather than comparing the means of the two groups of interest in the case of the t-test, the Mann-Whitney U test compares the medians.

The test converts the scores to ranks, across the two groups which is then used to evaluate whether the sum of the ranks for the two groups differ significantly. Thus, the actual distribution of the scores are irrelevant as the scores are converted to ranks. Additionally, there are two important assumptions to the test:

1. All observations are assumed to be random and independent of each other
2. The observations are on an ordinal scale (233)

The ABCD2 score takes whole values from 0 to 7 is regarded as ordinal data. Therefore, the Mann-Whitney U test was used to compare the ABCD2 groups (high-risk and low-risk) differences between the participants and non-participants.

3.4.11. Statistical analysis of categorical data

Pearson's chi squared test

In this sample the test was used to identify if there was a systematic difference between the non-participants and participants. The Pearson's chi squared test was calculated for the baseline characteristics apart from age, ABCD2 score, and IMD (as age was a continuous variable, and ABCD2 and IMD was ordinal data) (Table 3.4.1). Additionally, to assess any differences between the low-risk and high-risk ABCD2 groups and a specialist diagnosis of TIAMS, the Pearson's chi squared test was conducted using STATA 14.0.

Cohen's Kappa

Cohen's kappa statistic, κ, is a measure of agreement when the measurement scale is categorical or ordinal. Kappa was used to adjust the observed proportional agreement to consider the agreement which would be expected by chance. The following are interpretations of κ:

- <0: less than chance agreement
- 0.00–0.20 Poor agreement
- 0.21–0.40 Fair agreement
- 0.41–0.60 Moderate agreement
- 0.61–0.80 Good agreement
- 0.81–1.00 Almost perfect- perfect agreement

Kappa was used to measure the agreement between the interview data and clinic data. Maximum value of 1 represents perfect agreement, value of zero indicates no agreement better than chance, and a negative value signifies worse than chance (234). Because the data was binary i.e. did not consist of more than two categories, the weighted kappa was not used.

The definition for κ agreement frequently used (234) (suggested above) was applied when comparing the agreement for the two data sources particularly looking into the various Dawson clinical features used in the calculation of the Dawson score (history of stroke/TIA,

headache, diplopia, loss of consciousness, seizure, speech abnormalities, unilateral limb weakness, and unilateral facial weakness).

Odds ratio

An Odds Ratio (OR) is a measure of association between an exposure and an outcome. The OR represents the odds that an outcome will occur given a particular exposure, compared to the odds of the outcome occurring in the absence of that exposure (235).

The OR for TIAMS diagnosis by a clinic specialist in high-risk versus low-risk ABCD2 was calculated in order to evaluate whether the odds of the TIAMS diagnosis is the same for the two groups.

A contingency table presented the outcomes and the calculation for OR for TIAMS diagnosis in high versus low ABCD2 score was (a * d)/ (b * c). In this case it was (no diagnosis of TIAMS in low risk patients * TIAMS diagnosis in high-risk patients)/ (no diagnosis in high risk patients * TIAMS diagnosis in low risk patients).

3.4.12. Measures of diagnostic accuracy

Sensitivity, specificity and predictive values can be used to quantify the performance of a diagnostic test. The receiver operating characteristic (ROC) curve is a graphical plot showing the trade-off between sensitivity and specificity for every possible cut-off for a test to illustrate the diagnostic ability for each cut-off. The area under the receiver operating characteristic curve (AUC) is a measure of the usefulness/accuracy of a test in general, where a greater area means a more accurate test (236). A more detailed description of these measures is provided below.

Sensitivity and specificity

The choice of the cut-off of a test is based on a trade-off between sensitivity and specificity; as the sensitivity of a test increases the specificity reduces and vice versa.

The sensitivity is defined as the proportion of people with disease who will have a positive test result. A test with a high sensitivity is usually considered to be essential so that few patients with the disease are missed.

The specificity is defined as the proportion of people without the disease who will have a negative result. The specificity of a test is a measure of its ability to confirm the absence of the disease. A test with high specificity is usually considered to be desirable as it measures how accurate a test is in reducing false positives (237).

A false negative is when a patient is diagnosed as not having the disease, when truly they do have the disease. Alternatively, a false positive is when a patient is diagnosed as having the disease, when they really do not have the disease (237).

$$Sensitivity = \frac{Number\ of\ true\ positives}{Number\ of\ true\ positive\ +\ \ number\ of\ false\ negative}$$

$$Specificity = \frac{Number\ of\ true\ negatives}{Number\ of\ true\ negatives\ +\ \ number\ of\ false\ postive}$$

A contingency table was included after each of the ROC analyses where the sensitivity and specificity were calculated together with their 95% CI.

Positive and negative predictive value

The positive predictive value (PPV) and negative predictive value (NPV) describe the performance of a diagnostic test in a specific population. PPV is the proportion of people with a positive test result who actually have the disease, and the NPV is the proportion of people with a negative test result who do not have the disease (237).

The PPV and NPV are influenced by disease prevalence and the test's sensitivity and specificity. The point of a diagnostic test is to use it to make a diagnosis, and it is essential to know the probability that the test will give a correct diagnosis. This information cannot be obtained by the sensitivity and specificity results. Therefore, the predictive values were used to answer this.

$$PPV = \frac{Number\ of\ true\ positives}{Number\ of\ false\ positive\ +\ \ number\ of\ true\ positive}$$

$$NPV = \frac{Number\ of\ true\ negatives}{Number\ of\ true\ negative\ +\ \ number\ of\ false\ negative}$$

Both the PPV and NPV was calculated along with the sensitivity and specificity for each of the primary, secondary and exploratory analyses and the CI was provided for each.

ROC curve and AUC

The diagnostic performance of a test, or the accuracy of the test to distinguish between diseased cases and those without the disease is evaluated using the ROC curve analysis, and is a fundamental tool for diagnostic test evaluation (238). The ROC is a graphical approach where the sensitivity versus 1- specificity for the cut-off in the score being assessed is plotted (236)(sensitivity and specificity discussed above).

The closer the ROC curve is to the upper left corner, the higher the overall accuracy of the test (238). Whereas, a plot in the 45-degree diagonal (indicating an area under the curve of 0%) suggests that the discrimination is no better than chance. The 'top left' point indicated on a ROC curve is the cut-off for maximum statistical performance, but not necessarily the clinically appropriate cut-off (239).

Area under the curve (AUC) is in effect a measure of the overall performance of the risk score on the data you are applying it to. It is the gold standard measure and is always used for risk score work and represents the accuracy of the test. The ROC curve and AUC is the commonly used approach to diagnostic testing (238). The discriminative ability of the score e.g. separating people with the disease from without disease was looked into for a specific cut-off (5.4). In the Dawson paper (96), ROC curve for an optimal cut-off score of 5.4 in the development phase was used. Similarly, the discrimination of TIA diagnosis was assessed with the AUC derived from ROC curves in the Lasserson et al external validation study of the Dawson score (97). Due to this study also being an external validation of the Dawson score, the same diagnostic measure to assess the accuracy of the score using the 5.4 cut-off was used.

The AUC can be interpreted as the probability that the risk score correctly identifies if a patient has the disease or not. An area of 1 represents a perfect test whereas an area of 0.5 represents a worthless test. A general guide for classifying the accuracy of a diagnostic test is as follows (240):

- >0.9 high accuracy
- >0.7–0.9 indicates moderate accuracy
- >0.5–0.7low accuracy
- 0.5 chance result

The 5.4 cut-off used in the original Dawson paper from their Glasgow TIA clinic data (96) was applied in the primary analysis to assess the performance of the interview Dawson in predicting a diagnosis of TIAMS in an independent dataset (external validation). In order to test this, the ROC compared the interview Dawson diagnosis of TIAMS to the specialist diagnosis of TIAMS, providing an AUC value and the 95% CIs.

AUC statistic is commonly used as a way to compare diagnostic models (241). Once the primary analysis was carried out, the secondary ROC analyses were conducted (section 3.4.8). Additional exploratory analyses using the ROC with the 5.4 cut-off aimed to determine the performance of the Dawson score in particular sub-groups (section 3.4.8). The AUC between two ROC curves were compared with a p value calculated. If the p value was less than 0.05 this suggested the AUCs of the two ROC curves were significantly different.

Selection of cut-off

In the paper by Dawson et al (2009) (96) the method to determine the cut-off for interpreting a diagnostic score was the cost ratio approach. A cut-off was chosen according to most people correctly classified and the fewest incorrectly, which accounts for the prevalence of the event and the costs of misclassification in either direction (205).

Many alternative measures of accuracy for diagnostic tests can be used to identify a cut-off, most of which have been discussed earlier in this chapter and have been applied to the results. For example, an optimal cut-off according to a specific sensitivity or specificity usually with more emphasis on sensitivity (>80%) (237). Alternatively, desired likelihood ratios which shows how much a test result will change the odds of having a disease and can also be used to select a cut-off. This method involves dividing sensitivity and specificity rates to calculate the likelihood ratio (240). Additionally, the NPV can be used to select a cut-off and is the proportion of people with a negative test result who do not have the disease (237). Another possible approach is to choose the cut-off that maximises the total proportion of agreement between the diagnostic test and the gold standard.

An optimal cut-off for this study was identified through the cost misclassification method (cost ratio approach), where the assumption of a 2:1 cost ratio (used in the original Dawson

study) was made (i.e. assumed that the cost of misclassifying a cerebrovascular patient as non-cerebrovascular is twice as the cost of misclassifying in the opposite direction).

In the original Dawson paper, the cost ratio method was used. However, a journal reference or equation was not provided. Therefore, to confirm this cost ratio method, the formula to apply the cost ratio cited in the literature (205) would be applied to the cut-offs calculated in original paper to check if they were consistent with the ROC published by Dawson et al. This was to give an idea whether the same method cited in the literature was used in the original Dawson paper to determine the 2:1 and 3:1 cost ratios. The calculation cited in the literature (205) for the cost ratio method was the following:

A misclassification cost term = cost x prevalence x (1- sensitivity) + (1- prevalence) x (1- specificity)

The cost was either 2 for the 2:1 ratio or 3 for the 3:1 ratio and the prevalence was the proportion of TIAMS diagnosis in Dawson's sample which was 60%. The formula was then used for each point on the ROC curve to calculate the overall minimum value for the points in Excel for the 2:1 cost ratio.

The formula was then applied to this study using the 2:1 and 3:1 cost ratio (i.e. when it is assumed that the cost of misclassifying a cerebrovascular patient as non-cerebrovascular is three times the cost of misclassifying in the opposite direction). Dawson used the cost ratio method and it was thought best to use the same 2:1 and 3:1 so that the results can be compared to that reported by Dawson and for completeness of this study.

The prevalence differed to that of Dawson (60%) and was 35% in this study. The minimum value from both the cost ratios was used to establish the cut-off that would be appropriate. This then detailed the sensitivity, specificity, PPV and NPV associated with using that cut-off.

3.4.13. Acceptable level of diagnostic accuracy

Sensitivity and specificity for prediction of TIAMS was initially calculated using the cut-off point used in the Dawson paper (5.4). Sensitivity analysis was carried out to explore other cut-offs to explore the different thresholds, and establish if an alternative cut-off could be more useful clinically. Results in the original Dawson paper yielded a sensitivity of 93% and specificity of 34% (96).

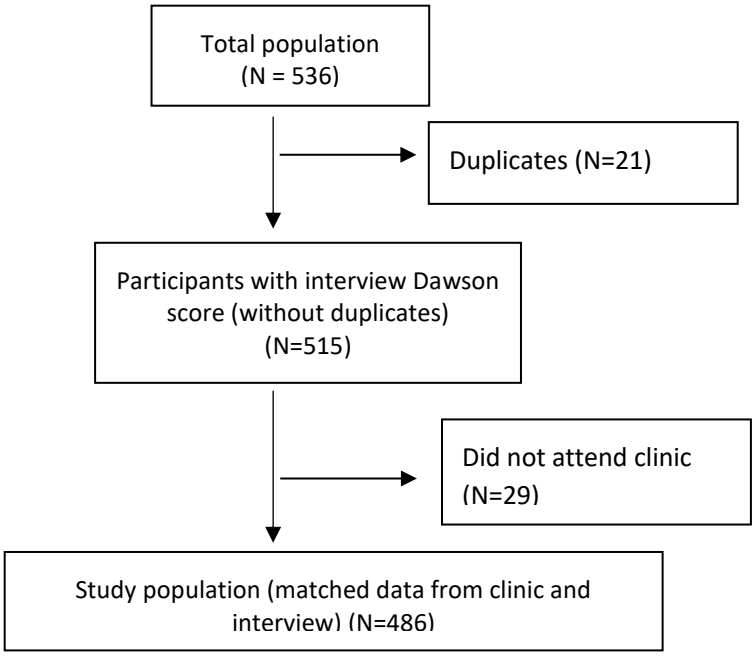
3.5. Results

This section provides detailed results of the external validation study. The results section starts by examining the representativeness of the sample, comparing participants and non-participants. The chapter is then split into sections, each of which tackles the primary and secondary objectives (section 3.3; 3.4.8). A brief discussion of the findings, the study's strengths and limitations and conclusion will then follow (sections 3.6–3.7).

3.5.1. Representativeness of the study sample

The data was collected over a 4-month period from 3rd October 2016 to 31st January 2017. The total number of interviews was 536. Once the duplicates were removed, the total of participants was 486 (Fig 3.5.1), and eight of these interviews were spoken in Hindi due to the patient not being able to fluently communicate in English. Similarly, two interviews were conducted with the carer/guardian rather than the patient because the patient was deaf, and the other patient had speech difficulties due to Parkinson's disease. During this period, an additional 273 patients attended the clinic but were not included in the sample due to no interview data for comparison. Overall, the sample included 486/759 (64%) of clinic attenders. A participant flow diagram that represent duplicate data, patients who were interviewed twice and interview only that represent patients who did not attend the clinic are shown in Figure 3.5.1 below:

Figure 3.5.1: Flow chart documenting the results of the data removed



Whether the sample was representative was explored using routine data collected in the clinic, as below. The interviews were conducted from Monday-Friday and some weekends (for logistical reasons, the researcher was not available on most weekends). This meant that patients referred and seen over most weekends were potentially more likely to be missed. A comparison of weekend versus weekday attendance for non-participants and participants was therefore carried out, the results of which are shown below (Table 3.5.1).

Table 3.5.1: Weekday versus weekend attendance for non-participants and participants

Variable	Non-participants	Participants	P value
Weekday (n= 636)	202 (32%)	434 (68%)	p <0.0001
Weekend (n=123)	71 (58%)	52 (42%)	

When comparing patients attended at weekend versus weekdays, a significantly higher percentage did not participate (58% versus 32%).

Baseline characteristics

Participants were compared to non-participants for each of the following variables derived from the clinical database: age (Table 3.5.2), gender, ethnicity, past history of vascular event, past history of diabetes vascular diagnosis, history of hypertension, history of atrial fibrillation, past history of TIA or stroke, clinic diagnosis, source of referral, ABCD2 score, IMD score and history of smoking (Table 3.5.3).

Table 3.5.2: Age of non-participants and participants

Label	Total	Mean age	Standard Deviation (SD)	Median	Interquartile range (IQR) 25%	75%	P value
Non-participants	273	64.94	16.85	67	54	78	p = 0.212
Participants	486	66.48	16.11	68	54	80	

Table 3.5.3 Baseline variables and specialist diagnosis for non-participants and participants

History	Non-participants 273	%	Participants 486	%	P value
History of hypertension	148	54	196	40	p <0.0001
History of diabetes	52	19	73	15	p = 0.151
History of Atrial fibrillation (AF) / or new AF	20	7	41	8	p = 0.589
Past history of TIA/Stroke	66	24	87	18	p = 0.039
Sex					
Female	138	51	241	50	p = 0.799
Male	135	49	245	50	
Referral					
Internal referral	189	69	195	40	p <0.0001
GP referral	84	31	291	60	
Smoking status					

Current smoker	38	14	52	11	p = 0.335
Never smoked	119	44	210	43	
Ex-smoker	64	23	129	27	
Index of multiple deprivation					
1st - ≤ 8.49 (Least deprived)	86	32	155	32	p = 0.876
2nd - 8.5 - 13.79	61	22	113	23	
3rd - 13.8 - 21.35	42	15	72	15	
4th - 21.36 - 34.17	45	17	78	16	
5th - ≥ 34.18 (Most deprived)	35	13	65	13	
Ethnicity					
White	204	75	366	75	p = 0.429
South Asian	34	12	55	11	
Black	4	1	6	1	
Other	16	6	16	3	
Specialist diagnosis					
Ischaemic stroke	55	20	64	13	p = 0.131
Transient ischaemic attack	61	22	108	22	
No formal diagnosis	67	25	132	27	
Migraine	28	10	62	13	
Other cerebrovascular	17	23	33	25	
Other non-cerebrovascular	45	16	87	18	
Diagnostic categories					
Total cerebrovascular diagnoses *	133	49	205	42	p = 0.082
TIAMS (TIA and minor stroke)	116	42	172	35	p = 0.053
Index of multiple deprivation					
1st - ≤ 8.49 (Least deprived)	86	32	155	32	p = 0.876
2nd - 8.5 - 13.79	61	22	113	23	
3rd - 13.8 - 21.35	42	15	72	15	
4th - 21.36 - 34.17	45	17	78	16	
5th - ≥ 34.18 (Most deprived)	35	13	65	13	
ABCD2 score					
High risk (> = 4)	175	69	228	53	p <0.0001
Low risk (< = 3)	79	31	205	47	

***Note: Cerebrovascular diagnosis included; ischaemic stroke, transient ischaemic attack, retinal artery occlusion, transient monocular blindness and transient global amnesia.**

Summary

Four variables showed statistically significant differences between non-participants and participants. Hypertension (non-participants 54% versus participants 40%), internal versus GP referrals (69% versus 40%), history of TIA/stroke (24% versus 18%) and those who were high risk according to the ABCD2 score (69% versus 53%).

The proportion with a clinic diagnosis of TIAMS was of borderline statistical significance; 35% in participants and 42% in non-participants (p = 0.053). For all the other baseline characteristics, the groups were non-significant (p ≥ 0.05). Overall, comparison of baseline characteristics suggested that patients with higher risk factors were under-represented.

3.5.2. Level of agreement between clinic and interview data

In the sample (N = 486), clinical features contributing to the Dawson score were collected at the telephone interview and were extracted from the clinic database to compare the two data sources. Table 3.5.4 presents the proportion of participants with each clinical feature recorded at interview and in clinic, level of agreement for each variable, the expected agreement and Kappa (κ) scores. The p value and 95% confidence interval (CI) of Kappa are also shown. The interpretation of κ is that advised by Landis and Koch, 1997 (234) (section 3.4.11).

Table 3.5.4: Proportion of agreement – interview and clinic data for Dawson score components

Dawson clinical elements	Interview data	Clinic data	Total proportion of agreement	Expected agreement	κ	95% CI	Interpretation of κ
History of stroke/TIA	14%	18%	89%	73%	0.58	0.50 to 0.67	Moderate
Headache	26%	19%	80%	65%	0.42	0.34 to 0.51	Moderate
Diplopia	8%	4%	92%	88%	0.33	0.25 to 0.41	Fair
Loss of consciousness	6%	5%	92%	90%	0.26	0.17 to 0.35	Fair
Seizure	2%	2%	96%	96%	0.08	-0.01 to 0.17	Poor
Speech abnormalities	38%	36%	88%	53%	0.76	0.67 to 0.85	Good
Unilateral limb weakness	34%	34%	83%	55%	0.62	0.53 to 0.71	Good
Unilateral facial weakness	15%	16%	89%	74%	0.59	0.51 to 0.68	Moderate

Table 3.5.4 highlighted variable agreement, with speech and unilateral limb weakness interpreted as good agreement, history of TIA/stroke, headache and unilateral facial weakness showing a moderate agreement. Diplopia, loss of consciousness reported fair agreement and seizure presented poor agreement.

For the three variables that had a 'poor or fair' κ, the proportion of positive cases (both in interview and clinic) was lower than the other variables and the expected level of agreement was higher. The prevalence was particularly low for seizure, which explains why the interpretation of κ was 'poor agreement' (242).

With both a very low or very high prevalence, the kappa statistic tends to be much lower than if the prevalence was around 0.5 for the same data because the prevalence is included in the kappa statistic calculation. A more detailed comparison of the agreement between the interview and clinic data can be viewed in Appendix 16.

Following on from the interpretations of κ for the interview and clinic Dawson clinical features, the Bland Altman (BA) plot shows the level of agreement between the clinic Dawson score versus the interview Dawson score and how closely they agree with each other. The probability of a positive specialist diagnosis for the two scores is also shown in sections 3.5.6 and 3.5.7. The findings can be used to establish whether both version of the score are sufficiently in agreement to be equally useful to triage referrals to the TIA clinic.

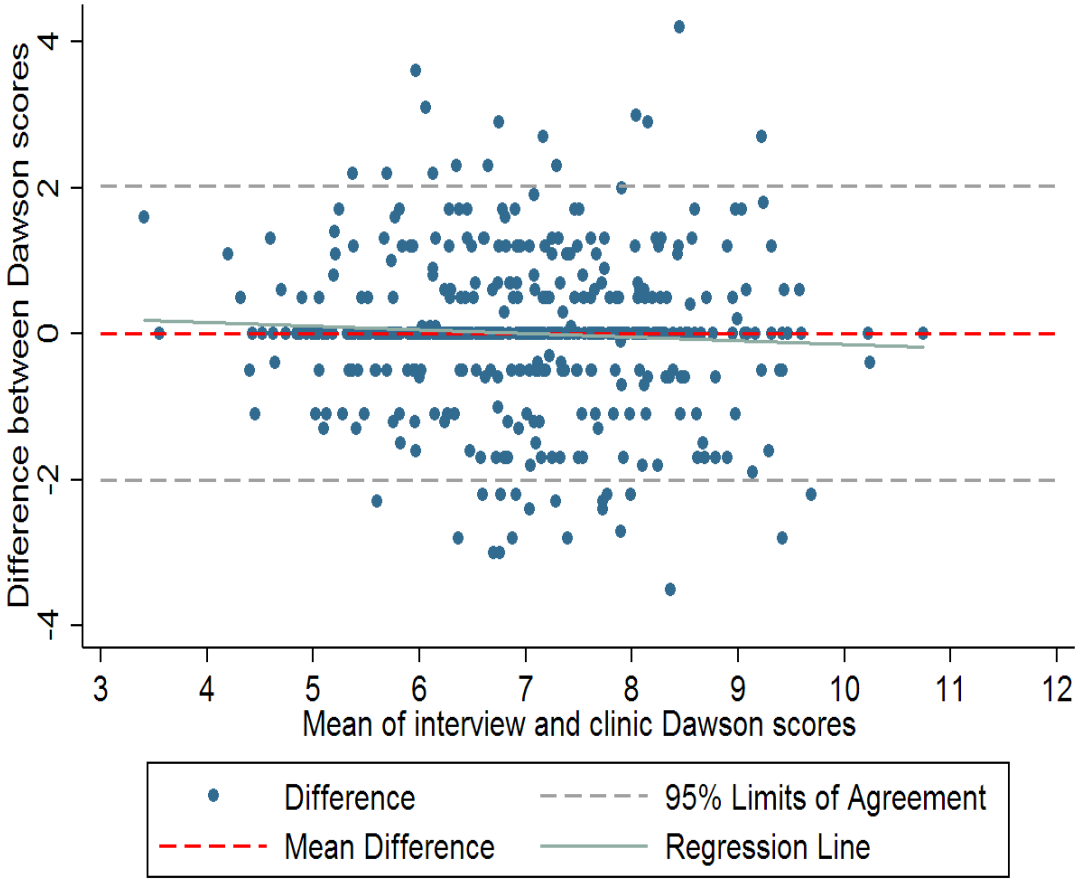
3.5.3. Comparison of the interview and clinic Dawson scores

Descriptive statistics for both the scores are presented in Table 3.5.5 below.

Table 3.5.5 Comparison of interview and clinic Dawson scores

Dawson score	Mean	SD	Min	Max
Interview	6.9626	1.28	3.55	10.74
Clinic	6.9570	1.34	2.61	10.81

Figure 3.5.2: Bland Altman plot comparing clinic and interview scores



The following method was used to calculate the mean difference and the limits of agreement:

Mean difference = 0.006

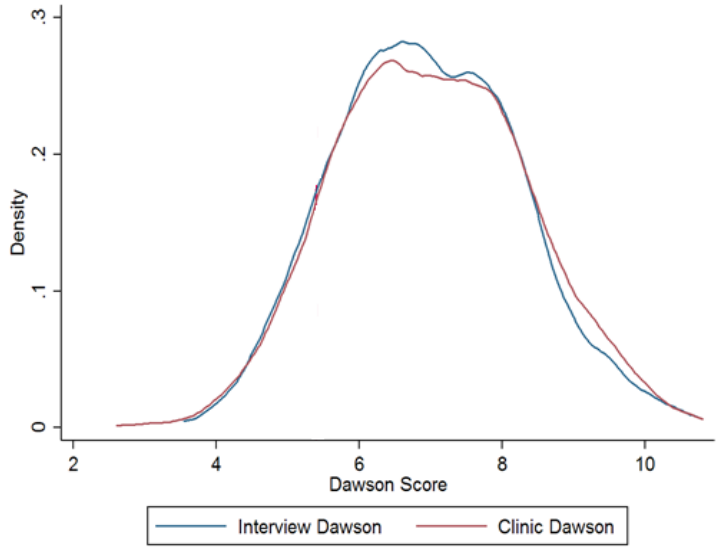
Lower limit = 0.006 – 2×SD (1.008) = -2.011

Upper limit = 0.006 + 2×SD (1.008) = 2.022

The BA plot (Fig 3.5.2) shows that in 34/486 cases (7%) difference between the scores lay outside the 95% limits of agreement. The mean difference (0.006) was close to zero and there was very little trend observed (R^2= 0.0037) between the difference and mean value of scores. This shows that the two measures have close to perfect average agreement and no systematic bias between them. It is expected that 5% of the scatter points would lie outside the limits of agreement. In this set of data, slightly more (7%) were outside the limits of agreement. However, it can be supposed that any differences are due to chance.

A probability density function describes the relative likelihood of the measure to take on a given value. From the PDF the probability of an event can be calculated. A figure of the PDF is shown below:

Figure 3.5.3: Probability density function of the interview and clinic scores



The area under the curve between two points on the x-axis shows the probability of the score being within this range. Both curves were normally distributed (Fig 3.5.3). This shows the distribution of the curves were both similar to each other. The results from both scores in identifying non-TIAMS and suspected TIAMS were then compared as shown above.

Table 3.5.6: Comparison of suspected TIAMS and non- TIAMS diagnosis between interview and clinic scores using the standard Dawson score cut-off of 5.4

Interview Dawson Score	Clinic Dawson Score		Total
	Non-TIAMS	Suspected TIAMS	
Non-TIAMS	36 (7%)	20 (4%)	56
Suspected TIAMS	22 (5%)	408 (84%)	430
Total	58	428	486

For both the interview and clinic Dawson data, 408, (84%) cases scores were classified as suspected TIAMS and in 3 cases 6 (7%) both data sources classified as non-TIAMS (Table 3.5.6).

Summary

Interpretations of κ comparing the interview and clinic Dawson clinical features suggested good to fair agreement across all variables apart from seizure. The 7% outside the limits of agreement shown in the BA plot (Fig 3.5.2) is close to the 5% expected and may have been due to chance. Overall it can be proposed that the two versions of the Dawson score are close enough to substitute one for the other. These findings suggest that if the Dawson score is to be used in practice, then the clinic score can be used to triage rather than collecting data by telephone.

3.5.4. Comparison of specialist diagnosis with the ABCD2 score

Specialist diagnosis was compared to participants' ABCD2 scores. An ABCD2 score of 4 or higher was considered high-risk and a score of 3 or less was low-risk. The results are shown below:

Table 3.5.7: Specialist diagnosis of TIAMS versus the ABCD2 score

Specialist diagnosis	ABCD2		Total	P value
	Low risk	High risk		
Other conditions – No diagnosis	189 (73%)	125 (55%)	314	p = <0.0001
TIAMS	69 (27%)	103 (45%)	172	
Total	258	228	486	

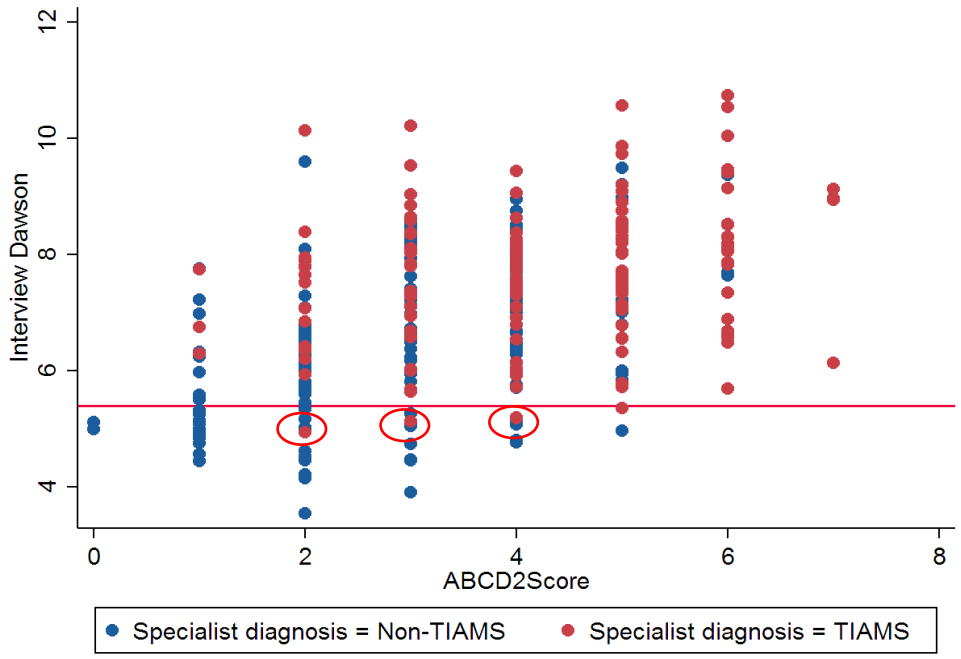
Of the high-risk patients, 45% were diagnosed as TIAMS compared to 27% of low-risk patients. The odds ratio for TIAMS diagnosis in high versus low ABCD2 score was calculated (189×103)/ (125×69) see section 3.4.11 for calculation (Table 3.5.7).

Odds of a specialist diagnosis of TIAMS was 2.25 times higher for those who had a high ABCD2 score, 95% CI: 1.52–3.36. This shows the ABCD2 score has some ability to predict diagnosis of TIAMS but that using a score of less than 4 to triage would exclude 69/172 (40%) of TIAMS. This was then compared with the diagnostic performance of the Dawson score (section 3.5.5 below).

3.5.5. Comparison of the interview Dawson and the ABCD2 score

To compare the utility for prioritisation for both scores it was important to compare the interview Dawson scores for patients to the ABCD2 scores, and to explore the proportion of patients who had both a TIAMS and non-TIAMS specialist diagnosis. The scatter plot results with the 5.4 cut-off (represented as the horizontal line) are shown below:

Figure 3.5.4: Scatter plot comparing the interview Dawson score to the ABCD2 score with the specialist diagnosis

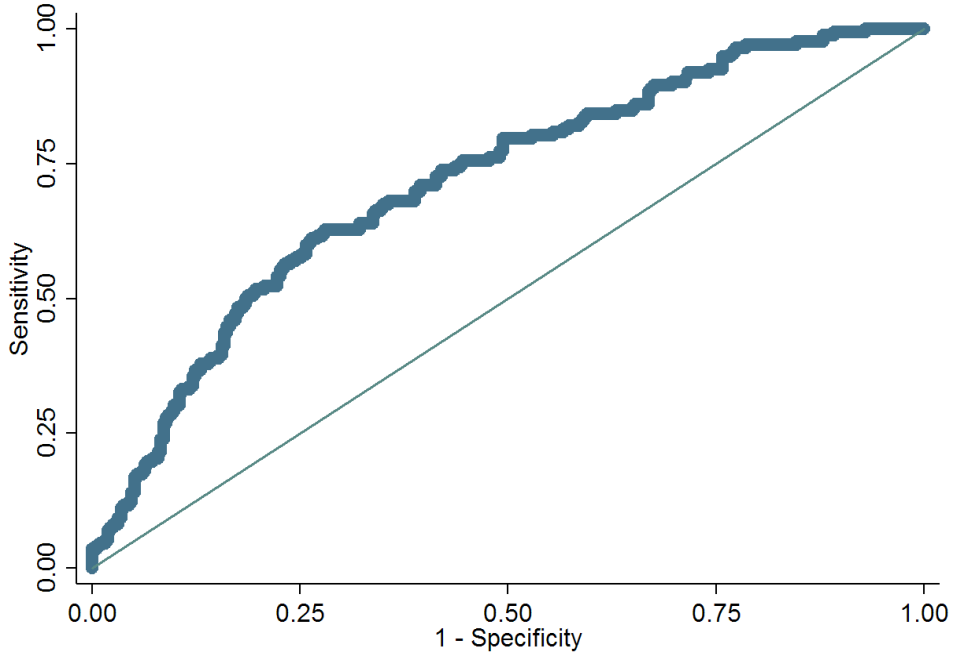


A high proportion of those who were low risk (≤ 3) according to the ABCD2 score had a specialist diagnosis of TIAMS. From the results it can be concluded that for prioritising patients the Dawson score would have more value than the ABCD2 score, as the majority of patients (apart from 3-circled in Fig 3.5.4) with specialist diagnosis of TIAMS and were above the 5.4 cut-off.

3.5.6. Specialist diagnosis and interview Dawson suspected TIAMS – Primary analysis

The primary objective was to assess the performance of the interview Dawson score using data collected before attendance at the TIA clinic in predicting a specialist diagnosis of TIAMS. The original (Dawson) cut-off for suspected TIAMS and non-TIAMS for the Dawson score was 5.4. The analyses below used this same 5.4 cut-off for the prediction of a TIAMS diagnosis. As clinically it is important for a score to have a minimum sensitivity (e.g. at least 80%) so that few cases are missed, the key performance of the score is towards the top right point of the ROC curve.

Figure 3.5.5: ROC curve comparing specialist diagnosis of TIAMS versus interview Dawson score



The area under the ROC curve was 0.71 (95% CI: 67% to 76%)

Table 3.5.8: Specialist diagnosis of TIAMS versus interview score suspected TIAMS

Specialist diagnosis	Interview Dawson		Total
	Other condition	Suspected TIAMS	
Other conditions or no diagnosis	51 (91%)	263 (61%)	314
TIAMS	5 (9%)	167 (39%)	172
Total	56	430	486

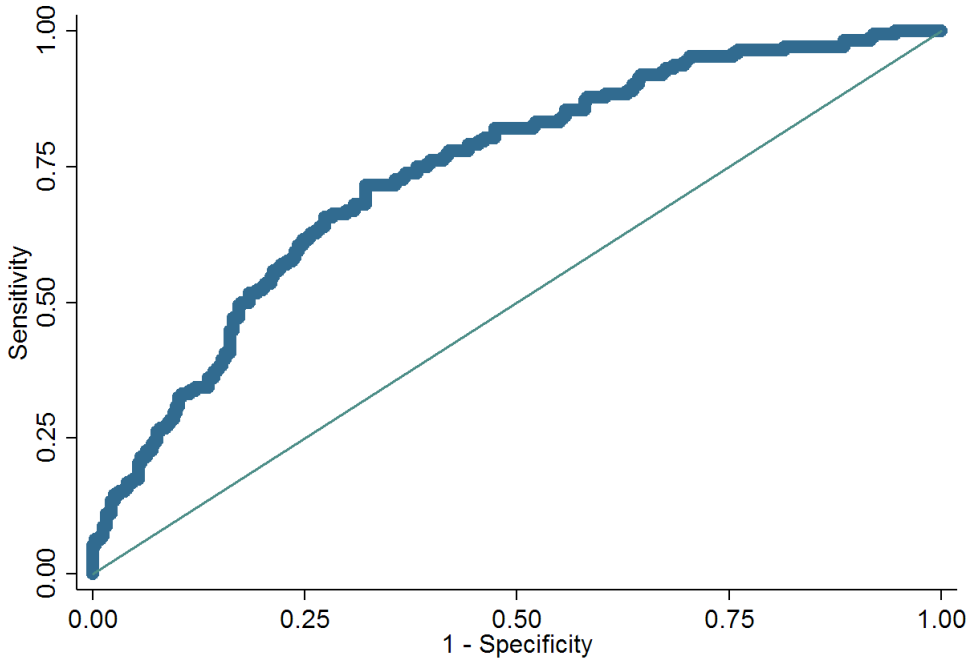
Using the 5.4 cut-off for the Dawson score, the following results can be derived from Table 3.5.8:

167 of the 172 patients where the specialist diagnosed TIAMS were correctly identified, a sensitivity of 97%, CI: 93% to 99%. 51 of the 314 patients where the specialist diagnosed other conditions were correctly identified, a specificity of 16%, CI: 12% to 21%. PPV of the Dawson score for the specialist diagnosis of TIAMS was 167/430, 39%, CI: 34% to 44%. NPV was 51/56, 91%, CI: 80% to 97%.

3.5.7. Specialist diagnosis and interview Dawson suspected TIAMS – Secondary analysis

A secondary objective was to assess the clinic score with the specialist diagnosis of TIAMS.

Figure 3.5.6: ROC curve comparing specialist diagnosis of TIAMS versus clinic score



The area under the ROC curve was 0.74 (95% CI: 69% to 78%).

Table 3.5.9: Specialist diagnosis of TIAMS versus clinic score diagnosis of TIAMS

Specialist diagnosis	Clinic Dawson		Total
	Other condition	Suspected TIAMS	
Other conditions or no diagnosis	53 (91%)	261 (61%)	314
TIAMS diagnosis	5 (9%)	167 (39%)	172
Total	58	428	486

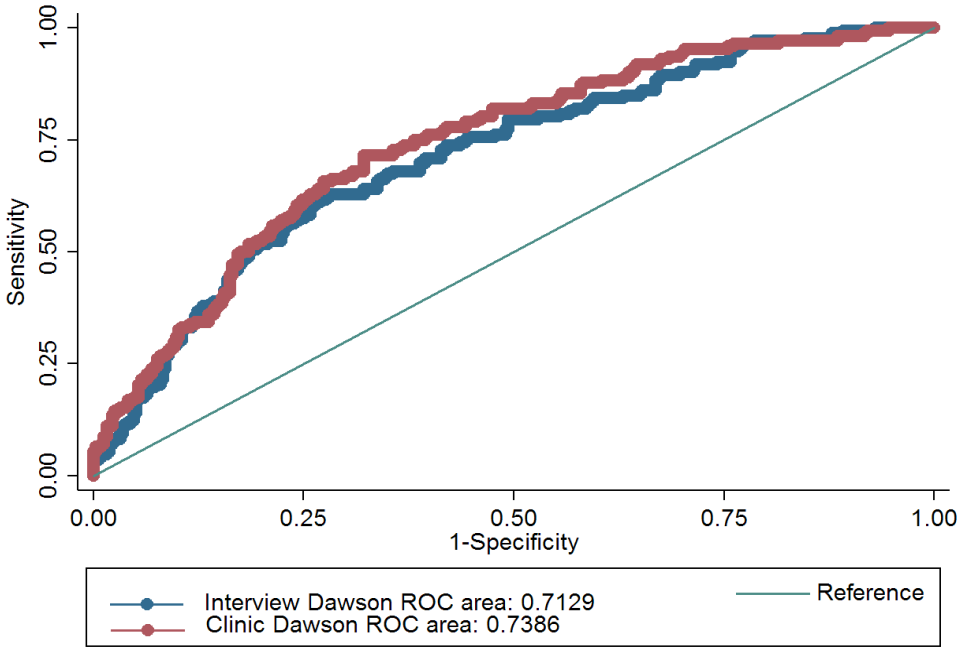
The same 5.4 cut-off used for the primary analysis (described above) was used to obtain the following results:

167 of the 172 patients where the specialist suggested a positive diagnosis of TIAMS was correctly identified, a sensitivity of 97% CI: 93% to 99%. 53 of the 314 patients where the

specialist suggested a diagnosis of non-TIAMS were correctly identified, a specificity of 17%, CI: 13% to 22%. PPV of the Dawson score for the specialist diagnosis of TIAMS was 167/428, 39%, CI: 34% to 44%. NPV was 53/58, 91% CI: 81% to 97%.

The primary objective assessed the performance of the interview score to the specialist diagnosis of TIAMS, whilst the secondary objective similarly assessed the performance of the clinic score to the specialist diagnosis. In Figure 3.5.7 the two ROC curves are compared against each other.

Figure 3.5.7: ROC curve comparing specialist diagnosis of TIAMS versus interview and clinic scores



The two versions of the score performed similarly in terms of the area under the ROC curve, with the clinic score reporting a slightly better performance than the interview score (0.74 versus 0.71).

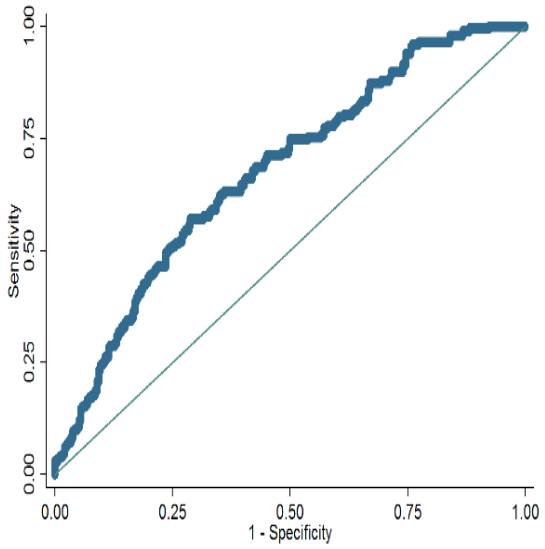
For each of the scores, using the specified cut-off of 5.4, 167 of the 172 participants with a positive specialist diagnosis of TIAMS also had suspected TIAMS identified by the Dawson score – giving a sensitivity of 167/172 = 93%. For the interview score, (51/314) had a non-TIAMS specialist diagnosis and were correctly identified as non-TIAMS by the interview Dawson, a specificity of 16% the clinic score identified (53/314) non-TIAMS specialist diagnosis, a sensitivity of 17%.

3.5.8. Specialist diagnosis of cerebrovascular disease

The original use of the Dawson score was to differentiate TIAMS/stroke from other conditions. Exploratory analyses presented in this section compared diagnoses of all cerebrovascular disease to the interview and clinic scores. The cerebrovascular categories included the following diagnoses; ischaemic stroke, transient ischaemic attack, retinal artery occlusion and transient monocular blindness. The results are shown below in figures 3.5.8a and 3.5.8b.

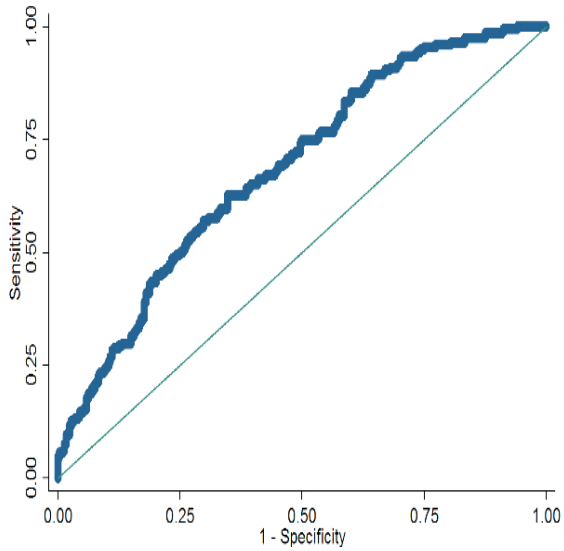
Figure 3.5.8: ROC curve comparison of cerebrovascular specialist diagnosis with the interview and clinic scores

3.5.8a. Interview



AUC of the ROC curve was 0.68 (95% CI: 63% to 72%)

3.5.8b. Clinic



AUC of the ROC curve was 0.68 (95% CI: 63% to 73%)

The 5.4 cut-off was used to obtain the following results:

3.5.9. Interview score results

Table 3.5.10: Specialist diagnosis of cerebrovascular versus interview score suspected diagnosis of TIAMS

Specialist diagnosis of cerebrovascular	Interview score		Total
	Other condition	Suspected TIAMS	
Other conditions or no diagnosis	49 (88%)	239 (56%)	288
Cerebrovascular diagnosis	7 (12%)	191 (44%)	198
Total	56	430	486

191 of the 198 patients where the specialist made a diagnosis of cerebrovascular disease were correctly identified, a sensitivity of 96%, CI: 93% to 99%. 49 of the 288 patients where the specialist made a diagnosis of no cerebrovascular disease were correctly identified, a specificity of 17%, CI: 13% to 22%. PPV of the Dawson score for the specialist diagnosis of cerebrovascular disease was 191/430, 44%, CI: 40% to 49%. NPV was 49/56, 88% CI: 76% to 95%.

3.5.10. Clinic score results

Table 3.5.11: Specialist diagnosis of cerebrovascular versus clinic score suspected diagnosis of TIAMS

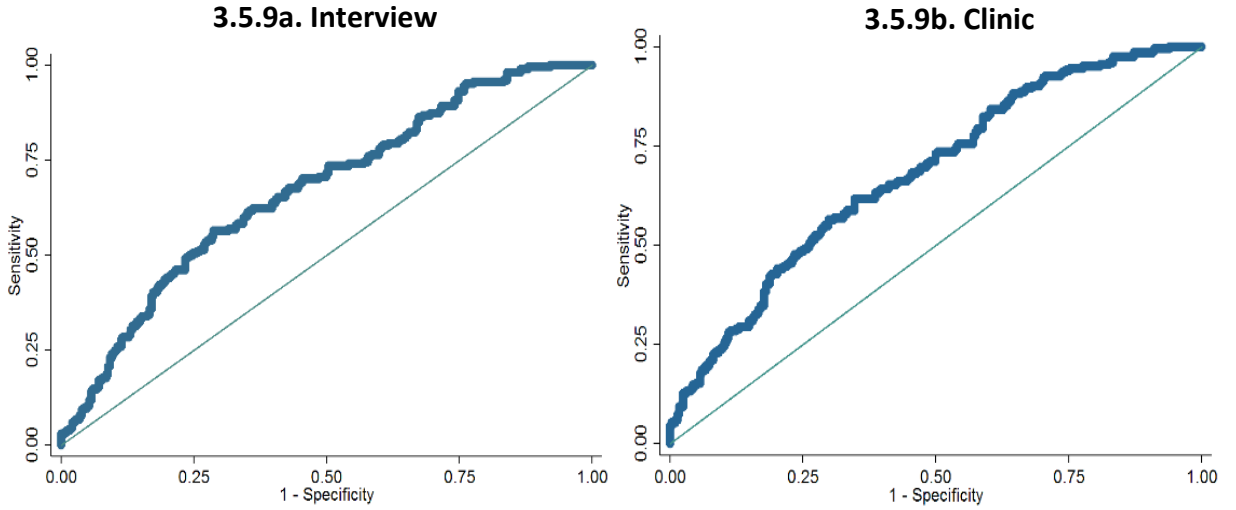
Specialist diagnosis of cerebrovascular	Clinic score		Total
	Other condition	Suspected TIAMS	
Other conditions or no diagnosis	51 (88%)	237 (55%)	288
Cerebrovascular diagnosis	7 (12%)	191 (45%)	198
Total	58	428	486

191 of the 198 patients where the specialist made a diagnosis of cerebrovascular disease were correctly identified, a sensitivity of 96%, CI: 93% to 99%. 51 of the 288 patients where the specialist made a diagnosis of no cerebrovascular disease were correctly identified, a specificity of 18%, CI: 14% to 23%. PPV of the Dawson score for the specialist diagnosis of cerebrovascular was 191/428, 45%, CI: 40% to 50%. NPV was 51/58, 88%, CI: 77% to 95%.

3.5.11. Specialist diagnosis of broader cerebrovascular disease

In this analysis, transient global amnesia (TGA) was added to cerebrovascular diseases. This group was labelled as 'cerebrovascular + TGA' and was compared to the interview and clinic scores indicating suspected diagnosis of TIAMS. The results are shown below in figures 3.5.9a and 3.5.9b.

Figure 3.5.9: ROC curve comparison of broader cerebrovascular specialist diagnosis with interview and clinic Dawson



AUC of the ROC curve was 0.67 (95% CI: 62% to 72%)

AUC of the ROC curve was 0.68 (95% CI: 63% to 73%)

3.5.12. Interview score results

Table 3.5.12: Specialist broader cerebrovascular diagnosis versus interview score suspected diagnosis of TIAMS

Specialist diagnosis of cerebrovascular + TGA	Interview score		Total
	Other condition	Suspected TIAMS	
Other conditions or no diagnosis	47 (84%)	235 (55%)	282
Cerebrovascular + TGA diagnosis	9 (16%)	195 (45%)	204
Total	56	430	486

195 of the 204 patients where the specialist made a positive cerebrovascular + TGA diagnosis were correctly identified, a sensitivity of 96%, CI: 92% to 98%. 47 of the 282 patients where the specialist made a non-cerebrovascular + TGA diagnosis were correctly identified, a specificity of 17%, CI: 13% to 22%. PPV of the Dawson score for the specialist diagnosis of cerebrovascular + TGA was 195/430, 45%, CI: 41% to 50%. NPV was 47/56, 84% CI: 72% to 92%.

3.5.13. Clinic score results

Table 3.5.13: Specialist broader cerebrovascular diagnosis versus clinic score suspected diagnosis of TIAMS

Specialist diagnosis of cerebrovascular + TGA	Clinic score		Total
	Other condition	Suspected TIAMS	
Other conditions or no diagnosis	49 (84%)	233 (54%)	282
Cerebrovascular + TGA diagnosis	9 (16%)	195 (46%)	204
Total	58	428	486

195 of the 204 patients where the specialist made a positive diagnosis of cerebrovascular + TGA were correctly identified, a sensitivity of 96%, CI: 92% to 98%. 49 of the 282 patients where the specialist made a diagnosis of non-cerebrovascular disease + TGA were correctly identified, a specificity of 17%, CI: 13% to 22%. PPV of the Dawson score for the specialist diagnosis of cerebrovascular + TGA was 195/428, 46%, CI: 41% to 50%. NPV was 49/58, 84% CI: 73% to 93%.

Summary

The Dawson score (interview and clinic) versus the specialist diagnosis of TIAMS reported an area under the ROC curve of 0.71 and 0.74 respectively (Fig 3.5.5, 3.5.6). The clinic Dawson score reported a slightly better performance. The ROC for both the interview and clinic Dawson score versus diagnosis of cerebrovascular showed a lower ROC of 0.68 for both interview and clinic (Fig 3.5.8a, 3.5.8b). Lastly, results for interview and clinic versus broader cerebrovascular diagnosis showed a similar ROC for interview (0.67) and clinic data (0.68) (Fig 3.5.9a, 3.5.9b).

The results in the TIAMS group were more accurate in comparison to the broader cerebrovascular categories. Although it was not a large difference, the results are expected to be better for this group as the Dawson score was intended to differentiate TIAMS from all other conditions. The risk score developed for TIAMS risk will include variables and/or weightings that could be different for other cerebrovascular categories. This would explain why the AUC was lower for these analyses. Table 3.5.14 summarises the NPV, PPV, sensitivity and specificity values according to each comparator.

Table 3.5.14: The NPV, PPV sensitivity, specificity according to the different comparators using the 5.4 cut-off

Comparator	NPV	PPV	Sensitivity	Specificity
Specialist diagnosis of TIAMS versus interview Dawson	91%	39%	97%	16%
Specialist diagnosis of TIAMS versus clinic Dawson	91%	39%	97%	17%
Specialist diagnosis of cerebrovascular disease versus interview Dawson	88%	44%	96%	17%
Specialist diagnosis of cerebrovascular disease versus clinic Dawson	88%	45%	96%	18%
Specialist diagnosis of cerebrovascular disease + TGA versus interview Dawson	84%	45%	96%	17%
Specialist diagnosis of cerebrovascular disease + TGA versus clinic Dawson	84%	46%	96%	17%

The results from the table show that the performance of the score was similar in terms of the sensitivity and specificity, regardless of specialist diagnosis of TIAMS, cerebrovascular or cerebrovascular plus TGA.

3.5.14. Sub group analyses

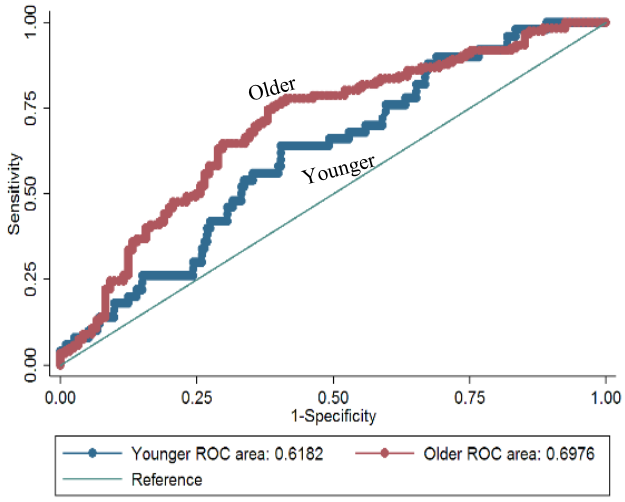
An exploratory objective was to determine the performance of the interview Dawson score in pre-specified sub-groups, and so, the ROC curves comparing sub-groups were plotted. To assess whether there was a statistical difference between the area under the curve for each sub group analysis, the Pearson chi-squared test was performed. The significance level of the p value was also adjusted according to the Bonferroni correction method to account for multiple testing. The p value was divided by the number of tests performed, which in this case was 8 (0.05/8 = 0.00625). Thus, statistical significance was defined as $p < 0.00625$.

Participants were divided according to whether they were above or below the median age of 68.4. Individuals with a South Asian ethnicity were then compared to those with a White ethnicity. There was a total of 22 individuals from other ethnic groups, however the numbers were too small to compare. The other groups included Chinese, black African, black Caribbean, black British, other black background and other ethnic groups.

Sub-group comparisons (presented below) were age, gender, diabetes, hypertension, ethnicity, socioeconomic status, ABCD2 score and referral.

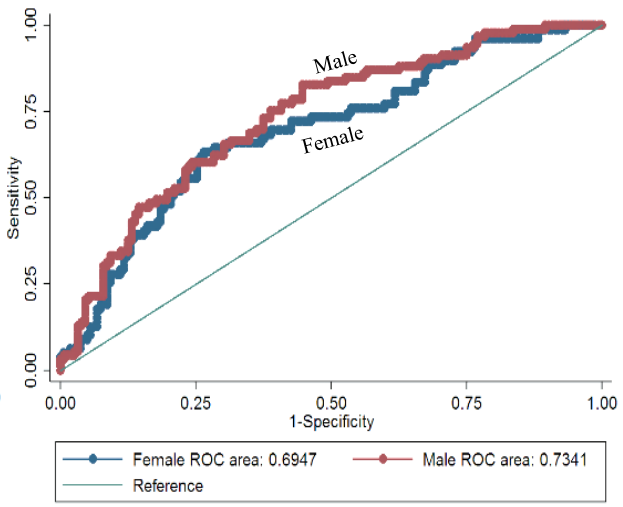
Figure 3.5.10: ROC curve comparison of sub-group variables

3.5.10a.



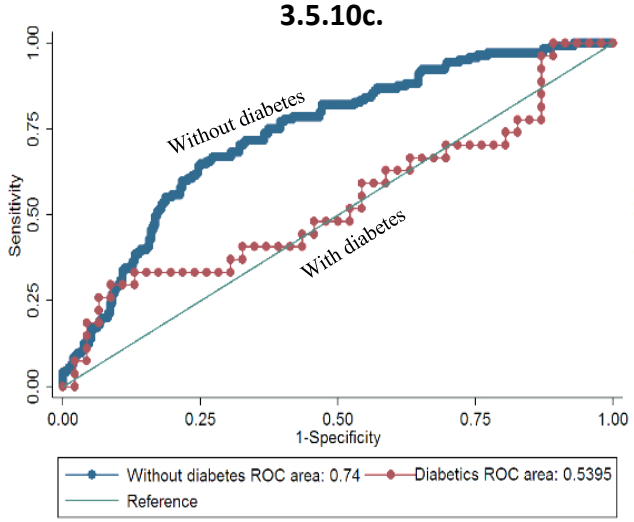
p = 0.141

3.5.10b.



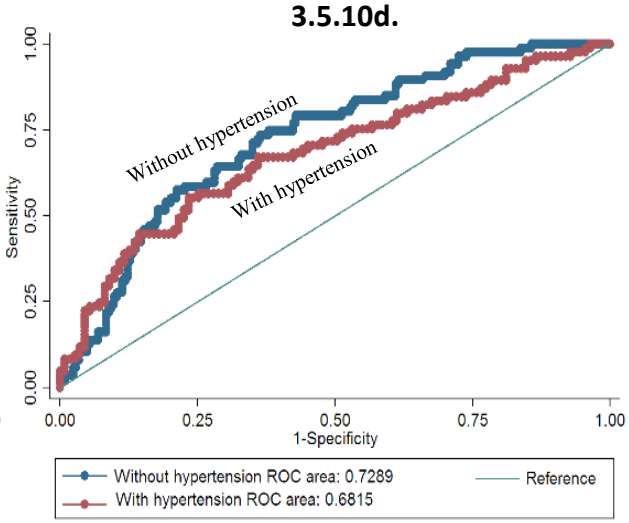
p = 0.417

3.5.10c.



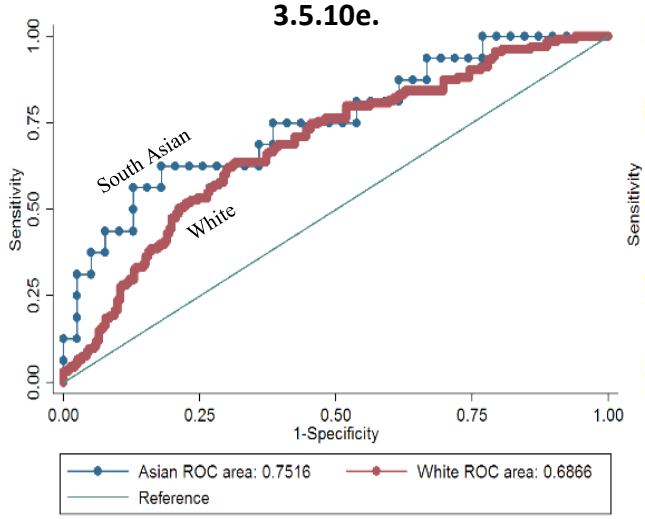
p = 0.011

3.5.10d.



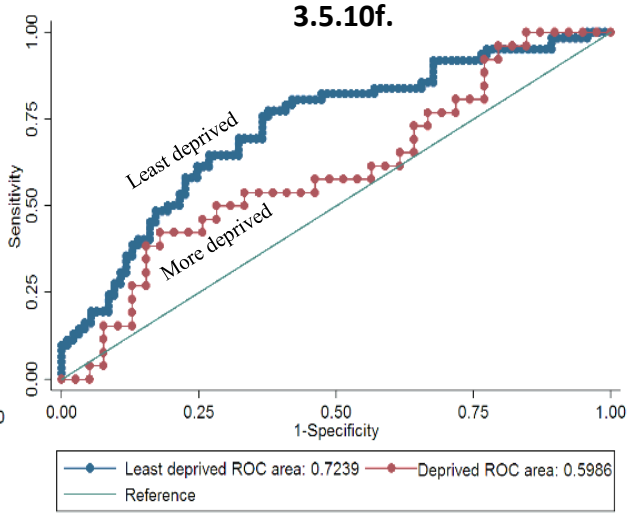
p = 0.343

3.5.10e.

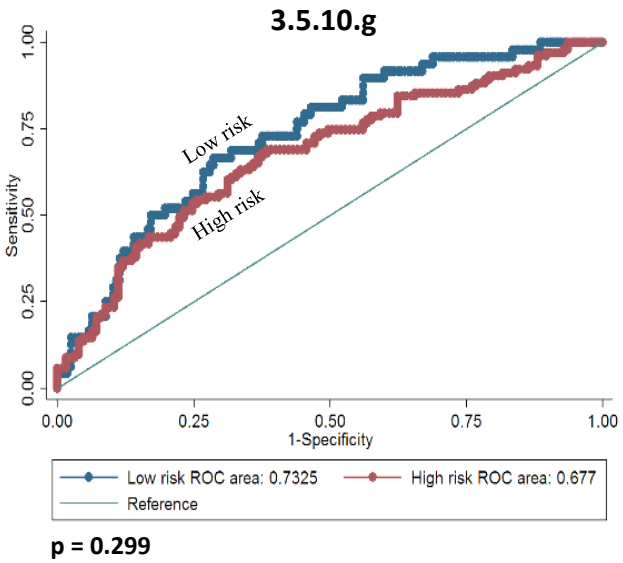


p = 0.421

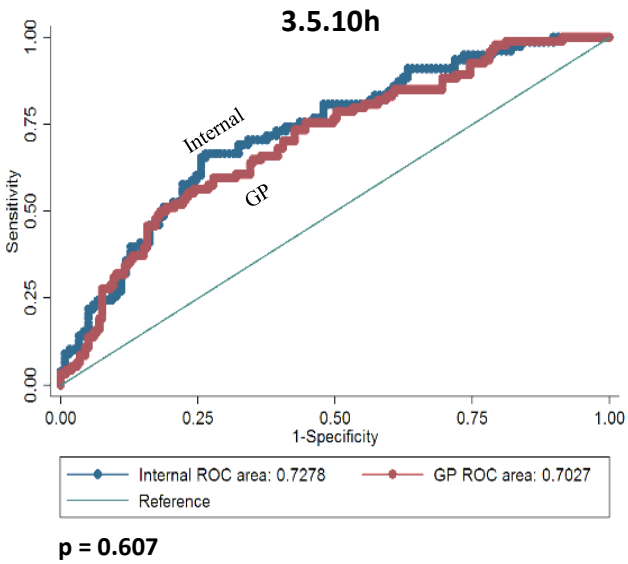
3.5.10f.



p = 0.137



p = 0.299



p = 0.607

For clearer comparisons between sub-groups, a descriptive table on the area under the ROC, the CI, sensitivity, specificity, PPV, NPV and percentage of TIAMs for each group are reported below.

Table 3.5.15: Summary of subgroup variables

Groups	Number	ROC AUC	95% CI		P-value	% TIAMS
Younger	243	0.62	54%	70%	p = 0.141	50%
Older	243	0.70	63%	76%		21%
Female	241	0.69	62%	77%	p = 0.417	33%
Male	245	0.73	67%	80%		38%
Without diabetes	413	0.74	69%	79%	p = 0.011	35%
With Diabetes	73	0.54	39%	69%		37%
Without hypertension	209	0.73	67%	79%	p = 0.343	30%
With hypertension	196	0.68	61%	76%		43%
South Asian	55	0.75	60%	90%	p = 0.421	29%
White	366	0.69	63%	74%		37%

Least deprived	155	0.72	64%	81%	p = 0.137	40%
Most deprived	65	0.60	46%	74%		40%
Low risk	205	0.73	65%	81%	p = 0.299	23%
High risk	228	0.68	61%	75%		45%
Internal referral	195	0.73	66%	80%	p = 0.607	40%
GP referral	291	0.70	64%	77%		32%

Summary

Differences between the two areas under the ROC was significant in the diabetes versus without diabetes group (0.54 vs 0.74) p = 0.011. However, once the Bonferroni correction was applied, all sub-group analyses were non-significant (Fig 3.5.10a-3.5.10h). The curves may not be as accurate as initially predicted for the diabetes group due to the smaller sample for those with diabetes. This was also the case for the South Asian and most deprived groups.

Although the Pearson chi-squared test for all the groups were not statistically significant, these results contrasted with the ROC figures (Fig 3.5.10a–3.5.10h). This is because the sensitivity and specificity relate to performance at the top right of the curve.

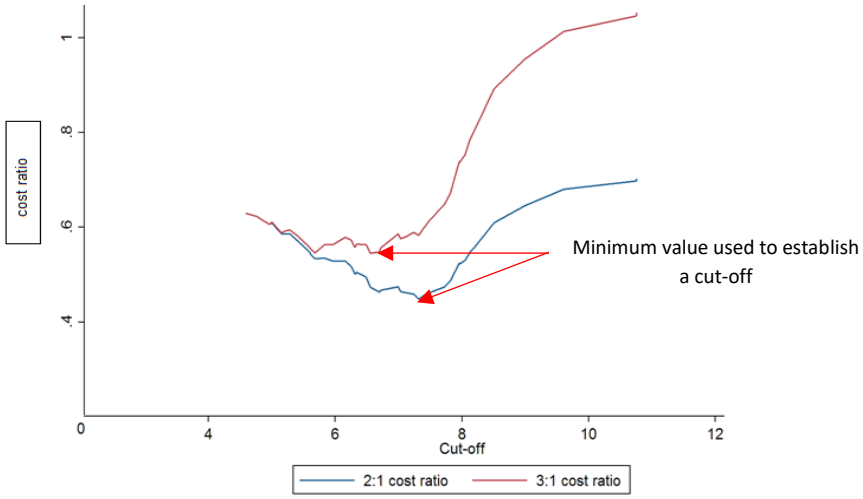
The results were similar across both IMD sub-groups with the most deprived group being slightly better. For the high-risk, low-risk, internal and GP referred patients the results were variable despite the ROC suggesting differences in low-risk and internal groups (Table 3.5.15).

In terms of the proportion of patients with a diagnosis of TIAMS in the sub-groups (Table 3.5.15) a large difference can be seen in the younger group than the older group (50% versus 21%). Those with hypertension had a higher TIAMS percentage than those without (43% versus 30%), and this was also the case for internal referrals than GP referrals (40% versus 32%). As expected, those who were high-risk according to the ABCD2 score had a higher TIAMS diagnosis percentage than those at low-risk (45% versus 23%). The rest of the results indicated a similar percentage of TIAMS for the sub-groups.

3.5.15. Applying cost ratios

In the Dawson paper, the recommended cut-off of 5.4 was derived using a 2:1 cost ratio. This assumed that the cost of misclassifying a cerebrovascular patient as non-cerebrovascular is twice as the cost of misclassifying in the opposite direction. The paper also presents a cut-off based on a 3:1 cost ratio. These principles were applied to the Leicester dataset to derive alternative cut-offs.

Figure 3.5.11: Applied cost ratio comparison



The weighting of both the sensitivity and specificity using the cost ratio formula reflected the ratio of the cost of misclassification (section 3.4.12). The minimum values were represented as the lowest point for both the 2:1 and 3:1 cost ratio, which proposed a cut-off of 7.26 for the 2:1, and 6.54 for the 3:1 (Fig 3.5.11).

Using these specific cut-offs, the sensitivity, specificity, PPV and NPV associated with each cut-off were calculated. The results of the 5.4 cut-off used in this study for the previous analyses and from the original Dawson paper are also shown in Table 3.5.16.

Table 3.5.16: Sensitivity, specificity, PPV and NPV associated with different cost ratios

Cost ratio	Cut-off	Sensitivity	Specificity	PPV	NPV
Leicester data	5.4	97%	16%	39%	91%
2:1	7.26	63%	72%	55%	78%
3:1	6.54	80%	50%	47%	82%
Dawson data					
2:1	5.4	93%	34%	68%	76%
3:1	6.1	99%	12%	Not reported	

Using the 2:1 cost ratio in the original Dawson paper, the optimal cut-off identified was 5.4, which was used for the previous analyses in the current study. However, applying the 2:1 cost ratio formula to the data in this study, a different cut-off emerged (7.26). The 3:1 cost ratio in the original Dawson paper gave a sensitivity of 99% but reduced the specificity to only 12%, and was therefore abandoned. In the Leicester sample, the 3:1 ratio gave a cut-off of 6.54 and therefore yielded a lower sensitivity but higher specificity, PPV and NPV than the 5.4 cut-off used in previous analyses.

3.6. Discussion

Summary of the findings

The clinical utility of the Dawson score was tested at the point in which both internal and GP referred patients attended the TIA clinic. The results demonstrated that using the 5.4 cut-off suggested by Dawson, a sensitivity of 97% and a specificity of 16% was achieved. Additionally, the use of the score in clinical practice could have some utility in reducing the number of non-cerebrovascular referrals to a fast track TIA clinic.

In regards to the secondary aims, the Dawson score from the interview and clinic data highlighted moderate agreement and achieved similar results when compared to specialist diagnosis of TIAMS. It was concluded that both methods of deriving the score produced results that were close enough to substitute one for the other. In regards to the clinic score however, it is uncertain how much of the data was truly based on GP recorded information as some details, although uncertain how frequently, may have been updated at clinic consultations. Additionally, the interview and clinic Dawson score performed similarly when comparing specialist diagnosis of broader cerebrovascular categories.

The Dawson score was better than the ABCD2 score in identifying patients at low risk of TIAMS. Therefore, the Dawson score had more potential than the ABCD2 score to prioritise referrals to the TIA clinic. Additionally, examination of the performance of the Dawson score in different sub-groups found no statistically significant results.

An exploratory analysis of the external validation study reported that with the applied 2:1 cost ratio to the Leicester data, a different cut-off to the 5.4 emerged; this was the 7.26 cut-off. Although the results reported a higher specificity, the sensitivity was deemed too low to be of any clinical use.

3.6.1. Comparison of the findings with other studies

Testing the clinical utility of the Dawson score demonstrated that using the 5.4 cut-off suggested by Dawson, a higher sensitivity was achieved (97% vs 93%), but a lower specificity was reported compared to the original study (16% vs 34%). The sensitivity reported in this study was also higher than found by Lasserson et al (92.3% in primary care and 93.4% in

secondary care) but the specificity was lower (18.1% in primary care and 29.3% in secondary care). The results from this study suggests that although the Dawson score correctly identified 97% of TIAMS cases, a large percentage of patients (61%) (Table 3.5.8) labelled as suspected TIAMS by the score turned out to have an alternative specialist diagnosis.

In the current study, applying the score at the 5.4 cut-off would reduce referrals by 12% as these are the patients that the score identified as not having a TIAMS; however, the score would exclude 9% who are diagnosed as TIAMS by the specialist (Table 3.5.8). These results are consistent with Lasserson et al who found that using secondary care data, the score would reduce referrals by 14% and would exclude 7% of TIA patients. Given the detrimental effects of a missed TIA, arguably, it would not be worth reducing referrals by 12%, when 9% would have a TIAMS diagnosis. In this study, there were a low percentage of referrals and a high proportion of missed TIAMS diagnosis. If the score is to be used in practice, then stroke physicians could contact the GP to discuss alternative strategies for the 12% of referrals whom they believe may not need be seen at the TIA clinic. It is important to note that the although the Dawson score was developed to aid accurate diagnosis of TIA and minor stroke, minor stroke was not assessed in Lasserson et al study. Therefore, this study highlights an accurate representation of reducing the burden at the TIA clinic by including both TIA and minor stroke patients.

Spectrum bias refers to the phenomenon that the performance of a diagnostic test may vary in different clinical settings because each setting has a different mix of patients. Therefore, the performance at one clinic may not be predictive of the performance of the test at another clinic (243, 244). This may explain the difference in sensitivity and specificity reported at the Glasgow TIA clinic, the Oxfordshire clinic and the Leicestershire TIA clinic in this study. This study may have included more atypical cases of TIA (cases with fewer classical symptoms) which are related to the difficulties in the diagnosis of TIA (245, 246), and may have affected test performance. When attempting to apply tests using data collected during secondary care, it has been suggested that GPs should be cautious (244). The lack of diagnostic test research in primary care means that primary care may be reliant on studies conducted in more specialist settings. However, it has been outlined that such studies may misrepresent the overall performance of the test in general practice populations, and affect individual patients because decisions on management are being

based on incorrect estimates of their probability of disease (244). If the score is to be used in primary care, GPs should be mindful of the complexities of the diagnostic process. The test's performance should be considered to be potentially affected by the presence of co-morbidities, the severity of the disease and prevalence in the patient population.

There was a higher prevalence of TIAMS in both Dawson (60%) and Lasserson (40%) studies in comparison to this study (35%) which contributes to differences in predictive values and suggests a very different population to the Dawson study. In this study PPV and NPV were 39% and 91% compared to 68% and 76% in Dawson's study. A recent systematic review found variation in PPVs for TIA across studies and that these differences can be explained by a combination of referral source and diagnostic criteria (78). For example, there was evidence to suggest that PPVs in primary care may be lower than those in ED. This is demonstrated in the current study which showed a higher proportion of TIAMS in internal referrals than GP referrals. A recent study also suggested that GPs' tolerance of uncertainty also influenced management decisions (166). GPs in the current study may have been less tolerant of risk now than 10 years ago when the Dawson study was published.

The prevalence of TIA in this study affected the 2:1 cost ratio result (section 3.5.15). The cut-off selection procedure is an informed decision that takes into account the epidemiological situation (e.g. prevalence in the target population) as well as the consequences of false negative and false positive results, which may differ according to different decision-making situation. For example, for a disease of low prevalence and high cost of false positive diagnoses, it may be recommended to choose a cut-off at the lower part of the curve to maximise specificity. Alternatively, if the disease prevalence is high and missing any disease individuals has serious consequences, a cut-off value towards the upper part of the curve would be selected to maximised sensitivity (204). In the original Dawson paper, a 5.4 cut-off was proposed with the applied 2:1 cost ratio; however, in this study, the 2:1 cost ratio method resulted in a cut-off of 7.26. In the original Dawson paper versus the results of this study using the 2:1 cost ratio the PPV was (68% vs 55%) and NPV was (76% vs 78%). At the recommended cut-off of 5.4 to reflect the need for greater sensitivity in TIA detection, the PPV remains around the overall level of 40% (98).

The specificities for both the 2:1 and 3:1 were higher than that reported in the original Dawson paper (72% versus 50%), but the sensitivities were only 63% and 80%, too low to be

of any clinical use. The sensitivity for the 2:1 and 3:1 cost ratio may differ because of the different test sample than that used in the original Dawson study. This would lead to different/incorrect weightings for the risk score used for the Leicestershire data. The cost ratio method could be used in the future to achieve the most clinically appropriate sensitivity and specificity to reduce the number of referrals seen at the specialist clinic.

The performance of the clinic score in predicting a specialist diagnosis of TIAMS was similar to the interview score, both with 97% sensitivity and 17% specificity (sections 3.5.6, 3.5.7). The PPV and NPV were the same for both; 39% and 91%. The AUC of the ROC curve were also similar for the interview and clinic scores, with the clinic results reporting slightly better results; 0.74 (95% CI: 69% to 78%) versus 0.71 (95% CI: 67% to 76%).

Interpretation of Kappa coefficient (κ) for the interview and clinic scores clinical features found good to fair agreement across all features, apart from seizure (Table 3.5.4). A limitation with κ however, is that a low prevalence is known to have an effect on the results (236). Thus, poor agreement in this study may be due to low prevalence. The results from the Bland Altman plot reported that 7% difference between the scores were outside the 95% limits of agreement (Figure 3.5.2). This however, may be down to chance and is not large enough to conclude that one version of the score differed from the other. The findings suggest that both methods of deriving the score were close enough to substitute one for the other. However, it is important to point out for the clinic score, it is uncertain how much of the data was truly based on GP recorded information as some details, although uncertain how frequently, may have been updated at clinic consultations. Therefore, the clinic score may not be reliable to triage GP referrals as it is based on perhaps the limited information provided by GPs. On the other hand, the interview Dawson score was collated by the researcher in a systematic way, was not updated at the clinic and showed promising results in predicting a specialist diagnosis of TIAMS. Therefore, it could be proposed that the interview Dawson score would be better suited to triage referrals.

It is important to consider ways in which the number of referrals can be reduced, enabling clinics to provide more time to manage patients with TIAMS and allow the clinic to assess patients promptly. If the Dawson score was to be used in primary care, then GPs could have a telephone conversation with specialists regarding patients they are unsure about prior to referral to the TIA clinic. In terms of the use of the score in secondary care, TIA clinic staff

could use the interview Dawson score to triage referrals by either referring back to the GP who did not meet the requirements at the TIA clinic, or could be sent to other clinics e.g. hypertension clinic where the patient can be managed accordingly.

The Dawson score performed slightly better for the TIAMS group compared with the cerebrovascular and broader cerebrovascular categories (section 3.5.8, 3.5.11). Although it was not a large difference, the results are expected to be better for this group as the Dawson score was intended to differentiate TIAMS from all other conditions. The risk score developed for TIAMS risk will include variables and/or weightings that could be different for other cerebrovascular categories, and therefore a score developed to diagnose TIAMS may not be representative for the diagnosis of cerebrovascular conditions.

The ABCD2 score was developed using data from patients with a confirmed diagnosis of TIA. Thus, it is unproven as a diagnostic instrument. Additionally, with regards to the use of the ABCD2 score, every individual with a significant risk of TIA should be assessed as soon as possible (247). Dawson et al did not explore whether the score would add further to the potential use of the ABCD2. In this study, the results comparing specialist diagnosis to participants' ABCD2 scores highlighted that of the high-risk patients, 45% were diagnosed as TIAMS compared to 27% of low risk patients. Furthermore, although the odds of a specialist diagnosis of TIAMS was 2.25 times higher for those who had a high ABCD2 score, and shows that the score has some ability to predict diagnosis of TIAMS, using a score of less than 4 to triage would exclude around 40% of TIAMS patients (section 3.5.4). This result is consistent with previous research which has concluded that he ABCD2 score has inadequate discrimination for the diagnosis of TIA (75, 78, 193).

With regards to the comparison of the interview Dawson score to the ABCD2 score to assess the scores utility to prioritise patients, the results suggested that a high proportion of patients who were low risk (≤ 3) according to the ABCD2 score had a specialist diagnosis of TIAMS. The Dawson score was better than the ABCD2 in identifying patients at low risk of TIAMS (section 3.5.4). Therefore, the Dawson score may be more effective for prioritising patients than the ABCD2 score. Since the ABCD2 score is no longer recommended from 2017 (11, 60), it is even more important that GPs are provided assistance to manage suspected TIA patients which may be achieved through the use of the Dawson score in terms of informing decisions about whether or not to refer. This was further supported by a

recent meta-analysis, which proposed that by using a diagnostic score by GPs, a better assessment can be facilitated for suspected TIAMS patients (248).

The performance of the Dawson score for the different sub-groups found that differences in performance between people with and without diabetes was not statistically significant once the Bonferroni correction was applied. It is important to note that there was a low sample size for the group with diabetes, so the difference could still be due to random error. Additionally, no statistically significant differences were found in the other subgroup comparisons (Fig 3.5.10a–3.5.10h).

Although it was not an objective to compare the proportion of TIAMS between sub-groups, the results highlighted that there was a large difference between the younger and older groups (50% versus 21%). This result suggests that GPs may have more diagnostic uncertainty about TIA in older people. The results also highlighted a higher percentage of TIAMS diagnosis in internal versus GP referrals (40% versus 32%). This may be because more severe cases of TIAMS are more likely to present to hospital rather than GP. Therefore, it can be suggested that the less severe cases presenting to GP may present more diagnostic uncertainty. Furthermore, as expected, those with hypertension had a higher TIAMS percentage than those without (43% versus 30%) (Table 3.5.15). These differences in percentages show that it may be beneficial to consider including these variables in future diagnostic tools or adjust the current Dawson in order to help diagnose TIAMS.

3.6.2. Strengths and limitations

Few diagnostic models undergo any external validation and very few are externally validated by different authors than those in the development study (216). A strength is that the results from this study can be used to further understand the diagnostic ability of the Dawson score and add to the external validation conducted by Lasserson et al.

A diagnostic tool for TIA would ideally be tested using data collected for the purpose by GPs when the diagnosis is being considered. Although in this study it was not feasible to ask GPs to calculate the score during the initial consultation, a major strength was that information to derive the interview score was collected soon afterwards, following referral to the clinic.

A specific strength is that data collection to derive the interview Dawson score was undertaken systematically. The data was collected from the patients by one researcher which improved the consistency of the process and the quality of the data. It is important to highlight that none of the patients declined verbal consent for the telephone interview, removing a potential source of bias. Furthermore, the researcher was able to speak to patients in Hindi if they were unable to communicate in English, which was a total of eight interviews in this sample. Due to the large population of South Asian community in Leicestershire, this was an advantage as these patients were not excluded, and the study was representative for these patients. Similarly, those that were unable to speak to the researcher due to cognitive disabilities, the researcher was able to speak to their guardian/carer on their behalf which was in two cases.

Collins et al.'s simulation study suggested that an external validation of a prognostic model requires a minimum of 100 events (in this case positive diagnosis of TIAMS) to have sufficient power. This was achieved in the current study as it included 172 events and 314 non-events. A higher sample size than that initially obtained without removal of duplicated and non-clinic attendees (536 patients) would have meant a longer recruitment period and the risk of not completing the study in the timeframe available.

The recent TRIPOD guideline (249) indicates that a model's predictive performance should be evaluated for key sub-groups such as age or sex, rather than across all combined individuals as any deficiencies can be masked this way. The test's performance was separately analysed in patient subgroups in this study and has been previously reported to be an essential part of reporting to inform clinical practice (244). This is an aspect that was not explored by Dawson et al, nor Lasserson et al. Furthermore, GP and internal referrals were examined separately in a sub-analysis recommended by the TRIPOD guidelines (249). The study included referrals from internal departments at the LRI (ED and in-wards) as well as GP referrals. Given that the focus was on GP referrals, it was a strength to explore differences in the performance of the Dawson score for both groups. However, although the overall sample for internal and GP referrals were 195 and 291 patients respectively, the specialist TIAMS diagnosis for the groups were 78 and 93 respectively. These numbers are less than recommended in Collins et al.'s simulation study which suggests a minimum of 100 and ideally more than 200 events for the results of a prognostic model to have sufficient

power (222). Therefore, it is likely that the sub-group analysis was underpowered and cannot suggest definitive conclusions. Prospective population-based cohort data of patients presenting to general practices and EDs has similarly shown a high early risk of recurrent stroke after TIA and minor stroke (207, 208). It was therefore thought best to include patient referrals from ED, which is an aspect Lasserson et al did not include in their study. Another justification for including ED referrals was because this study aimed to look at the Dawson score as a triaging tool. For this purpose, internal referrals were as important as GP referrals. Although there were no significant differences in the score performance between the two groups, the results suggest a higher percentage of positive TIAMS in the internal group than GP referrals.

Internal validity refers to the extent to which the conclusions of a study are true within the limits of the research methods and subjects or participants. It is a measure of accuracy of the study. A limitation of this study was that the sample was biased towards the milder end of the spectrum of clinic attenders. Patients with a higher cardiovascular risk were non-participants therefore, excluding a large number of TIAMS diagnosed patients and under-representing patients with higher risk factors. The proportion of patients with a clinic diagnosis of TIAMS was of borderline statistical significance resulting in fewer cases than expected for the statistical analysis and leading to less power. Many weekend attenders were missed as those who were high-risk patients according to the ABCD2 score were more likely to be assigned to a weekend appointment. This not only suggests that the sample was not completely representative of the clinic population in terms of high-risk patients, but also explains why the difference between participants and non-participants clinic diagnosis was borderline significant.

The clinic database did not consistently record hypercholesterolemia and to extract the data, two continuous variables (total cholesterol and low-density lipoprotein) would need to be retrieved. Due to the large volume of missing data for both, hypercholesterolemia was not used for analysis. Although this was accepted as a limitation of this study, it suggests that this study may have recruited fewer patients with high cholesterol, and therefore at higher risk of TIAMS. Furthermore, a major limitation with the clinic database related to the uncertainty of what extent the clinic score reflected GP data or added data at clinic consultations. Given that some elements of the clinic score may have been collected at

attendance, it can be concluded that the clinic score would not be appropriate for triaging referrals.

External validity is the extent to which the results/conclusions can be applied outside the setting of the study and whether they can be generalised. A limitation of this study was that it was small scale and conducted at a single site. Stroke prevention services are widely available in the UK (178). However, there is regional variation in terms of access to services, how clinics are run and the comprehensiveness of services (179). The data was collected at one clinic and other clinics may operate differently. For example, the setup, the referral forms, the procedure on the day of patient appointments will differ according to the clinic. In addition to this, Leicestershire is known to have a much higher proportion of South Asians than the rest of the UK population. Therefore, the results of the study may not be generalisable to places with different patient populations and clinic provision.

The accuracy of a diagnostic test may also vary across different study populations. For example, reported estimates cannot directly be translated to populations with a different case mix. This issue is also the case across different settings such as from secondary to primary care. The case mix in this study can explain the variation in results between Dawson's study and this study in terms of the reported sensitivities and specificities.

It is important to note that the gold standard diagnosis depended on the 10 different stroke specialists at the Leicester Royal Infirmary TIA clinic. A high rate of disagreement amongst stroke specialists with regards to the diagnosis of TIA has been consistently reported (129). Therefore, it could be argued that the final diagnosis of a patient may differ between the specialists at the clinic. Several studies on diagnostic accuracy have reported on the use of an expert panel to assign a firm diagnosis for various conditions such as TIA/stroke, dementia and heart failure (250-252). A consensus specialist view could have been sought for this study as a more accurate gold standard. However, this would have added to the expense and complexity of the study, and so the clinic diagnosis was accepted as a reasonable gold standard (253).

3.6.3. Future research

A key limitation is that the study was not able to capture data on patients that GPs ruled out and decided not to refer. This may include some missed TIA's that might have been recognised by the Dawson score had it been applied.

Since the ABCD2 score is no longer recommended for prioritising referrals, the burden of work and required capacity of TIA clinics will increase significantly. This is because clinics will have to cope with the fluctuating demand of referrals, making discrimination of TNA and TIA at referral level even more important. The clinics will not have information on how urgently to see patients. This makes it even more important to reduce over referral so all patients can be seen promptly. It can be proposed that a diagnostic tool/score is therefore needed that is derived and validated entirely from primary care data, and a need for a prospective study looking at all cases of TNA in primary care using large routine GP databases. Additionally, further research on a diagnostic tool implemented into practice is needed to fully understand its practicality and feasibility.

Disagreement exists between GP and specialists over clinical features of TIA, and specialists tend to document fewer features than described by the GP in TIA and non-TIA patients (Chapter 2). Given their clinical background, GPs may interpret responses contributing to the score differently from a researcher. To avoid any problems with miscommunication over the phone, it would have been better for the GP to record the data. Also, patients are more likely to recall symptoms and severity with the GP than at some point after the consultation. However, due to the complexity of this sort of study, it was not feasible during the timeframe of this study.

The predictive symptoms of TIA included in the Dawson score were identified 10 years ago and was not designed for retinal and some posterior circulation events e.g. bilateral visual loss, visual aura, monocular visual loss, ataxia (limb and gait), amnesia etc. Although the DOTS is a new internally validated web and mobile app based diagnostic tool which encompasses both brain and retinal TIA (193), it may be worth for future studies to further look into predictive symptoms of TIA. This study further showed predictive factors of TIAMS diagnosis that may be beneficial to consider for example, younger, patients with hypertension and referral source (GP or internal).

There was a total of 22 individuals from other ethnic groups, however the numbers were too small to compare. The other groups included Chinese, black African, black Caribbean, black British, other black background and other ethnic groups. Therefore, this study was not representative of the ethnicities other than the two included for sub-group analysis (White versus South Asian). Future extensions to this work may wish to look into the performance of the Dawson score for different ethnicities. Furthermore, although after adjustment for multiple comparisons (Bonferroni adjustment), the diabetes effect on ROC AUC was no longer statistically significant, there is currently an unknown reason for the apparent difference. Therefore, it may be of interest for future studies to look into the performance of the score on this subgroup (diabetic versus non-diabetic patients).

This study does not represent the national population, and the population in this sample does not reflect the population outside Leicestershire. A diagnostic tool/score is needed that is derived and validated entirely from primary care data. In addition, although the Dawson score has shown to have some diagnostic utility for TIAMS and can be used to triage, definitive conclusions on its use in primary care are difficult to draw from this study. Therefore, further work on this including a larger sample size that is representative of the national population would be beneficial to further assess the diagnostic accuracy of the score. The results from this study could further lead to research on a diagnostic tool (whether this is the Dawson or DOTS) implemented into practice to fully understand its practicality, feasibility and effectiveness of the score for TIA in general practice.

The findings from the systematic review in Chapter 2 outlined a need for more qualitative studies on GPs' views on the diagnosis and management of TIA, to better understand the nature of the condition, and the difficulties experienced in primary care. This will be explored in Chapter 4.

3.7. Conclusion

The findings from the systematic review (Chapter 2) suggested a need for further work on a diagnostic tool for TIA in primary care. The need for an external validation study to draw conclusions beyond the results of the original Dawson study led to the methodological approach of this study. Although the Dawson score has been externally validated using routinely collected primary and secondary care data, it had not been externally validated using data collected for the specific purpose of calculating the score. The purpose of this research was to determine whether applying the Dawson score before clinic attendance could reduce unnecessary clinic consultations. This study collated the information to derive the score soon after GP and internal referral to the clinic. The results of this study looking into the only diagnostic tool for TIA available at the time to optimise decisions about entry into specialist TIA services found the following key findings:

- The performance of the Dawson score differed to that found in both the Dawson and Lasserson study, which may be due to the difference in the sample. However, despite this the results from this study highlighted that the score could be used to reduce the number of non-cerebrovascular referrals to the TIA clinic through triage
- The performance of the clinic score in predicting specialist diagnosis of TIAMS was similar to the interview score. However, due to the uncertainty regarding the reliability of using the clinic score to triage GP referrals, the interview score may be better suited to triage both internal and GP referrals. In terms of practice, when the referrals are received at the TIA clinic, the clinic staff could contact the patients in order to calculate the score. If the Dawson score suggests that the patients' risk of TIA diagnosis is unlikely then these referrals could either be removed from the clinic list, referred back to the GP to be managed in primary care or referred to a different department within secondary care e.g. hypertension clinic
- The Dawson score could be used by GPs to aid their decision-making process, and used by TIA clinic staff to either send back referrals that did not meet the requirements at the TIA clinic or triage to an alternative department best suited for that patient e.g. the hypertension clinic

- Higher percentages of TIAMS were observed in referred patients who are younger, with hypertension and internal referrals. This may be useful for future diagnostic tools/scores to consider

Chapter 4: Qualitative study of GPs' views of TIA

Chapter 2 reported the existing literature on challenges that GPs experienced in the diagnosis and management of TIAs. The studies outlined were mainly quantitative; the need for more qualitative studies that reported GPs' views and experiences on this matter was identified. Chapter 3 looked at the performance of Dawson score after patients had been referred to the TIA clinic, and before their clinic consultation in order to reduce the number of non-cerebrovascular referrals. The validated diagnostic tool could be used to support diagnosis of TIA in primary care, potentially reducing the number of referrals to the TIA clinic, and to triage clinic referrals.

This chapter particularly focuses on GPs views on the diagnosis and management of suspected TIA patients, as well as exploring their views on a diagnostic tool for primary care. The chapter will introduce the study followed by the aims of the study, methods, results, discussion and conclusion (sections 4.1–4.6).

The paper was submitted for publication in Family Practice and was accepted on 16th March 2018 for which the researcher of this thesis was the first author. The final draft of the publication has been attached as an appendix, (Appendix 17). The publication focuses on a sub-set of the themes reported in this chapter (suspecting a TIA, diagnosis and presenting symptoms, making a referral decision and attitudes towards a diagnostic tool for TIA in primary care) which were identified as the most clinically relevant themes (Appendix 17).

4.1. Rationale for the qualitative study

There has been little qualitative work on TIA, particularly in the context of primary care. A study comprising qualitative interviews with GPs identified difficulties in applying generic guidelines to patients with complicated risk profiles with particular focus on prescribing. The study focused on secondary prevention of stroke but could be equally applied to TIA (254).

Qualitative studies have also explored patients' knowledge as a contributing factor to the delay in accessing healthcare after symptom onset (255, 256). However, these studies have predominantly focused on stroke and included hospital attendances as well as patients who sought help from GPs. The only qualitative work identified through the systematic review (Chapter 2) concentrated on the varying use of the ABCD2 score (125) which included views of GPs and hospital doctors.

Limited data are available to assess how GPs diagnose TIA in practice. The systematic review conducted in 2016 found that the Dawson score was the only diagnostic tool for TIA. An external validation of the score in secondary care was undertaken at the TIA clinic as part of the thesis (sections 3.3–3.7).

The study included testing the Dawson score by examining referrals made by GPs and internal departments, and using the Dawson score to collect clinical information from the patients and compare it to the hospital clinic database. As well as having value for triaging referrals at TIA clinics, the score could potentially play a role in diagnosing and managing referrals of TIA patients in the primary care setting.

The next step after the external validation study was to explore GPs' views through semi structured interviews on whether a diagnostic tool for TIA would be useful in a primary care setting. Also, to examine broader issues around diagnosis and management of TIAs. GPs' views on the usefulness of a diagnostic tool were explored which included the strengths and weaknesses of this approach, as well as a particular focus on thresholds for referrals. Thresholds for referrals were important to explore because the objective of the study was to reduce unnecessary referrals to the TIA clinic. By looking into GP preferred thresholds, it would drive an understanding of the clinical implications of the reduction in referrals

associated with the use of the score according to these thresholds. This was further explored in Chapter 5.

4.2. Aims

This study conducted telephone interviews with GPs to investigate their experiences and views on the diagnosis and management of TIAs, specifically assessing:

1. Their views on diagnosis and immediate management of suspected TIA patients
2. The potential utility and practicality of a diagnostic tool in a primary care setting

4.3. Methods

This chapter focuses on outlining important aspects of the study such as, the study design, ethical approval, recruitment, data collection, recording and transcription. As a novice researcher in order to understand the importance of these aspects and recognise the various qualitative research approaches, the researcher of this study enrolled in a qualitative research training workshop (Appendix 15).

4.3.1. Study design

A qualitative design using thematic analysis to interpret semi-structured telephone interview schedules with GPs. GPs from practices in Leicestershire were interviewed individually for up to 30-minutes (Table 4.4.1). The results from the systematic review informed as well as directed the interviews, and explored the areas identified. These included the difficulties of diagnosing and managing TIAs, factors influencing referrals and the impact this had in primary care (section 2.3).

4.3.2. Rationale for qualitative methodology

This study sought to interview GPs who have made referrals to the LRI TIA clinic and therefore, have experience consulting with patients they suspect may have sustained a TIA. The aim was to investigate GPs' personal experiences on the topic of the diagnosis and management of TIA in order to discover/uncover core elements and shared dimensions that may be visible across a diverse sample, whilst, offering new and unique variations. Research argues that individual experiences, patterns and meanings are difficult to investigate quantitatively (257). A qualitative research methodology for this study was chosen for a number of reasons outlined below.

Qualitative methodology lends itself well to exploratory and discovery-oriented research because it enables new insights to be developed in areas where there is limited existing knowledge. Qualitative methodology encourages participants to introduce ideas that they believe are pertinent to the topic of interest. Thus, a qualitative approach allowed for new concepts to develop that were not constrained by the researcher's preconceptions around the topic. Additionally, it facilitates knowledge around processes, patterns and meanings

(257). Thus, as the research aims were to explore GPs' experiences in an attempt to gain new understandings of their views of TIA diagnosis and management in primary care (as opposed to measuring variables or testing hypotheses), a qualitative methodological approach to data collection and analysis was deemed to be most appropriate.

4.3.3. Interviews

Individual GP interviews as a method of data collection was chosen as they allowed for an in-depth exploration of participant experiences. TIA is an under researched area and an in-depth understanding from GPs on this area would be beneficial to understand their views of diagnosing and managing a TIA. Interviews have been reported to be useful for examining clinical decision making by exploring and investigating doctors' views, experiences and their routine and rules they obey. Therefore, interviews are able to provide insights into individuals' meaning of the topic (258).

Qualitative interviews are flexible to varying degrees and are described as either unstructured, structured, or semi-structured (259). In an unstructured interview, participants can speak freely on the given topic and the interviewer responds with questions which they may have at certain points. Structured interviews enable the interviewer to ask each respondent the same questions in the same way whereas semi-structured interviews involve a series of open-ended questions based on the topic areas the researcher wants to cover. The open-ended nature of the question defines the topic under investigation but provides opportunities for both interviewer and interviewee to discuss some topics in more detail. The interviewer can also use cues and prompts to encourage the interviewee to consider the question further if needs be, or elaborate on the original response, or to follow a line of inquiry followed by the interviewee. Semi-structured interviews allow the researcher to use prior knowledge during the interview process (259). Thus, the use of semi-structured interviews allows the researchers to remain mindful of related literature whilst encouraging GPs to expand on their experiences.

The element of discovery is advantageous with semi-structured, open ended interviews. Researchers start with a few assumptions that may be obvious from the literature. However, they do not necessarily know in advance what will turn out to be important and an interview rather than a survey is able to enhance this process (260).

Semi-structured interviews were deemed to be the appropriate methodological choice for this study. The method allowed specific topics related to primary care diagnosis and management, which were defined from the literature to be addressed from GPs' points of view. Additionally, GPs were still able to elaborate on their views and allowed exploration of areas of interest arising spontaneously in interviews.

Whilst unstructured interviews would have been advantageous for providing flexibility for exploring new ground, Chapter 2 highlighted some potential areas worth exploring which was used to develop some research questions. These potential areas highlighted from Chapter 2 would be used as prompts to help the researcher remain focused on the research aims as a novice researcher, and make full use of GPs limited time. On this basis, semi-structured interviews were deemed to be the most appropriate method for data collection.

In terms of the validity of interviewing, it has been highlighted that the interviewer may influence or bias responses obtained from interviews (261). The researcher's aim is to avoid imposing their views and assumptions on the respondents. In terms of this study, the researcher's questions were intentially kept to a minimum to avoid limiting GPs' experiences or views. GPs were therefore seen as the experiental expert on the the phenomemon and were given maximum opportunity to verbalise their views.

Types of interviews

Face-to-face interviews are a common method for data collection within qualitative research. However, when participants are located at a distance from the researcher and are known for their busy schedule, face-to-face interviews can become expensive and time-consuming. To overcome such barriers and accommodate participants' schedules, telephones are considered to be an increasingly utilised method for data collection (262). Methodological literature has traditionally advised against the use of telephone interviews following concerns of the loss of non-verbal cues that are thought to convey subtle layers of meaning (263). However, research highlights that there is little difference in the resulting data of telephone and face-to-face interviews (264). In fact, an advantage of using telephone interview is that the interview process may feel less emotionally demanding. In contrast to face-to-face interviews, the absence of non-verbal cues means that everything needs to be articulated through verbal communication between the participant and

researcher, thereby potentially providing richer text for analysis (263). However, body language was not necessarily critical to this study, therefore such drawbacks were not viewed as being detrimental to the data collection process. Furthermore, face to face interviews have been particularly superior in terms of asking questions about sensitive issues such as drug and alchohol use (265). Again this is an aspect that did not apply to this study as patient cases were not discussed, and GPs provided their overall view and experience of the topic.

Although the length of telephone interviews is unlikely to be sustainable beyound 20–25 minutes, where as face to face interviews can be much longer (266), it was thought that GP time in consulatations would have not exceeded this timeframe due to their busy schedule. Telephone interviews were chosen for GPs convience due to GPs' high workload. It was thought that GPs can schedule in a time for a telephone interview that suits them and are easy to re-arrange if they are unavailable last minute. Telephone interviews were therefore deemed to be cost-effective, flexible, productive and valid methodological tools for maximising diversity within the sample.

4.3.4. Rationale for thematic analysis

Four different methodologies were considered in the process of designing this study: discursive, interpretative phenomenological analysis (IPA), grounded and thematic analysis. A discursive approach aims to explore identity and how people construct versions of themselves and justify their actions (267). Discourse analysis is thereby more concerned with the functional use of language and does not make inferences about how people feel or think (268). The aims of this study were more related to GPs decision making process in regards to TIA, rather than how GPs interact with patients and their perception of TIA. Therefore, discourse analysis was not the most appropriate methodology to study the research aims. IPA has a primary intent to describe lived experiences through identifying common meanings underlying a given phenomenon (269). The primary goal of IPA researchers is to investigate how individual's make sense of their experiences. This method is aimed at exploring in-depth patterns across a small sample and creating individual stories (270). The aim of this study was to identify themes and common patterns across a large sample. Therefore, a phenomenological approach was not considered as being appropriate for meeting the research aims. By comparison, a unique characteristic of grounded theory is

that of theory development. Grounded theory enables the researcher to move beyond description to a level of understanding of what is happening, and the processes that are occurring (271). It is argued to be the best method of analysis when investigating social events or situations to which people may have to adapt (272), when there is a need to challenge existing theories; or when the research field has relied on other forms of study or inquiry (273). This method however, is less well suited to research when researchers have specific research areas and topics that they wish to explore. It is an inductive approach whereby the theory evolves during the research process as a product of continuous interplay between data collection and analysis (274). Building on from systematic review (Chapter 2), the researcher of this study was starting to explore and be aware of some of the literature, and this study aimed to explore some of the areas highlighted from the systematic review. Therefore, there were existing areas that the researcher desired to explore, but equally the aim was also to look into new patterns in the data that had not been anticipated. In order to achieve this, thematic analysis was deemed to be the most appropriate methodology to meet the research aims.

Thematic analysis (Braun & Clarke, 2006) (275) aims to identify concepts with similar meanings in order to understand the phenomenon under investigation. It is largely used when the researcher is seeking to descriptively summarise an individual's account into thematic categories. Thematic analysis is argued to be the "building block" of any qualitative analysis (275). However, it remains unique in its theoretical flexibility in comparison to IPA or grounded theory, which some may view as being "theoretically bounded" (275).

The process of identifying codes can be deductive; (driven by theory from previous findings in a 'top down' approach) or inductive; (a 'bottom up' approach) where the themes are more grounded in the data. As mentioned earlier, the researcher desired to explore some pre-conceptions on specific questions whilst keeping an open mind to explore new themes and patterns that may be highlighted from the data. Therefore, both deductive and inductive processes were used. A deductive approach was used by outlining an initial coding framework drawing on from broad themes, informed by previous research (Chapter 2), which related to the research questions in this study. Some of the thematic areas under which codes were generated included barriers which influence referrals in primary care, difficulties diagnosing TIA patients, low referral rate issues etc. Inductive analysis then

allowed sub-themes to be generated from the data, in more of a grounded manner, through open coding and adding new themes.

4.3.5. Ethical Approval

The University of Leicester's sponsor green light review process was followed in order to ensure that this study was in line with all the relevant legislation and guidelines. Once sponsor authorisation was confirmed, ethical approval was gained from the University of Leicester ethics committee, Research and Governance (R&D) and HRA approval (Appendix 18). NHS ethics approval was not required since this study was interviewing GPs, rather than interviews with patients.

4.3.6. Participants

A description of the inclusion and exclusion criteria are provided below:

Inclusion criteria

- GPs who have referred to the Leicester TIA clinic
- GPs who are willing and able to give informed consent for participation in the study

Exclusion criteria

- Locums, GPs in training

The reason for excluding GPs in training was because we wanted to collate views on the topic from experienced GPs. The interview would include questions around their use of the ABCD2 score in primary care, referral of suspected TIA patients and also their views on using a diagnostic tool for TIA. It was thought that training GPs would not have the level of experience with diagnosing and managing suspected TIA patients. Additionally, trainee GPs would be debriefed after each session, and the decision to refer or not would be with the trainer. Therefore, they would not be acting autonomously, where as non-training GPs act on their decisions independently. The sampling frame for this study was GPs who had referred to the TIA clinic in the last two months. This restriction was added because GPs who had referred in the past two months would have recent experience of making a referral to the clinic. Therefore, these GPs would be able to answer the interview questions in terms of their recent referral decisions and difficulties with diagnosing a TIA, and may be more

likely to show interest in participating in the study. With this in mind, it was thought that there would be a substantial possibility that locums would be moving around and recruitment was thought to be difficult.

Sample size

Sample size in qualitative research is often determined by the concept of data saturation, defined as the point at which the addition of data does not contribute to the development of categories or no longer identify new points of interest. Thus, participants should be recruited until a sufficient number of points have been identified (259). In this study, sampling and recruitment continued until the analysis was considered to be thorough in terms of achieving data saturation. Saturation was reviewed after 10 interviews and a decision to not extend the recruitment was made.

Sample Selection

Purposive sampling was planned. The systematic review showed that GP age and years in practice did have some influence on GPs' referral decisions. However, there were no other factors e.g. ethnicity and environmental factors which influenced the results. Hence, the sample selection aimed to include a range of the following characteristics:

- Age
- Years in practice
- Size of practice

Consent process

Full informed consent was taken prior to starting the interview by the researcher (the author of this thesis) who had taken part in consent procedures training (Good Clinical Practice GCP1) (Appendix 19). The researcher requested verbal consent from GPs on the day of the interview which was recorded.

The selected GPs were emailed an information sheet (Appendix 20), a consent form (Appendix 21) and a shortened document of the Dawson paper to provide details of a possible diagnostic tool in primary care (Appendix 22).

GPs were advised that they need to respond to the email either stating that they accept or decline to participate in the study. Initially consent by email was proposed because GPs are

known to have a very busy schedule, thus, may not have the time to print and scan a consent form. However, when GPs were not responding via email, the researcher obtained verbal consent over the phone just before the telephone interview (Appendix 23). For each GP, verbal consent was obtained on the recorder, and the transcribed document of the interviews were saved on a password protected computer.

Data protection and patient confidentiality

The chief investigator (CI) (researcher) and principle investigator (PI) (stroke consultant at LRI) ensured that GPs' anonymity was maintained when data was stored. The GP's name and any personal information were not recorded. All documents were stored securely and were only accessible by authorised personnel.

The study complied with the Data Protection Act which requires data to be anonymised as soon as it is practical to do so. No personal identifiable data was asked in the interview and the interview did not commence until the participants had given consent. Also, when GPs were referred by their name on the call it was not recorded.

Each interview was typed into Word and anonymised which were shared only within the research team. The field notes and all copies of audio files, consent email and any other notes were kept securely on a password protected computer. Data files were imported into NVivo project where all transcripts were saved. All files/documents were backed up regularly and only shared within the study team and will be destroyed after 5 years.

4.3.7. Recruitment

The initial aim was to recruit between 15–20 GPs within Leicestershire, as this was considered large enough to gain a broad spread of GPs across different practices.
Three recruitment steps were taken for this study:

1. Email from a stroke consultant

The external validation study carried out at the LRI as part of the thesis (section 3.5) had research governance approval until March 2019. A stroke consultant emailed eligible GPs who were on the clinic database. The contents of the invitation document are outlined below. The email provided contact details of the researcher (university telephone number, address and email) and was countersigned by the stroke consultant (Appendix 24).

A total of 76 GPs who had referred to the TIA clinic within the past two months were emailed. This time frame was chosen because the diagnosis and management process would still be recent, therefore, allow GPs to relate to the latest events.

- 1st set of emails sent out on the 05-04-2017: 28 GPs
- 2nd set of emails sent out on the 21-04-2017: 48 GPs

Unfortunately, this method of recruitment did not provide any responses.

2. Invitation letter

The second option was to send out the invitation document, but in a letter format to the practices around Leicestershire, but this too did not provide any responses.

3. Email sent to practice managers

Practice managers were deemed an alternative point of contact, due to the high level of contact they have with GPs. The details of the practice managers were retrieved from the Research and development lead for the Leicester, and Leicestershire Clinical commissioning groups (CCGs). This included East Leicestershire and Rutland, West Leicestershire and Leicester City.

The research and development lead was able to access the practice managers' details. Therefore, she was requested to send out the invitation email, along with other documents deemed useful to the practice managers', which could be forwarded to the GPs. The researcher developed an email that was sent to the research and development lead who sent the email to the practice managers across 3 CCGs. The email detailed the study and requested GPs to contact the researcher if they wished to participate in the study (Appendix 25). Emails were sent to the following practice managers on the CCG boards:

- 31 practice managers in East Leicestershire and Rutland CCG
- 48 in West Leicestershire CCG
- 59 in Leicester City CCG

Invitation

The invitation briefly stated what the study was about, with a summary of the Dawson score and how it could potentially be used as both a diagnostic and management tool.

The invitation focused on the difficulties of managing and diagnosing TIA patients in primary care, and the problem with the number of over referrals at the TIA clinic. Additionally, emphasising the importance of the study and its relevance to primary and secondary care. GPs were made aware that the researcher was a thesis student and not a clinician. This would potentially encourage GPs to be open with how they felt in regard to the questions being asked.

Details of the interview were provided e.g. telephone interview, duration, reimbursement for the GPs' time and contact details if they were interested in participating. GPs were made aware that it was possible that not everyone who expressed interest would be interviewed. If a high number of GPs were to volunteer, then they would be asked some basic information such as, age, years in practice and size of practice so a diverse sample could be achieved. GPs were made aware that they would be reimbursed £50 (out of the thesis funding) for their time (Appendix 24 and 25).

Non-responders were re-emailed after 2 weeks if the study did not recruit enough participants. The Invitation email can be found in Appendix 25.

4.3.8. Data collection

The researcher of this thesis conducted 10 individual semi-structured interviews between Wednesday 7th June and Wednesday 9th August 2017. All GPs were interviewed individually in order to gain an in-depth exploration of their experiences. Each interview lasted between 25–36 minutes (Table 4.4.1).

Interview procedure

Participants taking part in a semi-structured interview still have a great deal of flexibility as they can respond to questions posed throughout the interview. The method allowed specific topics related to primary care diagnosis and management to be addressed from GPs' points of view. Additionally, GPs were still able to elaborate on their views and allowed new aspects to be formed. A draft topic guide was produced (discussed later) which was then piloted by two part-time GPs working at the University of Leicester.

A pre-draft interview topic guide was developed following the systematic review (Chapter 2), surrounding the challenges GPs faced with diagnosis and management of TIA in primary

care. Areas of interest were identified and several questions were conveyed to initiate a discussion. The initial interview schedule covered five broad areas which related to the research question. These areas included GPs' experience of diagnosing TIA patients and difficulties around this, GP referral, use of the ABCD2 score and the utility of a diagnostic tool in primary care. A copy of the topic guide can be found in Appendix 26.

Pilot interview

The topic guide was piloted with two part time GPs to improve content and flow of the interviews, which resulted in some minor changes to the topic guide. A full description of the suggestions made by both GPs in the pilot interviews, and how the topic guides were amended before the interviews are provided in Appendix 27. Two different approaches were taken to the pilot interviews:

1. Face to face interview with a GP
2. Telephone pilot interview with a GP

The first GP was unable to conduct a telephone interview and suggested a face to face interview instead. This allowed the GP to provide in-depth constructive criticism as there was an opportunity to pause after each section. The telephone pilot interview aimed to replicate the exact setting for the main interviews, and address any difficulties the GP or interviewer may experience.

Both pilot interviews provided an opportunity for the researcher to practise the technique required for a successful interview. For example, the opportunity to familiarise themselves with the questions on the topic guide and steer the interview in a way to bring out the best results possible (276).

With the pilot interviews, it was noted that the interviewer may influence participants' responses. It was necessary that the questions were used flexibly in response to participants' answers. In addition to this, the interviewer is responsible for leading the questions and has a responsibility for the overall structure of the interview (276). The pilot study helped with this as the researcher was able to reflect on the impact of these factors. The GPs' views were extremely helpful because they were able to give constructive criticism regarding the structure of the questions, how the questions were asked and if the topic guide was:

1. Clearly interpreted from GPs' point of view
2. Managed to tackle each aspect of the research question(s)

The topic guide was refined following pilot interviews.

4.3.9. Organising the interview

Once GPs agreed to participate in the main interview study, interviews were arranged on a convenient date and time for them.

Introduction to the interview

Information about the objective of the interview and overall study was reiterated. Confidentiality and anonymity were explained. The GPs were asked if she/he consents to be interviewed and for the interview to be recorded using a voice recorder. The GPs were informed that reimbursement for their time would be provided for.

Topic guide

The study was introduced to the GPs and the aims were stated.

The interviewer modified the interview schedule as the interviews progressed. A copy of how the topic guide evolved is provided in Appendix 28.

Questions did not need to be covered in a particular order, rather, the interview was conducted so that discussion could flow as freely and naturally as possible. If the interviewer felt additional information could be obtained from a particular question, then phrases such as 'can you tell me a little more about that?' 'why do you think that is?' and 'can you give me an example of that?' were used.

The topics covered in the questions are listed below:

1. GPs' experience of diagnosing TIA patients
2. Aspects GPs find difficult in regard to the above
3. Factors influencing referrals
5. The ABCD2 score
6. Strengths and limitations of the use of a diagnostic tool in primary care

Recording and transcripts

All 10 interviews were recorded on an Olympus DS-30 digital audio recorder and stored onto a personal computer. Due to time constraints, the interviews were transcribed by an experienced professional transcriber. Transcriptions allowed for a level of detail sufficient to identify various themes and conduct thematic analysis. Each transcript was read thoroughly whilst listening to the audio recording to check the quality and accuracy of them. This enabled the researcher to remain immersed in the data.

Using NVivo software

NVivo is a computer-assisted qualitative data analysis software (CAQDAS). Whilst CAQDAS takes qualitative analysis further than is possible with manual techniques (277), researchers argue that it may have the potential to transform qualitative analysis into a rigid automated process that neglects the role of human interpretation and reflection (278). However, for this study NVivo was used for organising and storing data, categories and sub-categories. NVivo enabled the researcher to instantly access original data behind each concept with the opportunity to link specific data to the different nodes. Thus, NVivo helped to keep the analysis process systematic, facilitated detailed comparisons within the data and encouraged theme development. Despite using computer software, the researcher continued to ask questions of the data to help make interpretations and decide what to code. This encouraged the researcher to remain close to the data.

4.3.10. Data analysis

The analysis started from the first interview and transcripts was entered into NVivo. Interviews were analysed using thematic analysis. In order to create meaningful patterns, thematic analysis was performed through the process of coding in six phrases, which complied with Braun and Clarke's model of thematic analysis (275):

- Familiarisation with data
- Generating initial codes
- Searching for themes among codes
- Reviewing themes

- Defining and naming themes
- Producing the final report

The specific steps to data analysis are highlighted below:

1. The researcher of this thesis (PB) read each transcript line by line. Word or phrases were highlighted to facilitate the process of "open-coding". Word or phases were highlighted in a different colour and notes were made for each GP response to check for similarities across each GP's answers. Coding checks were provided by the researcher's supervisor Carolyn Tarrant (CT) (Appendix 23 for example transcript with example open-coding). PB and CT discussed the key points highlighted in the transcripts along with aligning the discussion with previous literature found to be important from the systematic review identified in Chapter 2
2. The first step developed an initial coding frame that came from both initial coding of the transcripts, and from questions in studies in the literature. These were used to code the transcripts in Nvivo (Appendix 29 for Nvivo tables of parent and child nodes). Open codes were purely descriptive at this stage. For example, all GPs had similar definitions for TIA and all GPs agreed that distinguishing between a TIA and stroke was important. This process made it easier when coding in Nvivo, since each question had a few points noted from each GP response. Therefore, the points could be easily coded according to the points to generate 'nodes' in Nvivo. This was done for each question for the different topics: diagnosis, management and the utility of a diagnostic tool
   InVivo coding was also used whereby exact quotes from participants were used to label the codes e.g. definition of TIA – 'neurological deficit' 'ischaemic event' and reason for GP referral – 'confirm/refute a diagnosis', 'reassurance' etc (Table 4.3.1). This step encouraged the researcher to ask a range of questions to grasp what was being highlighted from the data. This included asking questions that were sensitising to the data for example, "what is going on here?", "what is the relationship between these categories?" This was particularly important to understand GPs' thought process and decisions around the diagnosis and management of the condition. For example, Chapter 2 highlighted that GPs tended to over-refer but there was a lack of understanding as to why this was the case. However, Table 4.3.1 outlines that there are various aspects that contribute to this such as, GPs seeking reassurance and value the investigations due to

the challenging nature of the condition and this may also contribute to their thinking on referring to confirm or refute a diagnosis.

Table 4.3.1: Example Nvivo parent and child nodes

Name	Sources	References
Definition of TIA		
Neurological deficit	4	5
Less than 24 hours	6	6
Ischaemic event	2	2
What are GPs referring for		
Reassurance	3	4
Investigations	3	4
Differs with patient	2	2
Diagnosis (confirm, refute)	2	2

3. Mind maps were developed to bring the themes together for interpretation and synthesis. A mind map was developed for each of the main topics (diagnosis, management and use of a diagnostic score in primary care) (Appendix 30). Salient themes throughout the transcripts were grouped together to form categories. This stage also involved re-visiting the data for evidence to further develop the categories and then identifying the core theme that tied all the categories together. It was a process of going forward and backwards between the mind maps and the coded data and then discuss with the supervisors (CT and AW) to define the themes. The constant comparison method was used to identify similarities and differences between the coded text within each batch of transcript data when grouping them into themes. For example, when GPs were asked if there were particular groups they found harder and easier to diagnose as suspected TIA, there was an even split between the categories easier versus harder for co-morbidities. The mind maps allowed a visual representation of the data and allowed the researcher to work with the concepts rather than details of the data. This process was helpful for considering the nature being relationships amongst the categories and sub-categories
4. This final stage included writing descriptions of the themes. It involved writing narratives for the different themes by reviewing the data and reflecting back to the coded data to highlight which aspects fell under which broad themes and whether they ‘fit’ in the

themes outlined. Throughout this and the rest of the process, the researcher was mindful of the data that did not fit the developing concepts. This enabled the researcher to maximise the dimensions of categories, and offer alternative explanations for particular patterns in the data. TIA is a challenging condition and the risk of missing a TIA can have a detrimental impact to the patient. Based on this, it is evident that GPs feel a huge sense of responsibility towards the correct management for these patients. Therefore, the researcher also focused on the GPs' emotional responses such as 'anxiety' 'frustration' 'pressure' etc as this helped to consider the potential meanings behind what was being discussed

Trustworthiness

Trustworthiness is one way researchers can persuade themselves and readers that their research findings are worthy of attention (279). Although thematic analysis as documented by Braun and Clarke, (2006) (275) has been presented here as a linear, six-phased method (section 4.3.10), it is actually an iterative and reflective process that develops over time and involves a constant moving back and forward between phases. In order to ensure the findings were an accurate representation of GP responses, it was a process of consistently looking back at the data for examples that did not fit. This involves highlighting all the statements, for example eight GPs agreed to the usefulness of a diagnostic tool in primary care; however, two GPs outlined a different view. It involved not making assumptions based on the majority of the GPs views, and questioning the interpretations. The researcher consistently questioned "is this the case for every GP" because every individual has a different view and the researcher attempted to account for this. Peer debriefing has been recommended to provide an external check on the research process. This process may increase credibility which refers to the fit between respondents' views and the researcher's representation of them (280). This process also enhances confirmability which is concerned with establishing that the researcher's interpretations and findings are clearly derived from the data requiring the researcher to demonstrate how conclusions and interpretations have been reached. A debrief between the researcher and the supervisors (CT, AW) was carried out for each of the stages of analysis. This also included consistently reflecting between the raw data and the description of the results. The reasons for theoretical, methodological and

analytical choices throughout the study was also highlighted to help others understand how and why decisions were made.

4.4. Results

The themes identified from the thematic analysis will be described with sections split into diagnosis, referrals, ABCD2 score, a diagnostic tool for primary care and thresholds for referrals. The chapter will further outline a summary of the findings including the strengths and weaknesses of this study. It is important to note that in this section, the write up of themes represented descriptions of the overall data generated through the analysis process (section 4.3.10); however, in the accepted publication in Family Practice (Appendix 17), the themes were refined further to emphasise the most clinically relevant themes.

The data was collected between June 2017 and end of August 2017. See Table 4.4.1 for interview details including the date, time and duration of the telephone interviews.

A total of 10 GPs volunteered to be interviewed, of which GPs 7, 8, and 9 and GPs 3, 5, and 6 were from the same practice. Due to the low response rate, GPs could not be purposively sampled, but the sample is reasonably diverse in terms of gender, size and locality of practice. Of the sample of 10, 4 were female and the majority worked in Leicester City.

Participating GPs were relatively experienced, with the majority having 6-11 years' experience of working in general practice (Table 4.4.2 for interviewee characteristics).

Table 4.4.1: GP interview details

GP	Date of telephone interview	Time	Duration
1	Wednesday 7th June 2017	11:00	29.56
2	Thursday 8th June 2017	09:00	34.22
3	Wednesday 14th June 2017	15:30	31.23
4	Friday 16th June 2017	14:30	24.13
5	Tuesday 20th June 2017	13:00	32.05
6	Wednesday 21st June 2017	14:00	30.00
7	Friday 28th July 2017	10:30	35.15
8	Tuesday 1st August 2017	14:00	26.01
9	Thursday 3rd August 2017	09:00	29.22
10	Wednesday 9th August 2017	14:00	30.50

Table 4.4.2: Interviewee characteristics

GP	Gender	Years in practice	Size of practice (Approx.)	Practice location	Practice
1	Male	6	6,000	(East Leicestershire and Rutland CCG)	Other
2	Male	11	10,000	(East Leicestershire and Rutland CCG)	
3	Male	2	3,500	Leicester city	Practice 1
4	Male	3	6,000	(East Leicestershire and Rutland CCG)	Other
5	Male	11	3,500	Leicester city	Practice 1
6	Female	11	3,500	Leicester city	Practice 1
7	Male	11	7,000	Leicester city	Practice 2
8	Female	11	7,000	Leicester city	
9	Female	7	7,000	Leicester city	
10	Female	11	9,000	Leicester city	Other

The themes highlighted below have been split into sections in order to facilitate ease of reading. The sections include diagnosis decisions followed by the themes that apply to this heading, followed by referral decisions, use of a scoring system and a diagnostic tool for TIA in primary care.

Prior to detailing the 8 themes identified from the GP interviews, the number of themes and associated heading titles are listed below in Table 4.4.3.

Table 4.4.3: Themes identified from GP interviews

Theme 1:	Suspecting a TIA, diagnosis and presenting symptoms
Theme 2:	TIAs and Stroke
Theme 3:	Referral decisions in the face of uncertainty
Theme 4:	Referral as a way of managing risk
Theme 5:	Referral decisions – disposal and gaming the system
Theme 6:	The role of the ABCD2 score in decision-making
Theme 7:	GPs' views of using a diagnostic tool for TIA
Theme 8	Thresholds for referrals

4.4.1. Section 1 – Diagnosis decisions

This section refers to GP diagnostic decisions. Under this heading two themes have been outlined which are suspecting a TIA, diagnosis and presenting symptoms (Theme 1), and TIAs and stroke (Theme 2).

1. Suspecting a TIA, diagnosis and presenting symptoms

The diagnosis of a TIA can be difficult depending on the presenting symptoms, as well as the GPs' experience and their ability to correctly suspect and diagnose a TIA. Generally, GPs found it difficult to answer how many patients they saw each year that they suspected as experiencing a TIA and suggested varied estimates; (2, 4-5, 10, 12-24, and 25-50).

GPs suggested that the number of suspected TIAs depended on various factors, for example, whether the GP was part time or full time, the size of practice and the population of the practice.

> *"I work part time in general practice so I only do five sessions a week so a colleague who was doing nine sessions a week would probably be sending more patients in I guess" (GP 7)*

> *"I suppose it depends on your practice size; it depends on the population of the practice" (GP 6)*

When asked for a definition of a TIA, the majority of GPs in the sample were able to describe presenting symptoms that caused them to suspect that the patients had experienced a TIA. A key criterion for them in suspecting TIA as opposed to stroke, was that the symptoms of a TIA resolved within 24 hours. However, one GP was unaware of how long the symptoms should last and was unable to answer.

> *"A focal loss of either muscle power or speech or – but that's to do with the muscle power – that is reversible, that reverses itself, and you're going to ask me within what time frame, but I don't know"* (GP 10)

For GPs the knowledge of the duration of symptoms lasting less than the 24-hour limit was the key criterion for the diagnosis of a TIA. This provided a sense of diagnostic confidence for a condition associated with few objective clinical or diagnostic findings.

GPs were more confident with the diagnosis of TIA in the presence of what they referred to as 'classical symptoms' e.g. leg, arm, face weakness, speech abnormalities and vision

impairment. These more obvious symptoms appeared to give GPs the confidence in their ability to diagnose a TIA. In contrast, the absence of these led GPs to consider existing conditions as the cause rather than a TIA.

A complication arose when GPs observed a patient as presenting with classical symptoms. GPs reflected on their previous experience of similar patients who turned out not to have a TIA, and therefore questioned the existence of a TIA. This uncertainty was elevated when the GPs had a number of previous experiences in which the symptoms were the result of different causes.

> *"I think the more supportive of the TIA would be just transient facial sort weakness or the sort of classical, curtain across the eye, any sort of transient weakness of the arm or leg, associated with tingling. So, I think, classical symptoms are those, more helpful in making the diagnosis"* (GP 6)

> *It's very difficult sometimes just to say that looks like a neurological event that's causing it and not something else masking it"* (GP 4)

> *I've had people with sensory symptoms i.e. they've had tingling and numbness in their right arm, right leg and headache. I have referred them to a TIA clinic on many occasions and the diagnosis comes back as migraine, and they've never had a migraine before"* (GP2)

When GPs saw patients with pre-existing risk factors such as diabetes, hypertension, high BMI etc. their threshold for suspecting TIA was lower. The risk factors made it more likely that the patients' symptoms could be a warning to developing a TIA. Therefore, GPs' suspicion in those groups was significantly higher.

> *"I've been more clinically aware if someone had sort of risk factors, so diabetes, hypertension, chronic smoker, over the age of 40. If they have high BMI, high cholesterol. So if there are other risk factors established or even previous sort of cardiac history, then having, you know, a higher index of suspicion and older population"* (GP 6)

Patients who were not seen as typical candidates for a TIA, for example, those of a younger age group, presented GPs with greater difficulties in making a confident judgement as to whether they had a TIA.

> *"Younger patient present with more of a diagnostic dilemma, because it's less likely for that group of patients to have TIA"* (GP 3)

> *"The time when I'm less certain is if you're faced with a very young person, say somebody in their 40s or 50s, because you think well they're not really in the right age group, but the symptoms really sound like a TIA, and perhaps you think well it's probably more like a migraine or something, but equally the*

history is very suggestive and just because they're young doesn't mean to say they can't have a TIA. So I guess that kind of leads to a little bit more uncertainty" (GP 8)

Increased uncertainty was also a feature of GP accounts of diagnosing patients with pre-existing neurological conditions, or those who had experienced previous strokes. When deciding whether the new symptoms were a new event or simply an exacerbation or deterioration in their existing condition, GPs found this to be challenging.

"People who have had previous strokes are always difficult because their symptoms can vary in intensity and deciding if a deterioration is actually a new vascular event can be difficult" (GP 1)

"I think the biggest challenge is in patients who have had a previous stroke where an intercurrent illness can kind of cause a re-emergence or a recurrence of some of their previous symptoms. So distinguishing a previous stroke that is kind of becoming manifest because of another intercurrent illness, especially in older and frailer person, you know, is I think quite difficult" (GP 7)

A significant finding was that GPs had more diagnostic difficulty when patients presented with just visual and sensory, or non-specific symptoms. As previously mentioned, the absence of classical symptoms led to uncertainty in diagnosis. In addition to this, there was a reliance on the patients' ability to articulate their symptoms and histories in a way that would have allowed a GP to associate them with the clinical definitions of a classical TIA.

The articulation of symptoms can be further hampered by language difficulties which may make it harder for the patient to be able to accurately describe the event, and for GPs to fully understand.

"Patients don't say 'oh I've got weakness in my arm and leg, my face dropped and my speech went a bit slurred for half an hour and it came back' they don't say that they say 'I felt funny in my arm or leg' or they have sensory symptoms of tingling and numbness in the right side of their body or left side of their body, based somewhere, base for different patients and also they complain of a different symptom side, they feel strange in themselves or they've got a headache. The history is very subjective and difficult to sort of peel out really. [Also] diagnosing a patient as suspected TIA is difficult in patients who has language difficulties- say people who English is not their first language"(GP 2)

"Somebody may have poor memory, sort of, not just a functional poor memory but actually someone who has dementia, communication difficulties, history retrieving difficulties, if that's an expression would make it difficult. [Also] somebody who yeah, say who was unable to give you a great history, whether that be just they're not very good at articulating what they are trying to tell you or they just have a bit of a vague memory of the event, or they haven't actually thought about it at the time, how long it lasted "Oh I'm not sure" (GP 10)

GPs described how patients often presented with vague and non-classical symptoms, for which TIA was one possible underlying cause. The challenge for GPs was to consider the likelihood of different underlying causes and to make a judgement about whether the possibility of TIA was high enough to merit a referral. The challenge therefore, was about working with levels of uncertainty caused by the lack of clarity of the presenting symptoms.

> *"There's a whole host of vague neurological symptoms that people present with that are not necessarily anything to do with a TIA that's a difficulty"* (GP 1)

> *"Vague can be perhaps just feeling dizzy. And we get a lot of patients where they just come in and say they just felt a bit dizzy, a bit light headed. And so then it's – you know, that can be quite challenging, because there can be so many different causes for that"* (GP 6)

Alongside patient characteristics and features of the patients' presenting symptoms, there were various practical factors surrounding the initial presentation that impacted on diagnosis. These included the availability of services and time pressure as a GP.

> *"Sometimes if you're running a busy clinic and you have somebody who comes in with a potential TIA those patients require more time than others because you've got to do a full neurological examination, then you've got to do a cardiovascular examination, make a decision based on the ABCD2 score and then refer them into hospital. So for me it's more the time pressures that make a diagnosis more challenging rather than the actual diagnosis of a TIA, because generally speaking the diagnosis of a TIA tends to be clear cut in terms of whether there's a possibility of them having one or not"* (GP 3)

2. TIAs and Stroke

Majority of the GPs recognised that stroke and TIA were managed differently and distinguishing between the two in a speedy manner, as well as taking the next course of action as fast as possible was essential, especially for stroke. GPs also argued for the importance of diagnosing TIAs as an opportunity for prevention. Diagnosing a TIA could enable action to be taken which would reduce the patients' subsequent risk of stroke. This therefore, enhanced an awareness of the value of preventative action and increased the importance that GPs placed on diagnosing a TIA.

> *"The management of the conditions are different and distinct in many ways and if we're going to get the best outcome for our patients, we need to be able to be quite clear in the diagnostic ability of both these conditions"* (GP 4)

"It gives the opportunity of instituting some forms of treatment at an earlier state, also carrying out other types of risk assessment, whether its measurements of blood pressure and cholesterol, triglyceride levels and other risk factors relative to the patient such as smoking and so those type of factors" (GP 5)

"One is a prodromal marker for something that can subsequently happen, which can lead to quite a degree of disability, rehabilitation and potential mortality. And the other obviously is the condition that we're trying to prevent, a full blow stroke from happening" (GP 4)

4.4.2. Section 2 – Referral decisions

Three themes have been outlined that relate to referral decisions. These include referral decisions in the face of uncertainty (Theme 3), referral as a way of managing risk (Theme 4) and referral decisions – disposal and gaming the system (Theme 5).

3. Referral decisions in the face of uncertainty

GPs suggested that an important reason for their referrals was to either confirm or refute the diagnosis. If a GP suspected a TIA was a possibility but was uncertain, they saw referral as a way of reducing uncertainty. They particularly valued referral to the TIA clinic to 'rule out' a TIA as an underlying cause of the patient's symptoms. As such, a referral was a way for the GPs to manage the fear of missing a diagnosis, through objective testing that could exclude TIA as a diagnosis. If the GP had a high level of suspicion that the patient had a TIA, they wanted confirmation of the diagnosis, through the investigations which TIA clinics delivered to provide more certainty.

"Clinics base that decision making on all those investigations, so I'm generally referring to confirm or refute a diagnosis" (GP 3)

"When you're referring to a TIA clinic this will be obviously specialists who are seeing TIAs constantly, one after another. So, in order to select somebody who is not a TIA at that time or is less likely to warrant a diagnosis of TIA would be, obviously easier made actually in a TIA clinic than it would be in General Practice. That combined with the availability of investigations which obviously leads to an exclusion of the TIA" (GP 5)

"On a personal level, probably because I refer things in that probably aren't TIAs but just for a confirmation. I guess there is a need for more education in what should and shouldn't be sent in, what is or isn't defined as a TIA or could be most likely a TIA, what symptoms and things are more likely, be confirmed as TIA" (GP 10)

The uncertainty caused by vague symptoms led to various challenges to managing a suspected TIA patient. Many patients "don't quite fit" and GPs must decide on their own threshold for referral which may be quite low, particularly if they are concerned to rule out a TIA. GPs suggested their threshold for referring would be lower if the patient had risk factors for stroke (e.g. diabetic, hypertensive patient, history of heart disease), even if the symptoms were less classical.

> *"It would apply to certain groups of patients where there is sudden onset of unsteadiness or potentially a fall which is a much more vague symptom. But again, if it's out of keeping with that patient you look for the underlying cause of that, one of which could have been a TIA"* (GP 5)

> *"It is based on probabilistic grounds that they've got risk factors and it is maybe something that needs to be ruled out"* (GP 7)

Seeking certainty was important both in terms of ruling in a TIA, as well as ruling one out. GPs were reluctant to start treatment before the diagnosis had been confirmed. The referral (and the confirmation of diagnosis that could be provided by tests done in the TIA clinic) provided them with the reassurance that they would be providing the correct treatment.

> *"If it hasn't been diagnosed before it makes it a bit harder really to prescribe"* (GP 2)

> *If I'm unsure if it's a TIA and I would like some assurance on the diagnostic possibility of this then I tend to hold back from prescription"* (GP 4)

It was evident from GP accounts that they were conscious of the balance between over and under referring. There was a discussion in the interviews around the proportion of referrals that were done for reassurance versus the confident TIA referrals.

> *"It's that initial deciding, could this be a TIA, you know how sure am I? How sure am I that it's not a TIA? That's where the difficulty is. I guess its initially deciding that you're worried about a TIA or maybe even more difficult is "ok I don't think it is but how certain am I that it's not?"* (GP 1)

Amongst GPs there was a clear recognition that there is a large amount of uncertainty surrounding the diagnosis of TIA. This begins with the concern around accurate presentation of symptoms, and is continued in the decisions to refer and/or prescribe medication. It is evident that there was no fixed protocol. The process of diagnosing the TIA was dependent on the GPs' judgement regarding the degree of symptoms, risk factors, past medical history, vague symptoms, detail of symptoms and initial presentation in consultation.

4. Referral as a way of managing risk

GPs' referrals can be considered as a strategy to manage risk, and this could be a reason for the high number of referrals at the clinic. GPs in the sample described a sense of personal and professional duty towards their patient due to the consequences a TIA can have on the patient. Additionally, referrals are a way GPs manage their level of awareness and anxiety about missing a TIA, which is strongly emphasised to them via professional education. Increased public expectations (through recent public awareness campaigns), and GP concerns about litigation also contributed to their method of managing referrals.

> *"Understanding that people who are referring in to the TIA clinic potentially are under a degree of pressure themselves and that they may have some anxieties themselves about missing something important like a TIA which, you know people get a lot of teaching on TIA and so that perhaps increases their level of anxiety and sort of changes their index of suspicion"* (GP 7)

> *"I think there is a medical legal factor as well, not to miss things, because if that person goes on to have a stroke because you've made a wrong diagnosis, you'd be worried about defensible your decision would be. So that becomes part of your decision-making process"* (GP 8)

When asked about the fact that 50% of referrals to the clinic are not diagnosed as stroke/TIA, GPs suggested this was partly due to the difficulty of diagnosing TIA with any certainty in the context of primary care, without conclusive diagnostic tests. GPs also suggested that it was important to have a high index of suspicion. For them, the risk of missing a TIA was greater than their concern about over-referral, and false positives were seen as a price they were willing to accept, to avoid missing TIAs.

> *"Maybe GPs aren't very good at making that difference without a diagnostic test"* (GP 6)

> *"It's always that thing of sensitivity versus specificity, because if every patient the GP referred to the clinic has had a TIA it would imply that GPs are not referring enough patients to the clinic. You would expect some false negatives in the mix because you're wanting to capture the TIA so you have to set the net a little wider. The wider you set the net, the more negatives you will get"* (GP 7)

GPs consistently reported that they would refer patients for reassurance for themselves as well as any clinical utility of the investigations which TIA clinics deliver. Additionally, GPs felt that the investigations provided to the patients because of making a referral, even if it did not lead to a diagnosis of TIA, could highlight risk factors that provided GPs with more of a lever to work with patients on their lifestyle choices.

> *"There is definitely an element of reassurance, because from our point of view in general practice, because we're seeing the patients actually, again we don't really want to miss the opportunity to actually take some preventative action for a patient with a TIA because the next time we might see them could be when they've actually had a stroke, which potentially we could have done something to prevent that"* (GP 5)

> *"If it excludes it then they're investigated but they're found to have some evidence that they may- that they are at risk, then that's again equally important because then they've got a sort of ammunition to support lifestyle changes. And prevention"* (GP 6)

Additionally, GPs suggested that this desire to use testing for reassurance was common across medicine, not just in relation to TIA clinics, and that this general tendency was a factor in explaining the high number of referrals to TIA clinics.

> *"Whenever you put a pathway together, right, and you make it easy for clinicians to refer in to that pathway then you're always going to find that the number of patients that you see will grow exponentially? Of which this is no different from my chest pain clinic that we used to run or a potential AF clinic. We found that the vast majority of patients didn't need to be there-, because and most of that is due to the clinician on the ground seeking reassurance about their own diagnostic ability. And that isn't anything new in medicine"* (GP 4)

5. Referral decisions – disposal and gaming the system

The TIA rapid access clinics were seen as an easy route for GPs to send their patients to. The fact that the clinics were easily and speedily available was a 'double-edged sword'. It meant that GPs could quickly resolve uncertainties about TIAs and move treatment forward. However, this ease of accessibility left the clinics open to over-use and misuse as defined by the GP themselves.

GPs suggested that TIA clinic referrals could potentially be used as a way of 'disposing' of patients (281). Overuse of TIA clinics could occur when doctors chose to refer to the clinic, even when they felt that the probability of TIA was remote, as a way of gaining access to quick investigations. One GP referred to this as the 'gaming technique' and stated that unfortunately *"that's one of the dark secrets of general practice"* (GP 7)

> *"The TIA clinic is so accessible, it becomes an easy place to send people who have that kind of softer symptoms that aren't classic TIA. It's a way of getting for example an MRI scan of the head or some investigations done quicker than you could get them done through a medical or neurological outpatient clinic. [Also], if you've got someone whose symptoms could potentially but deep down we know not really be likely to be a TIA, then*

you know that if you refer them to the TIA clinic then they'll get a decent work up and even if the diagnosis *that's reached isn't TIA, you know that they'll have some investigations and you know at least the ball will be rolling for the patient in terms of working out what's going on"* (GP 7)

4.4.3. Section 3 – The use of a scoring system

One theme applies to the use of a scoring system which is the role of the ABCD2 score in decision-making (Theme 6).

6. The role of the ABCD2 score in decision-making

GPs routinely use the ABCD2 score which is a risk stratification tool and stands for age, blood pressure, clinical features, duration of TIA and diabetes. The ABCD2 score is not a diagnostic tool, rather it is a score which was developed to enable the TIA clinic to prioritise referrals.

The questions around the score aimed to explore to what extent GPs found the score useful. Majority of the GPs viewed the ABCD2 score as a referral decision-making tool, and was primarily used to decide the *urgency* of the referral once the decision to refer had been made, rather than as part of the decision-making process around *whether or not* to refer.

The score gave GPs the evidence whether the patient was high-risk or low-risk and how soon they should be seen at the clinic. GPs reported finding the ABCD2 score useful as a decision support tool to aid with referral choices. It provided GPs with confirmation about the pathway for action in individuals who they had already decided to refer as a suspected TIA.

> *"The ABCD2 score is more useful in triaging the ones I already suspect [Also] I think it's helpful in identifying the people with TIAs that need more urgent assessment"* (GP 1)

> *"So it helps me to think about whether I need to be admitting the patient or not, without which it's a grey area, so at least you've got a guideline to help you make that decision"* (GP 3)

GPs perceived the ABCD2 as a useful score for prioritising the referrals appropriately. The score enhanced GPs' confidence about the decision to refer each time they made that decision. The score was a guideline used for reassurance that their decision mirrored with the result from the score, and to decide the urgency of the patient being seen in clinic. Importantly, the score legitimised the GPs' decision and facilitated speedy access to secondary care as it provided objective evidence of the need for fast access.

"The ABCD2 score gives you some reassurance that if a patient has a low score then less likely to have a crescendo situation, and if they've got a higher score then they are going to be seen more quickly in secondary care" (GP 7)

In relation to its role in supporting decisions around prioritising referrals, the score was also seen as supplementing, rather than guiding clinical judgement.

"GPs already have a good idea which category patients will fall into, so it's more of an additional aid" (GP 5)

"It is the combination of a score and consultation that would be useful for diagnosis, not just the score" (GP 5)

4.4.4. Section 4 – A diagnostic tool for TIA in primary care

This section refers to a diagnostic tool for TIA in primary care. Under this heading two themes have been outlined which are GPs' views of using a diagnostic tool for TIA (Theme 7) and thresholds for referrals (Theme 8).

7. GPs' views of using a diagnostic tool for TIA

There is currently no tool in primary care for the diagnosis of a TIA. Therefore, the questions around this section was to explore whether a tool for diagnosis would be helpful for GPs, whilst outlining some of the strengths and limitations of a diagnostic tool.

There are significant implications of a TIA diagnosis, such as future cardiovascular risk, medications patients would have to take, implications to their lifestyle etc. According to GPs' views, there is often significant uncertainty around the diagnosis of a TIA and the decision around whether to admit or refer a patient. Although GPs value their clinical judgement and experience, a consistent view across most GPs was that unlike the ABCD2 which was used to decide the urgency of the referrals, a diagnostic tool would have value in providing objective evidence to justify their decision about the diagnosis. Making GPs feel more confident in their decision, and providing confirmation.

"So sometimes if our diagnosis of a TIA solidified with an evidence based tool like a score which is known to increase the diagnostic predictability of a TIA then you can diagnose with a degree of certainty as opposed to ambiguity. Ultimately it's the clinical decision but something like that could be used to help solidify and consolidate that decision to use it" (GP 3)

> *"You want to just have a bit more evidence to support what your, the conclusion you're coming to. And there are some conditions where actually using a tool gives you a little bit more certainty"* (GP 8)

GPs felt a diagnostic tool would have particular value in confirming their judgement when a patient is low-risk, and legitimising decisions not to follow a TIA pathway.

> *"I guess for people who are very, very risk averse, and dealing with symptoms that are not classical, it might reassure them that not referring is OK"* (GP 1)

> *"Yeah, I think with non-referrals there probably would be some benefit in that actually because I expect if you, again, I think it's like everything else that we do, you have to look at the medical/legal aspect of it as well. So if there's a scoring system, because again, the safety element of referring patients or not referring patients, if you had a score and you've gone through an assessment, it probably does give you that"* (GP 5)

However, two of the GPs in the sample considered their clinical judgment alone to be sufficient:

> "*I place much more emphasis on my clinical ability to diagnose something rather than a score that'll help me diagnose*" (GP 4)

There were some practical concerns with using a TIA diagnostic tool in primary care, for example, filling out a form is time consuming and GPs are under time constraints. Also, a risk of a tool being superfluous and just adding to bureaucracy. However, the main concern was that a tool lacked the ability to consider patients' individual symptom presentations. This included anxiety and mental health issues, which may impact on the presenting symptoms. Therefore, GPs were concerned that the tool might not be an accurate representation as it could not consider all impacting variables.

> *"There is that risk of a small number of patients being disadvantaged who present with very atypical symptoms, not to sort of being excluded really"* (GP 2)

> *"I think it impairs clinical judgement, I don't think it adds to it, because I think again, with any particular symptom, so somebody might feel that their leg feels a bit weak actually just because they're anxious or they have been doing something that particular day. You can't account for variables within a patients presentation and I think these sort of tools don't take account of that"* (GP 5)

It is evident that some GPs would not be willing to take the risk of under-diagnosing or missing a TIA even after using a tool alongside their clinical judgement. Nevertheless, besides this, GPs pointed out the practicalities of using a diagnostic tool in primary care. For example, a tool would help with clinicians' time constraints as the tool could be used to

focus their mind on specific symptoms and signs. Also, it would reduce unnecessary referrals, investigations and possibly reduce patient distress.

Most GPs in the sample were positive about a diagnostic tool, proposing that using a diagnostic tool would strengthen the decision-making process about the best course of action for the patient. This included the decision-making about referral, and by adding the tool to clinical judgement, it would add value to not just diagnosis but management of suspected TIA patients. Additionally, if the tool suggested the patient was low-risk then GPs were more likely to re-evaluate the patient by asking for a more detailed history and evaluating if any other factors could explain the patients' symptoms.

It was proposed that those GPs who refer to have their patients seen quickly, then using a diagnostic may help them re-evaluate the patient and may challenge the GPs on their view on 'gaming';

> *"I'm referring really because I don't think it's a TIA but there's nowhere else to send the patient"* (GP 7)

A tool was proposed to be particularly useful for doctors who are less experienced and new to primary care as they may be less confident in managing TIAs in comparison to the more experienced doctors. A diagnostic tool was therefore seen as having the potential to increase their assurance to manage a suspected TIA patient.

> *"I think it might be helpful especially to less experienced doctors, so people coming into, who are new to Primary Care or maybe doctors who are a little bit less confident in sort of managing TIAs"* (GP 7)

It seems evident throughout the interviews that GPs would rather over-refer than to not refer a patient. This can be explained due to that feeling of uncertainty, which was proposed by every GP, and an objective diagnostic tool could eliminate or reduce that uncertainty. Furthermore, a diagnostic tool may reassure GPs, by potentially increasing diagnostic accuracy whilst reducing inappropriate referrals. Although there were some weaknesses of a diagnostic tool in primary care (discussed earlier), there was a clear consensus that a diagnostic tool would be helpful.

8. Thresholds for referrals

A final key issue discussed with GPs was the potential utility of providing cut-off points for referral based on a diagnostic score of 'likelihood' for TIA, presented as percentage likelihood. The choice of cut-off points relates to false positives and negatives of a TIA, so there are important implications of setting lower or higher thresholds. The thresholds therefore could be used as guidelines as to when to refer; hard thresholds take some of the responsibility for making the decision away from the GP and provides them with certainty and protection from legal challenge. GPs still felt that tool results would have to be used in conjunction with clinical judgement, which suggests that uncertainty was still present.

When GPs were asked about appropriate thresholds as a cut-off point to recommend definitely referring a patient, ambiguity again was present. GPs found it difficult to suggest a specific threshold they thought would be useful and responses varied. Figures suggested were; 5–10%, 20–50%, 1 in 3, and in one case, even less that 10% risk was felt to merit referral.

> *"Particularly if your basing it on the scoring system I think it's got to be slightly low, it's got to be- there's only 1 in 10 chance that it's a TIA then it might sway your decision"* (GP 5)

> *"I think lower than 10%- I'd feel quite uncomfortable because of the seriousness of that 10% so you're dealing with the low probability devastating event and the TIA itself obviously isn't devastating, but that translates into a significant risk of a permanent stroke down the line. So I think we've got to bear in mind that it's a low probability but of a devastating event and that's got to factor into judgement"* (GP 7)

A similar view to GP 7 was also suggested by GP 3 who believed that a patient with a 10% chance risk of a TIA should still be referred. This GP felt that if there was any suspicion of a TIA, then a referral would be made and the threshold would not affect this decision.

> *"If someone said to me a patients got a ten percent chance risk of a TIA then I think they should be investigated. That's one in ten chance and that's significant in my opinion [Also], the less than ten percent chance of a TIA is not sufficient for me not to investigate further, just because of the morbidity and mortality risk increases with positive diagnosis of TIA and you could under-diagnose TIA"* (GP 3)

When GPs were asked what threshold they would find useful as a guide as to when *not to refer*, some were happy to suggest a threshold; these included "10% or less" and other values included less than 2–5%, 1 in 100. One GP was uncertain of a value.

Clinical judgement was important and GPs acknowledged that they would need to account for individual patient history and presenting symptoms which would influence how happy they would be not to refer at 10% risk. In particular they would be happier not to refer if they were reasonably confident in an alternative diagnosis.

> *"Oh gosh that's a really difficult one. My personal view is that you probably need to set the bar quite low, you know, so I would be looking for- I would want higher sensitivity and that probably means lower specificity. So I think I'd be uncomfortable potentially certainly with anything above a sort of 10 to possibly 20% chance of symptoms in front of me being a TIA"* (GP 7)

> *"If there is a risk but its low and actually you've got your other diagnosis that you think is more likely then again you might come to a different decision about whether to refer or not. Whereas if it's the only thing you think that's happening but the score is [similarly] low then yeah you might be more likely to refer because you haven't got another idea of what is going on"* (GP 9)

When asked if a tool would be more useful in ruling out a diagnosis of TIA or ruling in, the answers varied with some proposing their views on ruling out, whilst others on ruling in. However, overall felt that they would maintain a low threshold for referral.

> *"I think I'd like to rule it out more, because if you're clear on who you're ruling out, then you know that the people that you are referring are more likely to have it. So, you want to be, you know very clear that you're ruling out those individuals where there's no risk, because you know, I would rather not commit anything and being over suspicious is probably better than being not suspicious at all"* (GP 6)

4.5. Discussion

Summary of the findings

This chapter explored the issues GPs face with the diagnosis and management of TIA and the utility of a diagnostic tool in primary care. A consistent theme identified from the thematic analysis was GPs' uncertainty around diagnosis and management. GPs reported that TIA was more likely to be suspected when patients were more obvious candidates for TIA (based on patient characteristics, past history and patient symptoms). Furthermore, GP referrals fell into four categories: 1. The GP was sure it is a TIA, but referred for confirmation, 2. The GP thinks it is a TIA but there is uncertainty. 3. The GP thinks TIA is unlikely but wants to exclude it, and is a way to seek reassurance and 4. The GP does not consider a TIA a realistic diagnosis, but wants to dispose of the patient. GPs felt that a diagnostic tool had the potential to improve the decision-making process and enhance GPs' confidence, particularly to rule out a TIA. In terms of a threshold GPs would feel comfortable to not refer suspected TIA patients, most suggested a threshold of 5% risk of TIA and lower to not refer, and a minority proposed a 10% or lower threshold.

4.5.1. Implications of the findings in the context of previous research

Overall, eight themes emerged from the semi-structured interviews exploring GPs' experiences on the diagnosis and management of TIAs and views on the utility of a diagnostic tool for TIA in primary care.

The theme of uncertainty was a key finding (thematic heading 3) (4.4.2 section 2) and had resonance throughout each of the other themes highlighted in the results section. This supports previous research on the diagnosis and management of TIAs in primary care. Previous research indicated deficiencies in GP knowledge and clinical practice (119, 120, 123, 124, 126, 128). TIA is challenging for GPs, given the heterogeneous presentations and diagnosis entirely based upon history (127, 166, 282). GPs' uncertainties around diagnosis and management, were reported due to the often-vague symptoms that may have numerous different causes but also could be suggestive of TIA (123).

Unsurprisingly, GPs reported that TIA was more likely to be suspected or diagnosed when more 'classical' symptoms were presented and the patient had known risk factors. GPs expressed diagnostic difficulties when symptoms were described as vague and in the absence of risk factors (thematic heading 1) (4.4.1 section 1). This suggests that GPs have an informal scoring assessment which rates the likelihood of diagnosis, depending on the nature of symptoms and the classical risk factors associated with a TIA. Patients who were not seen as typical 'candidates' for a TIA for example younger age groups presented GPs with more difficulty in making a judgement as to whether they had a TIA (thematic heading 1) (4.4.1 section 1). These patients were likely to be suspected as opposed to GPs being confident on the diagnosis of TIA. The challenge for GPs is assessing patients on the basis of their pre-existing characteristics and their presenting symptoms, whether they are a likely candidate for TIA (283). Some groups would be referred when GPs had significant uncertainty as GPs would not want to take the risk, and GPs highlighted that they would refer at times just to exclude diagnoses rather than confirm a diagnosis (thematic heading 4) (4.4.2 section 2). The practitioners' tolerance of uncertainty also influences management decisions (166).

GPs outlined the importance of diagnosing TIAs as an opportunity for prevention (thematic heading 2) (4.4.1 section 1). Diagnosing a TIA could enable action to be taken which would reduce the patients' subsequent risk of stroke. This therefore, enhanced an awareness of the value of preventative action and increased the importance that GPs placed on diagnosing a TIA. However, diagnosis of transient neurological symptoms was challenging (thematic heading 1) (4.4.1 section 1).

Referrals were in part a strategy to manage risk (either confirm a diagnosis or refute) along with an approach to seeking reassurance. GPs also used referrals as a strategy to get quick access to tests (thematic heading 3) (4.4.2 section 2). The TIA clinic was proposed as an 'easy' route for GPs and perhaps seen as the quicker solution to getting the investigations, even if that means sending patients who are less likely to have experienced a TIA, or those with less classical symptoms (thematic heading 5) (4.4.2 section 2). Results also suggested GPs' tendency to refer cases where TIA was thought unlikely which was partly driven by practicing defensively (thematic heading 4). This may include performing unnecessary diagnostic tests and invasive procedures, prescribing unnecessary treatment and needless

hospitalisation. The literature raises concerns about how healthcare professionals can get drawn into practising in ways that are influenced by a desire to protect themselves, rather than necessarily in the best interests of their patient (284).

As of 2017, guidance in the UK now excludes risk stratification using the ABCD2 score (11, 60), however the results from GPs stressed the value of a tool to aid with diagnosis and initial management. GPs' felt that the ABCD2 score was an additional aid to support decisions about urgency of referral and legitimise requests for urgent appointments. The score also provided reassurance that the risk of subsequent stroke was low (when the score corresponded with their own clinical judgement) (thematic heading 6) (4.4.3 section 3). A diagnostic tool would reduce the uncertainty by informing GPs on the likelihood of a TIA. A qualitative study in the UK consisting of interviews with GPs found that the ABCD2 scoring system was liked and that GPs complied with its use, as it offered a 'substantial means to navigate the referral system' (125).

The interviews found that GPs and emergency doctors may use the TIA clinics as a place to send patients they are unsure about even if they know the diagnosis is unlikely. This supports the findings from the current study which found that the ease of accessibility to the specialist TIA clinic left the clinics open to over-use and perhaps misuse (thematic heading 5) (4.4.2 section 2). GPs suggested that TIA clinic referrals could potentially be used as a way of 'disposing' of patients (281).

Most GPs believed that a diagnostic tool for TIA which could be used in primary care would be valuable, but suggested that it would not be used so much for informing diagnosis. Rather, it would be helpful as a validation of their clinical judgement. It was thought that it would provide objective evidence to defend their decision and back up their judgement. Additionally, GPs felt that the results from a diagnostic tool would need to be used alongside clinical judgement (thematic heading 7) (4.4.4 section 4). A study of GPs' experiences of using diagnostic tools for cancer found that clinicians may feel less confident to trust their clinical judgement alone and instead check patients' diagnoses through further testing. Also, a diagnostic tool was found to support GPs clinical decision-making and provided reassurance (285). This supports the results obtained from the current study as GPs valued an objective tool to back up their judgement (thematic heading 7) (4.4.4 section 4). This suggests that the uncertainty cannot be removed, but supports the evidence that

clinical risk scores/models combined with clinical judgement are better than clinical judgement alone (286).

GPs proposed that by using a diagnostic tool, patients can be re-evaluated and a diagnostic tool would therefore strengthen the referral and diagnostic process (thematic heading 7) (4.4.4 section 4). Similar findings emerged in a qualitative study exploring GPs' experiences of using diagnostic tools for cancer (285). The study reported that diagnostic tools assisted in the recognition of symptoms that previously might not have raised an alarm, by alerting the significance of more opaque signs and symptoms.

Although GPs were aware of the importance of diagnosing and managing suspected TIA patients, when asked about a suitable threshold for referrals, the majority in the sample found it extremely difficult to specify (thematic heading 8) (4.4.4 section 4). The uncertain nature of TIA diagnosis is demonstrated by the low agreement between stroke physicians when asked to rate the likelihood that patients' symptoms were consistent with TIA (287). The results of this were similar in the current study when GPs were uncertain about what likelihood would justify an appropriate threshold. If a score was introduced its utility could be supported by presenting the likelihood of TIA.

GPs consistently chose to refer to 'likelihood of TIA' rather than referring to sensitivity and specificity or predictive values (thematic heading 8) (4.4.4 section 4). Findings from a qualitative study looking into the difficulties experienced by healthcare decision makers identified that presenting GPs with a cut-off identifying sensitivity and specificity was difficult for them to fully understand (288). A growing evidence base is emerging on how best to present information about risk in general practice (289-291). GPs frequently base decisions on risk, however, it has been proposed that the nature and presentation of risk information available to GPs could be improved (292). The frequent use of risk score in daily practice suggests that GPs would feel confident using the risk presented in this study in daily clinical practice. Substantial efforts directed at the development and validation of more current and accurate risk scores for various population groups have helped improve the availability of risk scores in recent years (293, 294). These risk scores have shown to be useful for GPs for individual decision making (293, 295). GPs also use risk score to inform referral decisions based on the immediate likelihood of a diagnosis such as the Wells score, a diagnostic prediction model for deep vein thrombosis (87). In terms of the implications of

this for the next steps in this research, it was thought to be useful to explore how the Dawson score can be used to provide an explanation of the risk of TIA (Chapter 5).

4.5.2. Strengths and limitations

Through thematic analysis of qualitative interviews, this study has sought to explore the experiences of GPs, who are usually the first contact when a patient experience symptom(s) suggestive of TIA. This study of GPs' views on a diagnostic tool is a new area of research, as there are currently no diagnostic tools for TIA used in primary care. Therefore, the study adds to the evidence base on the diagnosis of TIA and management to secondary care.

A semi structured interview approach was used, allowing for an open dialogue exploring ideas in the current evidence base, whilst allowing for a degree of freedom in conversation. This meant encouraging GPs to reflect upon some areas which may not have arisen naturally, but that were the focus of the research and could be explored across the whole sample of GPs, as well as allowing for them to raise their own ideas and concerns. The interviews provided rich data from which to explore the challenges GPs face and the findings generated new insights on how uncertainty plays a key role in terms of GPs decisions on diagnosing and managing suspected TIA patients.

The questions used in this study were designed specifically to investigate the primary care diagnosis and management of suspected TIA patients, and used existing literature to support maximising response rates. A topic guide was piloted amongst two part-time general practitioners to assess usability and the quality of questions (Appendix 20 and 21).

The study intended to recruit 15–29 GPs with the aim to achieve data saturation (section 4.3.7), but only a sample of 10 GPs agreed to participate. Despite this, by the 10th interview, data saturation was reached with no new information being apparent.

Ten interviews across six different practices were completed (Table 4.4.1), and further interviews would have increased the diversity of GPs included. Time was a general limitation. GPs had limited time for interviews which explained the low response rate, and interviews were limited to up to 30 minutes. Although 30 minutes was reasonable, the interviews aimed to cover four particular areas (diagnosis, management, ABCD2 score and

utility of a diagnostic tool in primary care). Considering this, it meant that the amount of information ascertained for each topic was limited.

It is also important to consider the challenges that were encountered during the selection process for this study. This study aimed to recruit 15–20 GPs (mentioned earlier) which allowed broad demographic information to select from such as, age, years in practice and size of practice. However, as mentioned above, the sample was relatively small and therefore age was not collected; this was due to a need to protect anonymity in a small study. Furthermore, the GPs were self-selected and thus, more likely to have an interest in TIA. It can be argued that those included in the study may lack diversity of the population intended to be analysed.

Although the current study offers insights into an under-researched area, the benefits of this must be considered within the context of methodological limitations and unanswered questions. Firstly, although the study offers an account of GPs' views on diagnosis and how this may influence referrals to secondary care, it is limited by the exclusion of the views of less experienced GPs. GPs in this sample has between 6–11 years' experience (Table 4.4.1). Therefore, the sample was missing less and more experienced older GPs. This restricted the views from the interviews and only offered a partial view of the challenges faced in primary care. It may be that the newer and more experienced GPs with 20–30 years' experience had alternative views on the challenges on the diagnosis and management of TIAs. Newer GPs may also be more likely to value guidance from a diagnostic tool. However, the interviews did not provide insight in relation to this.

4.6. Conclusion

The interviews illustrated that the processes of diagnosis and referral were characterised by uncertainty, and there was a lack of consensus about acceptable thresholds for referral decisions. TIA does not have a gold standard diagnostic tool and having uncovered tensions that drive referrals, a diagnostic tool could have the potential to reduce uncertainty and reduce over-referral, if GPs were encouraged to use it alongside clinical judgement. For example, using the score (or risk calculation) as one of several sources contributing to referral decisions (including, confidence in alternative diagnosis).

Although the GPs outlined some practical concerns with using a TIA diagnostic tool in primary care, such as the need for an electronic form to avoid additional time expenditure, and the score's ability to consider individual symptom presentations such as, anxiety and mental issues that may have an impact on presenting symptoms, GPs emphasised the value of a score/tool to rule out TIA. Ruling out true negative cases could reduce the number of referrals to the specialist if referrals below the threshold were rejected. GPs suggested that the likelihood of TIA associated with a cut-off e.g. 5% or 10% risk of TIA would be useful. Therefore, the likelihood of TIA associated with various cut-offs were explored in the subsequent chapter (Chapter 5) in the attempt to demonstrate the use of the score associated with GP preferred thresholds. Although the external validation study (Chapter 3) similarly attempted to present the risk of TIA associated with the use of the score in different ways (sensitivity, specificity, PPV and NPV), it did not examine GPs' desired likelihood of TIA (percentage risk of TIA). Therefore, alternative cut-offs and risk estimation which took GPs' views into account were examined in Chapter 5, whilst exploring the implications for referrals if these were applied in practice.

Chapter 5: Alternative cut-offs for the Dawson score and estimation of risk of TIAMS

The results from Chapter 4 outlined GPs' preferred percentage risk of TIA for them to be comfortable not to refer suspected TIA patients. For GPs, knowing the risk of TIA against other diagnosis is helpful rather than other cut-offs. GPs also highlighted the need for a tool to rule out a TIA. Until this point, exploring alternative cut-offs with the associated NPV with the Dawson score was available; however, the next step was to use a logistic regression model to generate risk of TIA as this was what was preferred by GPs. Based on this, alternative cut-offs were examined whilst exploring the implications for referrals if these were applied in practice. This chapter begins by detailing the rationale of the study, followed by the aims of the study (section 5.1) methods and results (sections 5.2 and 5.3). Finally, a section presenting how the risk of TIAMS derived from the Dawson score could be presented to GPs are discussed along with conclusions of the study (5.4–5.5).

The qualitative interviews in Chapter 4 explored GPs' views on when they would be comfortable not to refer patients. GPs preferred to use a diagnostic tool to aid them with ruling out a TIA and expressed this as a level of risk. The majority of the GPs would be comfortable not to refer if the risk of TIA was 10% or less. The 5.4 cut-off does not include this and had an NPV which was deemed too low (91%). The analysis to date does not allow risk to be calculated. Therefore, NPV was explored as a proxy in the initial analysis, followed by an exploration of the risk of TIAMS which was deemed clinically relevant in directing management decisions. The difference between NPV and overall risk of TIA is that NPV is the probability that the individual with a negative test result truly does not have a TIA. Whereas risk of TIA is the percentage of patients who are likely to have a TIA diagnosis.

GPs also suggested that they would definitely refer if the likelihood of a TIA was 50% or more. Therefore, a cut-off with a PPV of 50% was examined. An important aspect to emphasise is that this chapter is exploratory and would need further work in a larger study before results are applied in practice.

When a new diagnostic test is validated in a different clinical setting the test's original cut-off is often examined to find if there is a more reliable and valid threshold for classifying cases as positive or negative (296).

The criteria for deriving cut-off values for diagnostic tools can be based on several different methods. The most commonly applied technique uses the receiver-operating characteristic (ROC) curve area under the curve (AUC) (section 3.4.12), and is the frequently used approach to diagnostic testing (238). The ROC curve is a graphical plot showing the trade-off between sensitivity and specificity for a cut-off of a test to illustrate the diagnostic ability. The area under the receiver operating characteristic curve is a measure of the usefulness/accuracy of a test in general, where a greater area means a more accurate test (236). From these statistical techniques, a suitable level for the sensitivity or the specificity can be established.

A perfect diagnostic test would have 100% sensitivity and 100% specificity which would make the AUC equal to 1 and would reach the upper left corner of the ROC curve as conventionally plotted, i.e. sensitivity against (1- specificity). The top left point of the ROC curve shows the statistical optimal performance of the test. However, this study was interested in the most clinically appropriate cut-off that included a high minimum sensitivity (>80%). Therefore, the emphasis was further to the right from the top left point of the ROC, (section 3.5.6). Higher cut-off values are related with lower sensitivities and higher specificities, whereas lower cut-offs lead to higher sensitivities and lower specificities (204). There is therefore a trade-off as changing the cut-off point to increase the sensitivity or specificity of a test will result in a reduction of the other. The results from a qualitative study on routine risk score use for primary care patients reported that studies of diagnostic accuracy should report alternative cut-offs (297).

Sensitivity and specificity can be combined into one measure: the likelihood ratio which shows how much a test result will change the odds of having a disease (240). The desired likelihood ratios can also be used to select a cut-off. This method involves dividing sensitivity and specificity rates to calculate the likelihood ratio. Additionally, the Youden index (also referred to as Youden's J statistic) is another way of combining sensitivity and specificity to define the optimal cut-off (298). This method takes a range of values between 0 and 1 where 1 indicates the perfect test. The J statistic calculates the distance between the ROC

curve and the diagonal line between the bottom left and top right of the ROC curve. Therefore, the higher the value the better the test (298). However, despite the various statistical methods for selection of cut-offs, the ultimate goal is to maximise diagnostic performances that are clinically meaningful (299). Therefore, it is recommended that researchers should select one that is most clinically relevant (299).

An alternative method to determine a suitable cut-off is the cost ratio approach (section 3.4.12). Although the approach is not as commonly cited in the literature than the ROC, it is still regarded as an appropriate method for selecting an optimal cut-off, as it allows clinical relevance to be statistically weighted in the selection of the cut-off (205). The method accounts for the prevalence of the event and the costs of misclassification in either direction. Another method uses negative predictive value (NPV) defined as the proportion of people with a negative test result who do not have the disease to select a suitable cut-off (237).

The ROC curve and AUC was used in Chapter 3 external validation study to test the discriminative ability of the Dawson score for the 5.4 cut-off (section 3.5). Therefore, it was useful to keep the method consistent for looking into the associated cut-off when exploring the NPV in this study. This study entailed looking into the NPV to rule out a TIA and the ROC curve before looking into percentage risk of TIA was thought to be the best method to determine the associated sensitivity, specificity and PPV figures, in addition to the cut-offs associated with the various NPV values.

Presenting GPs with a cut-off identifying sensitivity and specificity may raise difficulties in clinical interpretation as shown in the qualitative study (288). Exploring alternative cut-offs and estimated disease probabilities based on findings from GP interviews would provide GPs with sufficient assurance to rule out the suspected disease. GPs would then feel confident enough to take clinical decisions, because their treatment threshold for a specific disease e.g. 90% or 95% probability is presented (300).

Presenting results as estimated risk can greatly improve healthcare decision makers understanding of diagnostic accuracy. Healthcare professionals with limited understanding and experience of test accuracy experienced difficulties when information was presented as sensitivity and specificity. When the same information was presented as natural frequencies (e.g. percentage risk) along with the cut-offs, the implications of the results were

understood clearly. This was also the case for participants who had a good understanding of diagnostic test accuracy reviews (288).

The method frequently used to calculate risk is the logistic regression method which has been used by researchers to develop risk models (301, 302). By estimating the risk of an event, clinicians can make an informed choice regarding patients' treatment. For external validation studies the estimated coefficients from the development phase are used to predict risks for patients in the new sample. The logistic function or logistic curve can then be used to calculate the probability of the event i.e. risk of disease.

5.1. Aims

1. To explore alternative cut-offs based on findings from GP interviews
2. To examine clinical implications of using the cut-off/s in practice
3. To calculate individual risk of TIAMS according to the Dawson score

5.2. Methods

5.2.1 Exploring NPV's to establish a cut-off

NPV differs from risk of TIA as it is the probability of patients with a negative test result who truly do not have a TIA, and risk of TIA is the percentage of patients that are likely to have a TIA diagnosis. NPV associated with different cut-offs were available to explore, but the analysis does not allow risk to be calculated. GPs emphasised the importance of a tool to rule out a TIA (section 4.4.2). Therefore, it was deemed useful to explore the different NPV's to establish an alternative cut-off to suit the clinical requirements of GPs in the qualitative study (Chapter 4). A cut-off with an NPV of 95%, 90%, 85%, 80% and also the 91% NPV with the Dawson 5.4 cut-off were therefore examined. The study will then go into exploring GP desired percentage risk of TIA (5% and 10%) which they felt were comfortable thresholds to not refer cases.

5.2.2 Logistic regression

A method frequently used in external validation studies is logistic regression to estimate the risk of a disease (303, 304). Logistic regression is used when the dependent variable is binary (has only two values; 0 and 1 or diseased and not diseased). Logistic regression is a predictive analysis and estimates the coefficients as well as the confidence interval and significance level to predict the probability of presence of the characteristic of interest. Thus, for each variable that has predictive power a coefficient is derived (305). This method was used on the Leicester data to compare with the coefficients reported in the Dawson paper as part of the validation process. Dawson et al modelled all the variables jointly (all together in one model) as opposed to independently (one variable at a time). In order to replicate the same model as in the Dawson et al study, all variables were modelled jointly. This process was to observe whether the coefficients from this model was similar to what Dawson reported.

The logistic regression was used to derive the Dawson score in the first place. However, the step wise procedure used in the Dawson et al study was not applied to this study because this study aimed to validate the identified variables from the Dawson study, rather than

derive a new score. Therefore, the results from the logistic regression were used to compare the coefficients from the Dawson data to the coefficients and CI reported for this study.

Logistic regression is used to confirm the statistical prognostic significance of the included variables in the model. The regression coefficients describe the size and direction of the relationship between a predictor and the response variable. The coefficients can be used to determine whether a change in a predictor variable makes the event more or less likely. Positive coefficients are interpreted as the event being more likely and negative coefficients make the event less likely (306).

In terms of this study logistic regression was thought to be appropriate for a couple of reasons (307):

1. The data is categorical and the method is the only way to model categorical data
2. The outcome (TIAMS diagnosis; yes/no) is binary

5.2.3. Calibration and logistic re-calibration

Calibration refers to how close the output is to the true probability of an event by evaluating the degree of correspondence between the estimated probability of the event produced by the model and the actual experience of patients. Therefore, calibration looks at how accurate the estimates are in a model (308). Logistic recalibration adds a single coefficient referred to as the constant (intercept), which does not change the other coefficients reported in the logistic model. It is often referred to as the 'levelling factor' as it levels up or down according to the differences in prevalence (309).

Logistic regression was used as a basis of the modelling, the next step was to use Dawson's coefficients to present the probability risk of TIAMS according to the Dawson score for patients in this study. Firstly, the exponential function in STATA which is the expected probability function was applied using the Dawson's coefficients to adjust for the prevalence of TIAMS in this study. The prevalence of TIAMS in this study (35% prevalence in this study) was adjusted from 60% (in the Dawson study). A study using an example of a polygenic risk score explained that a risk score model together with risk stratification thresholds, built upon the data of one population, cannot be applied to another population without taking into account the target population's structure (310). There is a potential risk of misclassifying an individual into a wrong population which would lead systematically to a

wrong risk estimation, and highlights the importance of correct population detection (310). Due to differing prevalence rates between Dawson's study and this study, the calculation recalibrated the mean by adjusting the mean prevelance of TIAMS in the logistic regression model.

Through trial and error the prevalence of TIAMS was matched for this study e.g. 60% reported in Dawson's paper adjusted to 35% found in this study. The calculation for the probability risk of TIAMS using the exponential function was:

$$\frac{e^{Dawson\ score-7.75}}{1+e^{Dawson\ score-7.75}}$$

The aim of this thesis was not to develop a new score. Using coefficients from the logistic regression for this study as opposed to the Dawson's coefficients regression would present the probability risk of TIAMS based on a new score. Thus, using Dawson's coefficients, it will be a presentation of the Dawson score applied to this dataset.

Once the mean prevalence was adjusted, the probability of TIAMS for the Dawson score was presented on a logistic curve. The logistic curve tails away towards zero for the low end of the predictor and heads towards the high end of the predictor. Based on the logistic curve, a Dawson cut point corresponding to the desired probability suggested by GPs (5% and 10% risk) were calculated. The natural log function was used in STATA. The desired probability risk is included in the calculation i.e., 5% and 10%. The calculation then reports a cut-off based on the desired risk. The calculations were as follows:

$$5\%\ \text{Risk} = \log\left(\frac{0.05}{1-0.05}+7.75\right) \qquad 10\%\ \text{Risk} = \log\left(\frac{0.1}{1-0.1}+7.75\right)$$

5.3. Results

As can be seen in Table 5.3.1, the cut-off with 95% NPV value was 5.17. Therefore, this alternative cut-off was examined further. The cut-offs for this and other NPVs were explored along with the PPV, sensitivity and specificity to establish if a different cut-off could be more clinically useful. The alternative cut-offs examined focused on the NPV rather than other attributes. Cut-offs based on an NPV between 80 to 100 were examined and not any lower as these would be deemed too low to be of clinical use.

Table 5.3.1: The cut-offs, PPV sensitivity and specificity values according to the different NPVs

NPV (%)	Cut-off	PPV (%)	Sensitivity (%)	Specificity (%)	Number below cut-off (n= 486)	% below cut-off	Number of patients below cut-off with a specialist diagnosis of TIAMS (N = 150)	
100	4.93	37	100	7	22	5	0	0
97.5	5.12	38	99	11	34	7	1	0.7%
95	5.17	38	99	11	39	8	2	1.3%
91	5.4 (published cut-off)	39	97	16	56	12	5	3.3%
90	5.69	41	97	21	81	17	5	3.3%
85	5.93	41	91	28	106	22	16	11.0%
80	6.58	46	77	51	165	34	41	27.0%

The Dawson 5.4 cut-off from the external validation study (sections, 3.1–3.7) and 5.17 cut-off based on the qualitative study (sections, 4.1–4.6) performed as below:

- Dawson 5.4: Sensitivity 97%, referrals excluded 12%
- Alternative 5.17: Sensitivity: 99%, referrals excluded 8%

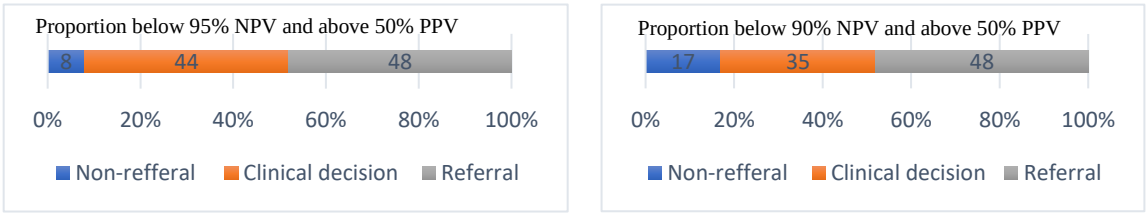
The score is intended to support clinical decision by quantifying the likelihood of a TIAMS diagnosis. A cut-off with a 95% NPV would be clinically useful in secondary care by marginally reducing the number of referrals.

5.3.1. Exploring two cut-offs to test the clinical implications

A cut-off of 5.17 and below was a level not to refer and if the risk was above 50% (cut-off of 6.39) GPs would definitely refer (section 4.4.4). Therefore, these two cut-offs were used to explore the proportion of patients below and above and the percentage between where referral could be a clinical decision, for example, on the GPs' confidence in an alternative diagnosis.

As a minority of GPs suggested a threshold of 10% and below to not refer, this was also examined. The two bar charts were split according to the two thresholds (proportion below cut-off versus proportion above cut-off). The bar charts show how many would not get referred if the score was to be used for triage, how many referrals will be left to clinical judgement and the number of definite referrals.

Figure 5.3.1: Proportion of patients below NPV and above PPV level



The bar charts show that if an NPV of 95% was to be used then 8% of patients would not be referred, compared to the NPV of 90% where 17% of patients would not be referred. The clinical decision would still be slightly higher with the 95% NPV (44%) compared to the 90% NPV (35%).

5.3.2. Logistic regression model

The first step in the logistic regression was to descriptively compare the coefficients for the predictive variables from the Dawson study to the coefficients and CI for the same predictive variables in this study. This was to observe the extent to which outcomes predicted by the logistic regression in this study in specified predictors were similar to those observed in the validation dataset (Dawson's).

Table 5.3.2: Comparison of the coefficients between this study and Dawson's study

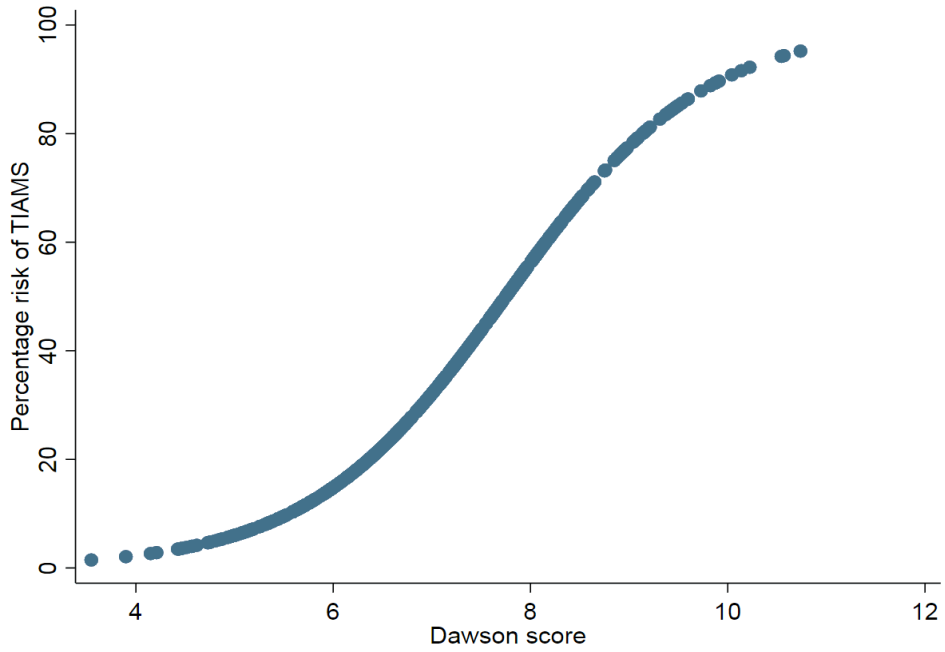
Variable	Coefficient	95% CI	Original Dawson coefficients
History of stroke or TIA	-0.43	-1.04 to 0.19	0.5*
Headache	-0.30	-0.77 to 0.26	-0.5
Diplopia	-0.53	-1.40 to 0.33	1.2*
Loss of consciousness	-2.0	-3.24 to -0.67	-1.1
Seizure	0.84	-0.75 to 2.44	-1.6*
Speech abnormalities	0.80	0.36 to 1.24	1.3*
Unilateral limb weakness	1.02	0.56 to 1.47	1.7*
Unilateral facial weakness	0.14	-0.50 to 0.78	0.6
Age (per year)	0.10	0.04 to 0.07	Multiply by 0.04
Note: The variables asterisked were outside the 95% CI in this study			

In the orginal Dawson paper, the variables listed in Table 5.3.2 were all statistically significant predictors of TIAMS. In this study, the aim was not to derive a score, rather to compare results to those reported in the Dawson paper. The coefficients for this study showed that the variables that were preditive of a TIAMS were: seizure, speech abnormalities, unilateral limb weakness, unilaternal facial weakness and age. History of stroke or TIA, headache, diplopia and loss of consciousness were negative predictors.
Five of the orginal Dawson predictors were outside the 95% CI reported in this study: history of stroke or TIA, diplopia, seizure, speech abnormalities and unilateral limb weakness (asterisked in Table 5.3.2). Whereas, the remaining four variables were inside this study's CI (headache, loss of consciousness, unilateral facial weakness and age). It could be proposed that the reason the Dawson coefficients differed to those reported for this study was due to the difference in case mix, as the true positive TIA population may have differed between the Dawson Glasgow study and this study.

5.3.3. Estimation of risk of TIAMS

Dawson's coefficents presented in Table 5.3.2 were used to derive a logistic curve showing the Dawson score against the risk of TIAMS. In order to use Dawson's coefficients to show the percentange risk of TIAMS in this study accurately, the Dawson score was re-calibrated. The mean was adjusted to 35% (the prevalance in this study) from 60% (the prevelance in the Dawson paper).

Figure 5.3.2: Logistic curve of percentage risk of TIAMS according to the Dawson score



The log calculation was used to derive a cut-off corresponding to the desired probability risk of TIAMS. A minority of GPs suggested a likelihood of TIAMS of 10% and below to not refer in the qualitative interviews (section 4.4.4). Therefore, the 10% risk was also examined. The calculation proposed a cut-off of 4.8 and 5.6 would be appropriate for GPs to identify patients with a 5% and 10% risk of TIAMS.

A table presenting the risk of TIAMS associated cut-off, sensitivity, specificity, NPV and PPV is shown below. The number and percentage below the cut-off and the number of those patients below the cut-off who had a specialist diagnosis are also provided. GPs also suggested they would definitely refer if over 50% risk, the results of which are also presented below.

Table 5.3.3: Descriptive details according to the GPs' desired percentage risk of TIAMS to refer

Risk of TIAMS	Cut-off	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)	Number below cut-off (n= 486)	% below cut-off	Number of patients below cut-off with a specialist diagnosis of TIAMS (N = 150)	
5%	4.81	100	5	100	37	17	3	0	0
10%	5.60	97	21	93	40	71	15	5	3.3%
(To not refer)									
50% (To refer)	7.75	49%	82%	74%	59%	256	53	88	59.0%

The cut-off of 4.8 would only exclude 3% of referrals. The 5.6 cut-off however, would exclude 15% of referrals. GPs may find it helpful to use the risk estimate to inform clinical decisions to assess the risk of TIA against alternative diagnoses

5.4. Discussion

In the first section of the results (section 5.3), the effect of a cut-off derived from the 95% NPV for ruling out a TIA as suggested in the qualitative interviews was examined. If this cut-off was to be applied then the clinical implication was that GPs would refer a lower percentage and in turn, would reduce the clinic burden. Using the alternative 5.17 cut-off with an NPV of 95% would potentially avoid 8% of referrals, therefore, marginally lowering clinic burden. Whereas, the 5.4 cut-off with an NPV of 91% would result in the reduction of 12% of the referrals. The sensitivities of the two cut-offs also differed with 5.4 reporting a sensitivity of 97% versus 99% for 5.17. The 5.4 cut-off would miss 5 true TIAMS patients out of the 56 patients that would not be referred, and the 5.17 would miss 2 cases of true TIAMS of the 39 patients. The NPV of 90% however, reduced the referrals by 17% with a sensitivity of 97%. A total of 81 patients would not be referred using the associated cut-off of 5.69, and would miss 5 true TIAMS patients.

Comparing the predictors found by Dawson et al, the model in this study shared few positive predictors of TIAMS. Based on the coefficients, the positive predictors for both studies were: speech abnormalities, unilateral limb weakness, unilaternal facial weakness and age. The negative predictors for both were headache and loss of consciousness. Whilst the coefficients for history of TIA/stroke, diplopia and seizure differed from Dawson's coefficients (Table 5.3.2).

Due to the difference in case mix, the performance of logistic regression models used in diagnostic and prognostic prediction research is generally known to be better on the dataset on which the model has been developed (derivation set), compared to the performance of the model on a new dataset (validation set). These studies have also shown differences in coefficients between the two, with much larger decrease in predictive performance on the validation set. Additionally, although the results were comparable, not all the predictors assured good performance (311-313). Five of the orginal Dawson predictors were outside the 95% CI reported in this study which were history of stroke or TIA, diplopia, seizure, speech abnormalities and unilateral limb weakness (asterisked in Table 5.3.2). Whereas the remaining four variables were inside this study's CI (headache, loss of consciousness, unilateral facial weakness and age).

Studies have concluded that logistic models need to include at least 100 events and 100 non-events, regardless of the predictive model being addressed (314, 315). However, others have suggested that in the case of scoring systems even with the required sample size, differences still may exist (316). In terms of this study, the majority of the variables did not reach the 100 events recommendation. These variables were: history of TIA, headache, diplopia, loss of consciousness, seizure and facial weakness (Appendix 16).

The differences in coefficients can be explained if the case mix in the validation sample differs from that of the derivation sample (317). For example, the true positive cases of TIA might differ noticeably. The predictors included in the Dawson model in the development study was identified around 10 years ago. The performance of a model has been suggested to change over time and re-evaluation may indicate differences in terms of the predictive variables and associated coefficients (317).

The regression coefficients of the predictors included in the model can be different in both the development and validation samples, as a results of differences in the methods used for data collection, or definition of the predictors (318). The data collection method was different for this study as the Dawson predictors were collected by a researcher via a telephone interview with patients before referral to the TIA clinic. Thus, this would be different to the interpretations from the clinicians.

Despite the differences in the coefficients for the predictor variables reported in this study and Dawson's, the score performance was found to be similar to the orginal Dawson performance even though sensitivity and specificity differed between the two. It has also been advised to keep variables known to be important risk predictors in the model, despite the non-significant results for the particular dataset (319).

In this study the coefficients were recalibrated to adjust for the prevalence of TIAMS from 60% in the original Dawson paper to 35% in this study (section 5.3.3). By doing so, the results from the logistic regression would be a representation of the Dawson score according to the patients from this study, rather than a new score derived from this dataset. Logistic regression models are important tools to provide estimates of patient outcome probabilities. The 5% risk of TIAMS with a cut-off of 4.81 according to the logistic curve would reduce refferals by 3% and no patients under this cut-off would not have a specialist

diagnosis of TIAMS. Alternatively, the 10% risk with a cut-off of 5.60 would reduce refferals by 15% and 5 out of 71 patients below this cut-off would have a TIAMS specialist diagnosis.

The presentation of NPV and probability risk highlighted that if GPs wanted a NPV of 95% or 90% to rule out a TIA then 8% and 17% of refferals would be reduced to the clinic, and would miss 2 and 5 TIAMS cases respectively. However, this is different to the 5% estimated risk, where 3% of refferals would be reduced, but no TIAMS cases would be missed. It was thought that reducing the refferals by only 3% would not have any clinical use.

The cut-off associated with 10% risk correlated well with the 5.4 cut-off derived using completeley different method (cost ratio). With the 5.4 cut-off, 5 cases of TIA (3%) would be missed, which is also the same for the 10% risk using the 5.60 cut-off. The performance overall for both were similar enough to propose that the orginal Dawson 5.4 cut-off used throughout this thesis would have very similar clinical implications to the 10% risk. However, it is important to note that if the prevalence of the clinic population was 70–80% TIAMS then the prediction risk would highlight different results to that reported in this study based on the 35% TIAMS prevalence.

The 10% risk presented the same results as the 5.69 cut-off with a NPV of 90% (Table 5.3.1), with a better performance than the Dawson 5.4 (NPV 91%), sensitvity (97% vs 97%), specificity (21% vs 16%) and PPV (41% 39%). The percentage of refferals was also higher (17% vs 12%) with 5 of those cases diagnosed as a TIAMS by a specialist. Therefore, if the Dawson score is to be used in clinical practice, then it could be proposed that the Dawson cut-off of 5.69 performs slighly better than the 5.4, but both could equally be used in practice, rather than using the risk presented in this study.

5.4.1. Strengths and limitations

Alternative cut-offs have been explored to fully understand the performance of the score at each level. A logistic regression analysis was done to present GPs with the risk of TIAMS in the form they reported would best help them with their decision-making. This is a particular strength of this study as this study has attempted to extend the research already done by exploring an aspect that has not been previously looked into. A weakness however, was that the Dawson's derivation study included a much larger sample of 3216 patients compared to

486 patients in this study. If access had been granted to Dawson's original data then the data could have been used to calculate risk.

5.5. Conclusion

This study included two sections that attempted to provide information on the Dawson score using findings from the GP interviews in Chapter 4. GPs emphasised a need for a tool to rule out a TIA and the alternative cut-offs based on NPV could marginally reduce the number of referrals to the TIA clinic. The importance of probability risk of TIA was also highlighted in the interviews. When these were examined, the results highlighted the following key messages:

- An NPV of 95% was used to identify an alternative cut-off of 5.17 as the 5.4 Dawson cut-off had a lower NPV (91%). The cut-off would exclude fewer non-cerebrovascular referrals to the TIA clinic than the 5.4 cut-off therefore, only marginally lowering the clinic burden. In contrast, using an NPV of 90% could reduce referrals by 17% and 5 of these patients would be labelled as TIAMS
- In terms of the risk of TIAMS; the 5% risk of TIAMS would not have any clinical use as the referrals would only be reduced by 3%. The 10% risk however, was similar to the 5.4 cut-off used in this study, reducing referrals by 15% and would miss 5 (3%) of TIAMS, similar to the 5.4 Dawson cut-off. The 10% risk with a cut-off of 5.60 also presented similar results when compared to the 5.69 cut-off with an NPV of 90%
- The cut-off associated with an NPV of 90% may be of clinical use in reducing referrals to the TIA clinic. Alternatively, the 10% risk of TIA could be a recommended threshold for not referring to the TIA clinic

The frequent use of risk scores in daily practice suggests that GPs would potentially feel confident using the risk presented in this study in daily clinical practice. Based on Chapter 4, it was important to address how best to communicate risk information to GPs. Both the external validation study (Chapter 3) and the qualitative study (Chapter 4) attempted to present the score in different ways to provide GPs with information they were comfortable with. For example, the external validation presented the Dawson score results based on sensitivity, specificity, PPV and NPV. Whereas, GP interviews highlighted they were more comfortable with likelihood of TIA (i.e. percentage risk of TIA) rather than sensitivity and specificity. Based on the results of this study, it can be concluded that the percentage risk can be presented, and that a 10% risk could be recommended as the threshold for not

referring, in combination with clinical judgement, and this may be more useful than rigid cut-offs. GPs would be comfortable knowing the risk of TIA against other diagnoses, rather than using cut-offs with associated sensitivity and specificity results.

Chapter 6: Final discussion

This chapter will begin with a summary of the studies: the systematic review, the external validation study, the qualitative study comprising of interviews with the GPs, and the exploratory study investigating percentage risk of TIAMS, in response to the interview findings. The key findings from each study will be outlined to demonstrate some of the barriers identified in the diagnosis and management of TIA in primary care. A discussion on the mixed methods approach will be outlined, followed by a comparison of the studies to other relevant research to provide a broader perspective of the strengths and limitations of the whole thesis. Lastly, recommendations for future research will be discussed, along with an overall conclusion.

6.1. Summary of research findings

The systematic review in Chapter 2 synthesising the evidence on the diagnosis and immediate management of TIA in primary care indicated deficiencies in GP knowledge and clinical practice. GPs tended to over-emphasise non-specific symptoms when considering a TIA diagnosis. Several studies showed that approximately half of referrals to secondary care TIA clinic were not diagnosed as TIA, and that in some countries this militates against services assessing patients promptly. Along with the evidence of under-referral to the TIA clinic, GPs may refer some patients to exclude as opposed to confirm a putative diagnosis which may explain high levels of referral at the TIA clinic. The review emphasised the need for further education, practical guidelines for GPs to improve knowledge and practice, and decision support tools to optimise referral patterns, and provide support with the diagnosis of this challenging condition.

The electronic decision support (EDS) tool from New Zealand (section 2.2.14) has shown promising results on the management of TIA, but further research looking into the diagnostic utility of the EDS would be useful to not only educate GPs but to support GPs with their decision-making process. The only diagnostic tool for TIA at the time of the start of the study was the Dawson score. Based on the Dawson publication study results, the score showed some potential in the diagnosis of TIA. The overall objective of the thesis was

to examine the diagnosis and immediate management of suspected TIA in primary care and how a diagnostic tool such as the Dawson score for TIA could be used to guide GPs' referral decisions, and to triage clinic referrals. Exploring the performance of the score in an external validation study would be valued in terms of supporting GP diagnosis and initial management, as well as the reduction of non-cerebrovascular referrals to minimise overall burden at the TIA clinic.

Following a feasibility study, an external validation was conducted at a TIA clinic in England. The study involved collecting the Dawson score data via telephone from suspected TIAMS patients who were referred to the TIA clinic, prior to their clinic consultation. The purpose of this study was to determine whether applying the Dawson score before clinic attendance could reduce unnecessary clinic consultations. If so, the score could potentially be used by clinic staff to triage referrals.

In the external validation study, the performance of the Dawson score differed to that found in both the Dawson and Lasserson study, which may be due to the difference in the sample. A higher sensitivity was achieved compared with Dawson and Lasserson et al studies, but the specificity was lower. This suggests that although the Dawson score correctly identified a high proportion of TIAMS cases, a large proportion of patients labelled as TIAMS by the score had an alternative specialist diagnosis. Despite this, applying the score would reduce referrals by 12% as these are the patients that the score identified as not having a TIAMS. Therefore, based on this, it was concluded that the score could have some utility in reducing the number of non-cerebrovascular referrals to a fast track TIA service.

The performance of the Dawson clinic score and Dawson interview score were similar in predicting a diagnosis of TIAMS. However, with regards to the clinic score, it was uncertain how much data were updated on the day of the patient's clinic appointment. Therefore, the evidence for the interview score is stronger compared with the clinic score to triage both internal and GP referrals.

A high proportion of patients who were low risk (≤ 3) according to the ABCD2 score had a specialist diagnosis of TIAMS. The Dawson score was better than the ABCD2 in identifying patients at low risk of TIAMS. Therefore, the Dawson score had more potential than the ABCD2 score to prioritise referrals to the TIA clinic.

In the original Dawson paper, it was assumed that the health related cost of misclassifying a cerebrovascular patient as a non-cerebrovascular is twice as much as the cost of misclassifying a non-cerebrovascular as a cerebrovascular (96). With adjustment to reflect the greater seriousness of missing true cerebrovascular patients at 2:1 cost ratio, an optimal cut-off score of >5.4 was used. It was thought best to use the same 2:1 cost ratio method so that the results can be compared to that reported by Dawson, and for completeness of this study. With the applied 2:1 cost ratio to the Leicester data, a different cut-off emerged to the 5.4 cut-off (7.26) which reported a higher specificity and PPV than the 5.4 cut-off used in this study, but a lower sensitivity and NPV. The cost ratio method could be used in the future to achieve the most clinically appropriate sensitivity and specificity to reduce the number of referrals seen at the specialist clinic.

With regards to the exploratory analysis for different patient sub-groups of those referred to the clinic, higher percentages of TIAMS compared to other patient groups were observed in those who are younger, had hypertension and were internal referrals. The next step after the external validation study was to explore GPs' views through semi structured interviews on whether a diagnostic tool for TIA would be useful in a primary care setting, and to examine broader issues around diagnosis and management of TIA. GPs' views on the usefulness of a diagnostic tool were explored which included the strengths and weaknesses of this approach, as well as a particular focus on thresholds for referrals.

The thematic analysis from the semi-structured telephone interviews with GPs revealed a range of difficulties faced when diagnosing a TIA. The major theme was uncertainty of symptoms which influenced their decision to refer. GPs reported that TIA was more likely to be suspected when patients were more obvious candidates for TIA (based on patient characteristics, past history and patient symptoms). Referrals were usually made based on uncertainty and a way to seek reassurance. GPs felt that a diagnostic tool had the potential to improve the decision-making process and enhance GPs' confidence, particularly to rule out a TIA. Interviews with GPs also explored a threshold they would feel comfortable to not refer suspected TIA patients. Most GPs suggested that if the likelihood of TIA was less than 5% then they would be comfortable to not refer and a minority proposed a 10% likelihood of TIA. This suggests that GPs would value a score if it presents percentage risk of TIA, and can be used in practice to help GPs decide whether to suspect or rule out TIA.

After completion of the external validation and qualitative work, it was evident that GPs preferred percentage risk of TIA for them to be comfortable not to refer suspected TIA patients. GPs also highlighted in the qualitative interviews the need for a tool to rule out a TIA. Although the external validation study similarly attempted to present the risk of TIA associated with the use of the score in different ways (sensitivity, specificity, PPV and NPV), it did not examine GPs' desired likelihood of TIA (percentage risk of TIA). Until this point, exploring alternative cut-offs with the associated NPV was available. The next step was to use a logistic regression model to generate risk of TIA. Based on this, alternative cut-offs which took GPs' views into account were examined whilst exploring the implications for referrals if these were applied in practice.

An NPV of 95% with an associated cut-off of 5.17 would exclude fewer non-cerebrovascular referrals to the TIA clinic than the 5.4 cut-off which had an NPV of 91%, only marginally lowering the clinic burden. In contrast to this, using an NPV of 90% could reduce referrals by 17% but 5 (3%) of these patients ruled out by this threshold would be confirmed as TIAMS.

Based on the logistic regression model results, the log calculation was used to derive a cut-off corresponding to the desired 5% and 10% probability risk of TIAMS (section 5.2.3). Probability risk of TIA differs from NPV as it is the percentage of patients that are likely to have a TIA diagnosis, whereas NPV is the probability of patients with a negative test result who truly do not have a TIA.

A referral threshold of 5% likelihood risk of TIAMS would not be of clinical use as referrals would only be reduced by 3%. Alternatively, the 10% risk was similar to the 5.4 cut-off used in Chapter 3, reducing referrals by 15% and missing 5 (3%) of TIAMS patients. The GPs suggested percentage risk could be combined with clinical judgement to aid decision making, and this may be more useful than cut-offs based on the score. Therefore, it may be more useful for a diagnostic tool for TIA to generate a percentage risk of TIAMS, as opposed to presenting a score with recommended cut-offs.

6.2. Reflection of using a mixed methods approach

This thesis took a mixed methods approach, using both qualitative and quantitative methods in a study of diagnosis for TIA. Mixed methods research is the use of both quantitative and qualitative methods in a single study or series of studies and is increasingly being used in health services research. Historically, most researchers have focused on the use of quantitative methodology. In the past decade however, qualitative methodology has been embraced, highlighting the contribution it can make to research in health care (320). As the importance of qualitative research has been recognised, there has been a growing interest in combining the two research methods. In health services research in England, the proportion of publications labelled as mixed methods increased from 17% in mid 1990s to 30% in the early 2000s (321).

Qualitative and quantitative approaches may be used in parallel, and with equal emphasis, in order to study research questions that mono-method approaches cannot adequately address. In this way, mixed methods research can bring a wider perspective in order to explore different aspects of the topic (322). Using mixed methods research has suggested to extend the breadth and range of inquiry by using different methods for different inquiry components (323). This concept is illustrated by a study that explored the factors impacting upon the quality of diabetes care in general practice. Qualitative methods such as focus groups with patients; interviews with healthcare professionals were combined with quantitative methods such as clinical audit or systematic literature review with meta-analysis to identify a wide range of factors, with some overlaps in the findings obtained via different approaches (324). Additionally, sub-studies can be generated from either the qualitative or quantitative studies to further explore identified areas. In principle, using these methods together generated greater insights and provided a wider perspective on the topic.

Justifications for using a mixed method approach usually relate to the need for comprehensiveness and the need for a range of methodologies to understand and evaluate complexities in health research (320, 325). Apart from comprehensiveness, there are other reasons for using mixed methods research, some of which are detailed below.

Methodological triangulation is an approach commonly used in mixed methods research, whereby qualitative and quantitative methods are used to study the same phenomena (326). This strategy has been found to be beneficial in increasing the validity of the research, providing confirmation of findings and amplifying the understanding and knowledge of the studied phenomena (326).

Although many researchers have been keen to embrace the mixed methods approach, mixed method studies in health services research can be challenging to combine, resulting in inadequate use of both the qualitative and quantitative components (321). The idea that quantitative and qualitative research are separate paradigms which cannot be connected has also been argued (211).

Fears relating to the validity and reliability issues of mixed methods research have emerged (327). Arguments around "design suitability" have been reported, which refers to whether the methods used in a study are appropriate for answering the research questions. Issues around the quality of mixed methods study in terms of "design adequacy" has also been raised. This is whether the methods are capable of capturing the effects, meanings or relationships from each approach, and do the components fit together across the study (within design consistency). Lastly whether the design analysis procedures are appropriate in addressing the research questions has been questioned ("analytic adequacy") (328) (p.113).

Mixing methods in this thesis

The different research approaches as highlighted above can be used to address multi-faceted research problems (329). Similarly, the purpose of mixing methods in this thesis was to provide a breadth of data relating to the barriers to the diagnosis and management of TIA in primary care, in order to inform the use of a diagnostic tool to reduce secondary care burden, whilst providing assistance to GPs on this challenging condition.

A mixed methods approach used in this thesis was to combine qualitative and quantitative research in a number of related studies. The studies are designed so that one method is informed by findings obtained from the alternative method (330). A mixed methods research design incorporates studies (or sub-studies) that can be used to "elaborate, enhance or illustrate the results from the other" (331) (p.266-7).

Mixing methods in this thesis was aimed at using the most appropriate methodological design to address and answer the research questions addressed in each study. The overall aim for using a mixed method approach was to investigate GP diagnosis and management of TIA which was addressed through both qualitative and quantitative studies (Chapters 3 and 4). Furthermore, the GP interview study in Chapter 4 was used to develop a further analysis plan for the quantitative data in Chapter 5 to address GPs' feedback from the interviews.

6.3. Implications of findings in the context of previous research

New policy guideline for the management of TIA

Considering that suspected TIA patients often present to primary care, and therefore that the initial management of TIA is with GPs, there are important findings for clinical practice and service organisation highlighted from this research. The research has shown that both diagnosis and referral are complex and demanding areas of clinical activity within primary care.

The NICE guidelines recommend that GPs immediately refer people who have a suspected TIA for specialist assessment and investigation to be seen within 24 hours of onset of symptoms (NICE, 2019) (41). In addition to this, from 2017, the UK stroke guidelines abandon the use of scoring systems such as the ABCD2 score to assess the risk of subsequent stroke or to inform urgency of assessment for those who have had a suspected or confirmed TIA (11, 41, 60). The 2017 Australian and New Zealand guidelines also outline that the ABCD2 score should not be used in isolation to decide the urgency an assessment of suspected TIA patients as this may delay the recognition of atrial fibrillation (AF) and carotid stenosis (55, 59). According to the NICE guideline, all TIA patients have significant risk of stroke, and therefore should be seen urgently. As mentioned in section 1.7 the NICE committee agreed on this recommendation based on the limited predictive performance of the risk score. Therefore, it is important to urgently confirm or refute the diagnosis of a suspected TIA with specialist opinion. The NICE guideline suggests that the immediate

assessment of suspected TIA patients had both better health outcomes and lower costs compared with assessment within a week, without the use of a risk stratification tool (NICE, 2019) (41). The updated recommendation is also supported by the literature which highlights that the ABCD2 score is frequently inaccurate, with a tendency to underestimate stroke risk (51, 54), with the specialist agreeing with the referring physician's total ABCD score in only 42% of cases (54). Furthermore, the ABCD2 does not identify patients with carotid stenosis or AF, as one in five patients with an ABCD2 score less than 4 have symptomatic carotid stenosis of >50% or atrial fibrillation, which underscores benefit from rapid diagnostic evaluation regardless of risk score (55). These findings emphasise the importance of urgent specialist assessment of suspected TIA patients, and that ABCD2 scores by non-stroke specialists cannot be relied upon in isolation to risk-stratify patients.

A small study in Leicestershire reported that approximately 10% of high-risk of stroke patients were seen within 24 hours of symptom onset and 40% of low risk referrals were seen within 7 days (36). In a 2009 study from North West England, median delay from referrals to specialist assessment was 12 days (40). Additionally, the Sentinel Stroke National Audit Programme (SSNAP) 2016 reported that over 50% of NHS sites could not offer a same day 7-days a week service for high-risk patients and just over 60% of low-risk patients were seen within a week (37). Similar results were found in Australian and New Zealand hospitals (38) (39). Given that there are delays for up to or more than a week for TIA clinics to assess patients, the updated NICE guideline recommendation (NICE, 2019) (41) will inevitably lead to further TIA clinic demand to assess these patients within 24-hours, and therefore, increase the burden of TIA clinics. Due to the new policy guideline, the number of high-risk patients at the Leicester TIA clinic have significantly increased. Currently approximately 50–60% of these patients are seen at the clinic within the 24-hour timeframe. The TIA clinics are prioritising high risk patients based on a national guidance. Patients who have symptoms suggestive of TIA within 1 week are considered high-risk and the rest of the patients are considered low-risk. TIA clinic staff currently look at the date of the symptoms on the referral form and prioritise patients based on this.

Since the update of the guideline of no longer using the ABCD2 score to prioritise referrals, the SSNAP has not yet published data on TIA clinic burden. It has however been

acknowledged that there are likely to be implementation challenges for some areas in providing an adequately responsive 7 days a week TIA clinic service. Setting up a 7 day a week service in trusts that do not currently offer this in order to achieve the updated 24-hour timeframe may have a substantial resource impact for the NHS in England (NICE, 2019) (41). This is supported by a recent report from a single stroke services based in Airedale and Bradford sites. Patients referred over the weekend at these sites are often seen on a Monday which is non-compliant with the updated 24-hour specialist assessment requirement[1]. This highlights the need for GPs to be supported with managing this challenging condition which in turn could reduce inappropriate referrals, and therefore clinic burden.

The principles of decision support tools

Clinical decision support (CDS) includes a variety of tools and interventions, computerised as well as non-computerised that are designed to provide physicians and other healthcare professionals assistance with clinical decision making tasks (332) (sections 1.10; 3.1.1). Additionally, a CDS can play a critical role in patient education by providing patients with relevant information in order to perform self-care. A well informed patient is in a greater position to perform self-management when confronted with health problems (333, 334).

Clinical decision support can be in many forms such as a score like the Dawson, DOTS, ABCD2, Wells and Alvarado score (7, 87, 88, 96) as well as electronic health record-based tools e.g. bipolar disorder in primary care patients with depression (335). Clinical decision support tools for cancer include the risk assessment tools (RATs) and QCancer to quantify the risk of an undiagnosed cancer in symptomatic patients (336, 337). Other methods that can be used in performing a diagnostic procedure include a set of guidelines such as the Ottawa Ankle Rules to help clinicians diagnose a possible bone fracture (89) as well as usage of medical algorithms.

There are many clinical decision support systems available that are used for different conditions in both primary care and secondary care settings. CDS can be used in the primary care setting to make referrals to secondary care such as the use of the ABCD2 score, the Dawson score, Wells score as well as cancer CDS e.g. QCancer RATs (7, 87, 96, 337). In contrast to this, there are also CDS systems used in primary care for prevention and

screening, drug dosing, medical management of diagnosis, rather than referral to secondary care (338-341). For example, the QRISK is a prediction algorithm which estimates the patient's 10-year risk of developing cardiovascular disease and is used to identify high-risk people for primary prevention (93). The patient health questionnaire (PHQ-9) has been validated for use in primary care to monitor the severity of depression and response to treatment. It can also be used to make a tentative diagnosis of depression in at-risk populations such as those with coronary heart disease or after stroke (342-345). Other CDS have focussed on managing in secondary care such as the HEART score used to predict a patient's 6-week risk for a major cardiac event in a patient who presents in the emergency room with chest pain (346). Furthermore, the APACHE II score provides estimate of intensive care unit mortality, and is helpful when discussing prognosis and care plans with family members (347).

A TIA/stroke electronic decision support computer algorithm from New Zealand identified in this study (section 2.2.14) (139, 140) incorporates diagnostic criteria and risk stratification according to the New Zealand guideline. The algorithm is multifaceted as it aims to improve GPs' diagnostic accuracy by providing GPs with definitions for neurological symptoms, guiding them into obtaining a focussed history and examination and confirms or rejects TIA/stroke as the likely diagnosis. The EDS also prompts secondary prevention immediately if specialist review is anticipated to be delayed. Studies on the EDS showed that the tool can be used to improve the initiation of best medical TIA therapy and reduce delays to specialist assessments (139, 140). Furthermore, the tool improved guideline adherence with no evidence to indicate any serious associated risk from the use of the tool. However, although the EDS tool showed some promising results, the authors proposed that further refinement may be required, along with larger studies to draw definite conclusions on the utility of the tool in improving clinical outcomes.

Discussion around the benefits of decision support tools

In general, in light of the growing body of medical information, a CDS offers support to clinicians in their clinical decision making. Implementation of CDS across various settings has led to improvements in patient care processes, healthcare costs and use of preventative medicine. Using CDS tools can help health care professionals recognise when tests may be unnecessary and when patients may be unable to avoid an unnecessary hospitalisation. They can also help clinicians personalise medicine by assessing an individual's risk for a particular condition to enhance patient care (348-350).

Although clinical decision support tools are not a new concept (351), the development of tools for the diagnosis of TIA is relatively novel. The need for further support for GPs to improve diagnosis and management of TIA have been consistently reported (352). The high number of patients referred to TIA clinics who have not suffered a TIA or stroke (135), coupled with evidence that some TIAs are missed or undertreated (132, 134), highlights the possible value of a decision support tool for GPs in diagnosing and managing suspected TIA.

This study highlights that there may be benefits of using a diagnostic score for TIA in primary care which were further supported by recent meta-analysis which proposed that by using a diagnostic score, a better assessment can be facilitated for suspected TIAMS patients (353). Furthermore, the use of diagnostic tools may function as a way of helping to resolve uncertainty about a set of symptoms (354), and are developed to aid clinicians' decision making (80). Findings from a qualitative study exploring GPs' experiences of using diagnostic tools for cancer reported that diagnostic tools assisted in the recognition of symptoms that previously might not have raised an alarm, by alerting the significance of more opaque signs and symptoms (285).

It has been suggested that clinical risk scores/models combined with clinical judgement are better than clinical judgement alone (286). A study of GPs' experiences of using diagnostic tools for cancer found that clinicians relied less on their clinical judgement alone, and instead check patients' diagnoses through further testing. Also, a diagnostic tool for cancer was found to support GPs clinical decision-making and provided reassurance (285). This supports the results obtained from the current study as GPs felt the need for an objective tool to back up their judgement (Chapter 4, section 4).

A large body of research addresses how to communicate risk information to GPs (355). Presenting GPs with a cut-off based on sensitivity and specificity can be difficult for them to fully understand (288). This has also been reported with the results of the AUC as it means very little to clinicians. It is well established that diagnostic tests are understood best when presented in terms of gains and losses to individual patients, but the AUC lacks clinical interpretability because it does not reflect this (356). A growing evidence base is emerging on how best to present information about risk in general practice (289-291). GPs frequently base decisions on risk, however, it has been proposed that the nature and presentation of risk information available to GPs could be improved (292). The frequent use of risk score in daily practice suggests that GPs are likely to feel comfortable using the risk presented in this study (Chapter 5). Substantial efforts directed at the development and validation of more current and accurate risk scores for various population groups have helped improve the availability of risk scores in recent years (293, 294). These risk scores have shown to be useful for GPs for individual decision making (293, 295). Such established models include the cardiovascular disease risk score (QRISK) to estimate individualised risk of cardiovascular disease, QDiabetes to identify people who may be at high risk of type 2 diabetes and the CHA_2DS_2-VASc stroke risk score for patients with atrial fibrillation. GPs also use risk scores to inform referral decisions based on the immediate likelihood of a diagnosis such as the Wells score, a diagnostic prediction model for deep vein thrombosis (87).

There are two ways of presenting the score as discussed earlier (section 3.1.1). This includes discrimination, which is where those with the disease are distinguished from those without the disease. On the other hand, calibration is the calculation of probabilities. Dawson et al had designed a score for discrimination, however GP interviews in Chapter 4 highlighted a preference for calibration. Therefore, it is important to point out that unlike the risk score models highlighted above, GPs may not be accustomed to using a diagnostic score such as the Dawson score which was not originally designed to present risk of TIAMS.

Although CDS are widely used and have led to various positive outcomes, there are examples of where the CDS has shown limited benefits or no changes in patient outcomes (357-360). It has also been highlighted that physicians are less likely to accept a CDS if the tool/score does not match their own decision-making processes (361). Furthermore, there are also practicality related issues, such as resistance to use the tool/score and increased

costs associated with implementation (362-364). Despite this, it has been suggested to be important to continue to develop tools that can improve patient care, particularly in areas of medicine and surgery that require complex and individualised decision making (350).

The Dawson score versus the DOTS

The only diagnostic tool for TIA at the time of the study was explored in terms of potentially reducing the number of referrals that are diagnosed at TIA clinics as non-TIAs. This could enable clinics to provide more time to manage patients with TIAMS, and allow the clinic to assess patients promptly. In the current study, applying the score at the cut-off recommended by Dawson would reduce referrals by 12% and exclude 9% of patients diagnosed as TIAMS (section 3.6.1). These results are consistent with Lasserson et al's study which found that using secondary care data, the score would reduce referrals by 14%, and would have excluded 7% TIA patients (98). Given the detrimental effects of a missed TIA, arguably, it would not be worth reducing referrals by 12%, when 9% would have a TIAMS diagnosis. This would be a big risk which GPs may not be willing to take. Ideally a score/tool should exclude a high number of referrals but the exclusion of true TIAMS should be low. However, in this study, there was a low percentage of referrals, and a high proportion of missed TIAMS diagnosis. Although it is important to acknowledge that some degree of misdiagnosis is unavoidable (365), the risk of missing a TIA diagnosis is detrimental. It could be proposed that if the score is to be used, then stroke physicians could contact the GP to discuss alternative strategies for the 12% of referrals whom they believe may not need be seen at the TIA clinic. Additionally, likelihood risk of TIA could be presented to GPs based on the score and used in conjunction with clinical judgement.

The DOTS is a new and internally validated web and mobile app based diagnostic tool which encompasses both posterior circulation and retinal TIA. The score was derived retrospectively from a single centre TIA clinic database, and an optimum cut-point was obtained for the score (-0.547). The derivation and validation cohorts were separate samples drawn from the years 2010/2012 and 2013 respectively (193).

There are many different factors which influence a GP's decision to refer. These include patient factors (clinical characteristics and personalities), GP knowledge and environmental

factors (support tools and referral processes) (366). The majority of these factors are not highlighted in the guidelines on the assessment of suspected TIA, which focus on neurological symptoms and cardiovascular risk factors (11, 33, 367). These results highlight the complexity of supporting decision making around whether to suspect TIA in those who present to primary care. GPs are consistently encouraged to take cardiovascular risk factors into account when diagnosing TIAMS (5,12,13). Therefore, diagnostic tools for TIA such as the Dawson score and the newly developed diagnosis of TIA (DOT) score focus on clinical characteristics and risk factors (96).

With regards to the Dawson score, the clinical characteristics that were predictive of TIA were included in the model around 10 years ago. The main advantage of the DOTS is that it includes a wider range of symptoms caused by retinal and some posterior circulation events that were not included in the Dawson model. Some of these include bilateral visual loss, visual aura, monocular visual loss, ataxia (limb and gait) and amnesia as well as including history of hypertension (193). In addition to the validation study (193), the DOTS has been subject to an external validation study for identification of TIA in a Chinese population in 2019 (368). The sensitivity compared with the DOTS validation study was lower (70% vs 89%) as well as the Dawson validation study (93%) (96) and this study (97%). In regards to the specificity, it was lower than the DOTS validation study (63% vs 76%) but higher than that reported in both Dawson (34%) and this study (16%). The study also highlighted a greater AUC of DOTS (0.728) compared with Dawson (0.681) (368). This was also consistent with the 2017 validation study of DOTS (DOTS AUC; 0.89 vs 0.77 Dawson score) (193). In terms of the limitations of the DOTS, the case mix was different to UK as it included a younger mean age (61.1 years), a lower percentage of TIA mimics (28%), and the data were not from primary care. Rather, it was collected retrospectively from a single centre in China. It is important to note that the discussion on how GPs may use a diagnostic score in this chapter are applicable to either the Dawson score or the DOTS.

How could the Dawson score be used in primary care?

Although suggestions have been outlined below on the use of the score in primary care, the use of the Dawson score in primary care consultation has not been tested in this thesis. This is an important avenue for future research (discussed later), as the work conducted has only shown that it can be used for triage in TIA clinics.

Communication between the GP and a specialist is important in order to provide the optimal care for patients (369). If a TIA is unlikely, then a telephone conversation with a specialist is suggested (11). Therefore, if the Dawson score is to be used in primary care and suggests that a TIA is unlikely, then it would be beneficial for the GP to speak with a specialist. Based on the discussion, it may be advised that the GP follows a less urgent referral stream if felt necessary. Alternatively, the specialist may suggest that the patient should be referred to be seen in the clinic.

It is important to note that the Dawson score has features of a diagnostic score and also a screening test. Its use is for those with symptoms of TIA which is the purpose of a diagnostic score, but on the other hand, it does not give a definitive diagnosis of TIA. Rather, the score provides an indication of those who should be seen by a specialist for investigation. Based on this, there is a risk of using the score without the adjunct of clinical judgement. Therefore, in primary care it should not be recommended to be used purely based on its diagnostic utility. Rather, it needs to be used alongside clinical judgement both in primary and secondary care to suspect or rule out a TIA. This is line with the literature which cites that diagnostic tools should be used alongside clinical judgement (286, 370). If the Dawson score is to be used alongside clinical judgement, patients may still need to be referred for specialist review. Working in partnership with patients and sharing responsibility for decision making with them is often discussed by clinicians as a key component of delivering good care (371). It is a discussion about the best course of action for the patient, which is a shared decision between the GP and the patient. This conversation can be made easier with the use of a tool, rather than based purely on GPs' clinical judgement.

GPs may use the TIA clinics as a place to send patients they are unsure about even if they know the diagnosis is unlikely, or to exclude rather than confirm a final diagnosis (125)

(281). Furthermore, given the challenging nature of diagnosis of transient neurological symptoms, the practitioners' tolerance of uncertainty also influences management decisions (166). This supports results from the qualitative study as many GPs referred TIA patients as a way to quickly resolve uncertainties about the diagnosis. Therefore, the use of the Dawson score in primary care may eliminate some of this uncertainty, and help reduce some unnecessary referrals, whilst providing reassurance to both the GP and the patient.

Previous research has shown that doctors are increasingly aware of the potential for complaints from patients and the risk of litigation (284). This means their practice is often more cautious and defensive (372). This may include performing unnecessary diagnostic tests, prescribing unnecessary treatment and needless hospitalisation. The literature raises concerns about how healthcare professionals can get drawn into practising in ways that are influenced by a desire to protect themselves, rather than necessarily in the best interests of their patient (284). Clinicians may feel less able to trust their clinical judgement and therefore, turn to the support of a diagnostic tool to back up their judgement. Furthermore, a diagnostic tool may provide reassurance that not referring is the right decision, provide documentary evidence of the decision-making process if the doctor is challenged about their decision, and support communication with patients about the best course of action.

How could the Dawson score be used in secondary care?

The Dawson score could be used in triaging referrals by either sending them back to be managed in primary care, or the clinic could refer them within secondary care to a different department such as the hypertension clinic. This is an important aspect because even though some patients may not have a TIA, they still may have risk factors that need managing. Similar to the suggestion above on the communication between GP and specialists, the specialist at the TIA clinic could have a telephone conversation with the GP to discuss management options for patients they believe should not be seen at the clinic.

In the validation study, it was not clear how much of the clinic score was updated at the time of the patient's clinic consultation. Therefore, if it was to be used for clinic triage, findings from the study provide more evidence for a member of the TIA clinic staff to collect the data for the Dawson score by phone, rather than relying on information from the GP

referral. This would include a telephone interview with patients to collect the Dawson data. Alternatively, it would be reasonable to suggest that if the score is to be used in primary care, then the GP could complete the Dawson score prior to referral to the TIA clinic. This way the Dawson clinical features are captured on the day of the consultation in primary care (although this has not been assessed in the current study). Similar to the ABCD2 score, the GP could add the patient's Dawson score to the referral form. The specialists at the clinic could then assess the referral letter and make a decision for the management of the patient. If the score is below a certain threshold, the specialist could communicate their decision reasons with the GP and agree how to best manage the patient. With internal referrals however, either a member of the clinic staff could collect the Dawson data once the patient presents to ED or inwards within secondary care, or a member of the clinic staff could interview the patient to collect this information.

It has been argued however, that the introduction of triaging GP referrals has created a further complication for the referral process and the quality of that process (373). Although the triaging process can enhance quality by helping ensure that the referral goes to the appropriate destination, and can reduce the burden at the TIA clinic, it has been argued that the triage function adds unnecessary steps in the patient pathway (373). Additionally, it can compromise clinical decision making and choice because of financial incentives at play (373). This is an important consideration because if the Dawson score is to be used in secondary care for triage the patient would have already had contact with secondary care at a cost of service use. Whereas, if the score is to be used in primary care to rule out a TIA then the cost of triage could potentially be avoided.

6.4. Strengths and limitations of the thesis

The overall aim of this thesis was to explore the diagnosis and management of suspected TIA in primary care, and how a diagnostic tool for TIA could be used to guide GPs' referral decisions and/or by secondary care to triage these referrals.

This thesis used both quantitative and qualitative methods to address the research questions within each chapter. The systematic review searched the literature in a structured way and synthesised findings to obtain a comprehensive account of current knowledge on the diagnosis and management of TIA. The external validation study assessed the utility of the Dawson score in predicting the diagnosis of TIAMS, and determined its potential to triage referrals at a TIA clinic. This led to the qualitative study interviewing GPs to explore their experiences and views of TIA and to investigate the potential utility and practicality of a diagnostic tool used in primary care setting. Lastly, Chapter 5 addressed the research question of exploring alternative cut-offs based on suggestions by GPs in the interviews using a logistic regression model that could present GPs with the risk of TIAMS using the Dawson score.

The strengths and limitations of each study were evaluated and discussed in the relevant earlier chapters. However, the strengths and limitations of the overall thesis are provided below.

A diagnostic tool for TIA would ideally be tested using data collected for this purpose by GPs when the diagnosis is being considered. Although in this study it was not feasible to ask GPs to calculate the score during the initial consultation, a major strength is that information to derive the interview score was collected soon afterwards, following referral to the clinic. Another strength is that information for the interview score was collected in a structured way, rather than relying on routine data collected by the GP.

The qualitative study examining GPs' views on the diagnosis of TIA addressed an area of research which has not been explored in-depth before. The study sought to explore the experiences of GPs, who are usually the first contact when a patient experience symptom(s) suggestive of TIA. An additional strength is that the topic guide for the qualitative study was

based on a systematic literature review, and was discussed and piloted with two GPs. This allowed the questions, structure and style to be amended according to their suggestions.

Semi-structured interviews allowed flexibility with the structure of the conversation and ultimately, provided rich data generating new insights on how uncertainty plays a key role in GPs decision-making process, and managing suspected TIA patients.

Another strength was the use of mixed methods. The clinical utility of the Dawson score study included exploring the cut-off originally used. The qualitative study provided insights into the cut-off that GPs would be comfortable with. This led to further analysis of the quantitative data to explore how the score could be used and presented in a way most useful to GPs.

A limitation of both the quantitative and qualitative studies was that they were small scale and conducted at single sites. Stroke prevention services are widely available in the UK (374) however, there is regional variation in terms of access to services, how clinics are run and the comprehensiveness of services (375). Therefore, the results of the clinic study may not be generalisable to places with different patient populations and clinic provision. Also, only referred patients were included, rather than all people for whom the GP considered a TIA diagnosis.

The sample included in the external validation study was biased towards the milder end of the spectrum of clinic attenders. A large proportion of those at high risk of TIAMS were missed from the study due to patient's being seen urgently on same day weekend appointments. Therefore, the sample was not completely representative of the clinic population in terms of high-risk patients. Furthermore, a major limitation with the clinic database related to the uncertainty of what extent the data was derived from GP data, or data added at clinic consultations.

The gold standard diagnosis used in this study was based on specialist diagnosis. There are 10 different stroke specialists at the Leicester Royal Infirmary TIA clinic. A high rate of disagreement amongst stroke specialists with regards to the diagnosis of TIA has been consistently reported (129). Therefore, a limitation of the study is that the final diagnosis for the patients relied on the judgment of a single specialist.

In terms of the qualitative study, time was a general limitation. GPs had limited time for interviews which explained the low response rate, and interviews were limited up to 30 minutes. Within the 30 minutes, four particular areas were covered which meant that the amount of information ascertained per topic was limited.

The sample consisted of 10 GPs from Leicestershire and some were from the same practices. The study aimed to initially recruit 15–20 GPs, which would have allowed for a range in terms of age, size of practice and years in practice. GPs in the final sample had between 6–11 years' experience (Chapter 4, Table 4.4.1). Therefore, the sample was missing less and more experienced GPs. In addition to this, it is possible that GPs who had a particular interest in the topic agreed to participate.

The main objective of this study was to explore GPs views on the diagnosis and management of TIA. Therefore, the patient's perspective was not explored. However, it may have been of interest to explore various patient focused areas. Examples include how GPs interact with patients on the diagnosis of TIA. The patient's understanding of TIA and their experience of the symptoms as well as their understanding and attitude of the risk of stroke associated with a TIA. Exploring these topics would have contributed to the large body of literature relating to the development of decision support systems designed to promote shared decision making with the clinician and patient together (376-378).

Shared decision making is a collaborative process through which healthcare professionals support their patient to reach a decision about their care. This includes current or future management decisions or planning. It involves healthcare professions working together with patients to choose tests, treatments, management or support options which are based on evidence and personal preferences, health beliefs and values. This involves ensuring that the patient understands the risks, benefits as well as possible consequences of different options through discussion and sharing information (379).

Sharing decisions, as opposed to clinicians making decisions on behalf of patients is gaining increasing prominence in health care policy (376). Furthermore, NICE is also developing a

guidance on implementing shared decision making which is expected to be published in April 2021. This will provide formal NICE guidance on implementing shared decision making[6]

The development of clinical support systems can aid clinicians form a partnership between the clinician and the patient to make a health decision. This joint process provides the opportunity for people to make decisions about their treatment and care that is right for them at that time (379).

6.5. Future research

Further research is needed to evaluate the feasibility and effectiveness of a diagnostic score for TIA in general practice, whether that is the Dawson score or DOTS. This would include whether the score would be accepted by GPs and its cost-effectiveness. Various studies have explored clinician views and attitudes on the acceptability of clinical decision support tools. The studies highlighted that clinicians' views on clinical decision support tools can shape the implementation process, and can help guide the preparation for adoption of future decision making tools in practice (380-382). As mentioned earlier, if a diagnostic score is to be used to triage in secondary care this may be associated with increased cost. It may be useful for studies to examine where a diagnostic score is best placed (primary or secondary care), and a health economic assessment of the use of the score.

Even though the Dawson score was derived from specialist assessments, in practice, a diagnostic tool/score would be more helpful for generalists. The score could also help to triage suspected TIA patients. The aim of this study was not to derive a score, rather it was a validation study of the Dawson score. However, this diagnostic tool has been suggested to perform less well in primary care than the original secondary care setting (98). A diagnostic tool/score is therefore needed that is derived and validated entirely from primary care data. This study only included referred cases and the issue of under-referral was not examined. Thus, there is a need for a prospective study looking at all cases of transient neurological attack in primary care.

[6] https://www.nice.org.uk/advice/ktt23/chapter/Evidence-context

Although calibration of the score was desired by GPs, the score was developed to be used based on its discriminative ability. Therefore, further work needs to be done if GPs want to establish the calibration aspect of the score. The score's purpose is not to be presented as percentage risk of TIA, rather, it is always going to be associated with a cut-off. If the risk calculation was to be implemented in practice, the percentage risk derived in the current study would not apply to someone who has not been referred by the GP. The assumption is that there are a number of cases in which the GP considers a diagnosis of TIA but do not refer. For these cases, the risk calculation would not apply, emphasising the need for more research in a primary care setting. Further research could derive a risk score not just on referred cases but on all cases of suspected TIA. Similar to the QRISK which was derived from national sample of practices which contributed to the database, further work is needed to develop the risk calculation so that it develops a risk output or probability output based on national data.

It may be worth for future studies to examine different factors which influence GPs' decisions on whether to refer. For example, patient factors (clinical characteristics and personalities), GP knowledge and environmental factors (support tools and referral processes) (366). The majority of these factors are not highlighted in the guidelines on the assessment of suspected TIA, which focuses on neurological symptoms and cardiovascular risk factors (11, 33, 367).

Various practical issues may also need to be considered if a score is to be used in practice. For example, the score needs to be embedded in electronic records that could be used in the practice and on home visits. A score could be further tested in an implementation trial where GPs are provided with information about likelihood of TIA.

Given GPs' preference for a score that provides individual risk of TIA, future research could also focus on how this could be linked with advice on referral with options including definitely refer, definitely do not refer and an option of seeking specialist advice about referral and management. A recent study found that collaboration with secondary care improved GPs confidence and skills in diagnosis (166). Thus, an option that includes an open line communication with a specialist may be beneficial.

In terms of the qualitative study, future studies could include newly qualified GPs and those with 20–30 years' experience to gain insight whether they have alternative views on the challenges of diagnosis and management of TIAs. Additionally, suspected TIA patient views on aspects relating to their diagnosis and management would be beneficial. This information could then be used to understand how a diagnostic tool could support shared decision making between the clinician and the patient to reach a decision about their care (376, 380). Furthermore, GPs may find explaining percentage risk to a patient less difficult as opposed to explaining cut-offs. The percentage risk of TIA may therefore support the communication of risk to the patients with the use of a diagnostic score.

6.6. Conclusion

The majority of patients with symptoms suggestive of TIA present to general practice. The three stands of the thesis demonstrated that GPs dealing with suspected TIA patients make decisions based on patient characteristics and symptom presentation.

The lack of support for general practitioners to aid with the diagnosis and management of suspected TIA patients is a barrier to achieving the NICE targets for prompt specialist assessment. GPs would value a diagnostic tool to help them by providing objective evidence to back up their judgement. The Dawson score is a tool that could be used to support diagnosis and referral decision, and would be most useful by providing a risk estimate to be used in combination with clinical judgement.

The external validation of the Dawson score found that the score could be used to reduce referrals to the TIA clinic. In the primary care setting, the Dawson score should be used alongside clinical judgement. However, in cases where the GP is uncertain on the appropriate management route, then GP should discuss these patients with a specialist at the TIA clinic. For using the Dawson score in triage, in a secondary care setting, it would be best for specialists to phone the patient to collect the Dawson score and then triage the patient accordingly. However, if the Dawson score is to be implemented in primary care then GPs could add the score on GP referral forms.

Further research on a diagnostic tool implemented into practice is needed to fully understand its practicality and feasibility. This would involve developing a risk calculation

based on national data, as well as testing the tool in a primary care setting. This thesis demonstrated the complexity of GPs' diagnostic and referral decisions and supported the need for a diagnostic tool to aid their decision-making process.

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Appendices

Appendix 1: Accepted systematic review publication

The below published article has been removed from the electronic and hard copy version of this thesis due to copyright restrictions:

Bose P, Wilson, A, Mistri A. Diagnosis and management of transient ischemic attacks in primary care: a systematic review. Journal of primary health care. 2017;9(2):114–30.

Appendix 2: Protocol updated on Prospero

Review question(s)
The diagnosis and immediate management of transient ischemic attack in primary care.

1. How are TIAs diagnosed in primary care?
2. How are TIAs initially managed in primary care?
3. How effective are interventions to improve the diagnosis and immediate management of TIAs in primary care?

Searches
MEDLINE 1995 – Present
EMBASE 1995 – Present
Scopus 1995 – Present
Web of Science1995 – Present

Types of study to be included

Published full text peer reviewed journal articles reporting empirical studies and systematic reviews will be included. There will be no restriction on language and no restriction on study design.

Exclusion criteria include papers restricted to stroke and long term management as well as reviews, editorials/letters, opinion pieces, conference abstracts, case reports and non-systematic reviews.

Condition or domain being studied

Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease. The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease. The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists (Easton et al., 2009).

Participants/ population

Participants will be GP (general practitioner), family doctor, family physician and patients with TIA presenting to primary care.

Exclusions include paramedics, Emergency department, and secondary care physicians, papers restricted to patients with stroke and studies of long term management /secondary prevention

Search strategy

The searches will include relevant databases from 1995-present. In the past 20 years, more has become known about the natural history of TIA and the importance of immediate management.

The search terms used are as follows;

- attack
- attack*
- care
- diagnos*
- diagnosis
- diagnostic errors
- doctor*
- family
- family doctor*
- family practice

- general
- general practice
- general practioner*
- general practitioners
- gp
- health
- isch?emic
- ischemic
- ischemic attack
- ischemic attack, transient
- misdiagnos*
- patient*
- physicians, family
- practice
- practioner*
- primary
- primary care
- primary health care
- tia
- transient
- transient isch?emic attack*

Outcome(s)

Primary outcomes
Diagnosis of TIA, immediate management of TIA (medication and referral)

Secondary outcomes
None

Selection of papers

Two review authors will independently screen all titles and abstracts in order to distinguish which papers are contributing to which question. Three questions will be analysed separately, thus, a table will be set up to help follow which papers fall under each category. An example is shown below

Studies:	Diagnosis	Management	Intervention
1	X		
2		X	X
3		X	

Data extraction

The papers identified by the electronic database searches will exclude obviously irrelevant titles using the detailed inclusion and exclusion criteria. Once the reviewers meet the finalised selection, a third reviewer may arbitrate if necessary. The selection process will be illustrated using a PRISMA flow diagram

Two review authors will assess the methodological quality independently and will resolve all disagreements through discussion or with the arbitration by a third review author.

Risk of bias (quality assessment)

Assessment of risk bias in the included studies;
The methodological quality of each study will be assessed using;

1. Mixed Methods Appraisal Tool (MMAT) (2011) (1)

Strategy for data synthesis

Individual data extracted will be structured around participant characteristics, intervention (if applicable), and outcomes and the three questions will be analysed separately.

Dissemination plans
We plan to disseminate our findings through scientific conferences and publications.

Contact details for further information
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Language
English
Country
United Kingdom
Stage of review
Ongoing
Date of registration in PROSPERO

Stage of review at time of this submission	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	Yes	Yes
Risk of bias (quality) assessment	Yes	No
Data analysis	No	No

Appendix 3: Database searches

This study aimed to review the available evidence about primary care physicians' (general practitioner/family doctor) accuracy in diagnosing transient ischemic attack. To structure the question for this review, the PICOS: (P: participation/population, I: intervention, C: comparator/control, O: outcome, S: study design) question formulation is specified below:

Participants	Patients with TIA
Intervention	GP diagnosis
Outcome	Diagnostic accuracy: the number of patients with specialist diagnosis probable or likely TIA
Study design	Qualitative and quantitative

Participants	Patients with TIA
Intervention	GP management and referral
Outcome	referral rates, urgency and medication
Study design	Qualitative and quantitative

Participants	General practitioners/physicians/family doctor
Intervention	Guidelines/diagnostic aids/ education to improve GP management
Comparators	GPs not receiving intervention
Outcome	Improved diagnosis and management
Study design	Qualitative and quantitative

The search below was on the diagnosis of TIA in primary care, the obtained results were also used to assess immediate management:

Medline: 239 papers

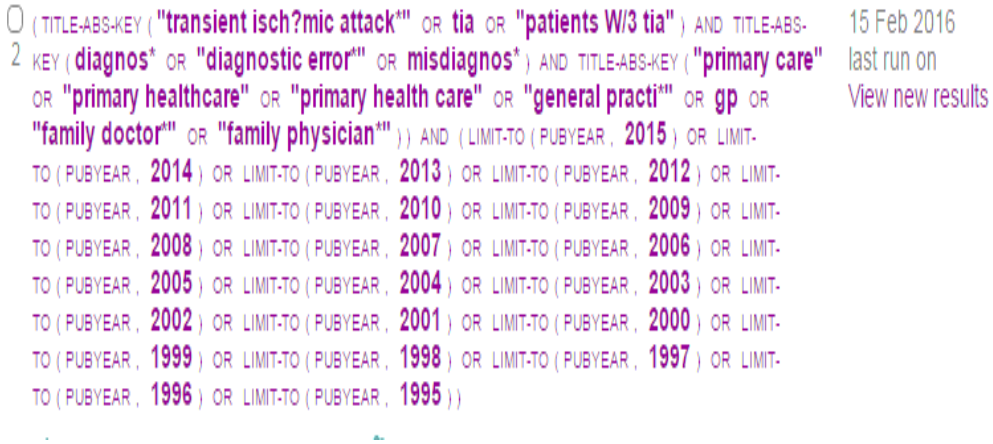
Number	Searches	Results
1	exp Ischemic Attack, Transient/ or ischemic attack.mp.	22089
2	Transient isch?emic attack*.mp.	10276
3	TIA.mp.	6090
4	(patient* adj2(TIA or transient isch?emic attack*)).mp.	2157
5	1 or 2 or 3 or 4	27328
6	exp Ischemic Attack, Tranient/di[Diagnosis]	2709
7	exp Diagnosis/	6993646
8	diagnos*.mp.	2242422
9	exp Diagnostic Errors/	102056
10	Misdiagnos*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word,	22961

	protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	
11	6 or 7 or 8 or 9 or 10	7919001
12	primary care.mp. or exp Primary Health Care/	133795
13	primary health care.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	68352
14	general practice.mp. or exp Family Practice / or exp General Practice/	84514
15	GP.mp.	30902
16	general practice.mp. or exp General Practitioners/	2739
17	Physicians, Family/ or family doctor*.mp.	18459
17	12 or 13 or 14 or 15 or 16 or 17	243596
18	4 and 10 and 17	239

Embase: 471 papers

Number	Searches	Results
1	ischemic attack.mp. or exp transient ischemic attack/	24035
2	Transient isch?emic attack*.mp.	24508
3	TIA.mp.	11285
4	(patient* adj2 TIA).mp.	2401
5	1 or 2 or 3 or 4	30093
6	exp transient ischemic attack/di[Diagnosis]	1770
7	exp diagnosis/	3521514
8	diagnos*.mp.	2407233
9	exp diagnostic error/	57222
10	misdiagnos*.mp.	27001
11	6 or 7 or 8 or 9 or 10	4324442
12	primary care.mp. or exp primary medical care/	114484
13	primary health care.mp. or general practice/	43722
14	Gp.mp.	54748
15	general practitioner/or general practitioner*.mp.	54021
16	family doctor*.mp.	76847
17	12 or 13 or 14 or 15 or 16 or 17	4216
18	5 and 11 and 18	263838
19	Limiy 19 to yr = “1995-current”	

Scopus: 243



Web of Science: 96 papers

Set	Run Search **Web of Science Core Collection Search History - " 30/10/2015"**
#14	#13 AND #9 AND #5 *DocType=All document types; Language=All languages;*
#13	#12 OR #11 OR #10 *DocType=All document types; Language=All languages;*
#12	**TOPIC:** (GP OR "family doctor*" OR "family physician*") *DocType=All document types; Language=All languages;*
#11	**TOPIC:** ("general practi*" OR "family practi*") *DocType=All document types; Language=All languages;*
#10	**TOPIC:** ("primary care" OR "primary health care" OR "primary healthcare") *DocType=All document types; Language=All languages;*
#9	#8 OR #7 OR #6 *DocType=All document types; Language=All languages;*
#8	**TOPIC:** (misdiagnos*) *DocType=All document types; Language=All languages;*
#7	**TOPIC:** (diagnos* near/2 error*) *DocType=All document types; Language=All languages;*
#6	**TOPIC:** (diagnos*) *DocType=All document types; Language=All languages;*
#5	#4 OR #3 OR #2 OR #1 *DocType=All document types; Language=All languages;*
#4	**TOPIC:** (patient* near/2 TIA) *DocType=All document types; Language=All languages;*
#3	**TOPIC:** (TIA) *DocType=All document types; Language=All languages;*
#2	**TOPIC:** ("transient isch?emic attack*") *DocType=All document types; Language=All languages;*
#1	**TOPIC:** ("isch?emic attack*") *DocType=All document types; Language=All languages;*

Appendix 4: Data extraction form

GP diagnosis and management of TIA

Data extraction Form

Study details

Study Details	
Refworks number:	
First author:	
Title:	
Journal:	
Publication date:	
Country of origin:	
Publication language:	

Eligibility

Eligibility Criteria	Yes	No	Comments
GP knowledge of diagnosis and/or immediate management of TIA			
GP practice in diagnosis of TIA			
GP practice in referral of TIA			
Intervention to improve GP diagnosis			
Intervention to improve immediate GP management of TIA			

Exclusion reason:

☐ Review
☐ Emergency department study
☐ Not diagnosis, management or intervention
☐ Not focused on TIA
☐ Long term management
☐ Restricted to stroke

Aim (as expressed by authors)

Design

General information	
Type of study: **Observational** ☐Cross-sectional/Survey Trial ☐ Cohort ☐ Prospective ☐ retrospective ☐ Case Control ☐ Other (State below) **Interventional** ☐ RCT ☐ non randomised controlled trial ☐ Controlled before and after ☐ Uncontrolled before and after - Interrupted time series ☐ Other (State below) ☐ **Qualitative** **Details of method**	**Second screen (if necessary) conducted by:** **Observational** ☐ Cross-sectional/Survey Trial ☐ Cohort ☐ Prospective ☐ retrospective ☐ Case Control ☐ Other (State below) **Interventional** ☐ RCT ☐ non randomised controlled trial ☐ Controlled before and after ☐ Uncontrolled before and after - Interrupted time series ☐ Other (State below) ☐ **Qualitative** ……
Quality score (MMAT 2011)	

Notes:

Participants (GPs)

Setting:	
Study Inclusion criteria:	
Study Exclusion criteria:	
Sample size/characteristics	
Exclusions / rate	
Years in practice/qualified	
Type of practice	
Other	

Participants (patients)

Inclusion criteria:		
Exclusion criteria:		
None		
Sample size		
Patient characteristics		

Interventions (if applicable)

Intervention type:	Educational and behavioural		Structural		Financial				
Location of intervention	Inpatient	Outpatient	Community	Mixed	Not clear				
Length of intervention period									
Person delivering intervention									
Timing of delivery									
Number, length and frequency of intervention components	Number:		Length:		Frequency:				
Details of intervention protocol:									
Details of control protocol:									

Results:

Primary Outcomes	

Results (interventions)

Primary Outcomes					
Intervention group sample size					
Control group sample size					
	Follow-up intervals from start of intervention	Method of measuring	Results for intervention group	Results for control group	Comparisons between groups

Author's conclusions:
Reviewer's conclusions:
Correspondence required:

Appendix 5: Mixed Methods Appraisal Tool template

Mixed Methods Appraisal Tool (MMAT) – Version 2011
For dissemination, application, and feedback: Please contact pierre.pluye@mcgill.ca, Department of Family Medicine, McGill University, Canada.

The MMAT is comprised of two parts (see below): criteria (Part I) and tutorial (Part II). While the content validity and the reliability of the pilot version of the MMAT have been examined, this critical appraisal tool is still in development. Thus, the MMAT must be used with caution, and users' feedback is appreciated. Cite the present version as follows.

> Pluye, P., Robert, E., Cargo, M., Bartlett, G., O'Cathain, A., Griffiths, F., Boardman, F., Gagnon, M.P., & Rousseau, M.C. (2011). *Proposal: A mixed methods appraisal tool for systematic mixed studies reviews.* Retrieved on [date] from http://mixedmethodsappraisaltoolpublic.pbworks.com. Archived by WebCite® at http://www.webcitation.org/5tTRTc9yJ

Purpose: The MMAT has been designed for the appraisal stage of complex systematic literature reviews that include qualitative, quantitative and mixed methods studies (mixed studies reviews). The MMAT permits to concomitantly appraise and describe the methodological quality for three methodological domains: mixed, qualitative and quantitative (subdivided into three sub-domains: randomized controlled, non-randomized, and descriptive). Therefore, using the MMAT requires experience or training in these domains. E.g., MMAT users may be helped by a colleague with specific expertise when needed. The MMAT allows the appraisal of most common types of study methodology and design. For appraising a qualitative study, use section 1 of the MMAT. For a quantitative study, use section 2 or 3 or 4, for randomized controlled, non-randomized, and descriptive studies, respectively. For a mixed methods study, use section 1 for appraising the qualitative component, the appropriate section for the quantitative component (2 or 3 or 4), and section 5 for the mixed methods component. For each relevant study selected for a systematic mixed studies review, the methodological quality can then be described using the corresponding criteria. This may lead to exclude studies with lowest quality from the synthesis, or to consider the quality of studies for contrasting their results (e.g., low quality vs. high).

Scoring metrics: For each retained study, an overall quality score may be not informative (in comparison to a descriptive summary using MMAT criteria), but might be calculated using the MMAT. Since there are only a few criteria for each domain, the score can be presented using descriptors such as *, **, ***, and ****. For qualitative and quantitative studies, this score can be the number of criteria met divided by four (scores varying from 25% (*) -one criterion met- to 100% (****) -all criteria met-). For mixed methods research studies, the premise is that the overall quality of a combination cannot exceed the quality of its weakest component. Thus, the overall quality score is the lowest score of the study components. The score is 25% (*) when *QUAL=1 or QUAN=1 or MM=0*; it is 50% (**) when *QUAL=2 or QUAN=2 or MM=1*; it is 75% (***) when *QUAL=3 or QUAN=3 or MM=2*; and it is 100% (****) when *QUAL=4 and QUAN=4 and MM=3* (QUAL being the score of the qualitative component; QUAN the score of the quantitative component; and MM the score of the mixed methods component).

Rationale: There are general criteria for planning, designing and reporting mixed methods research (Creswell and Plano Clark, 2010), but there is no consensus on key specific criteria for appraising the methodological quality of mixed methods studies (O'Cathain, Murphy and Nicholl, 2008). Based on a critical examination of 17 health-related systematic mixed studies reviews, an initial 15-criteria version of MMAT was proposed (Pluye, Gagnon, Griffiths and Johnson-Lafleur, 2009). This was pilot tested in 2009. Two raters assessed 29 studies using the pilot MMAT criteria and tutorial (Pace, Pluye, Bartlett, Macaulay et al., 2010). Based on this pilot exercise, it is anticipated that applying MMAT may take on average 15 minutes per study (hence efficient), and that the Intra-Class Correlation might be around 0.8 (hence reliable). The present 2011 revision is based on feedback from four workshops, and a comprehensive framework for assessing the quality of mixed methods research (O'Cathain, 2010).

Conclusion: The MMAT has been designed to appraise the *methodological quality* of the studies retained for a systematic mixed studies review, not the quality of their *reporting* (writing). This distinction is important, as good research may not be 'well' reported. If reviewers want to genuinely assess the former, companion papers and research reports should be collected when some criteria are not met, and authors of the corresponding publications should be contacted for additional information. Collecting additional data is usually necessary to appraise *qualitative research and mixed methods studies*, as there are no uniform standards for reporting study characteristics in these domains (www.equator-network.org), in contrast, e.g., to the CONSORT statement for reporting randomized controlled trials (www.consort-statement.org).

Authors and contributors: Pierre Pluye[1], Marie-Pierre Gagnon[2], Frances Griffiths[3] and Janique Johnson-Lafleur[1] proposed an initial version of MMAT criteria (Pluye et al., 2009). Romina Pace[1] and Pierre Pluye[1] led the pilot test. Gillian Bartlett[1], Belinda Nicolau[4], Robbyn Seller[1], Justin Jagosh[1], Jon Salsberg[1] and Ann Macaulay[1] contributed to the pilot work (Pace et al., 2010). Pierre Pluye[1], Émilie Robert[5], Margaret Cargo[6], Alicia O'Cathain[7], Frances Griffiths[3], Felicity Boardman[3], Marie-Pierre Gagnon[2], Gillian Bartlett[1], and Marie-Claude Rousseau[8] contributed to the present 2011 version.

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PART I. MMAT criteria & one-page template (to be included in appraisal forms)

Types of mixed methods study components or primary studies	Methodological quality criteria (see tutorial for definitions and examples)	Responses			
		Yes	No	Can't tell	Comments
Screening questions (for all types)	• Are there clear qualitative and quantitative research questions (or objectives*), or a clear mixed methods question (or objective*)?				
	• Do the collected data allow address the research question (objective)? E.g., consider whether the follow-up period is long enough for the outcome to occur (for longitudinal studies or study components).				
	Further appraisal may be not feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.				
1. Qualitative	1.1. Are the sources of qualitative data (archives, documents, informants, observations) relevant to address the research question (objective)?				
	1.2. Is the process for analyzing qualitative data relevant to address the research question (objective)?				
	1.3. Is appropriate consideration given to how findings relate to the context, e.g., the setting, in which the data were collected?				
	1.4. Is appropriate consideration given to how findings relate to researchers' influence, e.g., through their interactions with participants?				
2. Quantitative randomized controlled (trials)	2.1. Is there a clear description of the randomization (or an appropriate sequence generation)?				
	2.2. Is there a clear description of the allocation concealment (or blinding when applicable)?				
	2.3. Are there complete outcome data (80% or above)?				
	2.4. Is there low withdrawal/drop-out (below 20%)?				
3. Quantitative non-randomized	3.1. Are participants (organizations) recruited in a way that minimizes selection bias?				
	3.2. Are measurements appropriate (clear origin, or validity known, or standard instrument; and absence of contamination between groups when appropriate) regarding the exposure/intervention and outcomes?				
	3.3. In the groups being compared (exposed vs. non-exposed; with intervention vs. without; cases vs. controls), are the participants comparable, or do researchers take into account (control for) the difference between these groups?				
	3.4. Are there complete outcome data (80% or above), and, when applicable, an acceptable response rate (60% or above), or an acceptable follow-up rate for cohort studies (depending on the duration of follow-up)?				
4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the quantitative research question (quantitative aspect of the mixed methods question)?				
	4.2. Is the sample representative of the population understudy?				
	4.3. Are measurements appropriate (clear origin, or validity known, or standard instrument)?				
	4.4. Is there an acceptable response rate (60% or above)?				
5. Mixed methods	5.1. Is the mixed methods research design relevant to address the qualitative and quantitative research questions (or objectives), or the qualitative and quantitative aspects of the mixed methods question (or objective)?				
	5.2. Is the integration of qualitative and quantitative data (or results*) relevant to address the research question (objective)?				
	5.3. Is appropriate consideration given to the limitations associated with this integration, e.g., the divergence of qualitative and quantitative data (or results*) in a triangulation design?				
	Criteria for the qualitative component (1.1 to 1.4), and appropriate criteria for the quantitative component (2.1 to 2.4, or 3.1 to 3.4, or 4.1 to 4.4), must be also applied.				

*These two items are not considered as double-barreled items since in mixed methods research, (1) there may be research questions (quantitative research) or research objectives (qualitative research), and (2) data may be integrated, and/or qualitative findings and quantitative results can be integrated.

PART II. MMAT tutorial

Types of mixed methods study components or primary studies	Methodological quality criteria
1. Qualitative Common types of qualitative research methodology include: A. Ethnography The aim of the study is to describe and interpret the shared cultural behaviour of a group of individuals. B. Phenomenology The study focuses on the subjective experiences and interpretations of a phenomenon encountered by individuals. C. Narrative The study analyzes life experiences of an individual or a group. D. Grounded theory Generation of theory from data in the process of conducting research (data collection occurs first). E. Case study In-depth exploration and/or explanation of issues intrinsic to a particular case. A case can be anything from a decision-making process, to a person, an organization, or a country. F. Qualitative description There is no specific methodology, but a qualitative data collection and analysis, e.g., in-depth interviews or focus groups, and hybrid thematic analysis (inductive and deductive). Key references: Creswell, 1998; Schwandt, 2001; Sandelowski, 2010.	**1.1. Are the sources of qualitative data (archives, documents, informants, observations) relevant to address the research question (objective)?** E.g., consider whether (a) the selection of the participants is clear, and appropriate to collect relevant and rich data; and (b) reasons why certain potential participants chose not to participate are explained. **1.2. Is the process for analyzing qualitative data relevant to address the research question (objective)?** E.g., consider whether (a) the method of data collection is clear (in depth interviews and/or group interviews, and/or observations and/or documentary sources); (b) the form of the data is clear (tape recording, video material, and/or field notes for instance); (c) changes are explained when methods are altered during the study; and (d) the qualitative data analysis addresses the question. **1.3. Is appropriate consideration given to how findings relate to the context, e.g., the setting, in which the data were collected?** * E.g., consider whether the study context and how findings relate to the context or characteristics of the context are explained (how findings are influenced by or influence the context). "For example, a researcher wishing to observe care in an acute hospital around the clock may not be able to study more than one hospital. (…) Here, it is essential to take care to describe the context and particulars of the case [the hospital] and to flag up for the reader the similarities and differences between the case and other settings of the same type" (Mays & Pope, 1995). The notion of context may be conceived in different ways depending on the approach (methodology) tradition. **1.4. Is appropriate consideration given to how findings relate to researchers' influence, e.g., through their interactions with participants?** * E.g., consider whether (a) researchers critically explain how findings relate to their perspective, role, and interactions with participants (how the research process is influenced by or influences the researcher); (b) researcher's role is influential at all stages (formulation of a research question, data collection, data analysis and interpretation of findings); and (c) researchers explain their reaction to critical events that occurred during the study. The notion of reflexivity may be conceived in different ways depending on the approach (methodology) tradition. E.g., "at a minimum, researchers employing a generic approach [qualitative description] must explicitly identify their disciplinary affiliation, what brought them to the question, and the assumptions they make about the topic of interest" (Caelli, Ray & Mill, 2003, p. 5).

*See suggestion on the MMAT wiki homepage (under '2011 version'): Independent reviewers can establish a common understanding of these two items prior to beginning the critical appraisal.

Types of mixed methods study components or primary studies	Methodological quality criteria
2. Quantitative randomized controlled (trials) Randomized controlled clinical trial: A clinical study in which individual participants are allocated to intervention or control groups by randomization (intervention assigned by researchers). Key references: Higgins & Green, 2008; Porta, 2008; Oxford Center for Evidence based medicine, 2009.	**2.1. Is there a clear description of the randomization (or an appropriate sequence generation)?** In a randomized controlled trial, the allocation of a participant (or a data collection unit, e.g., a school) into the intervention or control group is based solely on chance, and researchers describe how the randomization schedule is generated. “A simple statement such as ‘we randomly allocated’ or ‘using a randomized design’ is insufficient”. *Simple randomization:* Allocation of participants to groups by chance by following a predetermined plan/sequence. “Usually it is achieved by referring to a published list of random numbers, or to a list of random assignments generated by a computer”. *Sequence generation:* “The rule for allocating interventions to participants must be specified, based on some chance (random) process”. Researchers provide sufficient detail to allow a readers’ appraisal of whether it produces comparable groups. E.g., blocked randomization (to ensure particular allocation ratios to the intervention groups), or stratified randomization (randomization performed separately within strata), or minimization (to make small groups closely similar with respect to several characteristics).
	2.2. Is there a clear description of the allocation concealment (or blinding when applicable)? *The allocation concealment protects assignment sequence until allocation.* E.g., researchers and participants are unaware of the assignment sequence up to the point of allocation. E.g., group assignment is concealed in opaque envelops until allocation. *The blinding protects assignment sequence after allocation.* E.g., researchers and/or participants are unaware of the group a participant is allocated to during the course of the study.
	2.3. Are there complete outcome data (80% or above)? E.g., almost all the participants contributed to almost all measures.
	2.4. Is there low withdrawal/drop-out (below 20%)? E.g., almost all the participants completed the study.

Types of mixed methods study components or primary studies	Methodological quality criteria
3. Quantitative non-randomized Common types of design include (A) non-randomized controlled trials, and (B-C-D) observational analytic study or component where the intervention/exposure is defined/assessed, but not assigned by researchers. A. Non-randomized controlled trials The intervention is assigned by researchers, but there is no randomization, e.g., a pseudo-randomization. A non-random method of allocation is not reliable in producing alone similar groups. B. Cohort study Subsets of a defined population are assessed as exposed, not exposed, or exposed at different degrees to factors of interest. Participants are followed over time to determine if an outcome occurs (prospective longitudinal). C. Case-control study Cases, e.g., patients, associated with a certain outcome are selected, alongside a corresponding group of controls. Data is collected on whether cases and controls were exposed to the factor under study (retrospective). D. Cross-sectional analytic study At one particular time, the relationship between health-related characteristics (outcome) and other factors (intervention/exposure) is examined. E.g., the frequency of outcomes is compared in different population sub-groups according to the presence/absence (or level) of the intervention/exposure. Key references for observational analytic studies: Higgins & Green, 2008; Wells, Shea, O'Connell, Peterson, et al., 2009.	**3.1. Are participants (organizations) recruited in a way that minimizes selection bias?** At recruitment stage: For cohort studies, e.g., consider whether the exposed (or with intervention) and non-exposed (or without intervention) groups are recruited from the same population. For case-control studies, e.g., consider whether same inclusion and exclusion criteria were applied to cases and controls, and whether recruitment was done independently of the intervention or exposure status. For cross-sectional analytic studies, e.g., consider whether the sample is representative of the population. **3.2. Are measurements appropriate (clear origin, or validity known, or standard instrument; and absence of contamination between groups when appropriate) regarding the exposure/intervention and outcomes?** At data collection stage: E.g., consider whether (a) the variables are clearly defined and accurately measured; (b) the measurements are justified and appropriate for answering the research question; and (c) the measurements reflect what they are supposed to measure. For non-randomized controlled trials, the intervention is assigned by researchers, and so consider whether there was absence/presence of a contamination. E.g., the control group may be indirectly exposed to the intervention through family or community relationships. **3.3. In the groups being compared (exposed vs. non-exposed; with intervention vs. without; cases vs. controls), are the participants comparable, or do researchers take into account (control for) the difference between these groups?** At data analysis stage: For cohort, case-control and cross-sectional, e.g., consider whether (a) the most important factors are taken into account in the analysis; (b) a table lists key demographic information comparing both groups, and there are no obvious dissimilarities between groups that may account for any differences in outcomes, or dissimilarities are taken into account in the analysis. **3.4. Are there complete outcome data (80% or above), and, when applicable, an acceptable response rate (60% or above), or an acceptable follow-up rate for cohort studies (depending on the duration of follow-up)?**

Types of mixed methods study components or primary studies	Methodological quality criteria
4. Quantitative descriptive studies Common types of design include single-group studies: A. Incidence or prevalence study without comparison group In a defined population at one particular time, what is happening in a population, e.g., frequencies of factors (importance of problems), is described (portrayed). B. Case series A collection of individuals with similar characteristics are used to describe an outcome. C. Case report An individual or a group with a unique/unusual outcome is described in details. Key references: Critical Appraisal Skills Programme, 2009; Draugalis, Coons & Plaza, 2008.	**4.1. Is the sampling strategy relevant to address the quantitative research question (quantitative aspect of the mixed methods question)?** E.g., consider whether (a) the source of sample is relevant to the population under study; (b) when appropriate, there is a standard procedure for sampling, and the sample size is justified (using power calculation for instance).
	4.2. Is the sample representative of the population understudy? E.g., consider whether (a) inclusion and exclusion criteria are explained; and (b) reasons why certain eligible individuals chose not to participate are explained.
	4.3. Are measurements appropriate (clear origin, or validity known, or standard instrument)? E.g., consider whether (a) the variables are clearly defined and accurately measured; (b) measurements are justified and appropriate for answering the research question; and (c) the measurements reflect what they are supposed to measure.
	4.4. Is there an acceptable response rate (60% or above)? The response rate is not pertinent for case series and case report. E.g., there is no expectation that a case series would include all patients in a similar situation.

Types of mixed methods study components or primary studies	Methodological quality criteria
5. Mixed methods Common types of design include: A. Sequential explanatory design The quantitative component is followed by the qualitative. The purpose is to explain quantitative results using qualitative findings. E.g., the quantitative results guide the selection of qualitative data sources and data collection, and the qualitative findings contribute to the interpretation of quantitative results. B. Sequential exploratory design The qualitative component is followed by the quantitative. The purpose is to explore, develop and test an instrument (or taxonomy), or a conceptual framework (or theoretical model). E.g., the qualitative findings inform the quantitative data collection, and the quantitative results allow a generalization of the qualitative findings. C. Triangulation design The qualitative and quantitative components are concomitant. The purpose is to examine the same phenomenon by interpreting qualitative and quantitative results (bringing data analysis together at the interpretation stage), or by integrating qualitative and quantitative datasets (e.g., data on same cases), or by transforming data (e.g., quantization of qualitative data). D. Embedded design The qualitative and quantitative components are concomitant. The purpose is to support a qualitative study with a quantitative sub-study (measures), or to better understand a specific issue of a quantitative study using a qualitative sub-study, e.g., the efficacy or the implementation of an intervention based on the views of participants. Key references: Creswell & Plano Clark, 2007; O'Cathain, 2010.	**5.1. Is the mixed methods research design relevant to address the qualitative and quantitative research questions (or objectives), or the qualitative and quantitative aspects of the mixed methods question (or objective)?** E.g., the rationale for integrating qualitative and quantitative methods to answer the research question is explained. **5.2. Is the integration of qualitative and quantitative data (or results) relevant to address the research question (objective)?** E.g., there is evidence that data gathered by both research methods was brought together to form a complete picture, and answer the research question; authors explain when integration occurred (during the data collection-analysis or/and during the interpretation of qualitative and quantitative results); they explain how integration occurred and who participated in this integration. **5.3. Is appropriate consideration given to the limitations associated with this integration, e.g., the divergence of qualitative and quantitative data (or results)?**

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Appendix 5: Applied Mixed Methods Appraisal Tool

Author	Type of study	Screening question (Yes, No)	Responses	Score
Roebers et al., (2007)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **No (53.5%)**	**67%**
Goldstein et al., (2000)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **Yes (full database)**	**100%**
Purroy et al., (2010)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **Yes** Are there complete outcome data (above 80% or above 60% response rate): **No (46.7%)**	**75%**
Middleton et al., (2003)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **Yes (60%)**	**100%**
Otten et al., (1995)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **Yes (66%)**	**100%**
Leung et al., (2012)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question:	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes**	**67%**

		Yes	In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **No (16%)**	
Mai et al., (2003)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **No (7%)**	**67%**
Lasserson et al., (2015)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **Yes (all referrals)**	**100%**
Gibbs et al., (2001)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **Yes (full database analysis)**	**100%**
Jackel et al., (2012)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **Yes (all 125 quota was reached)**	**100%**
Clarey et al., (2014)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **No (patient study)**	**67%**
Magin et al., (2013)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes (ABCD tool)** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate):	**67%**

			No (patient referral)	
Jagadesham et al., (2008)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **Yes (66%)**	**100%**
Ranta & Cariaga (2013)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **Yes** Are there complete outcome data (above 80% or above 60% response rate): **No (EDS programme)**	**75%**
Wiszniewska et al., (2000)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **No (53%)**	**67%**
Edwards et al., (2012)	Qualitative	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are the sources of qualitative data relevant to address the research question: **Yes** Is the process for analysing qualitative data relevant to address the research question: **Yes** Is appropriate consideration given to how findings relate to context (setting): **Yes** Is appropriate consideration given to how findings relate to researchers' influence: **No**	**75%**
Tomsaik et al., (2003)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **Yes (89%)**	**100%**
McNeill (2008)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate):	**50%**

			No (audit, referral letters)	
Ismail & Negm (2013)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **Yes (73.1%)**	**100%**
Lavin & Ranta (2014)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **No (EDS tool)**	**67%**
Wright et al., (2006 &2007)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **No**	**67%**
Ranta (2015)	Quantitative randomized controlled trial	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Is there a clear description of randomisation: **Yes** Is there a clear description of the allocation concealment **Yes** Are there complete outcome data (80% above): **Yes (all data)** Is there low withdrawal/drop out (below 20%): **No**	**75%**
Ranta et al., (2014)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **No**	**67%**
Mead et al., (1996)	Quantitative (non-randomised)	Are there clear qualitative/quantitative research questions (or objectives): **Yes** Do the collected data allow address the research question: **Yes**	Are participants recruited in a way to minimise selection bias: **Yes** Are the measurements used appropriate? **Yes** In the groups being compared are the participants comparable: **N/A** Are there complete outcome data (above 80% or above 60% response rate): **No**	**67%**

Appendix 6: Systematic review results tables

Knowledge based studies on diagnosis, recognition of emergency and prescription

Knowledge based studies						
Reference	***Country***	***Methods/Aim***	***GP details***	***Key findings***	***Type of study Quality score***	***Diagnosis (D) Referral (R) Prescription (P)***
Mead et al., (1996) (1)	***United Kingdom***	Cross sectional survey: Questionnaire **Aim:** To assess how GPs manage patients at risk of TIA/stroke	**Setting:** All GPs in Greater Manchester **Response rate:** 294/640 (46%) **Sample size:** 294 GPs	Median percentage of patients referred to specialist: **50% (**range 0-100%) 188 GPs **(64%)** would refer to general physicians 175 **(60%)** to geriatricians 65 **(22%)** to vascular surgeons 290 GPs **(99%)** would commence aspirin	***Quantitative (non-randomised)*** 67%	***R & P***
Reference	***Country***	***Methods/Aim***	***GP details***	***Key findings***	***Type of study MMAT score***	***Diagnosis (D) Referral (R) Prescription (P)***
Wiszniewska et al., (2000) (2)	***Poland***	Cross sectional survey: Questionnaire **Aim:** To assess GPs management of TIA/stroke	**Setting:** All GPs, practising GPs in 4 cities within Poland **Response rate:** 159/300 (53%) **Sample size:** 159 GPs **Age:** 27 to 66 (Average age: 42.2)	GPs would refer **50%** of patients **65%** were referred if they had speech problems **64%** doctors referred patients with motor impairments **54%** doctors referred patient with vision impairment **11%** GPs did not refer patients who already had a TIA **16%** of doctors prescribed antiplatelet	***Quantitative (non-randomised)*** *67%*	***R & P***

				21% prescribed vitamin B **55%** prescribed sedative drugs		
Reference	***Country***	***Methods/Aim***	***GP details***	***Key findings***	***Type of study*** ***Quality score***	***Diagnosis (D)*** ***Referral (R)*** ***Prescription (P)***
Middleton et al., (2003) (3)	***Australia***	Cross sectional survey: Questionnaire **Aim:** To examine GP knowledge about TIA/stroke and risk factors	**Setting:** Practising GPs from New South Wales, Australia **Response rate:** 296/490 (60%) **Sample size:** Male: 208 (70%) Female: 88 (30%) **Age (median)** age:47 years(range:28-81years)	**34 GPs (12%)** correctly estimated the risk of stroke **279 (94%)** GPs correctly identified modifiable stroke risk factors. Consider aspirin GPs responding highly likely **(54%)** **(32%)** responded somewhat unlikely to prescribing aspirin	***Quantitative (non-randomised)*** 100%	***D & P***
Reference	***Country***	***Methods/Aim***	***GP details***	***Key findings***	***Type of study*** ***Quality score***	***Diagnosis (D)*** ***Referral (R)*** ***Prescription (P)***
Nguyen-Huynh Mai et al., (2003) (4)	***United States***	Cross sectional survey: Structured telephone interviews **Aim:** To assess knowledge and reported management of TIA by primary care physicians (PCPs)	**Setting:** PCP in continental US **Sample size:** Quota sample of 200 **Response rate:** 1,289/2,978 (Quota sample 200) **Gender:** Male: 185 (93%) **Years in practice** (SD): 20 (11) **Patients seen monthly:**	Correctly identified 5 TIA symptoms: **44 (22%)** Only **86 (43%)** recognized that TIA symptoms should resolve within 24 hours. Correctly diagnosed: **62%** Incorrectly identified vertigo as symptom: **47%** **98-100%** was aware of risk factors. Referred to neurologist: **37%** GPs	***Quantitative (non-randomised)*** *67%*	***D & R***

			457 (243) **TIA patients seen monthly:** 14 (17)			
Reference	***Country***	***Methods/Aim***	***GP details***	***Key findings***	***Type of study Quality score***	***Diagnosis (D) Referral (R) Prescription (P)***
Tomasik et al., **(2003)** **(5)**	***Poland***	Cross sectional survey: Case vignettes, written questionnaire **Aim:** To assess the competence of Polish (PCPs) in diagnosing and managing patients with TIAs. Also, to assess the effect of age and type of TIA (mono-ocular blindness, versus hemispheric) on management	**Setting:** One healthcare district of Warsaw **Response rate:** 89/100 (89%) **Sample size:** GPs: 89 **Gender:** Female: 75% **Age (Mean, SD)** 43 (12) **Years in practice:** 17	The correct diagnosis of Monocular blindness was made by **63 (71%)** GPs Hemispherical ischaemia **52 (58%)** **No sig diff was found** For hemispheric ischaemia, correct diagnosis more likely if patient was aged over **65 (86, 97%)** than under **65 (74, 87%)**. More GPs would refer patients to neurologist with symptoms of hemispheral ischaemia than patients with monocular blindness: **61 (70%) v 31 (35%) p<=0.05** Antiplatelets given in **6 (7%)** of monocular blindness and **7 (8%)** of hemispheral ischaemia	***Quantitative (non-randomised)*** *100%*	***D, R & P***
Reference	***Country***	***Methods/Aim***	***GP details***	***Key findings***	***Type of study Quality score***	***Diagnosis (D) Referral (R) Prescription (P)***
Roebers et al., **(2007)** **(6)**	***Germany***	Cross sectional survey: PCPs current practice investigated by presenting 5 case scenarios **Aim:** To assess PCPs attitudes and practices of suspected stroke patients and factors which influence PCPs decisions on	**Setting:** All PCP in 4 regions of North Rhine-Westphalia, Germany **Response rate:** 395/714 (55%) **Sample size:** GPs: 395	**85% (335/395)** classified TIA as an emergency **132/395 (33%)** PCP would admit patients **Reasons for outpatient management:** Severe co-morbidities **(36.7%)**	***Quantitative (non-randomised)*** *67%*	***R***

		admission of patients with clear stroke symptoms	**Years in practice/type of practice:** 0-10: 146 (37%) 11-20: 142 (36%) >20: 96 (24%) Missing: 11 (3%) **Number of stroke patients in practice per year:** 0-5: 88 (22%) 6-10: 109(28%) 11-20: 97(25%) >20 69: (18%) Missing: 32 (8%)	Lack of therapeutic consequences of hospital admission **(32.9%)**		
Reference	***Country***	***Methods/Aim***	***GP details***	***Key findings***	***Type of study Quality score***	***Diagnosis (D) Referral (R) Prescription (P)***
Jagadesham et al., (2008) (7)	***United Kingdom***	Cross sectional survey: Postal questionnaires **Aim:** To assess the level of knowledge about the management of TIA among GPs and hospital trainees	**Setting:** General Royal Infirmary Leeds. GPs sampled from trust database **Response rate:** 40/60 GPs (66%)	All GPs correctly identified that TIA was an abbreviation for a transient ischaemic attack, and that this lasted <24 hours Risk of stroke underestimated: **23%** of GPs GP considered vertigo **(75%)** and confusion **(70%)** to be suggestive of a TIA **20%** would refer patients with motor or sensory deficits **22-40%** TIA patients would not be referred by GPs (depending on symptom type) All doctors were more likely to prescribe antiplatelet therapy with monocular visual loss **(P=0.03)** GPs less likely to initiate APT or statins than medical specialist registrars (**P <0.01)** 5-10 % GPs thought a carotid duplex ultra sound following a TIA was	***Quantitative (non-randomised)*** *100%*	***D, R & P***

				appropriate investigation and likely to request blood tests **(P<0.05)**		
Reference	***Country***	***Methods/Aim***	***GP details***	***Key findings***	***Type of study Quality score***	***Diagnosis (D) Referral (R) Prescription (P)***
Purroy et al.,(2011) (8)	***Spain***	Cross sectional survey: Questionnaire **Aim:** To assess the knowledge of doctors in Primary Care centres about TIA (definition, symptoms, diagnosis, management and risk of recurrence)	**Setting:** All medical staff in 24 Primary Care Centres (PCC) in one health area of Spain **Response rate:** 138/258 (53%) **Sample size:** GPs:138 **Gender:** Female 81 (59) **Age (SD):** 43 (8.4)	**124 (90%)** correctly identified the definition of TIA: **43 (31%)** answering less than one hour **81 (59%)** answering less than 24 hours. **59** PCPs **(43%)** recognised the risk of stroke recurrence. **65 (47%)** suggested the risk to be same as for an established stroke, **59 (43%)** proposed the risk was higher than that of stroke and **14 (10%)** suggested the risk was lower than that of stroke. Low awareness of visual symptoms: **(94, 68%)** Isolated vertigo incorrectly listed as symptom: **47 (34%)** Referral to ED: **(108, 78%)**	***Quantitative (non-randomised)*** ***75%***	***D & R***
Reference	***Country***	***Methods/Aim***	***GP details***	***Key findings***	***Type of study Quality score***	***Diagnosis (D) Referral (R) Prescription (P)***
Edwards et al., (2012) (9)	***United Kingdom***	Qualitative: Face to face interviews with GPs **Aim:** To understand how GPs use the ABCD2 sore	**Setting:** UK (West Mids and Cambs) within catchment area, recruited from mailing lists of local research networks **Sample size:** 9 GPs (6 of whom used the score)	Score used in multiple ways, beyond its original remit. Seen as boundary object to facilitate communication between GP and hospital. It was used for evaluation and swift referral, used as a diagnostic and prognostic tool	***Qualitative*** *75%*	***R***

				and also an educational tool for GPs and patients. Some GPs unaware of score and thought it was unnecessary		
Reference	***Country***	***Methods/Aim***	***GP details***	***Key findings***	***Type of study Quality score***	***Diagnosis (D) Referral (R) Prescription (P)***
Jackel et al., (2012) (10)	***France, Spain, Italy. US, Germany***	Cross sectional survey: Telephone interviews **Aim:** To identify global trends in the current clinical pathways underling the management of patients with TIA	**Setting:** Primary Care Group Practices in France, Germany, Italy, Spain, UK and US working in group practices of at least two (Europe) or five (US) physicians **Sample size:** GPs:24 Europe:20 US:4 **Years qualified (mean):** Europe:17 (5-25) US:21 (14-25) **Number of patients with TIA managed per month; Mean (range):** Number of patients with TIA managed per month; Mean (range): Europe: 6 (3-20) (n=18) US:34 (10-50)	In US different medications were prescribed according to risk level unlike UK, France and Germany	***Quantitative (non-randomised)*** *100%*	***P***
Reference	***Country***	***Methods/Aim***	***GP details***	***Key findings***	***Type of study Quality score***	***Diagnosis (D) Referral (R) Prescription (P)***
Leung et al., (2012) (11)	***Australia***	Cross sectional survey: Questionnaire **Aim:** To identify GP knowledge of TIA assessment and management and perceived barriers to tailor GP education	**Setting:** GPs (Adelaide Western general practice network) **Response rate:** 32/202 (16%) **Sample size:** Female: 16 (51.6%)	All correctly identified early risk of stroke **(N=32)** Correct diagnosis was made by 32/32 **(100%)** The barriers to effectively manage potential TIA cases were as follows:	***Quantitative (non-randomised)*** ***67%***	***D, R & P***

			Years in practice: 1 did not state 0-10: 4 (13%) 11-20:11(36%) 21-30:10(32%) 31-40:4(13%) >41: 2 (7%)	**13** identified difficulty accessing neurological expertise or acute stroke units as a barrier **(41%)** **6** lack of knowledge by GPs **(19%)** **5** suggested lack of time in general practice consultations **(16%)** **15/32 (47%)** correctly responded to anti-hypertensive treatment **20/32 (63%)** correctly responded to managing hyperlipidaemia		
Reference	***Country***	***Methods/Aim***	***GP details***	***Key findings***	***Type of study Quality score***	***Diagnosis (D) Referral (R) Prescription (P)***
Ismail, Negm **(2013)** **(12)**	***Egypt***	Cross sectional survey: Questionnaire administered in a structured interview **Aim:** To assess Knowledge and practices of Primary Health Care Physicians on TIA	**Setting:** Primary Health Care Physicians in Ismailia Governorate **Response rate:** 95/130 (73%) **Sample size:** Female: (53.7%)	**21%** identified duration of symptoms of TIA (within 1hr) **42%** defined (within 24hr) **37%** answered incorrectly **35%** chose symptoms not consistent with TIA: isolated hand numbness: **(38%)** isolated vertigo: (**37%)** **33.7%** referred as emergency Patient with history of TIA: **27%** referred to hospital admission. **86.3%** referred to a neurologist **14%** did not refer Antiplatelet **(57%)** Anti-coagulants **(22%)** **26%** prescribed inappropriate treatment (brain stimulants/anti-oxidants) **2%** did not prescribe any treatment at all	***Quantitative (non-randomised)*** *100%*	***D, R & P***

Reference	*Country*	*Methods/Aim*	*GP details*	*Key findings*	*Type of study Quality score*	*Diagnosis (D) Referral (R) Prescription (P)*
Ranta, Cariga **(2013)** **(13)**	***New Zealand***	Case Vignettes **Aim:** To assess guideline adherence and the potential role of software (EDS tool) to support referral to specialist	**Setting:** GP, general physician, stroke specialists **Sample size:** 10 GPs, 12 physicians; 12 stroke specialists	Stroke specialist care achieves higher guideline adherence compared to GPs and general physicians; GP diagnostic accuracy **76% (45-100%)** vs. general physician accuracy ***79%* (33-100%)** Cardiology referral made by **15 (5%)** Similar rates when recommending antiplatelet, statins and antihypertensive between GP and general physicians was found: **(27% and 31%)** than stroke specialists **(92%)**	***Quantitative (non-randomised)*** *75%*	***D, R & P***

Actual practice studies of diagnosis, recognition of emergency and prescription

Actual practice studies						
Reference	*Country*	*Methods/Aim*	*GP details*	*Key findings*	*Type of study Quality score*	*Diagnosis (D) Referral (R) Prescription (P)*
Otten et al., (1995) **(14)**	***Netherlands***	Cross sectional survey: Questionnaire **Aim:** To determine rate of referral to specialist, and factors predicting referral to specialist	**Setting:** All GPs in the area around the Academic Medical Centre in Amsterdam **Response rate:** 308/464 (66%) **Sample size:** 21 excluded 287 GPs **Gender:** Female: 165 (57%)	Neurology referral**:** **136 (47%)** Cardiology referral: **15 (5%)** Younger and independent patients were more likely to be referred. Younger patient **(OR 2.5; 95CI 1.5-4.2).** Independent in daily activities **(OR 2.2; 95%CI 1.1-4.3** **213/287 (74%)** prescribed aspirin	***Quantitative (non-randomised)*** 100%	***D & P***

Reference	*Country*	*Methods/Aim*	*GP & patient details*	*Key findings*	*Type of study Quality score*	*Diagnosis (D) Referral (R) Prescription (P)*
Goldstein et al., (2000) (15)	***United States***	Retrospective: Audit of medical records **Aim:** To audit outpatient management of first TIA and stroke by Primary Care Physicians	**Setting:** GPs:27 primary care practices in 2 separate communities in eastern US Patients: First recorded TIA **Sample size:** GPs: Community 1:8 practices Community 2: 19 practices Patients: 95	**2%** of patients were admitted to ED for evaluation and treatment on the day of the index visit **14%** were referred to neurologist **13%** to cardiologist **6%** to a vascular surgeon Antiplatelets were given to a total of **47%** and **63%** of patients who were not hospitalised or investigated	***Quantitative (non-randomised)*** *100%*	***R & P***
Reference	***Country***	***Methods/Aim***	***GP & patient details***	***Key findings***	***Type of study Quality score***	***Diagnosis (D) Referral (R) Prescription (P)***
Gibbs et al., (2001) (16)	***United Kingdom***	Cohort Incident Examination of GP database (1992-1996) **Aim:** To determine whether initial GP management of stroke and TIA was uniform across the UK and validity of diagnosis	**Setting:** GPs: UK practices contributing to GPRD Patients: New diagnosis of stroke and TIA (1992-1996) **Sample size:** 27 TIA cases 25 Stroke cases	Of the GP diagnostic code for TIA in 27 cases, a specialist agreed with a cerebrovascular diagnosis in **18 (66%)** of cases and confirmed as either TIA or stroke Of the 25 stroke cases, **20 (80%)** was confirmed by a specialist as either TIA or stroke Referral for TIA within 7 days of diagnosis was; Mean **18.8%** (range between regions **14-26**). Numbers not given Prescription rates for TIA within 7 days of diagnosis were; antiplatelet: Mean **38%** (range between regions **30-45%). P=0.0008** anticoagulants: Mean **1.3% (95%CI 0.72. 1.56)** range between regions not given.	***Quantitative (non-randomised)*** *100%*	***D, R & P***
Reference	***Country***	***Methods/Aim***	***Patient details***	***Key findings***	***Type of study Quality score***	***Diagnosis (D) Referral (R) Prescription (P)***
McNeill, (2008)	***United Kingdom***	Cross sectional survey: To assess diagnosis the history of the PCD was compared to	**Setting:** 1 UK TIA clinic Referral letters of Patients (for presumed acute stroke or TIA)	**In 17 cases (24%)** examination differed between GP and admission examination (admitting doctor not detecting signs documented by GPs)	***Quantitative (non-randomised)***	***D***

(17)		the notes from the admitting doctor. **Aim:** To assess the diagnostic accuracy of Primary Care Doctors (PCDs)	**Sample size:** 72 68 stroke 4 TIA **Gender:** Female: 33 (45%)	**22 letters (30%)** documented the speed of onset of the deficit **20 cases (27%)** the presumed diagnosis of stroke was correct **2 cases (3%)** a TIA was diagnosed Overall of **4** patients with a presumed diagnosis of TIA, **2** were diagnosed with TIA	*50%*	
Reference	***Country***	***Methods/Aim***	***GP & patient details***	***Key findings***	***Type of study Quality score***	***Diagnosis (D) Referral (R) Prescription (P)***
Magin et al., (2013) (18)	***Australia***	Cohort retrospective: All referrals from GPs and EDs first seen at the clinic **Aim:** To establish paths to care and outcomes for patients referred by GPs and EDs to an Australian acute access TIA service	**Setting:** Secondary referral clinic within the Hunter New England area Health Service, and the John Hunter TIA/minor stroke acute access clinic **Sample size:** 344 referrals 300 attendees 44 non-attendees **Attendees**: 127 referred by GP 104 referred by ED **Age mean (SD)** GPs: 64(16) ED 67(14) Total 65(15)	**231** patients were seen at clinic of whom; **121(52%)** were diagnosed as having TIA/stroke Of the 127 GP referred patients: 21 **(17%)** stroke 29 **(23%)**TIA 13 **(10%)** unclassified 64 **(50%)** not stroke Sig prediction of receiving a final diagnosis of TIA/stroke were higher ABCD2 score, being on antiplatelet or anticoagulant medication at clinic attendance	***Quantitative (non-randomised)*** *67%*	***D***
Reference	***Country***	***Methods/Aim***	***Patient details***	***Key findings***	***Type of study Quality score***	***Diagnosis (D) Referral (R) Prescription (P)***
Clarey et al., (2014) (19)	***Australia***	Prospective cohort (analysis of baseline data). Patients of 17 Australian general practices presenting as possible Transient ischaemic attack/minor stroke (TIAMS) or TIAMs mimic **Aim:** To evaluate the absolute cardiovascular risk (ACVR) of patients with incident TIAMS and with TIAMS mimics.	**Setting:** Patient base of 17 general practices in the regions of New South Wales, Australia **Response rate:** 179/365 (presenting TIAMS) (49%) **Sample size:** 87 TIAMS 92 TIAMS mimics	Migraine was the most common TIAMS mimic reported in **27 (29%)** Motor symptoms and BMI predicted TIA diagnosis. **120** presented to GP **14** referred to ED **68 (64%)** were exclusively managed in GP **39 (36%)** referred to clinic/ED	***Quantitative (non-randomised)*** *67%*	***D & R***

			Gender Male TIAMS mimics: 27 (39%) TIAMS: 42 (61%) **Other:** 72(40%) presented to ED 68 (38%) were managed in general practice	Of the **106** not referred to ED **44 (42%)** were assessed as TIAMS. Of the **14** referred to ED, **5 (36%)** were assessed as TIAMS Combining the above, **49** of the **120** GP patients **(41%)** were assessed as TIAMS		

Intervention studies on diagnosis, recognition of emergency and prescription

Intervention studies					
Reference	***Country***	***Methods/Aim***	***GP & patient details***	***Key findings***	***Diagnosis (D) Referral (R) Prescription (P)***
Wright et al., (2006 & 2007) (20, 21)	***United Kingdom***	Randomised controlled trail: Diagnostic guidelines, randomisation by Primary Care Trusts **Aim:** To evaluate effectiveness of guidelines to improve management of TIA	**Setting:** **GPs:** Practices in 3 Bradford PCTs **Sample size:** **GPs:** Total:76 practices Intervention: 43 practice Control: 33 practices **Patients:** Total: 375 Intervention: 230 Control: 145	Non-statistically significant increase in referrals to the TIA clinic in intervention practice. For controlled case: Odd ratio = 1.33, P= 0.089 For uncontrolled cases: Odds ratio = 1.82, P= 0.054 The guideline adherence (antiplatelets), Comparison of Intervention and control odds ratio: **0.9 (95% Confidence intervals 0.4, 1.8) P= 0.714**	**R & P**
Reference	***Country***	***Methods/Aim***	***GP & patient details***	***Key findings***	***Diagnosis (D) Referral (R) Prescription (P)***
Lavin & Ranta (2014) (22)	***New Zealand***	Cohort Retrospective: Diagnostic tool; a 14-month safety audit reviewing all patients managed with the help of the TIA/Stroke EDS tool. **Aim:** To assess the safety of a Transient Ischaemic Attack (TIA)/Stroke Electronic Decision	**Setting:** GPs: New Zealand general practices Patients: Managed using decision support tool from August 2009- October 2010 **Sample size:**	No evidence of harm due to use of tool was found 79 patients were managed with the EDS Admissions: **22 (28%)** Among the **11** TIA/Stroke–related admissions, **8** patients who were high risk of stroke was immediately admitted to hospital using the EDS. Additionally**, 3** patients originally triaged by the EDS to	**D**

		Support (EDS) tool in the primary care setting intended to aid general practitioners in the timely management of transient ischemic attacks	Number of GPs not stated Patients: 79	less urgent ‘‘outpatient’’ assessment because of a low-risk assessment, or initial management as recommended by the TIA/Stroke EDS tool had no adverse outcome. **No admissions for patients which tool rejected diagnosis of stroke**	
Reference	***Country***	***Methods/Aim***	***Patient details***	***Key findings***	***Diagnosis (D) Referral (R) Management (M)***
Ranta et al., (2014) (23)	***New Zealand***	Before and after study of the effect on process of care following the implementation of EDS assisting TIA management in primary care. All patients presenting with TIA to secondary services were included. **Aim:** To assess TIA Guideline adherence and patient safety and to assess if EDS was associated with reduction of avoidable delays without incurring additional risks	**Setting:** Patients referred to district’s TIA clinic or inpatient care with diagnosis of TIA. **Sample size:** Patient: Before EDS: 130 After EDS:139 **Patient characteristics:** Baseline characteristics similar except more with IHD and fewer smokers in before group	Time to specialist review (median) intervention group: 3 days, control group: 10 days **Hazard Ratio: 1.45 (95% CI 1.13, 1.86)** Results for comparison between groups; best medical therapy within 24 hours: Relative Risk: 1.33 (1.02, 1.71) P 0.04 and behavioural counselling: RR 1.68 (1.31, 2.16) P<0.0001	**R & M**
Reference	***Country***	***Methods/Aim***	***Patient details***	***Key findings***	***Diagnosis (D) Referral (R) Management (M)***
Lasserson et al., (2015) (24)	***United Kingdom***	Cross sectional study: Clinical and research records from TIA clinics and consultation and referral letters from Primary Care to physicians were used (populate the Dawson recognition tool). **Aim:** To examine the potential utility in Primary Care of the Dawson Score to compare the performance of the Dawson Score in Primary and Secondary care.	**Setting:** All vascular events in 92,000 patients registered at 9 general practices in Oxfordshire **Sample size:** 513/92,000 selected TIA: 209 Nonvascular cause: 304 **Age:** Mean (SD) age: TIA: 73 (12.8) nonvascular cause: 65.2 (1.6) P= <0.001 % male: TIA: 42 nonvascular cause: 47 **Other:**	209/513 **(40.7%)** Mean (SD) age: **68.5 (15.6)** years had a final TIA diagnosis Patients with TIA were older than patients without TIA: **73.2 (12.8)** versus **65.2 (1.6**) they also had a higher Dawson score (both Primary & Secondary) **7.21 (1.2) versus 6.34 (1.1), 7.48 (1.3) versus 6.01 (1.0)** The Dawson score had greater accuracy in diagnosing all TIA in specialist assessments than primary care assessments; **(c statistics 0.80 vs 0.70 P < 0.0001)** and performed particularly poorly in primary care for detecting posterior circulation territory TIA **(c statistic 95% CI, 0.52 (0.43-0.61)** The Cut-off point was **5.4**	**D**

			Mean (SD) Dawson primary care score: TIA: 7.2 (1.2) nonvascular cause: 6.3 (1.1) Mean (SD) Dawson secondary care score: TIA: 7.48 (1.3) nonvascular cause: 6.01 (1.0)	Both primary and secondary care scores had similar sensitivity in detecting TIA; **92.3% vs 93.4%** Specificity was higher in secondary care scores; **29.3% vs 18.1%**	
Reference	***Country***	***Methods/Aim***	***GP & patient details***	***Key findings***	***Diagnosis (D) Referral (R) Management (M)***
Ranta et al., (2015) (25)	***New Zealand***	Randomized controlled trial Diagnostic tool: Multicentre, single-blind, parallel-group, cluster randomized, controlled trial comparing TIA/stroke electronic decision support guided management with usual care. Main outcomes were guideline adherence and 90-day stroke risk. Secondary outcomes were cerebrovascular/vascular/ death/adverse events, **Aim:** To test if TIA/stroke electronic decision support in primary care improves management	**Setting:** **GPs:** General practices in 4 health districts of New Zealand Access to TIA pathway No prior exposure to tool Patients: Patients presenting to GP after symptoms interpreted as stroke/TIA by the GP **Sample size:** GPs: 56 practices 29 intervention 27 control Patients: Intervention: 172 Control: 119 **Patient characteristics:** Mean age 69.8 (I) 72.3 (C). no differences in demography, past history, medication history, ABCD2 score	Tool improves guideline adherence and might reduce stroke risk stroke: Ninety-day TIA or stroke occurrence was lower in the intervention group, 4/172 **(2.3%)** compared to 10/119 **(8.5%)** control, adjusted odd ratio: **(0.26; 95% CI 0.70–0.97; P = 5 0.045)** Fewer vascular events/ deaths occurred in intervention, 6/172 **(3.5%),** than in control patients, 14/119 **(11.9%)** adjusted odd ratio: **(0.27; 95% CI 0.09–0.78; P= 5 0.016)**	**D**

Appendix 7: Dawson paper

The following published articles have been removed from the electronic version of this thesis due to copyright restrictions:

Q J Med 2009; **102**:43–49
doi:10.1093/qjmed/hcn139 Advance Access publication 15 October 2008

Appendix 8: standardised questionnaire form

UNIVERSITY OF LEICESTER

University Hospitals of Leicester NHS
NHS Trust

Dawson score

Have you (or the patient) had any of the following symptoms at the time of event?
Tick Yes or No, and (optionally) add any comments if you have any queries.

Clinical features (at time of event)	***Text FOR PHONE INTERVIEW***	***Yes***	***No***	***Comments (if any)***
Headache	**Pain or ache in the head**	☐	☐	
Diplopia	**Double vision**	☐	☐	
LOC/Pre-syncope	**Blackout, loss of consciousness, or feeling of blacking out**	☐	☐	
Seizure	**Fit or twitching movements**	☐	☐	
Speech abnormalities	**Any abnormality of speech**	☐	☐	
Unilateral limb weakness	**Weakness on one side of arm or leg**	☐	☐	
UMN facial weakness	**Facial droop**	☐	☐	
History of stroke or TIA	**Previous stroke or ministroke**	☐	☐	
Age				

Time taken to complete form (mins)	
Difficulties encountered in the telephone interview process(if any)	
Date of phone interview	

Appendix 9: clinical utility of the Dawson score – service evaluation confirmation

RE: Query on Service Evaluation vs need for REC approval

From: Mistri Amit - Consultant In Stroke Medicine [mailto:amit.mistri@uhl-tr.nhs.uk]
Sent: 05 September 2016 09:28
To: Maloney Carolyn - Head of Research Operations <carolyn.maloney@uhl-tr.nhs.uk>
Cc: Bose, Priyanka <pb274@leicester.ac.uk>
Subject: RE: Query on Service Evaluation vs need for REC approval

Very useful, thanks very much.
We will get on with the project.

Best wishes
Amit

From: Maloney Carolyn - Head of Research Operations
Sent: 05 September 2016 09:19
To: Mistri Amit - Consultant In Stroke Medicine
Cc: Bose, Priyanka (pb274@leicester.ac.uk)
Subject: RE: Query on Service Evaluation vs need for REC approval

Dear Amit

I would suggest that Service Evaluation would also fit your proposal if it is based on the text within your email. Therefore no requirement for REC or R&I Approvals. Makes no difference whether it's a PhD study or not.

With Best Wishes
Carolyn

Mrs. Carolyn Maloney
Head of Research Operations

0116 258 4109 (LGH) Mon, Tues & Fri
07903 877501 (Mobile) Weds & Thurs
LRI Base Weds / GGH Base Thurs

From: Mistri Amit - Consultant In Stroke Medicine
Sent: 02 September 2016 10:21
To: Maloney Carolyn - Head of Research Operations
Cc: Bose, Priyanka (pb274@leicester.ac.uk)
Subject: Query on Service Evaluation vs need for REC approval

Dear Carolyn

As you know, I am in the protracted process of resolving REC issues regarding LeiSTAR (for use of TIA & Stroke database data).
Currently, stuck with Ewan (I don't seem to get reply to emails) so that he can get Andrew Furlong's approval (as Caldecott Guardian).

Meanwhile, I am involved in an evaluation of a scoring tool (within a PhD project) in the TIA clinic.

This involves a subtle change of asking a few clinical questions, earlier in the process.
i.e. these questions would be asked anyway by the nurse or consultant at interview, but we want to ask them at the initial phone contact.
We would be looking at whether these questions can be asked in a robust fashion, and whether the answers we get match those we get later on.
The score would then be matched with the final diagnosis, with the eventual aim to assess if this score helps us streamline our process and enable rejection of unlikely TIA patients / prioritisation of likely TIA patients.

Because this falls within a PhD project, I have been advised to seek your advice/approval.
Whilst this would be covered under the umbrella of LeiSTAR, that is proving to be a rather slow process, and I do not wish to delay this current evaluation.

You may recall that David Eveson is doing something similar using information from the database (for another score), and I gather that was deemed service evaluation.
Your advice on the matter will be much appreciated.

With best wishes
Amit

PS Please call if a brief discussion would help 07541490481

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Appendix 10: Interview questions and response from clinic aide

Structured interview with the Clinic Aid: Monday 12th September 1:30 (duration 30 minutes)

The interview started with thanking the clinic aid for taking part in the data collection process and further asking questions regarding her experiences and attitudes towards the Dawson Score.

A total of 12 forms was collected, so we didn't get a form for every patient. I'd like to know if we can improve the approach to getting the forms filled in, so we can get better data?

At first the forms were put in a drawer so when making the appointments the forms were being forgotten about and not filled in. However, after missing out patients at the beginning of the week, the forms were attached to the patients faxed referral letters, so that when the file was opened first thing in the morning they are not forgotten about.

Attaching notes and reminders (post notes) to the staff filing the form out and attaching the forms to the patients' files will make the approach better.

Do you have data to show how many eligible patients were missed?

The S number was provided on the form, however, the forms were not photocopies so there is no way of identifying missing patients at the clinic.

How was it for you filling the forms? (did you find it difficult to collect the data whilst handling the workload at the TIA clinic?)

Handling the workload at the TIA clinic has to be done at a fast phase. Multi-tasking is needed as it involves dealing with patients on the phone, in the clinic, sorting through files, making sure patients are timely going for each tests, therefore the forms were being forgotten about. The forms itself was easy to fill out and did not take long (maximum 2-3 minutes), it was remembering to ask at the end of each call (after the appointment details were given) which was slightly challenging.

Were the forms filled in every time a phone appointment was arranged If not, then what sort of challenges occurred for the forms not to be filled in every time?

At first the forms were stored in an envelope in the drawer, it was organised that way by the staff, therefore the forms would not be remembered about until after the call. The issue with remembering after the call is that after giving the patients descriptive information about the appointment (e.g. time, date, venue appointment, what to bring on the day, what to expect etc.) you don't want to ring them back to disturb them with explaining about the data collection questions which may sometimes confuse them. Also, sometimes the clinic aid made the calls in the consultation room if it was free, and if the form was forgotten in the draws she would have to put the patients on hold to get this which showed unprofessionalism and may irritate the patients.

How easy was it to collect the data from the patient (if easy, then what was easy about the process)?

The clinic aid suggested that the data collection process was easy. Only one case where the relative was speaking on behalf of the patient, but once the data collection process was explained, both the patient and relative was happy to proceed with no questions asked.

Sometimes when speaking to the patient they could not remember what happened, so they took a bit of time to re call the event. The majority remembered and all answered each question asked, but instead of taking 2-3 minutes it maybe took around 5 minutes.

It was beneficial to have tick boxes, if it wasn't for the tick boxes then the staff wouldn't have had time to write statements out. It was easy because an option to elaborate is also provided and when adding the additional information, it can be quiet brief you can do it in a sentence or even a word.

Did any of the following individual items collected cause any difficulty (headache, diplopia, loss of consciousness/pre-syncope, seizure, speech abnormalities, unilateral limb/facial weakness, history of stroke/TIA)?

Some patients wanted to go through all the episodes (headache, diplopia, seizure etc). the patients wanted to give an extensive history and explain what happened in depth rather than answering the questions in a few minutes. They were trying to re call and describe everything which not only happened at the time of event, but what may have happened 10 years ago. An example of this was a patient describing history of stroke/TIA. The patient went into detail about each event which happened in the last few years rather than a 'yes' or 'no' answer and maybe a date if remembered.

Loss of consciousness: Lay term provided (blackout) was asked to be explained by the patient. Sometimes the patient thought a faint was a blackout and clinic aid had to explain that unless they were fully unconscious it is not a blackout.

Did you experience any issues whilst collecting the data for example:

Where there some patients you could not get the information from (refusal from the patient or any other challenges experienced by the patient?)

No patient refused to answer, but some patients who had speech problems due to the event were difficult to understand. Also those who spoke little English was hard to understand as the sentences were broken and took time to piece together to make sense of it.

Any issues with getting information from third party?

All third party was happy to give information. If it was a relative the clinic aid asked if she could speak to the patient herself, but if the patient could not speak for any reason then verbal consent was taken from patients, and if the patient was happy if the relative went through some questions on behalf of him/her. If the relative/guardian was not at the time of event when this happened, then it may be difficult for them to answer the questions (Dawson Score questions)

Were you asked to expand on/explain any questions?

Blackout was asked to be explained, sometimes they thought that a faint was a blackout and some patients thought that if they have a headache during the phone appointment then they answered 'yes'. But the clinic aid had to then explain that the headache can be accepted as a 'yes' if it occurred at the time of event.

Were you asked any clinical questions?

No clinical questions were asked

Any other issues you may be able to think of?

The clinic aid suggested that if the patient is unable to answer the questions and the relative/guardian is prepared to answer on their behalf, then the patients' verbal consent is needed. An issue the clerk proposed with this is that the patient may not be available to talk or give consent. Also, the clerk stated that she had an experience in the interview when the relative questioned why they cannot answer on the patients' behalf without consent. The clerk explained that in this situation she had to inform the guardian to request the patient to call the clinic back at a convenient time, in order to either speak about the questions, or give consent for the relative/guardian to answer on their behalf.

I am aware that you do not work 7 days a week and the days you have off another member of staff replaces you. Did this change over affect the data collection? And if so how?

The clinic aid is full time with two different shift patterns. This shift patterns did affect the data collection especially when they were not put in the files as they were forgotten about when making the calls to the patient.

Do you feel this is a legitimate role for a clinical aid/clinic clerk or that it should be done by a nurse?

The clinic aid suggested that their role probably has more experience than a clinic clerk to collect the data. The clinic clerk however, because she is experienced enough now (because of the staff) can also tackle the clinical questions, but a new clinic clerk or a clinic clerk at a different department who may have not got the help from other staff members may be unaware of how to tackle the questions.

If the clinic clerk is unable to answer questions which may be asked they will need to confirm with a member of clinical staff or doctors which will:

1. Show unprofessionalism as the patient will have to be put on hold
2. Waste of time as doctor/clinical staff may not be available
3. The clinic clerk may say she is unsure and maybe have a guess

The clinic aid suggested that the staff members who have enough knowledge and experience about details of the tests at the clinic should make the appointments to the patients and collect the data. This should be either the clinic aid or nurse or someone who has medical knowledge or enough experience.

Any improvements you could suggest if this process is to be repeated in the future? Would you do anything to make sure more forms get completed, and that the data is of good quality?

A big improvement would be to put the forms in with the patients notes the day before the files are taken out, preferably the night before as this is when the files are ready for the appointment the next day and the forms should be attached to the file.

There is not always time to ring the patients again and it isn't professional to put them on hold to go get the data collection form and the patient may be disturbed if you ring again. Therefore, organising the form and making sure the staff remembers to fill it will be easier.

The staff/person who will be collecting the data needs to introduce themselves properly so the patient understands why the data is being collected and who the person collecting the data is, as some patients can be quite sensitive about giving details and information.

The staff/person needs to understand the process and appointment details which are given to the patient and also ask for verbal consent from the patient to speak to the relative. If the patient comes to know patient consent was not given it causes a lot of issues.

Appendix 11: Results of the feasibility study

Data details

The overall missing and non-missing data are provided below:

Table 1: Missing and non-missing data

	Clinic database	Pilot results
Missing data	11%	11%
Non-missing data	88%	88%

Descriptive summaries of Dawson score and demographic feature of patients

Table 2: Descriptive summary of the Dawson scores: clinic database versus interview Dawson

	N	Mean	SD	Min	1st Quartile	Median	3rd Quartile	Max
Dawson database	10	6.7	1.1	5	6	6.7	7.9	8.1
Dawson interview	10	7.2	1.5	5.3	6	7.1	8.8	9.4

Demographic feature: Age

Majority of the patients were around 60–70, with some falling in the 40s category and the rest fell in the 80s. A summary of the patients' ages is shown in Table 3.

Table 3: Descriptive summary of age

Variable	Obs	Mean	Std. Dev	Min	Max
Age	11	62	15.7035	40	86

Comparison of the clinic database Dawson score and interview Dawson score

Table 4 below compared recording of each Dawson score components from the clinic database and pilot.

Table 4: Database versus pilot patient responses according to the Dawson score clinical features

Clinical features	**Headache**		**Diplopia**		**Loss of consciousness**		**Seizure**		**Speech abnormalities**		**Unilateral Limb weakness**		**Unilateral facial weakness**		**History of Stroke or TIA**	
Database vs Pilot	**Db**	**Pil**	**Db**	**Pil**	**Db**	**Pil**	**Db**	**Pil**	**Db**	**Pil**	**Db**	**Pil**	**Db**	**Pil**	**Db**	**Pil**
Patient 1 Age: 64	Null	No	Null	No	Null	Yes	No	No	Null	Yes	Null	Yes	Null	Yes	No	Yes
Patient 2 Age: 66	No	No	No	No	No	No	No	No	Yes	Yes	No	No	No	No	No	No
Patient 3 Age: 40	Yes	Yes	No	No	No	No	No	No	Yes	Yes	No	No	No	No	No	No
Patient 4 Age: 40	Yes	Yes	No	Yes	No	Yes	No	No	No	Yes	Yes	No	No	No	No	No
Patient 5 Age: 64	No	No	No	No	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes	No	No
Patient 6 Age: 66	No	No	No	No	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes	No	No
Patient 7 Age: 44	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No
Patient 8 Age: 60	No	No	No	No	No	No	No	Yes	No	Yes	No	No	Yes	No	No	No
Patient 9 Age: 85	No	No	No	No	No	No	No	No	Yes	Yes	No	No	No	No	No	Null
Patient 10 Age: 67	No	No	No	No	No	No	No	No	Yes	Yes	No	No	No	No	No	No
Patient 11 Age: 86	Yes	Yes	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No

Note: NULL means missing

Level of agreement between the clinic database and interview pilot Dawson score results and confidence intervals

To test the level of agreement between the pilot study Dawson score results collected by the clinic aide and the database Dawson score, each clinical feature collected in the pilot were compared with the same clinical feature retrieved from the database using STATA (Version 14.0).

An aspect of the pilot was to test the analyses to be used in the main study. Although the CI was too wide to be useful for the pilot study due to the small sample size, the analysis was still carried out in STATA and included in the table below for completeness.

Table 5: Percentage of agreement between clinic database and interview Dawson

Clinical feature	Total number	Number of agreements	Proportion (lower CI)	Proportion (upper CI)
History of stroke or TIA	10	9/10	55%	100%
Headache	10	10/10	69%	97.5% (1*)
Diplopia	10	9/10	55%	100%
Loss of consciousness	10	9/10	55%	100%
Seizures	11	10/11	59%	100%
Speech disturbance	10	4/10	12%	74%
Unilateral limb weakness	10	9/10	26%	88%
Unilateral facial weakness	10	9/10	26%	88%

Note: * means one sided confidence interval

Appendix 12: R&D letter of approval to conduct study at the TIA clinic

University Hospitals of Leicester NHS
NHS Trust

RESEARCH & INNOVATION

Research & Development Office
Leicester General Hospital
Gwendolen Road
Leicester
LE5 4PW

DIRECTORATE OF RESEARCH & DEVELOPMENT

Director: **Professor Nigel Brunskill**
Assistant Director: **David Hetmanski**
Head of Research Operations: Carolyn Maloney

Direct Dial: (0116) 258 4199
Fax No: (0116) 258 4226

12th August 2016

Miss Priyanka Bose
University of Leicester
Medical School
Centre for Medicine
Lancaster Road
Leicester
LE1 7HA

Dear Priyanka,

This letter confirms your right of access to conduct research through **University Hospitals of Leicester NHS Trust** for the purpose and on the terms and conditions set out below. This right of access commences on **12th August 2016** and ends on **31st March 2019** unless terminated earlier in accordance with the clauses below.

You have a right of access to conduct such research as confirmed in writing in the letter of permission for research from this NHS organisation. Please note that you cannot start the research until the Principal Investigator for the research project has received a letter from us giving permission to conduct the project.

The information supplied about your role in research at **University Hospitals of Leicester NHS Trust** has been reviewed and you do not require an honorary research contract with this NHS organisation. We are satisfied that such pre-engagement checks as we consider necessary have been carried out.

You are considered to be a legal visitor to **University Hospitals of Leicester NHS Trust** premises. You are not entitled to any form of payment or access to other benefits provided by this NHS organisation to employees and this letter does not give rise to any other relationship between you and this NHS organisation, in particular that of an employee.

While undertaking research through University Hospitals of Leicester NHS Trust, you will remain accountable to your employer **University of Leicester** but you are required to follow the reasonable instructions of **Amit Mistri** in this NHS organisation or those given on her/his behalf in relation to the terms of this right of access.

Where any third party claim is made, whether or not legal proceedings are issued, arising out of or in connection with your right of access, you are required to co-operate fully with any investigation by this

RESEARCH & INNOVATION

NHS organisation in connection with any such claim and to give all such assistance as may reasonably be required regarding the conduct of any legal proceedings.

You must act in accordance with **University Hospitals of Leicester NHS Trust** policies and procedures, which are available to you upon request, and the Research Governance Framework.

You are required to co-operate with **University Hospitals of Leicester NHS Trust** in discharging its duties under the Health and Safety at Work etc Act 1974 and other health and safety legislation and to take reasonable care for the health and safety of yourself and others while on **University Hospitals of Leicester NHS Trust** premises. You must observe the same standards of care and propriety in dealing with patients, staff, visitors, equipment and premises as is expected of any other contract holder and you must act appropriately, responsibly and professionally at all times.

You are required to ensure that all information regarding patients or staff remains secure and *strictly confidential* at all times. You must ensure that you understand and comply with the requirements of the NHS Confidentiality Code of Practice (http://www.dh.gov.uk/assetRoot/04/06/92/54/04069254.pdf) and the Data Protection Act 1998. Furthermore you should be aware that under the Act, unauthorised disclosure of information is an offence and such disclosures may lead to prosecution.

You should ensure that, where you are issued with an identity or security card, a bleep number, email or library account, keys or protective clothing, these are returned upon termination of this arrangement. Please also ensure that while on the premises you wear your ID badge at all times, or are able to prove your identity if challenged. Please note that this NHS organisation accepts no responsibility for damage to or loss of personal property.

We may terminate your right to attend at any time either by giving seven days' written notice to you or immediately without any notice if you are in breach of any of the terms or conditions described in this letter or if you commit any act that we reasonably consider to amount to serious misconduct or to be disruptive and/or prejudicial to the interests and/or business of this NHS organisation or if you are convicted of any criminal offence. Your substantive employer is responsible for your conduct during this research project and may in the circumstances described above instigate disciplinary action against you.

University Hospitals of Leicester NHS Trust will not indemnify you against any liability incurred as a result of any breach of confidentiality or breach of the Data Protection Act 1998. Any breach of the Data Protection Act 1998 may result in legal action against you and/or your substantive employer.

If your current role or involvement in research changes, or any of the information provided in your Research Passport changes, you must inform your employer through their normal procedures. You must also inform your nominated manager in this NHS organisation.

Yours sincerely

Lisa Wann
R&I Team Leader

cc: Copy to University of Leicester HR (Lesley Green)
Nicola Junkin HR UHL
Amit Mistri UHL
Copy for File

Appendix 13: TIA clinic consultation observation notes

TIA clinic Leicester Royal Infirmary consultation observation notes – Thursday 7th May 2015

- Patient notes are logged into the system (saves stroke consultations from going into individual paper format notes)

Patient 1: Expressive dysphasia

- Patient blanked out for a couple of hours, loss of control and loss of memory (did not know where he was or what he was doing)
- Consultant suggested an MRI due to pain in the neck (otherwise consultant would not suggest an MRI)
- Consultant thought the symptoms may be due to a benign cause
- Consultant advised the patient not to drive until MRI scan was done and the result has been confirmed
- Non-urgent MRI scan in the next two weeks would be arranged

Patient 2: Expressive dysphasia

- Patient woke up one Tuesday morning and could not get words out for most of the day. However the patient was able to understand others
- 4–5 minutes of tingling in right arm (lower part of the arm) (7–12 noon, less than 12 hours)
- The patient has cancer in his lings and liver and is taking cerefolin and nexavar for the cancer
- Consultant suggested that the patient may have high cholesterol due to eye bagging under the eyes
- Patient had an ultrascan but no MRI – ultrascan results were fine
- MRI scan needs to be done on the day
  Conclusion – Mini-stroke and cholesterol may be high or symptoms due to spreading of cancer. If the scan shows mini stroke then will be provided with medication in order to address risk factors and prevent a stroke from happening again, as a stroke has already occurred.

  Note for researcher: there are two types of dysphasia:
  - Expressive: Understand others but cannot speak/difficulty speaking
  - Receptive: can speak fluently but cannot process what others are saying

Patient 3

- AF is a major risk factor of stroke. The patient keeps having a stroke and needs to be put on a new medication
- High blood pressure puts the patient at high risk of stroke

- Cholesterol needs to be below 5, anything above this is high
- Normal blood pressure in patients with stroke 140/190
- Medication was provided to get the cholesterol down

Patient 4

- Patient felt light headed and unsteady
- No weakness and no expressive or receptive dysphasia
- Patients vision was good
- White blood cells dropped due to cold
- Consultant recommended that the patient should go to the GP and get a full blood count again and is given permission to drive as the patient has not had a stroke

Patient 5

- Patient has had a stroke – due to vision (lack of vision) meaning blockage in artery and has got a line across the eye
- Heart goes into a different rhythm
- Cholesterol is 6.3 – needs to go down to ideally 4/5
- The patient was prescribed 3 treatment medications
    - Statin to get the patient's cholesterol down – may experience muscle pain due to this
    - Clopidogrel to thin blood
    - Amlodipine to lower patient's blood pressure
- Patient was advised to see an optician after a month if the deficit in the eye is still present then may be advised not to drive
- DVLA needs to know only if symptoms are the same 1 month after
- The clot may gradually reduce, however the vision impairment (line in the eye) may not necessarily vanish. Needs to see an optician who will then send the patient to an eye clinic and address if the patient is fit enough to drive

Patient 6:

- Patient has had a lot of strokes in the past and experienced an episode of dysphasia whilst shopping
- The patient has had 4 strokes identified from brain scans in the past
- Consultant recommended to do a heart scan (within the next 6 weeks) and a non-urgent ultra-scan
- Driving is OK as no new stroke has been detected
- The strokes will always be there in the scan as it has affected the brain

Appendix 14: Researcher's script

Study Number: ☐☐☐

UNIVERSITY OF LEICESTER

University Hospitals of Leicester NHS
NHS Trust

Researchers' script

UHL number: **S☐☐☐☐☐☐☐**

GP referral ☐ **Internal referral ☐**

Introduction (for GP referral)

Hi am I speaking with Mr/Mrs/Ms….

If the patient answers:

"We have received your GP referral letter and would like to book you in for an appointment at the TIA clinic" **(inform the patient on the appointment date and time from electronic system).**

"We need you to be here for 8:30 am on …… and you can eat and drink as normal. You will just need to bring your medicine history with you on the day of your appointment. It is a full day clinic where the doctor will decide which tests are appropriate for you, and you may go straight for your scans if required".

Directions to the clinic:

"You will need to enter through the Balmoral building, and then take a right past the urgent care centre following the sign for TIA clinic and we are based just there".

"I need to ask some questions about your symptoms to aid with some initial decisions about your management at the TIA clinic". Are you happy to answer 8 simple Yes/No questions?

Yes ☐ **No ☐**

If the respondent is not the patient:

Can I speak to (Mr/Mrs/Ms)? **(if the patient is unavailable then advise them that you will ring back later)**

If the patient is available but unable to answer the questions (for whatever reason):

Reason why the respondent is not patient?

……

Is the patient able to give consent for you to answer questions on his/her behalf?

"Can you just put him/her on the phone so that we can get verbal consent from him/her so that we can go through the appointment details with you and you can answer some questions on his/her behalf"?

Has the patient given consent to speak to carer/relative/guardian?

Yes ☐ No ☐

Who is the respondent (carer/relative/guardian)?

"We have received the GP referral letter and would like to book an appointment at the TIA clinic" **(inform the carer/relative/guardian on the appointment date and time from electronic system).**

"We need (Mr/Mrs) to be here for 8:30 am on …… and you can eat and drink as normal. He/she will just need to bring his/her medicine history with him/her on the day of his/her appointment. It is a full day clinic where the doctor will decide which tests are appropriate for you, and he/she may go straight for your scans if required".

Directions to the clinic:

"You will need to enter through the Balmoral building, and then take a right past the urgent care centre following the sign for TIA clinic and we are based just there".

"I need to ask some questions to aid with the patients ongoing management at the TIA clinic"

Introduction (for internal referral)

"Hi am I speaking with Mr/Mrs/Ms…" **(If patient is not at home then ring back later)**

"I am calling from the TIA clinic at the Royal Infirmary. Just to remind you that you have an appointment for the **(DATE & TIME)**"

"I need to ask some questions about your symptoms to aid with some initial decisions about your management at the TIA clinic". Are you happy to answer 8 simple Yes/No questions?

Yes ☐ No ☐

Dawson score

Have you (or the patient) had any of the following symptoms at the time of event?
Tick Yes or No, and (optionally) add any comments if you have any queries.

Clinical features (at time of event)	***Text FOR PHONE INTERVIEW***	***Yes***	***No***	***Comments (if any)***
Headache	**Pain or ache in the head**	☐	☐	
Diplopia	**Double vision**	☐	☐	
LOC/Pre-syncope	**Blackout, loss of consciousness, or feeling of blacking out**	☐	☐	
Seizure	**Fit or twitching movements**	☐	☐	
Speech abnormalities	**Any abnormality of speech**	☐	☐	
Unilateral limb weakness	**Weakness on one side of arm or leg**	☐	☐	
UMN facial weakness	**Facial droop**	☐	☐	
History of stroke or TIA	**Previous stroke or ministroke**	☐	☐	
Age				

Time taken to complete form (mins)	
Difficulties encountered in the telephone interview process(if any)	
Date of phone interview	
Language spoken (Hindi/English)	

Appendix 15: Qualitative research methods workshop

Collaboration for Leadership in Applied Health Research and Care East Midlands

NHS National Institute for Health Research

East Midlands Centre for BME Health

WORKSHOP ON

"QUALITATIVE RESEARCH FOR ETHNICITY AND HEALTH"

This workshop, led by two qualitative research experts, Dr Sarah Salway and Dr Robert Akparibo, will help to enhance researcher's expertise to produce ethically inclusive research to address ethnic health disparities in research and health care.

A combination of presentations, individual work and small group exercises, will take place to promote the following learning objectives for participants:

- Be able to identify the contribution of qualitative research approaches to understanding ethnicity-health links and informing action on ethnic healthcare inequalities
- Be able to critically assess the quality of such research studies
- Be aware of key challenges for qualitative research on ethnicity and health and be able to offer plausible solutions:
  - operationalising ethnicity and constructing a sample
  - working across languages
  - understanding cultural influences on health and healthcare
  - exploring processes of exclusion and discrimination
  - promoting inclusive research practice

The workshop is suitable for health researchers, as well as those who commission or use health-related research.

Date and time: 23rd October 2015, 11.00am – 4.30pm

Registration: 10.30am, Buffet lunch: 1.00pm

Venue: Leicester Diabetes Centre, Leicester General Hospital, Gwendolen Rd, Leicester LE5

To register, email bmehealth@le.ac.uk.

Spaces will be limited so book early to avoid disappointment.

Biographies

Dr Sarah Salway, BA (Hons) Oxon, MSc, PhD. Dr Salway has 20 years research, consultancy and teaching experience in the field of public health, with a particular focus on three axes of inequality: race/ethnicity, gender and poverty. Her work includes a focus on understanding the perspectives of service users/clients and improving the fit between services and needs. Dr Salway's work on race/ethnicity spans the social welfare and health arenas illustrating an interest in the intersection between different dimensions of inequality and exclusion.

Dr Robert Akparibo, BSc, MSc, MPH, PhD. Dr Akparibo has expertise in Mixed Methods Research, Programme Evaluation using Realist Approach Evidence Synthesis and systematic review. His research interests are maternal and child health and nutrition, health care planning, management and systems.

Collaboration for Leadership in
Applied Health Research and Care
East Midlands

NHS
National Institute for
Health Research

East Midlands
Centre for BME Health

This certifies that

Priyanka Bose

Completed the workshop:

QUALITATIVE RESEARCH, ETHNICITY AND HEALTH

On

23rd October 2015

at the Leicester Diabetes Centre

Professor Kamlesh Khunti

Professor Sarah Salway

Appendix 16: Level of agreement between the interview data and clinic data

To test the level of agreement between the interview and clinic Dawson data, each clinical feature collected in the interview was compared with the same clinical feature retrieved from the clinic database. The results are shown below:

Comparison between interview and clinic for history of TIA/stroke

History interview	History clinic		Total
	(No)	(Yes)	
(No)	382 (96%)	37 (43%)	419
(Yes)	17 (4%)	50 (57%)	67
Total	399	87	486

More patients were recorded as experiencing a previous stroke/TIA in clinic than reported in the interview (87 versus 67). Just over half (57%) suggested having a history of stroke/TIA in both the interview and at the clinic, and 96% declined a previous history according to both data sources. The overall agreement for previous history of TIA/stroke was (89%).

Comparison between interview and clinic for experience of headache at the time of event

Headache interview	Headache clinic		Total
	(No)	(Yes)	
(No)	330 (84%)	32 (35%)	362
(Yes)	65 (16%)	59 (65%)	124
Total	395	91	486

124 patients were recorded as experiencing a headache in the interview versus 91 at the clinic stage, and 65% reported a headache during both the interview and clinic discussion. 84% declined feeling a headache from both the clinic and interview source, and the overall agreement was reported to be 80%.

Comparison between interview and clinic for experience of double vision (diplopia) at the time of event

Diplopia interview	Diplopia clinic		Total
	(No)	(Yes)	
(No)	437 (94%)	9 (45%)	446
(Yes)	29 (6%)	11 (55%)	40
Total	466	20	486

According to the interview data, more patients experienced a diplopia (double vision) than reported in clinic (40 versus 20). 55% agreed in both the interview and clinic and 94% declined to the symptom in both data sources. The overall agreement was reported to be 92%.

Comparison between interview and clinic for experience of loss of consciousness at the time of event

Loss of consciousness interview	Loss of consciousness clinic		Total
	(No)	(Yes)	
(No)	441 (96%)	17 (68%)	458
(Yes)	20 (4%)	8 (32%)	28
Total	461	25	486

28 patients reported loss of consciousness at the interview stage, versus 25 in the clinic, however a total of 32% agreed in both the interview and clinic and 96% declined to experiencing the symptom according to both data. The overall agreement for loss of consciousness was 92%.

Comparison between interview and clinic for experience of seizure at the time of event

Seizure interview	Seizure clinic		Total
	(No)	(Yes)	
(No)	467 (98%)	8 (89%)	475
(Yes)	10 (2%)	1 (11%)	11
Total	477	9	486

28 patients in the interview suggested experiencing a seizure, in comparison to 9 at the clinic. 11% agreed from both the data, and 98% declined experiencing the symptom from both datasets. The overall agreement was found to be (96%).

Comparison between interview and clinic for experience of speech abnormalities at the time of event

Speech interview	Speech clinic		Total
	(No)	(Yes)	
(No)	279 (89%)	20 (12%)	299
(Yes)	34 (11%)	153 (88%)	187
Total	313	173	486

More patients reported experiencing speech abnormalities with 187 at interview versus 173 in clinic. 88% agreed from both data, and 89% declined an encounter of speech abnormality according to both sources. The overall agreement was found to be 88%.

Comparison between interview and clinic for experience of unilateral limb weakness at the time of event

Unilateral limb weakness interview	Unilateral limb weakness clinic		Total
	(No)	(Yes)	
(No)	280 (87%)	42 (25%)	322
(Yes)	41 (13%)	123 (75%)	164
Total	321	165	486

A total of 165 patients suggested suffering unilateral limb weakness at the time of event in the clinic, compared to 164 in the interview. 75% reported limb weakness in both datasets, and 87% declined experiencing the symptom at both the interview and clinic stage. The proposed overall agreement was 83%.

Comparison between interview and clinic for experience of unilateral facial weakness at the time of event

Unilateral facial weakness interview	Unilateral facial weakness clinic		Total
	(No)	(Yes)	
(No)	384 (95%)	30 (37%)	414
(Yes)	22 (5%)	50 (63%)	72
Total	406	80	486

More patients reported unilateral facial weakness in clinic than at the interview stage (80 versus 72). 63% agreed on both databases and 95% declined to experiencing facial weakness from in data sources. The overall agreement was proposed as 89%.

Appendix 17: Accepted qualitative paper publication

The below published article has been removed from the electronic and hard copy version of this thesis due to copyright restrictions:

Bose P, Tarrant C, Mistri AK, Wilson, A. Managing uncertainty: a qualitative study of GPs' views on the diagnosis and immediate management of transient ischaemic attack and the potential of a diagnostic tool. Family practice. 2018;35(6):738–43

Appendix 18: University sponsor approval

UNIVERSITY OF LEICESTER

Research & Enterprise Division
University of Leicester
Research Governance Office
Fielding Johnson Building
University Road
Leicester
LE1 7RH
Email: uolsponsor@le.ac.uk
Admin Tel 0116 373 6410 / 223 1660

10 March 2017

Miss Priyanka Bose
University of Leicester
Centre for Medicine
3rd Floor Room 3.06
Leicester, LE1 7HA

Dear Miss Priyanka Bose

Ref:	**UOL 0602 / IRAS project ID: 217845**
Study title:	**The Diagnosis & Management of Transient Ischaemic Attack (TIA): A Qualitative Interview study on the use of the Dawson Score for TIA in Primary Care.**
Status:	**Approved**
End Date:	**30/06/2017**
Site:	**University Hospitals Leicester NHS Trust**

I am pleased to advise you that following confirmation of a Favourable Opinion from an Ethics Committee, HRA, NHS Trust R&D Approval, and where relevant regulatory authority agreements have been received, the University are able to confirm sponsorship for the above research at the above site.

Please note you are required to notify the Sponsor and provide copies of:

- Changes in personnel to the Study
- Changes to the end date
- All substantial amendments and provisional and favourable opinions
- All minor amendments
- All serious adverse events (SAEs) and SUSARS
- Annual progress reports
- Annual MHRA (DSUR) safety reports (if applicable)
- End of study declaration form
- Notifications of significant breaches of Good Clinical Practices (GCP)or Protocol

Please copy the Sponsor into all correspondence and emails by using uolsponsor@le.ac.uk.

Please note it is essential that you notify us as soon as you have recruited your first patient to the study.

I would like to wish you well with your study and if you require further information or guidance please do not hesitate to contact me.

Yours sincerely

Diane M. Delahooke

Dr Diane Delahooke
Acting Research Governance Manager

University Ethics Sub-Committee for Medicine and Biological Sciences

Appendix 18: Ethical approvals

07/03/2017

Ethics Reference: 10423-pb274-healthsciences

TO:
Name of Researcher Applicant: Priyanka Bose
Department: Health Sciences
Research Project Title: The use of the Dawson Score for TIA in Primary Care

Dear Priyanka Bose,

RE: Ethics review of Research Study application

The University Ethics Sub-Committee for Medicine and Biological Sciences has reviewed and discussed the above application.

1. Ethical opinion

The Sub-Committee grants ethical approval to the above research project on the basis described in the application form and supporting documentation, subject to the conditions specified below.

2. Summary of ethics review discussion

The Committee noted the following issues:
Thank you to the team for responding to the series of queries and suggestion that we had.

3. General conditions of the ethical approval

The ethics approval is subject to the following general conditions being met prior to the start of the project:

As the Principal Investigator, you are expected to deliver the research project in accordance with the University's policies and procedures, which includes the University's Research Code of Conduct and the University's Research Ethics Policy.

If relevant, management permission or approval (gate keeper role) must be obtained from host organisation prior to the start of the study at the site concerned.

4. Reporting requirements after ethical approval

You are expected to notify the Sub-Committee about:

- Significant amendments to the project
- Serious breaches of the protocol
- Annual progress reports
- Notifying the end of the study

5. Use of application information

Details from your ethics application will be stored on the University Ethics Online System. With your permission, the Sub-Committee may wish to use parts of the application in an anonymised format for training or sharing best practice. Please let me know if you do not want the application details to be used in this manner.

Best wishes for the success of this research project.

Yours sincerely,

Dr. Chris Talbot
Chair

Appendix 18: HRA approval

Health Research Authority

Miss Priyanka Bose
PhD student
University of Leicester
Centre for Medicine, 3rd Floor, Room 3.06
15 Lancaster Rd
LEICESTER
LE1 7HA

Email: hra.approval@nhs.net

20 February 2017

Dear Miss Bose

Letter of HRA Approval

Study title:	**The Diagnosis & Management of Transient Ischaemic Attack (TIA): A Qualitative Interview study on the use of the Dawson Score for TIA in Primary Care.**
IRAS project ID:	**217845**
REC reference:	**17/HRA/0634**
Sponsor	**University of leicester**

I am pleased to confirm that **HRA Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications noted in this letter.

Participation of NHS Organisations in England

The sponsor should now provide a copy of this letter to all participating NHS organisations in England.

Appendix B provides important information for sponsors and participating NHS organisations in England for arranging and confirming capacity and capability. **Please read *Appendix B* carefully**, in particular the following sections:

- *Participating NHS organisations in England* – this clarifies the types of participating organisations in the study and whether or not all organisations will be undertaking the same activities
- *Confirmation of capacity and capability* - this confirms whether or not each type of participating NHS organisation in England is expected to give formal confirmation of capacity and capability. Where formal confirmation is not expected, the section also provides details on the time limit given to participating organisations to opt out of the study, or request additional time, before their participation is assumed.
- *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* - this provides detail on the form of agreement to be used in the study to confirm capacity and capability, where applicable.

Further information on funding, HR processes, and compliance with HRA criteria and standards is also provided.

It is critical that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details and further information about working with the research management function for each organisation can be accessed from www.hra.nhs.uk/hra-approval.

Appendices

The HRA Approval letter contains the following appendices:

- A – List of documents reviewed during HRA assessment
- B – Summary of HRA assessment

After HRA Approval

The attached document *"After HRA Approval – guidance for sponsors and investigators"* gives detailed guidance on reporting expectations for studies with HRA Approval, including:

- Working with organisations hosting the research
- Registration of Research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics and is updated in the light of changes in reporting expectations or procedures.

Scope

HRA Approval provides an approval for research involving patients or staff in NHS organisations in England.

If your study involves NHS organisations in other countries in the UK, please contact the relevant national coordinating functions for support and advice. Further information can be found at http://www.hra.nhs.uk/resources/applying-for-reviews/nhs-hsc-rd-review/.

If there are participating non-NHS organisations, local agreement should be obtained in accordance with the procedures of the local participating non-NHS organisation.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please email the HRA at hra.approval@nhs.net. Additionally, one of our staff would be happy to call and discuss your experience of HRA Approval.

HRA Training

We are pleased to welcome researchers and research management staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

Your IRAS project ID is **217845**. Please quote this on all correspondence.

Yours sincerely

Rekha Keshvara
Assessor

Email: hra.approval@nhs.net

Copy to: *Dr Diane Delahooke*
Mrs Carolyn Maloney

Appendix A - List of Documents

The final document set assessed and approved by HRA Approval is listed below.

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Verification insurance]		13 January 2017
Interview schedules or topic guides for participants [Schedule of questions for GPs]	V1	21 December 2016
IRAS Application Form [IRAS_Form_31012017]		31 January 2017
IRAS Application Form XML file [IRAS_Form_31012017]		31 January 2017
IRAS Checklist XML [Checklist_31012017]		31 January 2017
Letter from sponsor [Indemnity insurance letter]		05 January 2017
Letters of invitation to participant [Invitation to participate email]	V1	21 December 2016
Other [Dawson paper]		14 December 2016
Other [GCP certificate]		22 November 2016
Other [Feasibility assessment CCG]		06 December 2016
Other [Feasibility assessment site]		06 December 2016
Other [SoE CCG]	1	17 February 2017
Other [SoE UHL]	1	17 February 2017
Other [SoA CCG]	1	17 February 2017
Other [SoA UHL]	1	17 February 2017
Participant consent form [Consent form]	V1	21 December 2016
Participant information sheet (PIS) [Participant information sheet]	V1	21 December 2016
Research protocol or project proposal [Study protocol]	V1	21 December 2016
Summary CV for Chief Investigator (CI) [Curriculum Vitae]	V0.1	29 November 2016
Summary CV for student [Curriculum Vitae]		29 November 2016
Summary CV for supervisor (student research)		29 November 2016

Appendix B - Summary of HRA Assessment

This appendix provides assurance to you, the sponsor and the NHS in England that the study, as reviewed for HRA Approval, is compliant with relevant standards. It also provides information and clarification, where appropriate, to participating NHS organisations in England to assist in assessing and arranging capacity and capability.

For information on how the sponsor should be working with participating NHS organisations in England, please refer to the, *participating NHS organisations*, *capacity and capability* and *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* sections in this appendix.

The following person is the sponsor contact for the purpose of addressing participating organisation questions relating to the study:

Dr Diane Delahooke
Email: dd78@leicester.ac.uk
Tel: 0116 252 5308

HRA assessment criteria

Section	HRA Assessment Criteria	Compliant with Standards	Comments
1.1	IRAS application completed correctly	Yes	No comments
2.1	Participant information/consent documents and consent process	Yes	No comments
3.1	Protocol assessment	Yes	No comments
4.1	Allocation of responsibilities and rights are agreed and documented	Yes	Statement of activities will act as an agreement of an NHS organisation to participate.
4.2	Insurance/indemnity arrangements assessed	Yes	Where applicable, independent contractors (e.g. General Practitioners) should ensure that the professional indemnity provided by their medical defence organisation covers the activities expected of them for this

Section	HRA Assessment Criteria	Compliant with Standards	Comments
			research study
4.3	Financial arrangements assessed	Yes	No application for external funding has been made.
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	IRAS A22 states 'Participation in this research may involve a loss of privacy.' However, the applicant has clarified that this is an error and participant confidentiality will be maintained.
5.2	CTIMPS – Arrangements for compliance with the Clinical Trials Regulations assessed	Not Applicable	No comments
5.3	Compliance with any applicable laws or regulations	Yes	No comments
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Not Applicable	No comments
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Not Applicable	No comments
6.3	Devices – MHRA notice of no objection received	Not Applicable	No comments
6.4	Other regulatory approvals and authorisations received	Not Applicable	No comments

Participating NHS Organisations in England

This provides detail on the types of participating NHS organisations in the study and a statement as to whether the activities at all organisations are the same or different.

There are two site-types:

1. The University Hospitals of Leicester NHS Trust will carry out the eligibility check and send participation invitation emails.
2. At the GP sites (CCGs), GPs will confirm consent via email. Participant (telephone) consent confirmation and interviews will be carried out by the research team.

The Chief Investigator or sponsor should share relevant study documents with participating NHS organisations in England in order to put arrangements in place to deliver the study. The documents should be sent to both the local study team, where applicable, and the office providing the research management function at the participating organisation. For NIHR CRN Portfolio studies, the Local LCRN contact should also be copied into this correspondence. For further guidance on working with participating NHS organisations please see the HRA website.

If chief investigators, sponsors or principal investigators are asked to complete site level forms for participating NHS organisations in England which are not provided in IRAS or on the HRA website, the chief investigator, sponsor or principal investigator should notify the HRA immediately at hra.approval@nhs.net. The HRA will work with these organisations to achieve a consistent approach to information provision.

Confirmation of Capacity and Capability

This describes whether formal confirmation of capacity and capability is expected from participating NHS organisations in England.

Participating NHS organisations in England **will be expected to formally confirm their capacity and capability to host this research**.

- Following issue of this letter, participating NHS organisations in England may now confirm to the sponsor their capacity and capability to host this research, when ready to do so. How capacity and capacity will be confirmed is detailed in the *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* section of this appendix.
- The Assessing, Arranging, and Confirming document on the HRA website provides further information for the sponsor and NHS organisations on assessing, arranging and confirming capacity and capability.

Principal Investigator Suitability

This confirms whether the sponsor position on whether a PI, LC or neither should be in place is correct for each type of participating NHS organisation in England and the minimum expectations for education, training and experience that PIs should meet (where applicable).
Principal Investigator or Local Collaborators are not expected for this study as the study activities will be carried out by the research team via email and telephone contact only. The study participants will be contacted directly by the researcher via email. GCP training is not a generic training expectation, in line with the HRA statement on training expectations.

HR Good Practice Resource Pack Expectations

This confirms the HR Good Practice Resource Pack expectations for the study and the pre-engagement checks that should and should not be undertaken
The applicant has confirmed in the study supporting documents that she has access to the names of GPs who have referred to the clinic as part of her job role. Therefore, Honorary Research Contracts and Letter of Access are not expected for this study, as research is limited to involvement of staff as participants.

Other Information to Aid Study Set-up

This details any other information that may be helpful to sponsors and participating NHS organisations in England to aid study set-up.
• The applicant has indicated that they do not intend to apply for inclusion on the NIHR CRN Portfolio.

Appendix 19: GCP certificate

Assessment Certificate

Issued to

PRIYANKA BOSE

For completion of the University Hospitals of Leicester NHS Trust

Good Clinical Practice GCP1

For clinical trials NOT involving Investigational Medicinal Products

Training and Assessment on

10th February 2016

Authorised on behalf of the University Hospitals of Leicester

Julie James
Aldona Kirkham
Anne Moore
Clinical Trial Monitors and Trainers

Valid until 09th February 2018

Updated October 2014

UNIVERSITY OF LEICESTER

Appendix 20: Participant information sheet

Study Title: The use of the Dawson Score for TIA in Primary Care

Participant Information Sheet

Please read this information and feel free to ask any questions or to request further information.

Introduction

This research study is part of a PhD project at the University of Leicester. I intend to increase understanding of how TIAs are diagnosed and managed in Primary Care.

The purpose of this research is to investigate GPs' views on the diagnosis and immediate management of TIA patients, and the potential utility of a diagnostic tool (Dawson Score). This information will contribute to interventions to assist GPs in diagnosing this condition and selecting patients for referral.

Do I have to take part?

GPs working in Leicester, Leicestershire and Rutland have been invited to participate in this research. Your participation in this study is voluntary and you may choose not to participate, however your participation is very valuable. If you decide to participate, you may withdraw at any time without stating a reason.

What will happen if I take part in this study?

An email consent will be taken prior to the interview and reconfirmed at the time of the telephone interview. I will arrange a convenient date and time for you so that the telephone interview can take place. It will take up to 30 minutes. I would like to ask you some questions regarding general diagnostic and immediate management issues of TIA patients, and gain your perspective on the utility of a diagnostic Score to diagnose TIAs and triage referrals. You will be sent a copy of the Score before the interview

I will take notes of the discussion, and a recording will also be made using an encrypted digital voice recorder. The recording will then be transcribed and stored on a computer, after which the tape will be erased.

There will be no identifiable data in the transcripts, therefore your name will not be recorded. All the information gathered will be treated as confidential. The information I collect will be presented in meetings and journals, but no personal identifiable information will be used in any reports. Direct quotes from the recordings may also be used, but these will be anonymised.

Are there benefits to taking part in the study?

There will be no direct benefit to you from participating in this study. However, the information that you provide will help me understand your experiences and factors that might contribute to issues relating to the diagnosis and management of TIAs.

You will be reimbursed £50 for your time and contribution to the study.

Who has reviewed the study?

Academic supervisors, sponsor representative from the University of Leicester, University of Leicester Ethics Committee, University Hospitals of Leicester R&I Team, Health Research Authority Team have reviewed the study. In addition, Leicester, Leicestershire and Rutland (LLR) Clinical Commissioning Groups' (CCG) Research and Development lead has reviewed this study.

Representatives of the sponsor or host NHS Trust may examine the study records for monitoring and audit purposes, and by agreeing to take part in this study, you agree to this.

If you have any questions about the research study, please contact Priyanka Bose on pb274@le.ac.uk

Appendix 21: Consent form

CONSENT FORM

Study Title: The use of the Dawson Score for TIA in Primary Care

Researcher: Priyanka Bose

1. "I confirm that I have read and understand the participant information sheet (V1 Date 21/12/2016) for the above study" I have had the opportunity to consider the information provided, to ask questions and to have these answered satisfactorily.
2. I understand that my participation is voluntary and that I am free to withdraw following its completion, without giving a reason and without my legal rights being affected.
3. I understand that representativeness of the sponsor or host NHS Trust may examine study records for monitoring purposes.
4. I confirm that consent has been obtained by email, and agree for the consent to be reconfirmed prior to the interview taking place.
5. I agree to the interview being tape recorded.
6. I understand that the recordings will be transcribed anonymously and they will then be deleted. I give permission to this.
7. I agree to take part in the above study.

Anonymised quotations: The name of the participants will not be used to label any recordings. Any additional names, places or other identifying information mentioned during the interview will be anonymised when a final transcript is made. Any quotations used will have details altered as further assurance of anonymity. Any quotations or descriptions used in reports of the study will be anonymised.

Appendix 22: Dawson score details sent to GPs

A RECOGNITION TOOL FOR TRANSIENT ISCHAEMIC ATTACK

Reference: *Dawson J, Lamb KE, Quinn TJ, et al. A recognition tool for transient ischaemic attack. QJM 2009; 102 (1): 43-9.*

Abstract

Background:
Scoring systems exist to assist rapid identification of acute stroke but not for the more challenging diagnosis of transient ischaemic attack (TIA).

Aim:
To develop a clinical scoring system to assist with diagnosis of TIA.

Methods:
We developed and validated a clinical scoring system for identification of TIA patients. Logistic regression analysis was employed.

Results:
Our development cohort comprised 3216 patients. The scoring system included nine clinically useful predictive variables. After adjustment to reflect the greater seriousness of missing true TIA patients (a 2:1 cost ratio), 97% of TIA and 24% of non-TIA patients were accurately identified. Our results were confirmed during prospective validation.

Conclusions:
This simple scoring system performs well and could be used to facilitate accurate detection of TIA.

Dawson score

The figures below are the sum calculated depending on the patients answer to each variable and the patients age multiplied by 0.04. To generate a final Dawson score, each score from the 8 independent variables plus age had to be summed to give the total. **If the total was more than 5.4 then it would be classified as TIA.**

Variable	Score if yes	Score if no
History of stroke or TIA	0.5	0
Headache	0	0.5
Diplopia	1.2	0
Loss of consciousness/Pre-syncope	0	1.1
Seizure	0	1.6
Speech abnormalities	1.3	0
Unilateral limb weakness	1.7	0
Unilateral facial weakness	0.6	0
Age	Multiply by 0.04	

Appendix 23: GP transcription with verbal consent

File Name: Interview 1

Transcribed by: Clayton Research Support (DW). 49, Towcester Road, Old Stratford, Northamptonshire, MK19 6AH. Tel: 01908 562778 Email: claire.clayton88@gmail.com

Interviewer

The purpose of this interview is to look into GPs' experience of diagnosis and management of suspected TIA patients and the use of the ABCD^2 score and the potential utility of a diagnostic and management tool in primary care. So before I go onto the questions I would like to seek agreement to audio record this interview if that's OK with you?

Respondent

That's fine yeah.

Interviewer

And also I would like to seek verbal consent, so are you happy to participate in the study?

Respondent

Sure.

Interviewer

So the transition to the first topic is diagnosing suspected TIA patients. So the questions being asked are related to the general diagnosis of patients rather than specific patients themselves. So as a GP there are difficulties in diagnosing suspected TIA patients as you know, so the first question is do you think it is useful to distinguish between a stroke and a TIA?

Respondent

Yes.

*Agreed important

Interviewer

Is there a specific reason why you would think that?

Respondent

Well because a stroke is a permanent neurological defect and a TIA is a big risk factor for developing it so it's an opportunity for prevention.

① stroke is a permanent neurological defect
② TIA is a risk of developing stroke
③ opportunity for prevention

Interviewer

So what would be your definition of a TIA?

Respondent

Neurological deficit of vascular cause that reverses within twenty four hours.

Interviewer

And roughly how many people a year do you diagnose with suspected TIA?

Appendix 24: Invitation to participate document

The use of the Dawson Score for TIA in Primary Care

Dear General Practitioner,

I am writing to ask if you would be willing to take part in my research study.

My name is Priyanka Bose and I am a PhD student at the University of Leicester. My research is about the diagnosis and immediate management of Transient Ischaemic Attack in Primary Care.

It is well established that TIAs are difficult to diagnose in Primary Care and that only around half of patients referred to TIA clinics have their diagnosis confirmed. A diagnostic tool named the Dawson Score has been found to be helpful in a Secondary Care clinic setting, but I do not know if it would assist GPs in making decisions about diagnosis and referral. This interview study is designed to seek GPs views and investigate whether the Dawson Score may be helpful. To explore this question, I am seeking to organise telephone interviews with a sample of GPs. The interviews will take up to 30 minutes and will take place on a day and time that is convenient for you. Additionally, you will be reimbursed £50 for your time. For further information please see the participant information sheet.

Please note that not everyone who expresses interest in taking part will be selected. If you are to be selected for the study, I will contact you to arrange a convenient day and time for the interview. Please feel free to email me on pb274@le.ac.uk with any further questions which you may have.

Regards,

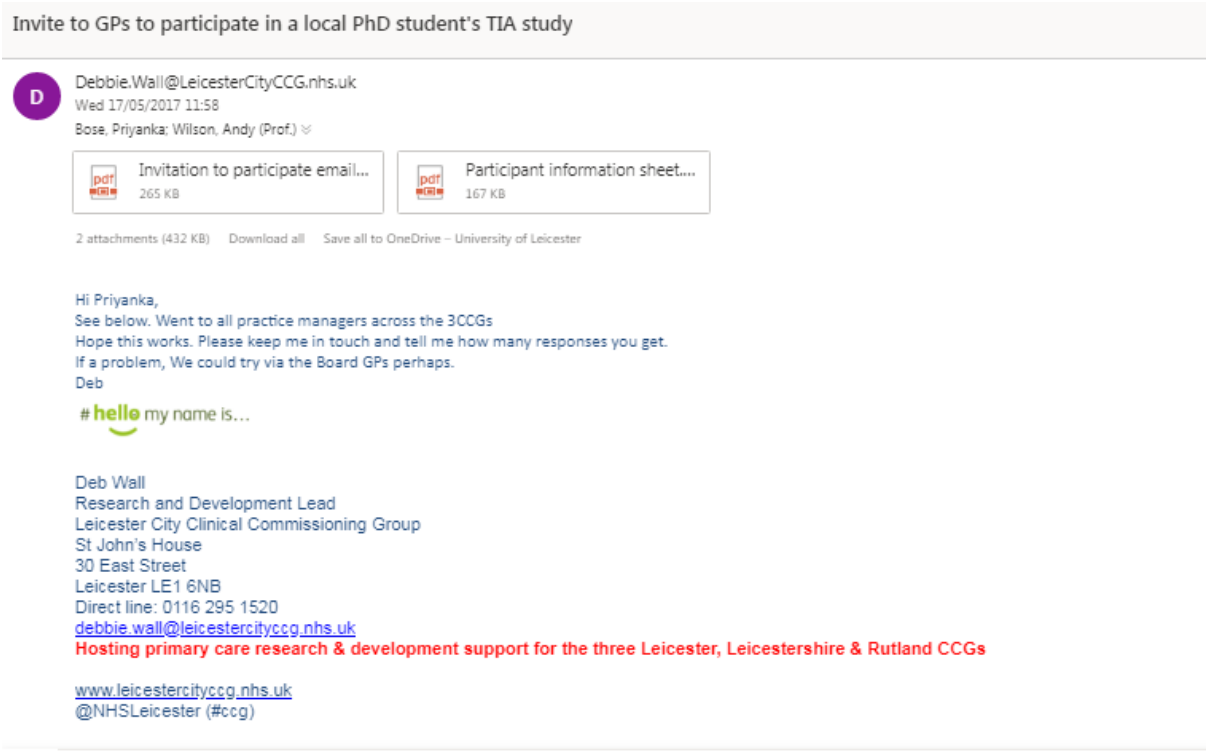
Priyanka Bose
Postgraduate student

University of Leicester
Department of Health Sciences
Centre for
Medicine

pb274@le.ac
.uk 0116 252
5449

Dr Amit Mistri
Consultant Physician _ Stroke Medicine
Leicester Royal Infirmary
Leicester LE1 5WW
Secr: 0116 2585060

Appendix 25: Email sent to practice managers



Invite to GPs to participate in a local PhD student's TIA study

D

Debbie.Wall@LeicesterCityCCG.nhs.uk
Wed 17/05/2017 11:58
Bose, Priyanka; Wilson, Andy (Prof.)

Invitation to participate email... 265 KB

Participant information sheet.... 167 KB

2 attachments (432 KB) Download all Save all to OneDrive – University of Leicester

Hi Priyanka,
See below. Went to all practice managers across the 3CCGs
Hope this works. Please keep me in touch and tell me how many responses you get.
If a problem, We could try via the Board GPs perhaps.
Deb

#hello my name is...

Deb Wall
Research and Development Lead
Leicester City Clinical Commissioning Group
St John's House
30 East Street
Leicester LE1 6NB
Direct line: 0116 295 1520
debbie.wall@leicestercityccg.nhs.uk
Hosting primary care research & development support for the three Leicester, Leicestershire & Rutland CCGs

www.leicestercityccg.nhs.uk
@NHSLeicester (#ccg)

From: Wall Debbie
Sent: 17 May 2017 11:56
To: ELRCCG All Practice Managers; West Leicestershire CCG - Practice Managers; Leic City CCG Practice Managers
Cc: Wall Debbie
Subject: Invite to GPs to participate in a local PhD student's TIA study

Dear Practice Manager,

I am trying to help Priyanka, a PhD student, get started with her work. Please could you bring her request (see below and attachments) to the attention of GPs in your practice?
Best wishes,
Deb Wall, R&D Lead LLR CCGs

.....

I am a PhD student at the University of Leicester conducting a study on the diagnosis and management of TIAs in Primary Care under the supervision of Professor Andrew Wilson and Dr Amit Mistri (Consultant in Stroke Medicine). As part of this work I would like to interview GPs on their experiences and views of diagnosing this condition. If you referred patients to the LRI for suspected TIA in the last two months, I hope that you will be willing to take part. Interviews will be conducted by telephone, and will last up to 30 minutes. £50 will be paid in recognition of the GPs time invested.

More details of this study have been provided in both the invitation, and participant information sheet attached.

I would be grateful if GPs could let me know if they are interested in taking part by contacting me at pb274@le.ac.uk

Regards,

Priyanka Bose
Postgraduate student
University of Leicester

Email: pb274@le.ac.uk
Telephone: 0116 252 5449

Dr Amit Mistri
Consultant Physician – Stroke Medicine
Leicester Royal Infirmary
Leicester LE1 5WW
Secr: 0116 2585060

Appendix 26: GP interview topic guide

Hi am I speaking with Dr….

My name is Priyanka Bose, I am a PhD student at the University of Leicester. I would like to thank you for volunteering to take part in this research, your participation is much appreciated.

Just to recap on the research aims, the purpose of this interview is to look into GPs experiences of diagnosing and managing suspected TIA patients, the use of the ABCD2 score and the potential utility of a diagnostic tool in Primary Care that may discriminate TIA from mimics, and thus aid the subsequent management pathway.

Before I go onto to the questions, I would like to seek agreement to audio record this interview, is this okay with you? Also, I would like to seek verbal consent, are you happy to participate in this study?

The transition to the first topic is **DIAGNOSING SUSPECTED TIA PATIENTS**.
The questions being asked are related to the general diagnosis of patients, rather than specific patients. Published evidence indicates that there are difficulties in diagnosing suspected TIA patients in primary care, with more than half of those attending a TIA clinic turning out to be "another condition" ie. A TIA mimic, so the first question is:

- Do you think it is useful to distinguish between a stroke and a TIA?
- What would be your definition of a TIA?
- Roughly how many people a year do you diagnose with suspected TIA?
- What are the challenges in diagnosing TIA?
- Are there any groups in particular, where you found difficulty diagnosing as a suspected TIA? (e.g. diabetics, or elderly etc)
- What specific symptoms (if any) do you find difficult in terms of diagnosing TIA? And what symptoms do you find easy/or easier to diagnose TIA?
- Is there anything else you think might contribute to the issues around diagnosis?

The transition to the second topic is **MANAGING SUSPECTED TIA PATIENTS**
TIA clinics usually have a high number of referrals making it very difficult to see all patients within the recommended timeframe; high risk within 24 hrs and low risk within 7 days.

- How do you make a decision to refer a suspected TIA patient?

Perhaps if you think about the last patient you managed it might be easier (just a reminder please do not state any particular patient information or details, just general details about management)

- What specific symptoms do you look for in suspected TIA patients?
- What are you usually referring the suspected TIA patients for (e.g. is it for a neck scan? Confirm the diagnosis? Exclude a diagnosis? Reassure yourself?)
- What are the difficulties in making that decision to refer?
- Where would you usually refer patients, and why?
- Are there any instances when you would admit a patient with suspected TIA or send them to ED rather than refer to the TIA clinic? If yes, is there a particular reason why you choose ED or hospital admission or referring to clinic?
- Are there patients with TIA whom you would manage yourself i.e. not refer or admit (explore if yes)
- As you may know, about 50% of referrals to the clinic are not diagnosed as stroke/TIA. What are your views on this? Why do you think this happens? (explore)
- If you choose not to refer or admit the patient, would you usually prescribe treatment?
- If answer is yes, what treatment would you provide?
- If answer is no, then what are your reasons for not providing treatment
- For patients, you do refer, do you prescribe any treatment yourself?

"The transition to the next section is on the **ABCD2 Score**".

- Have you heard of the ABCD2 score?
- No: It's a risk stratification tool, stands for Age, Blood pressure, Clinical features, Duration and Diabetes and can usually be found at the bottom of TIA clinic referral forms.
- Yes: I know you suggested you have heard of the ABCD2 score, but I'm just going to briefly state what it stands for. It's a risk stratification tool, stands for Age, Blood pressure, Clinical features, Duration and Diabetes and can usually be found at the bottom of TIA clinic referral forms.
- If no, is there a reason why you do not use the ABCD2 score? And how do you see the ABCD2 score if you don't really know what is it?
- If yes, what are your views about using the ABCD2 score? Is it useful to you?
- Do you think the score is of any value in making a diagnosis of TIA?
- Are there any other scores which you use?
- If yes, which ones?

"The transition to the final section is on the **UTILITY OF A DIAGNOSTIC TOOL**".

Scores have been developed to give the likelihood of a positive diagnosis of TIA and are designed to assist, not over-ride, clinical judgement. For example the score which was sent to you via email may be useful in Primary Care to help with diagnosis and the decision whether to refer.

The Dawson Score includes age of patient, previous history of stroke or mini-stroke and seven variables relating to the clinical event (headache, loss of consciousness, seizure, diplopia, speech disturbance, unilateral facial and limb weakness).
In principle, would you value a score to help diagnose TIA? Please explain the rationale for your answer?

- What do you think the strengths and weaknesses would be of using a diagnostic tool in Primary Care?
- Would you find it useful to use a score to help with the diagnosis of TIA?
- If yes, then what are the reasons for this?
- If no, then why not?
- Please explain the rationale for your answer (is a better non-confrontational way of putting it)

A score would give you a % probability of a TIA diagnosis, using clinical features. We would like to explore at what likelihood level, primary care referrers may choose to REFER or NOT TO REFER to a TIA clinic.

If the likelihood of a TIA was more than 50%, would this help you to decide **to** refer?

What, if any threshold would you find most helpful in deciding **to** refer (eg 10% i.e. 1 in 10, 20% 1 in 5, 50% 1 in 2)?

If the likelihood of a TIA was less than 10%, would this help you to decide **not** to refer?

What, if any, threshold would you find most helpful in deciding **not** to refer (eg 1% 1 in 100, 5% 1 in 20, 10% 1 in 10, 20% 1 in 5)?

In summary, would you find a score more helpful in 'ruling in' or 'ruling out' a diagnosis of TIA?

How, if at all, do you think using a score in this way would alter your referrals to the TIA clinic?

E.g. do you think you would refer more or less patients; would it make you more comfortable with non-referral in certain circumstances?

Just before finishing, I would like to ask are there any ways in which you think referral pathways for TIA could be improved?

Closing and thanks – conclude by thanking him/her for their time and contribution.

Thank you very much for your time today, just to inform you, you will receive a cheque from the University of Leicester as a gratitude for your time today. I will send an email after this interview and you will just have to get back to me with some basic details about yourself which are needed to process the payment.

Appendix 27: How the topic guide was amended

Face to Face pilot interview: Schedule of questions for telephone interview with GPs who have made suspected TIA patient referrals with GP 1: Wednesday 7th December 2016: 11am.

Background: General Practitioner

Current position: National Institute for Health Research (NIHR) Clinical Lecturer in General Practice

The interview only started to record after the researcher asked if "I was speaking with Dr (name) (as no identifiable information was recorded)

Once it had been confirmed the researcher was speaking with the intended participant, the recording had begun.

The recording started with an introduction; "my name is Priyanka Bose, I am a PhD student at the University of Leicester. I would like to thank you for volunteering to take part in this research, your participation is much appreciated". The research aims were then briefly stated:

"Just to recap on the research aims, the purpose of this interview is to look into GPs experiences of diagnosing and managing suspected TIA patients, the use of the ABCD2 score and the potential utility of a diagnostic and management tool such as the Dawson Score in Primary Care".

Permission to audio record the interview and verbal consent was then asked.

"Before I go onto to the questions, I would like to seek agreement to audio record this interview, is this okay with you? Also, I would like to seek verbal consent, are you happy to participate in this study?"

Once consent for the recording and the verbal consent to participate had been taken the questions were asked.

"The transition to the first topic is diagnosing suspected TIA patients. The questions being asked are related to the general diagnosis of patients, rather than specific patients. As a GP, there are difficulties in diagnosing suspected TIA patients, so the first question is what would be your definition of a TIA?"

Instead of asking GPs to give a definition of a TIA, perhaps to consider providing a definition to the GPs, and then asking "do you agree with this definition" "is it a useful definition for you as a GP"

This suggestion was very helpful as it allowed me to think about my questions and what I really want to know from the GPs. From the systematic review conducted in 2015, it was reported that the definition stated by GPs varied, with some GPs suggesting symptoms lasting less than 1 hour, others suggesting the traditional less than 24 hrs and others proposing incorrect definitions >24 hrs. Therefore, it was thought that rather than providing a definition, it would be best to see which definition the GPs suggests which define as TIA in their perspective, and which one they use in Primary Care.

From this, the question "do you think it is useful to distinguish between a stroke and a TIA"? was developed, ti allow further details on the two conditions. This would also enable GPs' to go further into detail about the two definitions and perhaps their views on this.

The rest of the questions were asked and it was stated that the questions which followed for the first topic "diagnosing suspected TIA patients" was well structured and would allow the GPs to go into detail.

"The transition to the second topic is managing suspected TIA patients" and it was described that TIA clinics experience high number of referrals, making it difficult to see patients within the recommended time frame (high risk, 24 hours, low risk, 7 days).

Whilst going through the questions for this section in the pilot interview, the GP suggested to add the question "what specific symptoms would you look for in suspected TIA patients"? GPs may not go into much detail with the questions, therefore this question followed on from the previous questions being

asked. It would allow GPs to go more in depth with the level of detail they provide. It may also show differences or even patterns in regards to what GPs' look for when diagnosing and managing the patients.

"The transition to the next section is on the ABCD2 score". Whilst going through the questions on this topic, the GP proposed that I should ask whether they have heard of the ABCD2 score. The questions were implying that every GP knew of the ABCD2 score. However, although some GPs may know of the score, others may not know, or may use it but are not aware that it is labelled as the 'ABCD2', as it can usually be a small section GPs fill out at the bottom of the referral forms.

It was advised to ask GPs if they had heard of the score, and if the answer was no, then to briefly describe what the score is. Taking on this advice, a section describing the ABCD2 score was added, e.g. it is used as a risk stratification tool, which stands for Age, Blood pressure, Clinical features, Duration and Diabetes, and can usually be found at the bottom of TIA clinic referral forms.

This information may be a reminder to the GPs who have come across such a score, just not in its labelled form. However, if the GPs' have never used this then it also informs them about the score.

Within this section the question "do you think the score is of any value in making a diagnosis of TIA" if the GP answers "no" then this follows on with the question "are there any reasons why you do not use the score".

It was suggested that instead of asking "are there any reasons why not" just ask the first question and then see what the GPs' answers are. Most GPs would suggest a reason as to why they will or will not use a score like this when asked about the value of a score. Therefore, asking "why not" may make the questions repetitive. If the GPs do not tackle the "why not" question, then this can be asked after the first question.

The questions in the last section was asked:

"The transition to the final section is on the Dawson Score". Brief details of the Dawson Score was provided;

"The score includes age of patient, previous history of stroke or mini-stroke and seven variables relating to clinical event (headache, loss of consciousness, seizure, diplopia, speech disturbance, unilateral facial and limb weakness)" GPs were informed that the score which was sent via email may be helpful in Primary Care to diagnose and triage referrals.

The first suggestion on this section was to state whether the Dawson Score has been validated? And if so has it been validated as a diagnostic tool? The GP suggested that this would give the GPs a better understanding of the potential utility of the score. Additionally, as GPs have such a busy timescale, they may not have read the full paper on the Dawson Score. Therefore, providing brief but useful information would help tackle the questions which follows within the section.

Taking this on board the statement "The score has been validated as a diagnostic tool in secondary care" was added.

It was further advised that the GPs would not know enough on the sensitivity and specificity of the score to answer some of the questions that was asked. For example;

"Do you think the Dawson Score would be useful in Primary Care?"

If yes, then "what would be useful about it?"

It was proposed that it would be better to restructure the questions so that it reads as though questions are being asked about a diagnostic tool, rather than focusing primarily on the Dawson Score. For example;

"What do you think the strengths and weaknesses would be of using a diagnostic tool in Primary Care?"

"Would you find it useful to use a score to help with the diagnosis of TIA?"

"Would you be willing to use a score like this for risk stratification for suspected TIA patients?"

From the discussion with the GP in the pilot interview, the researcher learnt that the structure of the interview was vital. The topic guide needed to be carefully structured so that each question was asked appropriately, and the questions that follow are relevant and can get the best details possible. The pilot interview brought up sections and questions which needed more attention and correcting, and conveyed parts which needed to be constructed in a better way.

Additionally, each GP would have a different response, some will be very detailed and other not so much. Therefore, each question needed to be asked in a way that there was room for them to further explain most of the questions, and to talk about their experiences in as much detail as possible.

Topic guide 1 and topic guide 2: The differences

The overall suggestion was to add a few extra questions as each GP will vary from one another. Some GPs will go into detail about their experience of diagnosing and manging suspected TIA patients, whilst others will be limited to their answers.

The topic on diagnosing suspecting TIA patients started with asking GPs what their definition of a TIA is, this is the same with topic 1 and 2. However an extra sentence asking GPs if they think it is useful to distinguish between a stroke and TIA was added. They will be asked to go into detail about their answer whether it is 'yes' or 'no'. Both topic 1 and 2 follows on asking GPs their experience of diagnosing suspected TIA patients, how many people a year do they diagnose with suspected TIA and the challenges relating to diagnosing.

Taking on the suggestions, two additional questions were added to topic 2 at the end of this section by asking GPs "are there any groups in particular they found difficult diagnosing as a suspected TIA?" and "what specific symptoms (if any) they found difficult diagnosing?" This intended to cover most aspects relating to the difficulties of diagnosing suspected TIA patients, and could potentially allow GPs to go into detail when asking the various questions.

The topic on the management of suspected TIA patients started with the question "how do you as GPs make a decision to refer a suspected TIA patient"? However, in topic 2, a sentence on "are there any specific symptoms which GPs look for in patients?" was added, which then followed on to asking about the difficulties in making the decision to refer. Again this sentence was added to cover most aspects relating to the difficulties with diagnosing suspected TIA patients. The rest of topic 1 and topic 2 remained the same, by asking GPs where they would usually refer patients, would they provide any treatment and what treatment (if any).

Both topic 1 and 2 followed through by asking GPs about the ABCD2 score. In topic 1 GPs were asked if they are using the ABCD2 score in Primary Care. However, in topic 2 this was changed to asking GPs if they have heard of the ABCD2 score. If their answer was no then it would be explained what the score was (e.g. risk stratification tool, which stands for Age, Blood pressure, Clinical features, Duration and Diabetes, and can usually be found at the bottom of TIA clinic referral forms). GPs will use the TIA clinic referral forms for suspected TIA patients and will state the age, blood pressure, clinical features etc, but may not be aware that it actually stands for the ABCD2 score. Therefore, clarifying this to the GPs would give them a full understanding of the score.

If the GPs answer no to using the ABCD2 score then it will be asked if there is a reason as to why they do not use the ABCD2 score, and if they answer yes to using the score then they will be asked on their views on using it and if they think it is of any value in making a diagnosis of TIA. Both topics will end this section with asking if there are any scores or other scores which they use for TIA.

The final section was on the Dawson score, both topic guides started with introducing briefly the purpose of the Dawson score. For example The Dawson Score includes age of patient, previous history of stroke or mini-stroke and seven variables relating to the clinical event (headache, loss of consciousness, seizure, diplopia, speech disturbance, unilateral facial and limb weakness). Furthermore, it was stated that the score which was sent to the GPs via email. May be helpful in Primary Care to diagnose and triage referrals. However an additional sentence was added to topic 2, stating that the score has been validated

as a diagnostic tool in Secondary Care. This was provided to give GPs more detail about the score and its potential purpose.

The first question on topic 1 asked GPs if they think the Dawson score would be useful in Primary Care. The pilot interview with suggested that asking GPs this will not allow an appropriate answer. The reason for this is because GPs are not aware of the sensitivity and specificity of the score, and will not be able to answer this question. In topic 2 this question was changed to asking GPs what they thought the strengths and limitations of using a diagnostic tool in Primary Care would be.

In topic 1 GPs would be asked what they would find useful about the Dawson Score in particular. Again this does not provide GPs with enough information to talk of the score in terms of its diagnostic ability. In topic 2 this question was changed to asking if they would find it useful to use a score to help with the diagnosis of TIA and if yes then what are the reasons for this, and if no then what are their reasons for this.

Lastly, in topic 1, the GPs would be asked to sum up some strengths and limitations of using the score in Primary Care. The GPs would not know enough about the score to determine the strengths and limitations in Primary Care. This question was altered in topic 2 to asking GPs if they would be willing to use a score like this for diagnosis and management in Primary Care.

Both topic 1 and topic 2 finished by asking if the GPs thought of any ways which referral pathways for TIA could be improved, and further with a closing sentence thanking GPs for their participation.

Telephone pilot interview: Schedule of questions for telephone interview with GPs who have made suspected TIA patient referrals with GP 2: Wednesday 8th March 2017: 12:00

The aim of the telephone pilot interview was to replicate the exact setting for the main interviews which will be conducted with GPs.

A room was booked for an hour at the University Of Leicester (Centre for Medicine), and the University phone within that room was used to contact the GP.

Once the call had been made, the recording of the interview using the encrypted digital recorder only started to record after I had asked if "I was speaking with Dr (name)?" as no identifiable information will be recorded.

Overall the interview duration was 29.59 minutes. The interview went smoothly with the GP answering all the questions on the topic guide.

The topic "diagnosis of suspected TIA patients" started with asking GPs what their definition of a TIA. The GP felt that this question was slightly direct, and perhaps easing GPs in would be more beneficial. Taking this on board, the first and second question (do you think it is useful to distinguish between a stroke and a TIA?) was swapped. The question "what is your experience of diagnosing suspected TIA patients?" was felt to be quiet vague and perhaps re wording would provide more use to answering the specific question. The question was reworded to "is there anything else you think might contribute to the issues around diagnosis?" and was put at the end of that section. This was done so that any additional information which the GPs thinks that is not covered in the diagnosis section can be added.

Appendix 28: How the topic guide evolved

For each interview, any difficulties answering questions, uncertainties and GP responses were noted briefly on each topic guide. The notes were then discussed with an academic supervisor to consider if any amendments needed to be applied to the topic guide, before the next interview. The purpose of this was to enable changes to the topic guide to tailor to GPs' answers, some of the changes are stated below:

Topic: DIAGNOSIS

- "Is there anything else you think might contribute to the issues around diagnosis?"

The intention of this question was to give the GP a chance to add to the difficulties surrounding diagnosis of suspected TIA patients, which could have been missed or were not covered in the questions asked. Two GPs were unsure how to answer the question, and suggested the important points had been covered.

The indication that the question did not add to anything, and that there were no additional points, it was thought best to not ask the question going forward, as it may allow more time for alternative questions.

- Elaborated on question: "Are there any groups in particular you found difficult diagnosing?" Examples were given, e.g. diabetes younger versus older, to prompt their thoughts. In the first interview, the answer to this question was brief, however once the examples were provided, it enabled a more detailed answer of various groups, therefore the examples were added to the topic guide.

- Start of interview 4, amended question to asking what symptoms they found harder and easier, rather than just the symptoms they found difficult, which was thought to generate any similarities or inconsistencies.

Topic: MANAGEMENT

- "About 50% of referrals are not diagnosed as a TIA/stroke, do you think this is reasonable?" was changed to "What are your views on this? Why do you think this happens?" The altered question encouraged the GP to go into more detail rather than a one word answer.

Topic: UTILITY OF A DIAGNOSTIC TOOL

Most questions in this section was changed from "what are your reasons for this" to "please explain the rationale for your answer" as it was more of a non-confrontational way of asking the question.

- What if any threshold would you find most helpful in deciding to refer (e.g. 10%, 20%, and 50%) changed to (10% 1 in 10, 20% 1 in 5, and 50% 1 in 2).
- What if any threshold would you find most helpful in deciding not to refer changed to (1% 1 in 100, 5% 1 in 20, 10% 1 in 10, and 20% 1 in 5).

The first few GPs found it difficult to answer on a specific percentage, and once the question was altered, more GPs managed to pin point on an answer, as it gave a wider perspective of the figures.

Appendix 29: Nodes in Nvivo

Name	Sources	References	Memo Link	Created By	Created On	Modified By	Modified On
Would a score change referral process	0	0		PB	17/07/2017 11:53	PB	17/07/2017 11:53
Yes	4	7		PB	17/07/2017 11:53	PB	17/07/2017 11:59
No	2	3		PB	17/07/2017 11:53	PB	17/07/2017 11:57
What specific symptoms do GP look for	0	0		PB	13/07/2017 11:34	PB	13/07/2017 11:34
Weakness	4	6		PB	13/07/2017 11:34	PB	13/07/2017 11:44
Vision	3	4		PB	13/07/2017 11:34	PB	13/07/2017 11:45
Speech	4	4		PB	13/07/2017 11:34	PB	13/07/2017 11:45
Classical, neurological, sensory symptoms	3	4		PB	13/07/2017 11:35	PB	13/07/2017 11:42
What GPs are referring for	0	0		PB	13/07/2017 11:58	PB	13/07/2017 11:58
Reasurrance	3	4		PB	13/07/2017 11:59	PB	13/07/2017 12:07
Investigations	3	4		PB	13/07/2017 11:58	PB	13/07/2017 12:05
Differs with patient	2	2		PB	13/07/2017 12:04	PB	13/07/2017 12:05
Diagnosis (confirm, refute)	2	2		PB	13/07/2017 11:58	PB	13/07/2017 12:06
Using a diagnostic tool in PC	0	0		PB	14/07/2017 15:55	PB	14/07/2017 15:55
Strengths	5	8		PB	14/07/2017 15:55	PB	14/07/2017 16:07
Weakeness	6	9		PB	14/07/2017 15:55	PB	14/07/2017 16:07
Threshold found useful to refer	0	0		PB	17/07/2017 10:55	PB	17/07/2017 10:55
Threshold found useful to refer	0	0		PB	17/07/2017 11:13	PB	17/07/2017 11:13
Other	2	2		PB	17/07/2017 11:14	PB	17/07/2017 11:20
10% or less	4	5		PB	17/07/2017 11:14	PB	17/07/2017 11:20
Other	3	3		PB	17/07/2017 10:56	PB	17/07/2017 11:03
10% or less	3	4		PB	17/07/2017 10:56	PB	17/07/2017 11:18
Specific symptoms	0	0		PB	04/07/2017 10:51	PB	04/07/2017 10:51

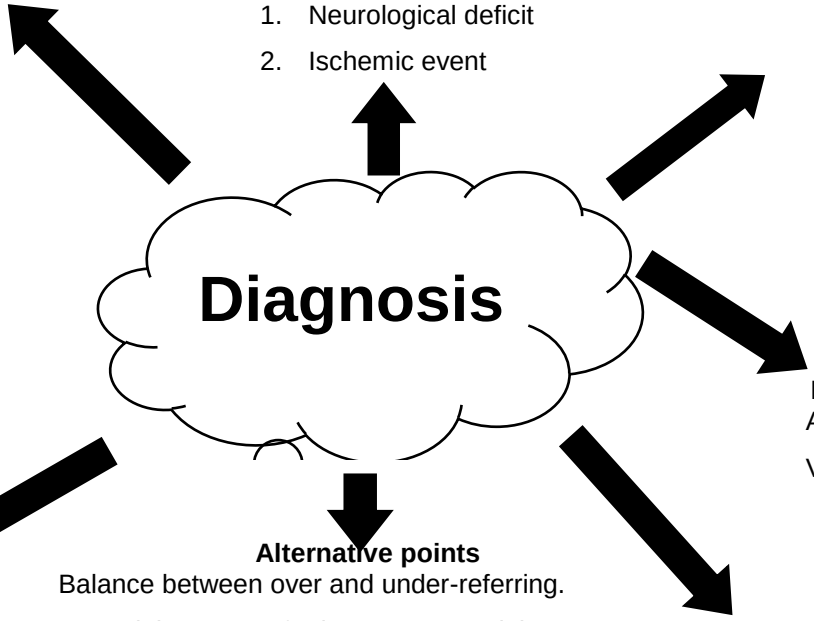
Easier	0	0		PB	04/07/2017 11:02	PB	04/07/2017 11:02
Classical symptoms	3	4		PB	04/07/2017 11:03	PB	04/07/2017 11:15
Difficult	0	0		PB	04/07/2017 11:01	PB	04/07/2017 11:01
Vague or no specific symptoms	3	5		PB	04/07/2017 11:02	PB	04/07/2017 11:14
Speech	1	2		PB	04/07/2017 11:02	PB	04/07/2017 12:16
Sensory and visual	3	9		PB	04/07/2017 11:01	PB	04/07/2017 11:11
Score to help with diagnosis	0	0		PB	14/07/2017 13:25	PB	14/07/2017 13:25
Would value a score	4	4		PB	14/07/2017 13:25	PB	14/07/2017 13:33
Would not value a score	2	4		PB	14/07/2017 13:25	PB	14/07/2017 13:32
Score more helpful with ruling in or out	0	0		PB	17/07/2017 11:40	PB	17/07/2017 11:40
Ruling out	4	4		PB	17/07/2017 11:41	PB	17/07/2017 11:44
Ruling in	1	1		PB	17/07/2017 11:41	PB	17/07/2017 11:42
Both	1	1		PB	17/07/2017 11:41	PB	17/07/2017 11:42
Prescribing treatment	0	0		PB	13/07/2017 16:05	PB	13/07/2017 16:05
Dont refer, Variable results	6	8		PB	13/07/2017 16:05	PB	13/07/2017 16:15
Do refer, variable results	5	6		PB	13/07/2017 16:09	PB	13/07/2017 16:15
Particular groups (harder)	0	0		PB	03/07/2017 16:08	PB	03/07/2017 16:13
Previous strokeTIA	2	3		PB	03/07/2017 16:20	PB	03/07/2017 16:24
Other difficulties	2	5		PB	03/07/2017 16:18	PB	03/07/2017 16:30
Other co-morbidities	3	3		PB	03/07/2017 16:08	PB	03/07/2017 16:28
Elderly	1	1		PB	03/07/2017 16:09	PB	03/07/2017 16:23
Younger	1	1		PB	03/07/2017 16:09	PB	03/07/2017 16:25
Particular groups (easier)	0	0		PB	03/07/2017 16:14	PB	03/07/2017 16:14

With co-morbidities	3	6		PB	03/07/2017 16:15	PB	03/07/2017 16:32
Elderly	2	2		PB	03/07/2017 16:16	PB	03/07/2017 16:32
Liklihood of TIA less than 10% NOT REFER	0	0		PB	17/07/2017 11:29	PB	17/07/2017 11:29
Help not to refer	5	5		PB	17/07/2017 11:30	PB	17/07/2017 11:34
No	1	1		PB	17/07/2017 11:30	PB	17/07/2017 11:33
Liklihood of a TIA more than 50%	0	0		PB	17/07/2017 10:23	PB	17/07/2017 10:23
Unsure about referring	1	2		PB	17/07/2017 10:25	PB	17/07/2017 10:27
Help to refer	5	5		PB	17/07/2017 10:24	PB	17/07/2017 10:31
Importance of distinguishing TIAstroke	0	0		PB	03/07/2017 11:16	PB	03/07/2017 12:02
TIA warning sign	1	1		PB	03/07/2017 12:08	PB	03/07/2017 12:08
Seperate entities	3	6		PB	03/07/2017 11:41	PB	03/07/2017 12:06
Similar pathology	1	1		PB	03/07/2017 12:12	PB	03/07/2017 12:14
Prevention	2	2		PB	03/07/2017 11:58	PB	03/07/2017 12:09
Managed differently	2	2		PB	03/07/2017 11:41	PB	03/07/2017 12:07
Managed differently	0	0		PB	03/07/2017 11:50	PB	03/07/2017 11:41
All 6 GPs agreed important	0	0		PB	03/07/2017 12:04	PB	03/07/2017 12:04
Difficulties deciding to refer	0	0		PB	13/07/2017 13:29	PB	13/07/2017 13:29
Symptom conflict	2	2		PB	13/07/2017 13:30	PB	13/07/2017 13:37
Practical issues	3	6		PB	13/07/2017 13:30	PB	13/07/2017 13:40
Other factors	2	3		PB	13/07/2017 13:30	PB	13/07/2017 13:37
Diagnose annually with suspected TIA	0	0		PB	03/07/2017 12:36	PB	03/07/2017 12:36
Varied	5	8		PB	03/07/2017 12:39	PB	03/07/2017 12:44

estimates							
Found difficulty answering	2	3		PB	03/07/2017 12:37	PB	03/07/2017 12:39
Definition of TIA	0	0		PB	03/07/2017 12:10	PB	03/07/2017 12:10
Neurological deficit	4	5		PB	03/07/2017 12:20	PB	04/07/2017 11:40
Less than 24hours	6	6		PB	03/07/2017 12:11	PB	03/07/2017 12:26
Ischemic event	2	2		PB	03/07/2017 12:20	PB	04/07/2017 11:40
Decision to refer	0	0		PB	13/07/2017 10:43	PB	13/07/2017 10:43
Combination of factors	4	6		PB	13/07/2017 10:52	PB	13/07/2017 11:17
Past history	1	3		PB	13/07/2017 10:53	PB	13/07/2017 11:13
ABCD2 to decide urgency	3	5		PB	13/07/2017 10:52	PB	13/07/2017 11:09
Challenges to diagnosing	0	0		PB	03/07/2017 13:37	PB	04/07/2017 11:36
Uncertainty of symptoms	5	13		PB	03/07/2017 13:40	PB	03/07/2017 14:24
Time pressure	1	3		PB	03/07/2017 14:09	PB	03/07/2017 14:16
Patient researchers	1	2		PB	03/07/2017 14:08	PB	03/07/2017 14:11
History	2	3		PB	03/07/2017 14:09	PB	03/07/2017 14:25
Availability of service	1	2		PB	03/07/2017 14:08	PB	03/07/2017 14:20
Anyway referral pathways can be imporoved	0	0		PB	17/07/2017 12:12	PB	17/07/2017 12:12
Yes	4	6		PB	17/07/2017 12:12	PB	17/07/2017 12:18
No	3	3		PB	17/07/2017 12:12	PB	17/07/2017 12:17
Any patients you would not admit or refer	0	0		PB	13/07/2017 14:22	PB	13/07/2017 14:22
Varied answers	5	5		PB	13/07/2017 14:33	PB	13/07/2017 14:58
Patients refuse	2	2		PB	13/07/2017 14:26	PB	13/07/2017 14:37
Admitting patients rather than referring	0	0		PB	13/07/2017 13:58	PB	13/07/2017 13:58
Whilst in consultation	2	2		PB	13/07/2017 13:59	PB	13/07/2017 14:00
Varied answers	4	6		PB	13/07/2017 13:58	PB	13/07/2017 14:36

Recurrent TIAs	2	2		PB	13/07/2017 14:01	PB	13/07/2017 14:02
ABCD2	0	0		PB	14/07/2017 11:39	PB	14/07/2017 11:39
Not useful for diagnosis	4	5		PB	14/07/2017 11:40	PB	14/07/2017 11:53
Useful for diagnosis	1	1		PB	14/07/2017 11:40	PB	14/07/2017 12:05
Found it valuable	6	10		PB	14/07/2017 11:40	PB	14/07/2017 12:05
50% referrals to TIA clinic	0	0		PB	13/07/2017 15:14	PB	13/07/2017 15:14
Reasonable	3	5		PB	13/07/2017 15:14	PB	13/07/2017 15:23
Other comments	3	4		PB	13/07/2017 15:15	PB	13/07/2017 15:24

Appendix 30: Mind maps



Challenges to diagnosing suspected TIA patients

Various practical factors:

1. Availability of services
2. History
3. Time pressure as a GP
4. Patient research symptoms beforehand

However, majority of GPs suggested that it was the uncertainty of symptoms.

"Not textbook like"

Very vague symptoms (challenging) regularly noted in challenges and specific symptoms found difficult

Specific symptoms

Harder:

Vague symptoms, as there can be so many different causes for the vague symptoms.

Visual and sensory symptoms

Visual symptoms subjective perspective than objectively being able to define.

Sensory symptoms sometimes over exaggerated:

"Pins and needles described as loss of sensation or numbness"

Easier:

Classical symptoms

Definition

All GPs defined TIAs as resolving within or less than 24hrs

Similar definitions split into two;

1. Neurological deficit
2. Ischemic event

Alternative points

Balance between over and under-referring.

Potential to over refer in cases you might want to over investigate for any neurological symptom.

A lot of people **"don't quite fit"** but still suspicious enough to want to rule it out.

All points above link to specific symptoms. Vague symptoms lead to uncertainty and leads to all of the above.

Diagnosing annually with suspected TIA

Varied estimates; 4-5, 12-24, 25-50, 10, 2

How many GPs diagnose depends on various factors:

- Part time or full time GP
- Size of practice
- Population of practice

Importance of distinguishing between TIA and stroke

All GPs agreed important

Varied answers with majority suggesting:

1. TIA and stroke are separate entities
2. Managed differently

Particular groups

Even split between categories:

(easier vs harder for co-morbidities).

Other difficulties included:

1. Language difficulties
2. Existing neurological condition and previous TIA/stroke

More suggested elderly groups were easier:

"High level of suspicion in that group"

MANAGEMENT

ANY CASES YOU DID NOT ADMIT/REFER

Refusal from patients to be referred or admitted

Varied answers

- Those who are in their final year of life
- Those who have had a stroke & are in residential homes & disabled
  - No change to their management

Don't subject to hospital admission, referral & interventions!

Not an acute scenario to not admit or refer
Happened in a chronic setting

GP would still refer to a TIA clinic if they do not admit to confirm/refute, but will put them on preventive meds/aspirin statin & control BP.
ABCD2 more than 5 send them on to hospital

ADMITTING PATIENTS RATHER THAN REFERRING

1. Recurrent TIAs within a short space of time
2. Whilst in consultation (having an episode)

Varied answers:

The ambulatory TIA clinic has made it easier to refer. Depends on the ABCD2 score > 5 admit
Those clinically unstable needs admitting
- symptomic
- visual disturbance
- uncontrollable BP.

DECISION TO REFER

1. ABCD2 to decide urgency of referral
2. Combination of factors
   - ABCD2 + referral form
   - Clinical experience
   - Risk factors, clinical presentation & ABCD2 score.
   - Background knowledge of patient & patients history

SPECIFIC SYMPTOMS GP LOOK FOR

Top symptoms were;
1 → weakness
2 → speech
3 → vision
4 → classical, neurological & sensory symptoms.

50% REFERRALS TO THE TIA CLINIC

Majority of GPs agreed that this was a reasonable percentage.
Other comments included; seeking reassurance with their diagnostic ability is not new in medicine

- Easier for clinicians to refer
- Easier to make a diagnosis @ the TIA clinic than in general practice, due to investigations or looking at early ongoing symptoms of another condition.
- If its a easy pathway, numbers will grow exceptionally.
- It is important to have a high index suspicion, "maybe GPs aren't very good at making that difference without a diagnostic test"

DIFFICULTIES IN DECIDING TO REFER

Time contraints: GPs time, time it takes to refer & organise everything
Pressure from CCGs NOT to refer
Accessability, access to hospitals for patients.
Symptom conflict: Whole host of other conditions make it difficult versus no difficulty with symptoms.
Other factors included - Degree of symptoms, risk factors, past med history (differed patient 2 patient)

the initial decision whether to refer or not is difficult; more so deciding NOT to refer!

WHAT ARE YOU REFERRING FOR

- Investigations
- Reassurance

} Seen as a form of Prevention

Diagnosis (confirm or refute).

Some GPs answered that it differs patient to patient, e.g
mainly to confirm diagnosis & or for ongoing management for patients who had symptoms in the last hour or last week & resolved"

MANAGEMENT

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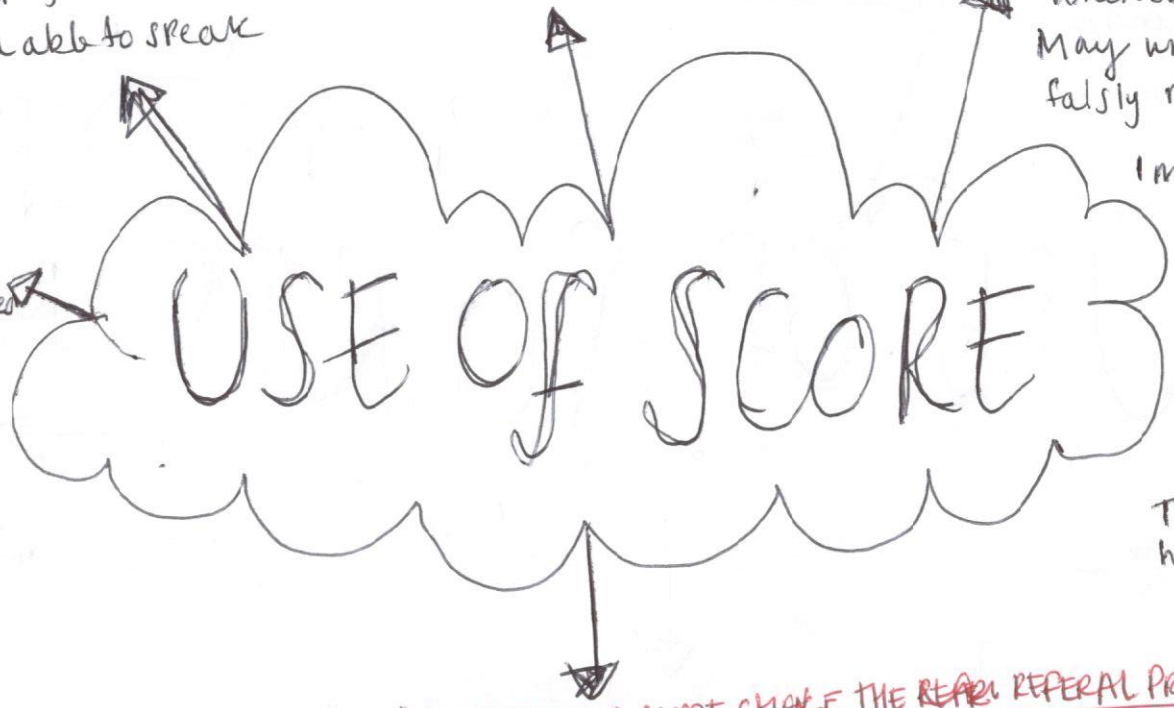

CAN REFERRAL PATHWAYS BE IMPROVED?

- Being able to meet the timescale guidelines
- keeping it simple (1 page referal)
People hate ticking lots of boxes - Simplyfying it
- fast track access is very important (integrated with computer systems).
Clear pathway, maybe be able to speak directly to a clinician?

SCORE MORE USEFUL IN RULING IN OR OUT?

Majority of GPs suggested a score would be more useful in ruling out 4/6
& 1 said ruling in & 1 said both ruling in & ruling out.

USING A DIAGNOSTIC SCORE IN PC

WEAKNESSES:

Not easily memerable
form filling is time consuming
Adds another layer of bureaucracy when suspect is clearly a TIA
May under diagnose TIAs, falsly reassuring Patients (false negatives)
Impairs clinical judgement
tools don't take into account variables within a Patient Presentation
A lot of clinicians are dependent on them.
They don't make a huge difference how clinicians would behave generally.

NO CHANGES TO PATHWAY

Pathway is fantastic
The ability to use the resources around it is difficult
Needs to be increased
Provision made to have clinics run Properly.

WOULD USING A SCORE CHANGE THE ~~REFRL~~ REFERAL PROCESS

Majority of GPs said yes;

- using a score will increase referals, but waiting time will be longer
- will give more evidence to refer/refute or not refer.
- will strengthen the referral process.
- increase confidence, not missing anything in individuals
- if there was a low risk on the score then would re-evaluate (take more time) asking for a more detailed history & seeing any other factors which explain their symptoms.
- Safety element of referring or not referring patients

WOULDN'T ALTER REFERREL

No change in referral from 2 GPs.
If the GP is worried about a TIA then would send them in, a score would not be helpful for referral.

USE OF SCORES

USING A DIAGNOSTIC SCORE IN PRIMARY CARE

STRENGTHS:

Reassuring that NOT referring is OK
Guidance to sharpen GPs diagnosis
clinicians have time Contraints, it helps focus their mind on specific symptoms & signs.
Avoid unnecessary investigations, will reduce Patient distress.
If your always use to tools more likely to use it
Better use of GPs time, better for patient, targets HR Patients

ADDITIONAL COMMENTS

The Dawson score numbers are quite difficult to remember.

Electronic score would be good for surgery, but not for home visits, usually visits homes every day 3X a day.

More accurate way of making a diagnosis

Making a good electronic version that emerged within clinical systems would be good.

ABCD2 SCORE

USEFUL FOR GPS?

Useful for identifying people with TIA who needs urgent assessment

Pointers to take you in the right direction

Its a guideline which;

- Provides uniformity on how to make a diagnosis
- Help make that decision

The score helps reassess the features on the score which sometimes can be overlooked.

VALUE IN MAKING DIAGNOSIS

NO; Majority suggested NO

Not valueable in diagnosis rather Pre-diagnosis to risk assess;

1. When patients need to be seen
2. Whether the patient needs to be admitted.

More for GP confirmation, a decision tool just to help!

GPs already have a good idea which category patients will fall into, so its more of an additional aid.

Combination of tool & consultation that is useful for diagnosis not just the score.

YES;

Has value in diagnosis; increases the chances or likelihood of be it being a TIA.

SCORE FOR DIAGNOSIS

WOULD NOT VALUE A SCORE FOR DIAGNOSIS

Would not use it as Places more emphasis on clinical ability

usual symptoms that GP should know anyway

Will be good as a reminder, but a score adds to confusion.

SCORE FOR DIAGNOSIS

WOULD VALUE A SCORE FOR DIAGNOSIS

Diagnosis is the most difficult part, deciding how certain that it is/isn't a TIA

If the score has been validated & if the score achieves 70% hit rate, but if it stays the same, whats the point?

Significant implications of what a TIA involves;

- future cardiovascular risk
- medications they will have to take

A tool / score will increase certainty as opposed to ambiguity. Can be used to reassure GPs & solidify & consolidate that decision to use it

Makes the chance of that condition being likely Present more