Transient Ischaemic Attack and Stroke
Electronic Decision Support to Improve
Stroke Care in New Zealand

PhD Thesis

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Abstract

Background

Transient Ischaemic Attacks (TIA) and minor strokes indicate a high risk of early recurrent stroke and other vascular events. Early implementation of secondary preventive measures provided through rapid access specialist stroke services reduces the 90-day stroke risk from 10% to 2%. Same day stroke specialist access is challenging in some areas due to resource constraints, geographical distances, or cultural barriers. The use of electronic decision support tools can help to improve guideline adherence and in some cases improve patient health outcomes and reduce treatment costs. This thesis explores the utility of a TIA/stroke electronic decision support tool in primary care to improve TIA/stroke care in New Zealand.

Methods

The intervention is a web-based electronic decision support tool that integrates into general practitioners’ practice management systems. This tool was developed by the candidate in collaboration with BPAC\textsuperscript{INC}. Four preliminary observational studies are reported. The focus of this thesis is a multi-centre, single-blind, parallel-group, cluster randomised, controlled trial comparing TIA/stroke electronic decision support guided TIA management with usual care in general practices. Eligible participants presented to a participating general practice with symptoms of TIA or stroke. Main outcomes were guideline adherence and 90-day stroke risk. Secondary outcomes included total cerebrovascular and vascular events or death, treatment cost, adverse events, and user feedback. The main analysis was by cluster-adjusted logistic regression.

Findings

The preliminary studies suggested that the tool was effective and safe, but their design limitations precluded definite conclusions. In the multi-centre trial 29 clinics were randomly assigned to the intervention group and 27 to the control group, recruiting 172 and 119 patients respectively. More patients received guideline adherent care in the intervention group 131/172 (76.2%), compared to the control, 49/119 (41.2%); adjusted odds ratio (OR) 4.57; 95% confidence interval (CI) 2.39-8.71; p<0.001. The 90-day stroke
rates were 2/172 (1.2%) in the intervention and 5/119 (4.2%) in the control group; OR 0.27, 95%CI 0.05-1.41; p=0.098. The 90-day TIA and/or stroke rates were lower at 4/172 (2.0%) in the intervention compared with 10/119 (8.5%) in the control group; adjusted OR 0.26; 95%CI 0.70-0.97; p=0.045. There were also fewer, 6/172 (3.5%), vascular events or deaths in the intervention group compared with 14/119 (11.9%) in the control group; adjusted OR 0.27; 95%CI 0.09-0.78; p=0.016. Finally, the intervention was associated with a lower treatment cost ratio of 0.65 (95%CI 0.47-0.91; p=0.013) without an increase in adverse events. A pre-specified sub-group analysis looked at patients with specialist confirmed TIA/stroke and their 90-day stroke rate was 2/99 (2.2%) in the intervention and 5/69 (7.3%) in the control group; unadjusted OR 0.26; 95%CI 0.05 to 1.4; p=0.097. User-feedback from both general practitioners and stroke specialists was favourable.

**Interpretation**

Primary care use of a TIA/stroke electronic decision support tool improves guideline adherence, reduces the risk of recurrent cerebrovascular and vascular events, safely reduces treatment cost, and is well received by clinicians. With increasing health care complexity inter-sectorial collaboration and exploration of new management strategies are important. The TIA/stroke electronic decisions support software is an example of such collaboration and innovation. The journey from inspiration through implementation and rigorous scientific evaluation has been successful in demonstrating the utility of this tool for New Zealanders and perhaps beyond.
Preface

This thesis describes a six year project about the use of a primary care based Transient Ischaemic Attack (TIA) electronic decision support tool to improve TIA management and stroke prevention in New Zealand. The focus of the thesis is a cluster randomised controlled trial, the Efficacy and Safety of a TIA/Stroke Electronic Support Tool (FASTEST) trial. This trial is the most formal scientific assessment of an electronic decision support tool for this disorder to date. This thesis also provides comprehensive background about TIA, its clinical importance and management, and the rationale and context for the use of electronic decision support. The tool is described in detail together with a description of its evaluation.

The candidate, a neurologist, conceived the idea of the tool, developed the underlying logic algorithm, and contributed significantly to software design. She worked closely with Jason Hall, software engineer at BPACINC to develop the current product. Throughout the development process the candidate recruited active input from general practitioners, information technologists, stroke specialists, and district health board managers.

The candidate would like to thank and acknowledge the contributions of the following individuals: Prof Susan Dovey, primary PhD supervisor and FASTEST trial collaborator, Prof Mark Weatherall, PhD supervisor and FASTEST trial collaborator, Dr John Gommans, PhD advisor and FASTEST trial collaborator, Prof Murray Tilyard, CEO of BPACINC and FASTEST Trial collaborator, and Prof John Campbell who was initially a PhD supervisor before he retired due to ill health. In addition, the candidate would like to extend her gratitude to the many general practitioners, general physicians, and stroke specialists who have contributed to the development of the tool and its evaluations. Last, but not least, the candidate would like to thank her husband, John Ranta, for his ongoing and unwavering support and invaluable editorial input.

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List of Tables

Table 1: ABCD2 Score ........................................................................................................... 7
Table 2: Risk stratification by ABCD2 score......................................................................... 8
Table 3: Comparison of non-inpatient based TIA service models (Models 2-6)* .................. 10
Table 4: New Zealand TIA Guideline table defining TIA symptoms .................................. 12
Table 5: Patients admitted following electronic decision support use ................................. 44
Table 6: Binary outcomes before (2009) and after (2011) the introduction of a TIA/Stroke decision support tool ......................................................................................... 47
Table 7: Service costs ......................................................................................................... 55
Table 8: General practice characteristics by region and randomisation ................................. 65
Table 9: Characteristics of patients by study group ............................................................. 66
Table 10: Outcome measure comparisons by randomised group ........................................ 67
Table 11: Final specialist diagnosis ..................................................................................... 72
Table 12: Outcomes calculated for sub-group of patients with TIA/Stroke ......................... 73
Table 13: Intervention general practitioner questionnaire responses .................................. 74
Table 14: Examples of intervention general practitioner free text questionnaire responses about the electronic decision support tool ......................................................... 74
Table 15: Intervention general practitioner questionnaire responses about the time it took them to complete the initial screen to reach a triage decision and the time it took to implement a management plan using the tool ................................................................. 75
Table 16: Examples of intervention general practitioner free text responses about the time it took them to use tool and implement management ........................................... 75
Table 17: Free text comments about training/instructions on tool use ................................. 75
Table 18: Control group general practitioners single scored question responses .................. 76
Table 19: Control general practitioner free text comments about perceived tool utility ...... 76
Table 20: Interventions achieved ......................................................................................... 79
Table 21: Time to investigations and medication initiation (days) .......................................... 79
Table 22: Individual outcomes in cerebrovascular and vascular composites ....................... 80
Table 23: Cost data stratified by category .......................................................................... 81
Table 24: Diagnostic/triage outcomes rendered by the tool if the diagnosis of TIA or stroke is uncertain .................................................................................................................. 83
Table 25: Proportions of patients with final specialist diagnosis (TIA/stroke or non-TIA/stroke) over generalist/tool diagnoses by treatment arm .................................................. 84
Table 26: Features of ten patients with tool identified atypical features who received a final specialist diagnosis of TIA or stroke ........................................................................ 85
Table 27: Patients who underwent community work-up without specialist input .................. 86
Table 28: Guideline adherence and 90-day cerebrovascular/vascular risk in patients managed by general practitioners who attended a pre-trial TIA training session compared with those managed by general practitioners who did not attend the training session ................................................... 87
Table 29: Guideline adherence and efficacy outcome event rates stratified by training plus/minus electronic decision support use ........................................................................ 87
Table 30: 90-Day Stroke Risk by ABCD2 score in FASTEST patients .................................. 89
Table 31: 90-Day Stroke Risk by Risk Category comparing ABCD2 score alone with New Zealand Guideline criteria ................................................................. 89
Table 32: Study outcomes stratified by ethnic origin .......................................................... 91
List of Figures

Figure 1: Summary of the TIA diagnostic and triage algorithm .......................................................... 26
Figure 2: Single page data entry form with sub-menu for ‘Communication/speech problems’ ..... 31
Figure 3: Box displayed if user hovers of next to ‘Visual Symptoms.’ ......................................... 32
Figure 4: Sample outcome page for a low risk patient with typical TIA symptoms ..................... 32
Figure 5: Sample outcome page with ‘community Management’ option selected ......................... 33
Figure 6: High risk TIA patient triage page .................................................................................. 34
Figure 7: Outcome page if the only selected symptom is ‘syncope.’ ........................................... 34
Figure 8: Sample outcome page in a patient with both unilateral weakness and syncope .......... 35
Figure 9: Example of special advice box added to triage page ....................................................... 35
Figure 10: Advice for a patient with persistent right sided weakness .......................................... 36
Figure 11: Extended community stroke management while awaiting ambulance ....................... 36
Figure 12: Management consistency with NZ TIA Guidelines: general practitioners, general physicians, stroke experts, and electronic decision support software ........................................... 39
Figure 13: Time to event Kaplan-Meyer Graph ........................................................................... 47
Figure 14: Trial Profile: Number of general practices enrolled and randomised and number of patients registered and included in analysis .................................................................................. 64
Figure 15: Average per patient cost .............................................................................................. 70
Figure 16: Cost Residuals .............................................................................................................. 70
Figure 17: Mean cost by practice .................................................................................................. 71
Figure 18: Mean cost residuals ..................................................................................................... 71
List of Appendices

Appendix I: Validation Study
Appendix II: Feasibility Study
Appendix III: Safety Audit
Appendix IV: Cohort Study
Appendix V: FASTEST Trial Protocol Paper
Appendix VI: FASTEST Trial Protocol (Grant Application)
Appendix VII: Ethics Approval
List of Abbreviations

ARR  Absolute Risk Reduction
CEA  Carotid Endarterectomy
CI   Confidence Interval
CT   Computed Tomography
DRG  Diagnosis Related Group
ECG  Electrocardiogram
FASTEAST  Efficacy and Safety of a TIA/Stroke Electronic Support Tool trial
GP   General Practitioner
HR   Hazard Ratio
ICD-10-AM  International Statistical Classification of Diseases and Related Health Problems Tenth Revision, Australian Modifications
M3T  Monash Transient Ischaemic Attack Triaging Treatment – refers to an urgent TIA service model
MIMS  Monthly Index of Medical Specialties
MRI  Magnetic Resonance Imaging
NNT  Number Needed to Treat
OR   Odds Ratio
RRR  Relative Risk Reduction
SOS-TIA  International Distress Code plus Transient Ischaemic Attack – refers to an urgent TIA service model
TIA  Transient Ischemic Attack
Table of Contents

Abstract .......................................................................................................................... i
Preface ......................................................................................................................... iii

Chapter 1: Background ................................................................................................. 1
  1.1. Stroke and Transient Ischaemic Attack (TIA) ....................................................... 1
      1.1.1. Introduction .................................................................................................. 1
      1.1.2. Definitions of stroke and TIA ...................................................................... 1
      1.1.3. Stroke risk following TIA ............................................................................ 3
      1.1.4. Available secondary preventive measures .................................................. 3
      1.1.5. Implementation of secondary stroke prevention ......................................... 4
      1.1.6. Barriers to implementation ......................................................................... 11
      1.1.7. New Zealand TIA guidelines ..................................................................... 11
      1.1.8. The idea of a TIA/stroke electronic decision support tool ......................... 13
  1.2. Electronic decision support .................................................................................. 14
      1.2.1. Introduction .................................................................................................. 14
      1.2.2. Definition ..................................................................................................... 14
      1.2.3. Characteristics of electronic decision support systems ............................... 15
      1.2.4. Evidence of effectiveness of electronic decision support systems .............. 16
      1.2.5. Uptake of electronic decision support systems ........................................... 17
      1.2.6. Safety of electronic decision support systems ............................................ 18
  1.3. Electronic decision support to guide stroke management .................................... 18
      1.3.1. Introduction .................................................................................................. 18
      1.3.2. Prior application of electronic decision support in TIA/stroke management .... 19
      1.3.3. Prior applications of electronic decision support in stroke diagnosis .......... 20
      1.3.4. Other applications of electronic decision support ....................................... 21
      1.3.5. Summary of electronic decision support use in TIA and stroke .................. 21

Chapter 2: TIA/stroke electronic decision support development, description, and pre-
FASTEST trial evaluations ......................................................................................... 22
  2.1. Introduction ........................................................................................................ 22
  2.2. Electronic decision support for TIA/minor stroke management: tool description ......................................................... 22
2.2.1. Diagnosis and triage .............................................................................................................. 23
2.2.2. TIA/stroke electronic decision support management recommendations .................. 27
2.2.3. Other features of the TIA/stroke electronic decision support ......................... 28
2.2.4. Sample screenshots ........................................................................................................ 31

2.3. Validation of the electronic decision support tool ............................................................. 37
2.3.1. Overview .............................................................................................................................. 37
2.3.2. Method of the validation study ...................................................................................... 37
2.3.3. Results ................................................................................................................................. 38
2.3.4. Non-medic use of the tool ............................................................................................... 39
2.3.5. Interpretation ...................................................................................................................... 40

2.4. Feasibility of the electronic decision support tool .............................................................. 41
2.4.1. Introduction ......................................................................................................................... 41
2.4.2. Method of the feasibility study ...................................................................................... 41
2.4.3. Results ................................................................................................................................. 41
2.4.4. Interpretation of the feasibility study ............................................................................ 42

2.5. Post-Implementation safety audit ....................................................................................... 43
2.5.1. Introduction ......................................................................................................................... 43
2.5.2. Method of the post-implementation audit ................................................................. 43
2.5.3. Results of the post-implementation audit ................................................................. 43
2.5.4. Interpretation ...................................................................................................................... 45

2.6. Cohort study of electronic decision support tool use ..................................................... 45
2.6.1. Introduction ......................................................................................................................... 45
2.6.2. Method of the cohort study ............................................................................................ 45
2.6.3. Results of the cohort study ............................................................................................. 46
2.6.4. Interpretation of the cohort study ................................................................................. 48

Chapter 3: FASTEST Trial ................................................................. 49
3.1. Introduction ............................................................................................................................ 49
3.2. Hypotheses ............................................................................................................................ 49
3.3. Methods ................................................................................................................................. 49
3.3.1. Trial design ....................................................................................................................... 49
3.3.2. Participants ...................................................................................................................... 50
3.3.3. Intervention ...................................................................................................................... 50
3.3.4. Outcomes .......................................................................................................................... 51
3.4. Results ................................................................. 62
3.4.1. Numbers randomised, recruited, and analysed .................. 62
3.4.2. Baseline data ...................................................... 65
3.4.3. Efficacy outcomes ............................................... 67
3.4.4. Safety outcome .................................................. 68
3.4.5. Economic analysis ............................................... 69
3.4.6. Sub-group analysis ............................................. 72
3.4.7. User feedback .................................................... 73
3.4.8. Supplementary data ............................................ 78
3.5. Exploratory analyses ............................................... 81
3.5.1. Introduction ....................................................... 81
3.5.2. Diagnostic accuracy ............................................. 82
3.5.3. Impact of general practitioner training ......................... 86
3.5.4. Risk stratification to predict stroke recurrence ................ 87
3.5.5. Ethnicity .......................................................... 90
3.5.6. General practitioner imaging access .......................... 92
3.6. Trial registration ................................................... 93
3.7. Funding ............................................................. 93
3.8. Ethics ............................................................... 93

Chapter 4: Discussion ................................................... 94
4.1. FASTEST trial ....................................................... 94
4.1.1. Efficacy .......................................................... 94
4.1.2. Safety ........................................................... 100
4.1.3. Treatment cost .................................................. 101
4.1.4. User feedback .................................................... 103
4.1.5. Exploratory analyses .......................................... 103
4.1.6. Limitations ...................................................... 108
4.1.7. Strengths ................................................................................................................. 111
4.1.8. Overall FASTEST conclusion .................................................................................. 112
4.2. FASTEST trial results in the context of prior studies ................................................. 113
  4.2.1. In the context of prior TIA/Stroke electronic decision support research 113
  4.2.2. In the context of prior TIA service research ............................................................ 114
  4.2.3. In the context of prior electronic decision support research ................................. 115
4.3. TIA/stroke electronic decision support in the broader context ............................... 116
4.4. Next steps .................................................................................................................. 118
4.5. Future studies ............................................................................................................. 120
4.6. Final conclusion ......................................................................................................... 120
References ......................................................................................................................... 121
Appendices ......................................................................................................................... 130
  Appendix I: Validation Study .......................................................................................... 130
  Appendix II: Feasibility Study ......................................................................................... 137
  Appendix III: Safety Audit ............................................................................................... 140
  Appendix IV: Cohort Study .............................................................................................. 144
  Appendix V: FASTEST Trial Protocol Paper ................................................................. 158
  Appendix VI: FASTEST Trial Protocol (Grant Application) ........................................... 167
  Appendix VII: FASTEST Trial Ethics Approval ............................................................... 186
Chapter 1: Background

1.1. Stroke and Transient Ischaemic Attack (TIA)

1.1.1. Introduction

Stroke is the second most common cause of death worldwide and the most common cause of long term adult disability in developed countries.\textsuperscript{1,2} Each year approximately 9,000 people will suffer a stroke in New Zealand with an associated cost of over $450 million.\textsuperscript{3} If current trends in stroke incidence and mortality continue,\textsuperscript{4-6} the number of stroke survivors living in New Zealand will reach 50,000 by 2015, and the estimated overall annual cost of stroke to the country will be greater than $700 million.\textsuperscript{3}

The impact on individuals, and their families, whānau and caregivers is substantial. Approximately one third of people with stroke will die within the first 12 months and one third will be reliant on others for assistance with activities of daily living.\textsuperscript{7} Stroke is also the second most common cause of dementia, the most frequent cause of epilepsy in older people, and a frequent cause of depression.\textsuperscript{8-10}

Reducing the burden of stroke is a key goal for health service planning.

1.1.2. Definitions of stroke and transient ischaemic attack

A stroke, sometimes also referred to as ‘brain attack,’ is the loss of brain function due to the disruption of blood supply to the brain. Disruption of blood supply is caused either by ischaemia (lack of blood flow through a blocked blood vessel) or haemorrhage (bleeding from a ruptured blood vessel), usually as a consequence of atherosclerosis. As a result of inadequate supply of essential nutrients such as oxygen and glucose, the affected brain area cannot function properly and this leads to neurological deficits such as inability to move one or more limbs, inability to speak, or visual impairment.\textsuperscript{11} Risk factors for vascular diseases that lead to stroke include diabetes, high blood pressure, tobacco smoking, high cholesterol, advanced age, and atrial fibrillation.\textsuperscript{12} In addition,
some ethnic groups, including New Zealand Māori and Pacific people, are at higher risk of experiencing stroke.\textsuperscript{13}

Transient ischaemic attack (TIA) refers to stroke like symptoms that are ‘transient’ i.e. they rapidly and fully resolve. TIAs identify people at particularly high risk for subsequent stroke and are sometimes referred to as ‘mini strokes.’\textsuperscript{12} The exact definition of ‘TIA’ is a topic of debate. The classic definition of TIA is \textit{‘a sudden, focal neurologic deficit that lasts for less than 24 hours, is presumed to be of vascular origin, and is confined to an area of the brain or eye perfused by a specific artery.’}\textsuperscript{14} This definition arose at a time of almost no available neurodiagnostic techniques to assess brain tissue damage.\textsuperscript{15} The 24-hour time cut off point is arbitrary. Some patients have transient or nearly transient symptom duration of more than 24 hours (often referred to as ‘minor stroke’), yet are managed the same and share a similarly high risk of a further catastrophic stroke as TIA.\textsuperscript{16} Conversely, recent imaging studies have demonstrated that a large proportion of people with TIAs lasting between one and 24 hours will have brain Magnetic Resonance Imaging (MRI) changes consistent with completed infarction indicating actual stroke rather than a truly transient phenomenon.\textsuperscript{17-19} Most truly transient events are in fact very brief, lasting less than an hour, an observation made already back in the 1950s and 60s\textsuperscript{20-23} and later confirmed by Levy and colleagues.\textsuperscript{24} This longstanding observation along with the recent imaging evidence has led stroke experts, particularly in North America, to promote a new ‘tissue based’ diagnosis of TIA where TIA is defined as a \textit{‘transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischaemia, without acute infarction.’}\textsuperscript{15,25}

In New Zealand and the United Kingdom the time-based definition of TIA has been maintained in part because MRI imaging is not routinely obtained for all TIA patients and early computed tomography (CT) imaging frequently misses strokes, especially small infarcts.\textsuperscript{26,27} The present predominantly primary care based research will use the time-based TIA definition and include patients with minor stroke in discussions under the term ‘TIA’ unless clearly stated otherwise, because the risk of further catastrophic stroke is similar. Ultimately, transient or nearly transient symptoms with or without evidence of tissue damage indicate cerebral circulatory compromise with potentially salvageable tissue at risk. Currently, primary care level management to reduce the risk of stroke remains the same for both patient groups.
1.1.3. Stroke risk following TIA

TIA precedes a full stroke in approximately 25% of ischaemic stroke victims\textsuperscript{28} and 10.5% - 18.2% of TIA patients will experience a stroke within 90 days of their TIA.\textsuperscript{29-31} TIA also signals increased risk for other complications. A Northern California study of 1707 TIA patients also showed a 25.1% risk of overall adverse events within 90 days of TIA (stroke (10.5%), cardiovascular hospitalisation (2.6%), death (2.6%), or recurrent TIA (12.7%)).\textsuperscript{29}

The pathological basis of TIA varies although atheromatous tissue that compromises arterial blood flow through the large intracranial (middle, anterior, or posterior cerebral) or ophthalmic arteries is most common.\textsuperscript{32} Large cerebral arteries supply substantial volumes of brain tissue and if transient compromise is followed by permanent tissue loss significant disability may arise. As a result 85% of strokes following TIA are severely disabling or fatal.\textsuperscript{33} The risk of symptom recurrence is greatest in the first few hours and days after the initial event while the atheromatous tissue remains fresh and stroke rates of as high as 8.1% within 48 hours of TIA have been reported in high risk patients.\textsuperscript{34,35} The high risk of severely disabling and fatal stroke within just a few days of a TIA is the basis for clinical guidelines recommending urgent intervention.\textsuperscript{26,27}

1.1.4. Available secondary preventive measures

The key intervention following TIA that has been shown to reduce subsequent stroke risk is urgent review by a stroke specialist followed by rapid initiation of existing recommended treatments.\textsuperscript{26,27,30,36,37} Existing medical treatments are chosen based on TIA aetiology with most patients benefiting from one or two antiplatelet medications (relative risk reduction (RRR) 13-28%, absolute risk reduction (ARR) 1.0-1.9%, number needed to treat (NNT) 53-104),\textsuperscript{27,37,38} a HMG CoA reductase inhibitor (statin) (RRR 16%, ARR 0.44%, NNT 230),\textsuperscript{39,40} and an anti-hypertensive medicine (RRR 24-31%, ARR 0.85-2.20%, NNT 45-118),\textsuperscript{41} unless there is evidence of atrial fibrillation. Patients with atrial fibrillation benefit most from treatment with an anticoagulant agent such as warfarin (RRR 67%, ARR 8%, NNT 13).\textsuperscript{42}

The New Zealand TIA Guidelines\textsuperscript{27} recommend diagnostic work-up to include head imaging with either CT or MRI to exclude TIA mimics such as seizure due to a space-occupying lesion. Cardiac investigations should, at a minimum, include an
electrocardiogram (ECG) with optional additional testing to investigate for atrial fibrillation. Imaging work-up should also include investigation of the carotid arteries to screen for carotid artery stenosis. In some patients carotid imaging may be forgone if symptoms are clearly caused by a different aetiology, not referable to brain areas supplied by the carotid system, or patients are not surgical candidates. Patients with a carotid stenosis of at least 50% ipsilateral to the involved brain tissue should be considered for carotid endarterectomy within 2 weeks of initial symptoms (NNT 6-25). The guideline recommends additional tests in special circumstances.

Behavioural counselling on diet, lifestyle, smoking cessation (RRR 33%, ARR 2.3%, NNT 43), and driving are also important to provide to patients and their families. These recommendations are discussed in more detail and fully referenced in the New Zealand TIA Guidelines.

1.1.5. Implementation of secondary stroke prevention

Implementing these secondary preventive measures rapidly and comprehensively is a complex and resource intensive task and the best way to accomplish this is unknown. This section discusses six different proposed models.

Model 1:

One option is to admit all patients with TIA to an inpatient specialist stroke service. This has the two fold advantage of offering rapid expert driven implementation of secondary prevention and providing close observation. Close observation helps to monitor for stroke recurrence in the early high risk period post TIA and allows for prompt administration of intravenous Alteplase, a stroke thrombolytic medication. Whether inpatient observation for this purpose is justified has been debated. Undifferentiated admission of all potential TIA patients will mean that 20-50% of admissions will be for unnecessarily admitted non-TIA patients due to the high false positive rate of initial non-expert TIA diagnosis. In addition, unless facilities are staffed to allow for immediate specialist and diagnostic assessments higher risk TIA patients hidden amongst the also admitted low risk and TIA-mimic patients may actually experience delayed interventions and longer hospital stays, especially if admitted over the weekend. This is unlikely to be good use of health care resources and
the most recent research suggests that outpatient management of at least some TIA patients is probably more cost-effective.\textsuperscript{47,48}

The next four service models describe feasible and safe alternatives to admitting all potential TIA patients to hospital.\textsuperscript{30,36,49,50}

**Model 2:**

The Australian Monash Transient Ischaemic Attack Triaging Treatment (M3T) model proposes emergency department assessments under the guidance (at times telephone guidance only) of the inpatient stroke team with urgent carotid and CT imaging accomplished while patients are in the emergency department followed by immediate antiplatelet initiation if deemed safe.\textsuperscript{51} Some patients are still admitted for further management but many are discharged home from the emergency department with outpatient TIA clinic follow-up within ‘a few weeks’ of initial presentation.

Researchers compared this model with routine inpatient admission of all potential TIA patients and found that stroke recurrence within 90 days non-significantly dropped from 4.7% (7/150) to 1.5% (7/468); adjusted odds ratio (OR) 0.46; 95% CI, 0.12-1.68; \( P = 0.24 \).\textsuperscript{51} While a direct cost analysis was not included in the report it is reasonable to assume that this system might reduce hospital related treatment cost due to the reduction of hospital admissions without compromising patient outcomes.

**Model 3:**

The Paris based ‘SOS-TIA’ model (where ‘SOS’ refers to the international Morse code distress signal) offers 24/7 telephone advice by a nurse with senior vascular neurologist back-up, specialist TIA clinic review, and a complete diagnostic work-up all within just six hours of the initial event. This resource intensive model bypassed some emergency department assessments and achieved a 90-day stroke rate of 1.2% (95% CI 0.72-2.12) compared with a predicted risk of 5.96%.\textsuperscript{36}

Both models three and four reduced hospital admissions. However, 24 hour, seven day a week availability of stroke specialist input and diagnostic work-up is still required and while emergency department costs are likely reduced in the SOS-TIA model it could be argued that hyper-acute vascular neurology review is potentially more costly than hyper-acute generalist emergency department assessments. Furthermore, this model may be only applicable to very large metropolitan populations served by major tertiary
centres. Conversely, limiting hyper-acute assessments to general emergency doctors with specialist telephone advice, as in the M3T model, risks a high rate of misdiagnosis.\textsuperscript{52} Neither system places a significant emphasis on reducing hyper-acute assessments for TIA mimickers. In SOS-TIA some mimics might be vetted through the nurse telephone triage advice. However, 384 out of 1085 patients (35\%) accepted for hyper-acute specialist clinic assessment still ended up with non-TIA diagnoses.

In an attempt to reduce requirements for hyper-acute vascular neurology input the subsequent three models employ a two-tiered risk stratification system that referring clinicians may use without requiring immediate stroke specialist input. In these systems only the ‘most at risk’ TIA patients undergo inpatient or hyper-acute stroke specialist assessments and others are referred to ‘less urgent’ outpatient specialist clinics.\textsuperscript{35,53}

**Model 4:**

The first such application was reported by the Oxford Group in 2007.\textsuperscript{30} Rothwell and colleagues proposed a two tier system in which general practitioners refer suspected TIA or stroke patients to a routine outpatient TIA/minor stroke clinic unless they feel that the patient ‘requires immediate hospital admission’. This approach reduces the need for emergency department and hyper-acute vascular neurology clinic presentations and thereby offers a further opportunity for cost savings. This system alone (EXPRESS study phase 1) was associated with a relatively high 90-day stroke risk of 32/310 (10.3\%). However, subsequent refinement (EXPRESS study phase 2) changed the outpatient clinic to a ‘same day open access clinic’ avoiding the need for patient appointment booking and related delays. This rapid access clinic operated weekdays during regular office hours. In addition, stroke specialists initiated best medical therapy immediately rather than writing back to patients’ general practitioners with recommendations for them to initiate therapy later. These phase 2 interventions were associated with a significant improvement in 90-day stroke risk which dropped to 6/281 (2.1\%), adjusted hazard ratio (HR) 0.20, 95\% CI 0.08-0.49; \textit{p}=0.0001.\textsuperscript{30} The open access system reduced the median time from general practitioner to specialist review from 3 days (inter-quartile range (IQR) 2 to 5 days) to 1 day (IQR 0 - 3); \textit{p}<0.0001. Median time to initiation of relevant non-antiplatelet medications dropped from 20 days (IQR 8 - 53) to 1 day (IQR 0 - 3); \textit{p}<0.001. Point estimates and confidence intervals were not reported for these outcomes. A weakness of this study is that criteria for assigning in- versus out-patient assessments were not clearly described in the paper.
Model 5:

Olivot and colleagues offered a more specific description of their triage strategy. Their ‘Stanford’ model used a validated stroke risk assessment score, the ‘ABCD2’ score, to triage patients for inpatient admissions (ABCD2 score of >3) or outpatient (≤3) assessments combined with early head and intra- and extra-cranial vessel imaging.

Table 1: ABCD2 Score

<table>
<thead>
<tr>
<th>A = Age:</th>
<th>60 years</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>B = BP:</td>
<td>&gt; 140/90mm Hg</td>
<td>1</td>
</tr>
<tr>
<td>C = Clinical features:</td>
<td>unilateral weakness or speech impairment w/o weakness</td>
<td>2</td>
</tr>
<tr>
<td>D = Duration of symptoms:</td>
<td>10-59 minutes</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>≥ 60 minutes or</td>
<td>2</td>
</tr>
<tr>
<td>D = Diabetes:</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Olivot’s observational cohort study compared observed stroke rate with predicted stroke rate based on ABCD2 score (table2). The observed 90-day stroke rate was 0.9% (0.3%-3.2%), which was significantly less than expected based on ABCD2 scores (P=0.001). Point estimates were not provided. The use of a validated scoring system with clear triage parameters is a strength of this study and model. However, in order to access this triage system all potential patients (including the 20-50% TIA mimics) still had to present to the emergency department where triaging took place. Of these 49% (108/224) ended up with a specialist non-TIA diagnosis, but still underwent vascular imaging immediately. Therefore, this system still heavily relies on availability of acute secondary services including rapid access to diagnostics and potentially inefficient use of health care resources.
Table 2: Risk stratification by ABCD2 score

<table>
<thead>
<tr>
<th>ABCD2 score:</th>
<th>0 – 3</th>
<th>4 – 5</th>
<th>6 – 7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low Risk</td>
<td>High Risk</td>
<td></td>
</tr>
<tr>
<td>Proportion of all TIAs</td>
<td>34%</td>
<td>45%</td>
<td>21%</td>
</tr>
<tr>
<td>Stroke risk (%) at:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 days</td>
<td>1.0</td>
<td>4.1</td>
<td>8.1</td>
</tr>
<tr>
<td>7 days</td>
<td>1.2</td>
<td>5.9</td>
<td>11.7</td>
</tr>
<tr>
<td>90 days</td>
<td>3.1</td>
<td>9.8</td>
<td>17.8</td>
</tr>
</tbody>
</table>

Both the Oxford and the Stanford models employ a two-tiered triage model to reduce hyper-acute specialist assessments and improve health care efficiency. However, in both models most patients still underwent urgent specialist assessment within 1-2 days of initial presentation. In the ‘Stanford’ model all patients still underwent emergency department visits and imaging. Neither study reported data on presumed cost savings.

**Model 6:**

Wasserman et al. tested a two tier system allowing longer delays until specialist outpatient assessments in two Ottawa hospitals. They grouped Patients into ‘low’, ‘intermediate’, and ‘high-risk’ relying predominantly on the ABCD2 score with outpatient specialist clinic review occurring between 0-7 days for high risk and more than 14 days for low risk patients. Similar to the M3T and Stanford models all patients were seen in the emergency department and underwent immediate head CT imaging and ECG although they generally did not receive immediate specialist input into their care. In addition, all potential TIA patients also underwent urgent outpatient echocardiograms, 24-hour Holter monitoring, and carotid Doppler examinations. The 90-day stroke rate in this case series was 31/982 (3.2%) which compared favourably to a predicted risk of 9.1% (95%CI 2.1-4.3) based on the ABCD2 score (p<0.0001). This provides some evidence that longer delays in outpatient specialist assessments may be

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*24-hour Holter monitoring involves electrocardiogram electrodes placed on the patient’s chest for a 24-hour recording. This increases the chance of capturing an irregular heart rhythm compared with a routine electrocardiogram, which captures only a few seconds.

* Carotid Doppler involves the use of an ultrasound probe to measure the arterial blood flow direction and velocity in the carotid arteries and sometimes the vertebral arteries to detect any blockages or stenosis.
feasible. However, reliance on secondary services for initial assessments and rapid undifferentiated diagnostic work-up of all potential TIA patients regardless of triage score remains an issue. Unfortunately, the authors did not present a figure for the accuracy of their emergency physician TIA diagnoses.

It has to be recognised that these different models evolved in a variety of health systems. Some of these systems (e.g. United Kingdom) rely more heavily on primary care referral to secondary services than others (e.g. United States of America) and this may have influenced the resultant service models. Nonetheless it can be concluded that acceptable 90-day stroke rates following TIA are achievable without universally admitting all potential TIA patients to hospital. Risk stratification performed at the time of first health care contact, be it by the general practitioner, the emergency room physician, or a different front line clinician, may help to prioritise patients in greatest need of admission/urgent comprehensive investigations and/or immediate specialist review. However, reported international models (table 3) that have explored alternative TIA management strategies continue to rely on either rapid specialist input and/or rapid emergency department assessments coupled with comprehensive diagnostic work-up of all potential TIA patients, including up to 50% TIA mimickers.
<table>
<thead>
<tr>
<th>Model</th>
<th>Trial Design</th>
<th>Patient inclusion criteria†</th>
<th>Patient inclusion</th>
<th>90 day Stroke risk (active) n/n (%)</th>
<th>90 day Stroke risk (control) n/n (%)</th>
<th>Adjusted odds or hazard ratios (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 2</td>
<td>Sequential cohort</td>
<td>All patients evaluated in emergency department with possible TIA</td>
<td>Per protocol</td>
<td>7/468 (1.5%)</td>
<td>7/150 (4.7%)</td>
<td>0.46 (0.12-1.68)</td>
<td>0.24</td>
</tr>
<tr>
<td>M3T (2012)</td>
<td>Specialist confirmed or possible TIA/stroke</td>
<td></td>
<td></td>
<td>7/296 (2.4%)</td>
<td>7/114 (6.1%)</td>
<td>0.43 (0.12-1.59)</td>
<td>0.21</td>
</tr>
<tr>
<td>Model 3</td>
<td>Case Series</td>
<td>All patients evaluated in by vascular neurologist following RN telephone screen</td>
<td>Per protocol</td>
<td>13/1052 (1.2%)</td>
<td>(5.96%)**</td>
<td>-</td>
<td>n/a</td>
</tr>
<tr>
<td>SOS-TIA (2007)</td>
<td>Specialist confirmed or possible TIA/stroke</td>
<td></td>
<td></td>
<td>13/824 (1.6%)</td>
<td>-</td>
<td>-</td>
<td>n/a</td>
</tr>
<tr>
<td>Model 4</td>
<td>Sequential Cohort</td>
<td>Specialist confirmed or possible TIA/Stroke referred to outpatient TIA clinic</td>
<td>Per protocol</td>
<td>6/281 (2.1%)</td>
<td>32/310 (10.3%)</td>
<td>0.20 (0.08-0.49)†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EXPRESS (2007)</td>
<td>Including inpatient referrals to aid comparison to other studies</td>
<td></td>
<td></td>
<td>27/644 (4.2%)</td>
<td>63/634 (9.9%)</td>
<td>-</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 5</td>
<td>Case Series</td>
<td>All patients evaluated in emergency department with possible TIA</td>
<td>Per protocol</td>
<td>2/223 (0.9%)</td>
<td>(7.1%)**</td>
<td>-</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stanford (2011)</td>
<td>Specialist confirmed or possible TIA/stroke</td>
<td></td>
<td></td>
<td>2/116 (1.7%)</td>
<td>(7.9%)</td>
<td>-</td>
<td>0.03</td>
</tr>
<tr>
<td>Model 6</td>
<td>Case Series</td>
<td>All patients evaluated in emergency department with possible TIA</td>
<td>Per protocol</td>
<td>31/982 (3.2%)</td>
<td>(9.1%)</td>
<td>-</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Model 1, inpatients based TIA care, is considered the ‘gold standard’ but current data of its efficacy if used in 100% of TIA patients are not available. †The denominator for calculating stroke rate differed between studies. Notably EXPRESS excluded all TIA mimickers and inpatients, while all other researchers included these groups. Data are provided to assist with allowing comparisons. **These studies used published risk predictions for ABCD2 scores rather than their own controls.
1.1.6. Barriers to implementation

Rapid specialist and diagnostic access for all potential TIA patients may not be feasible in New Zealand and many other parts of the world because of the resource implications of providing 24 hour, seven days a week, or even working-hour rapid access specialist TIA clinics.\textsuperscript{54} Rapid diagnostic access is similarly difficult.\textsuperscript{55} This is especially the case in non-urban healthcare settings, where patient volumes often cannot support a sufficient number of specialised clinicians to staff these services.\textsuperscript{51} In addition to economic constraints, rural health systems in particular also struggle with other access barriers. Recruiting physicians for non-urban centres is a long standing challenge worldwide as jobs in these locations are viewed as less desirable by clinicians.\textsuperscript{56} In addition, the geographic distances patients have to travel to reach even small rural hospitals often impede timely access or even preclude it entirely.\textsuperscript{57} The associated transport costs and time away from work are frequently not acceptable to patients, particularly those from disadvantaged groups, both in rural and urban settings.\textsuperscript{58,59} Furthermore, cultural barriers can significantly impact on patients’ desire or ability to effectively access relevant health services, which is a well described problem faced by people in both New Zealand and Australia as well as other countries with culturally diverse populations.\textsuperscript{60-62}

1.1.7. New Zealand TIA guidelines

The 2008 New Zealand TIA Guidelines\textsuperscript{27} have tried to address these resource limitations by recommending a two tier triage system based on the experience of the Oxford EXPRESS study, the ABCD2 risk prediction score, and several other high risk indicators.\textsuperscript{30,35} Other international guidelines have adopted a similar approach.\textsuperscript{26} The guidelines initially list typical TIA symptoms (table 4). If none of these are present further TIA management is discouraged.
Table 4: New Zealand TIA Guideline table defining TIA symptoms

<table>
<thead>
<tr>
<th>Typical symptoms of TIA</th>
<th>Not typical of TIA (If occur in isolation, without typical symptoms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral weakness - face, arm, leg</td>
<td>Confusion (note - exclude dysphasia)</td>
</tr>
<tr>
<td>Unilateral altered sensation</td>
<td>Impaired consciousness or syncope</td>
</tr>
<tr>
<td>Dysphasia</td>
<td>Dizziness or light headedness</td>
</tr>
<tr>
<td>Monocular Blindness</td>
<td>Generalised weakness or sensory symptoms</td>
</tr>
<tr>
<td>Hemianopia</td>
<td>Bilateral blurred vision or scintillating scotoma</td>
</tr>
<tr>
<td></td>
<td>Incontinence – bladder or bowel</td>
</tr>
<tr>
<td></td>
<td>Amnesia</td>
</tr>
</tbody>
</table>

If typical TIA features are present patients are grouped into a ‘high risk’ category if they also have an ABCD2 score (table 1) of >3, suffer from atrial fibrillation, are on anticoagulation medication, have experienced two or more events over the past 7 days, and/or experienced ongoing symptoms or symptom duration for more than 24 hours. ‘High risk’ patients are to be referred for specialist assessment within 24 hours usually via inpatient admission, but if rapid specialist outpatient assessment including imaging is achievable this represents an alternative. Patients with typical TIA symptoms, but a ‘low risk’ profile, can be referred to an outpatient TIA clinic for assessment within 7 days or in some instances can be managed by their general practitioner in the community if the general practitioner can access the relevant diagnostics and achieve completed work-up within the 7 day period.27

Although the guideline is based on expert opinion in conjunction with available evidence, it is unknown if this two-tier system can in fact be implemented in New Zealand, whether it is cost-effective, and whether the intended treatment benefits will accrue. This is in part because while the ABCD2 score has been validated to accurately predict recurrent stroke risk, the assertion that deferring assessment for low risk patients for up to 7 days has no robust evidence base. The studies supporting a two-tier approach in fact either involved immediate secondary level emergency department and brain imaging assessment regardless of triage category or if tiered triage occurred at the...
general practitioner level even low risk patients were seen within a couple of days of primary care assessment. $^{30,49,50}$

Most TIA patients initially present to their general practitioner$^{63}$ and the success of an up to 7 day delay for specialist review following initial general practitioner assessment for ‘low risk’ patients heavily depends on appropriate early general practice level care, which may be beyond the scope of many general practitioners. Under the New Zealand TIA Guidelines, general practitioners are now asked to diagnose, triage, and provide initial, and in some instances comprehensive management without specialist support. The scope of clinical conditions managed in general practice is very broad and individual general practitioners will have patients presenting to them with TIA/stroke like symptoms only 4-5 times per year, making it challenging for them to remain skilled and up to date.$^{52,64,65}$ General practice TIA diagnostic accuracy is accordingly very low at only 50-80%$^{27}$ and the expectation that all general practitioners are aware of and consistently use the latest TIA guidelines may be unreasonable for clinicians who encounter a particular condition only a few times a year.

In summary, the current evidence indicates that (a) stroke risk is highest early after TIA, (b) early implementation of secondary prevention through inpatient specialist or rapid access outpatient specialist TIA clinics can reduce the risk of stroke after TIA, (c) multiple barriers exist to achieving rapid specialist and imaging access, (d) to address this problem current New Zealand Guidelines propose a two-tier triage system that relies heavily on general practitioners to manage early TIA, which may be risky given their limited TIA expertise.

### 1.1.8. The idea of a TIA/stroke electronic decision support tool

In 2008 I learned about the BPAC$^{\text{INC}}$ cardiovascular risk assessment tool from Dr Jonathon Morton, a Palmerston North general practitioner, at a MidCentral Health Tipping Point Summit centred on primary/secondary integration. BPAC stands for Best Practice Advocacy Centre and is a Dunedin based not-for profit organisation that promotes best practice care in general practice. As part of this effort the organisation has developed electronic tools to assist implementation of primary care guidelines, including a cardiovascular risk assessment tool. Jonathon asked if I could imagine any application for electronic decision support in the field of neurology. The TIA
conundrum immediately sprang to my mind. I envisioned a tool that could aid general practitioners in making an accurate diagnosis of TIA or stroke, reduce inappropriate referrals of TIA mimics to my service, triage patients according to best practice guidelines to ensure high risk patients are seen promptly, and encourage general practitioners to initiate best medical therapy in patients who would otherwise have delayed specialist or no anticipated review to protect them from early stroke recurrence. I envisioned a tool that improved patient care and was inherently educational with built in resources for both general practitioners and patients to improve processes of care. This, it seemed, would address pressures on secondary care, support general practitioners with expert advice yet maintain or even enhance their autonomy, and ensure urgent treatments are not delayed. It appeared that this method could lead to even faster treatment than awaiting specialist review, even if specialist review was delayed by only a few hours.

1.2. Electronic decision support

1.2.1. Introduction

Electronic decision support tools have increasingly emerged throughout the health sector over the past 10-20 years. Several names describe the same concept and designations that appear in the literature include ‘computerised clinical decision support,’ ‘electronic clinical decision support,’ ‘clinical decision-support,’ ‘computerised decision support,’ ‘decision support,’ and ‘computer-based medical decision support.’ In this thesis the term ‘electronic decision support’ will be used. Electronic decision support systems, including the TIA/stroke electronic decision support tool presented in this thesis, are essentially an effort to facilitate knowledge translation of up to date scientific knowledge into improved patient management and outcomes.

1.2.2. Definition

No official definition of electronic decision support is available, but the excerpts below capture the flavour of the major characteristics:
Any electronic system designed to aid directly in clinical decision making, in which characteristics of individual patients are used to generate patient-specific assessments or recommendations that are then presented to clinicians for consideration.

Information systems intended to improve clinical decision-making where [electronic decision supports] match individual patient data to a computerized knowledge base that uses software algorithms to generate patient-specific recommendations that are delivered to healthcare practitioners.

Software applications that use patient data, a database of clinical knowledge and ‘conditional’ logic (e.g. ‘if-then’ and ‘do while’) to generate patient-specific recommendations related to care.

Stand alone electronic guidelines or flow charts are generally not considered under the category of electronic decision support because they do not incorporate individual patient data and as a rule provide general rather than patient specific guidance.

1.2.3. Characteristics of electronic decision support systems

Electronic decision support systems vary widely depending on (a) the task they are designed to support (e.g. diagnostics, prognostication, or therapeutics), (b) the approach to incorporating individual patient data (e.g. direct manual input by the health care provider versus automatic retrieval from integrated electronic health records, or both), (c) the type of knowledge base drawn upon (e.g. risk scores, clinical guidelines, expert opinions), (d) the inference mechanism used (e.g. hierarchical versus Bayesian logic models), (e) the types of outputs generated (e.g. treatment advice or warning alerts), and (f) the ways outputs are communicated to health providers (e.g. electronic pop up boxes, generated e-referrals, or printable individualised patient information leaflets).

Examples of classic electronic decision support systems include alerts, reminders, order sets, drug-dose calculations that automatically remind clinicians of specific actions, or care summary dashboards that provide performance feedback on quality indicators.

Another variation among electronic decision support systems is the setting and broader area of application. Systems used in primary care tend to focus on primary preventive care and chronic disease management while secondary care applications preferentially
support diagnostic test ordering and drug prescribing including therapeutic drug monitoring and dosing. Targeted health care providers differ as well and include doctors, nurses, pharmacists, and others.

1.2.4. Evidence of effectiveness of electronic decision support systems

Electronic decision support systems have been in use for two to three decades and several systematic reviews have assessed their overall efficacy, safety, and cost-effectiveness. The general conclusion is that many assessments of electronic decision support systems convincingly demonstrate improved processes of care, practitioner performance, or guideline adherence. Hard clinical endpoints such as patient morbidity and/or mortality are, however, scarcely reported and this has been repeatedly raised as a general criticism. For example, a 2012 systemic review by Bright et al reported that only 16/148 (11%) randomised controlled trials assessing electronic decision support published results on patient morbidity and mortality. Furthermore, the few available studies that do report on patient health outcomes do not provide a consistent message as regards overall efficacy of these tools. Bright’s meta-analysis found an overall benefit on averting adverse health outcomes in the setting of electronic decision support use (RR 0.88; 95%CI 0.80 to 0.96). However, a systematic review by Sahota and colleagues found that only 3/20 (15%) studies assessing the effect of electronic decision support in the acute medical care demonstrated improved patient outcomes. A third review found that only 7/52 (13%) studies reporting on health outcomes were able to demonstrate clear benefit.

Similarly sparse and inconclusive are results on cost-effectiveness. Bright found that out of their 148 reviewed studies only 22 (15%) reported treatment costs and 6/148 (4%) included a formal cost-efficacy analysis, which considers costs in relation to treatment benefit. Of the 22 offering results on cost savings, 13 (59%) demonstrated some benefit in this regard with electronic decision support use. Of the six studies reporting on cost-efficacy, results were equivocal with 3/6 (50%) indicating that electronic decision support was cost-effective and 3/6 (50%) indicating that it was not.

The overwhelming conclusion by all reviewers is that the comparison of different electronic decision support systems in a meta-analysis is challenging due to the
heterogeneity of the tool designs, intended purpose, clinical condition that is supported, and healthcare setting. Therefore their true value may currently be underestimated. They also agree that future studies should focus on patient outcomes and cost-effectiveness.

### 1.2.5. Uptake of electronic decision support systems

Despite their heterogeneity, one commonality that all electronic decision support systems share is the importance of end-user buy-in.\(^68,80,81\) Success in large part relates to end-user preferences and whether their needs are being met. Healthcare professionals have to perceive the tools as useful for their work before they use it\(^68,80\) and feel reassured that use of the tool does not impede their work flow or lengthen consultation times.\(^82\) Furthermore, developers have to accept the possibility of clinicians’ unwillingness to alter their workflow even if clinicians believe that a given tool could benefit patients.\(^83\)

The importance of end-user preferences was highlighted by Kawamoto and colleagues\(^73\) who examined specific predictors of successful outcomes of electronic decision support tools. They identified the following key features: (1) automatic provision of decision support as part of clinical workflow, (2) provision of recommendations rather than just assessments, (3) provision of decision support at the time and location of decision making, and (4) computer based decision support. All of these features relate to the electronic decision support/end-user interface. Among systems that incorporated all of these features 92% (30/32) were able to demonstrate significantly improved clinical practice. Other features that these authors identified as favourable included ‘provision of periodic feedback,’ ‘sharing recommendations with patients,’ and ‘requesting documented reasons for not following recommendations.’\(^73\)

Other researchers have highlighted additional challenges that may influence end-user buy-in. These include the perception that electronic decision support tools may potentially harm the doctor-patient relationship, obscure responsibilities, and threaten clinicians’ autonomy.\(^84\) The availability of relevant hardware, sufficient technical support, and adequate training all need to be considered before implementation.\(^85\)
Therefore, developers need to involve the end-users early in the process of developing and implementing electronic decision support. A collaborative and co-operative approach with appropriate goal setting and achieving early user acceptance are paramount for success. Systems endorsed by colleagues minimise perceived threats to professional autonomy and alleviate concerns about compromised doctor-patient interactions. To achieve user acceptance developers generally have to ensure that their systems integrate well into clinician workflow, are flexible, but reliable, not too prescriptive, and are viewed by end-users as a positive development with high potential utility. In addition, ongoing review and feedback leading to periodic modification needs to be considered when assessing required time investment into the decision support development project.

1.2.6. Safety of electronic decision support systems

In addition to efficacy, cost, and user-buy in, safety is an important consideration because electronic tools can make mistakes for a variety of reasons and clinicians need to audit any recommendation delivered by an electronic decision support system. For example automation bias has been raised as a serious safety concern. Automation bias is defined as ‘the tendency to over-rely on automation.’ Educating clinicians about this is therefore important. Another problem relates to users overly relying on the software, but then inadvertently ignoring rendered advice either because it was not displayed prominently or advice was formulated in a non-user friendly manner (e.g. too much text). It has therefore been emphasised that research on electronic decision support tools should include reports on adverse events, including incidences related to inappropriate use.

1.3. Electronic decision support to guide stroke management

1.3.1. Introduction

A literature review in February 2014 using the PubMed search engine and the search terms ‘electronic,’ ‘computer,’ and/or ‘decision support,’ plus ‘Stroke’ and/or ‘Transient ischemic attack’ revealed several prior applications of electronic decision support in the area of stroke care. The two most relevant studies are discussed in detail below.
1.3.2. Prior applications of electronic decision support in TIA/stroke management

In 2003 Weir et al. published a cluster randomised controlled trial of a computer-based decision support system that provided patient-specific estimates of the expected ischemic and haemorrhagic vascular event rate depending on the anti-thrombotic therapy chosen. This was a hospital-based tool to assist physicians with the selection of the most appropriate anti-thrombotic medication to use in ischaemic stroke and TIA patients. They randomised 16 hospitals (9 intervention and 7 control) and analysed 637 patients (200 intervention and 437 control). The relative risk of a subsequent adverse outcome, defined as recurrent ischaemic or haemorrhagic stroke, was reduced by 2.7% (95% CI 0.3-5.7) in the intervention group. The odds ratio for implementing optimal therapy was favourable at 1.32 (0.83-1.80), but neither result reached statistical significance at the 0.05 level. User feedback from representative clinicians at the intervention hospitals indicated that 5/9 (55%) of clinicians believed the electronic decision support had influenced their prescribing. Several methodological issues were encountered: most notably that at the time that the study was conducted no definite consensus on optimal preventive therapy was in place and a wide range of prescribing practices were noticed in both control and intervention arms. Nonetheless, the authors concluded that the use of an electronic decision support system in stroke prevention was feasible although did not substantially influence prescribing practice after ischaemic stroke. 88 This study demonstrates that end-users have to be receptive to the advice offered. If the target audience is sufficiently expert or believes itself to be sufficiently expert they may have a low threshold to override decision support advice. This reduces the impact such a tool will have on patient management and outcomes.

In 2007 Brown et al published results of their cohort pilot study that assessed the implementation of an emergency department-based TIA clinical pathway incorporating what they refer to as ‘computer-based clinical support.’ Their main objective was to assess whether such a pathway is feasible and could assist with reducing admissions to hospital by offering rapid investigations in the emergency department, initiating antiplatelet therapy, and improving overall guideline adherence. They analysed 75 TIA patients and found that in 85.3% of cases physicians adhered to the guideline, 90.7% of patients were started on anti-thrombotics, and 93.3% underwent relevant imaging. The rate of event recurrence at 90 days was 7/75 (9.3%) for TIA, 1/75 (1.3%) for stroke, and
11/75 (14.6%) for vascular event or death. Hospitalizations occurred in 40/75 TIA patients (53%). They did not have a comparison group, but concluded that their electronic decision support system was feasible and justified a larger study. This study successfully demonstrates that flow-charts and electronic check-list reminders could be useful in TIA management. Such simple tools are used widely and the utility of check lists is accepted even beyond health care. Missing from Brown’s system is any actual computer generated advice based on individual patient characteristics. This omission limits the conclusions that can be drawn from this study about the utility of comprehensive electronic decision support in the setting of TIA management.

1.3.3. Prior applications of electronic decision support in Stroke diagnosis

One of the key aspects of clinical decision making that neither of these researchers considered is the significant challenge of rendering an accurate diagnosis before instituting a management plan. It is reasonable to expect stroke physicians as investigated by Weir to achieve appropriate accuracy, however, this is much less certain in the emergency department setting without stroke team support. The very low 90-day stroke rate reported by Brown and colleagues may in part be related to a potentially quite significant number of TIA mimics in their data set.

The only identified reference in the literature addressing computer-based stroke diagnosis comes from work by Klaus Spitzer and Louis Caplan published in 1989. They explored the feasibility of computer assisted stroke syndromic allocation (MICROSTROKE) and localisation (TOPOSCOUT). These systems demonstrated accuracy in stroke syndrome allocation in 181/250 (72.5%) cases, which was similar to expert diagnosis. Experts, however, outperformed computers when it came to localisation. Computers did well with correctly classifying hemispheric symptom distributions 215/250 (86%), but struggled with brainstem distribution 140/250 (56%). Experts achieved accurate localisation on clinical grounds in 80-86% of cases regardless of brain distribution. These early attempts confirm that computerised algorithms are feasible in the field of stroke diagnosis and localisation although it appears that ongoing

5 Syndromic allocation here refers to thrombosis, embolus, lacune, intracerebral haemorrhage, and subarachnoid haemorrhage; localisation refers primarily to hemispheric versus brain stem, but also incorporates well described syndrome such as ‘top of the basilar’ and ‘Wallenberg’s syndrome.'
refinement was not pursued or at least not reported. The only subsequent publication on computerised stroke diagnosis is a 2012 paper by Nam et al that reports a hand-held tool using a simple algorithm to assign TOAST\textsuperscript{93} classifications called iTOAST. TOAST classifies stroke by aetiological sub-type ((1) large artery atherosclerosis, (2) cardioembolic, (3) small-vessel occlusion, (4) stroke of other determined aetiology, (5) stroke of undetermined aetiology). The iTOAST system relies on availability of diagnostic results and is useful for therapy implementation and registry data collection, but does not aid in the process of confirming the initial diagnosis of stroke or TIA and would thus not be of major utility in primary care.

1.3.4. Other applications of electronic decision support

Other relevant reported uses of electronic decision support systems in stroke management include a tool developed for inpatient inter-disciplinary teams aiming to improve clinical documentation,\textsuperscript{94} patient education tools,\textsuperscript{95} a tool to assist with the management of atrial fibrillation in stroke,\textsuperscript{96} and tools to assist hospital physicians with stroke thrombolysis decision making.\textsuperscript{97-99} One conference abstract from 2008 proposed a clinical decision support system for acute stroke aiding with differential diagnosis, an interactive stroke protocol map, and a patient specific overview of workflow status. This tool aimed to improve continuity of care and reaches a higher level of complexity than the simpler and more focused tools thus far discussed. However, no further publication since their 2008 description for planned alpha-testing is available, suggesting that further implementation has not yet occurred.\textsuperscript{100}

1.3.5. Summary of electronic decision support use in TIA and Stroke

Electronic decision support tools address different challenges across the stroke care continuum. They aim to improve specific aspects of TIA or stroke care and all target secondary hospital clinicians. To date no other research group has published on the efficacy of TIA/stroke electronic decision support tools addressing either the specific challenges faced by general practitioners and/or attempting to provide comprehensive diagnostic, triage, and treatment support.
Chapter 2: TIA/Stroke electronic decision support development, description, and pre-FASTEST trial evaluations

2.1. Introduction

The development of the TIA/Stroke electronic decision support tool started in July 2008 and was initially based on international best practice clinical guidelines.37,101 The first New Zealand TIA Guidelines became available in October 200827 and were subsequently incorporated into the tool. This chapter describes the electronic decision support tool used in the FASTEST trial (Chapter 3) including the underlying logic concepts, content, format, and special features. A summary of electronic decision support evaluations carried out as part of the implementation process is also provided. From this point onward ‘TIA/Stroke electronic decision support,’ ‘TIA/Stroke electronic decision support tool,’ ‘electronic decision support,’ or simply the ‘tool’ refer to the electronic decision support tool created by the candidate in collaboration with BPACINC and used in all subsequent evaluations including the FASTEST trial described in chapter 3.

2.2. Electronic decision support for TIA/minor stroke management: tool description

The overall goal of the electronic decision support tool that is the subject of this research is to improve best practice stroke and TIA care through improved general practitioner best practice guideline adherence. To this end the tool assists with three main clinical tasks: diagnosis, triage, and management.
2.2.1. Diagnosis and Triage

2.2.1.1. Diagnosis

An accurate diagnosis of TIA and stroke is important to advise subsequent management steps. Diagnostic features of the tool aim to improve the diagnostic accuracy of clinicians.

Diagnosing TIA can be challenging. By the time patients see a doctor their symptoms have usually resolved and clinicians therefore have to rely on patients’ historical accounts. There are six key features that are usually present and help to support a diagnosis of TIA. First, symptom onset is usually sudden. Second, patients usually report a focal neurologic symptom that can be attributed to compromise of one or multiple cerebrovascular territories. Examples of these symptoms include unilateral weakness, numbness, speech or language disturbance, or a focal vision defect. Third, the presence of one or more atypical features, such as syncope, is unusual. Fourth, patients will typically have one or more vascular risk factors. Examples of these risk factors include older age, tobacco use, and hypertension. Fifth, symptoms resolve within 24 hours. Sixth, patients usually will present with a high blood pressure (>140/90) if the TIA occurred very recently. If all of these features are present a diagnosis of TIA is highly likely. If symptoms last more than 24 hours a stroke is the more appropriate diagnosis.27,102

For a diagnosis of TIA to be considered likely the electronic decision support tool requires at least one typical TIA symptom. If both typical and an atypical symptoms co-exist then they are weighed against each other. For example, unilateral weakness will always elicit a strong concern for a diagnosis of TIA even if there are multiple atypical features. However, upper limb numbness if it occurs concurrently with syncope, a highly atypical feature, would indicate that while a TIA is still possible other diagnoses should be considered as well (see figure 1 for a simplified decision algorithm flow chart).

2.2.1.2. Triage

The electronic decision support tool also offers advice on the appropriate triage destination for a patient to undergo further management after general practice
consultation. This recommendation is based on the diagnosis and incorporates the New Zealand TIA Guideline risk stratification system of dividing patients into ‘high’ and ‘low’ risk categories as described in Section 1.1.7 in Chapter 1.

Patient triage depends primarily on the predicted risk of early stroke, which in turn depends on the likelihood that a TIA has in fact occurred. In addition to diagnostic certainty, time features inform risk. If symptoms occurred more than a week ago the high risk period has already passed making urgent assessment less important. If multiple events occurred over the past week, even if they were atypical, the concern for a further event increases. Early recurrence risk, however, is not the only aspect that advises triage recommendations. Some patients require urgent assessments for other reasons. For example, if a patient is taking anticoagulant medications they will require an urgent head CT scan to exclude bleeding before these medications should be continued. A delay in imaging means interruption of effective therapy, whether for stroke prevention or some other condition, and may expose patients to unacceptable risk. Another scenario that generally requires immediate hospital referral is the lack of complete symptom resolution. If symptom onset was within three hours of initial consultation with a doctor, the patient may be a thrombolysis candidate. If this scenario arises the tool instructs general practitioners to abort use of the tool immediately and call an ambulance for hyper-acute hospital transfer. Regardless of time of onset, all patients with ongoing symptoms should undergo a rehabilitation assessment, which is challenging to organise in a timely fashion as an outpatient and therefore the tool places these patients into the ‘high risk’ category prompting hospital transfer.

Because of the considerable overlap between the diagnostic and triage decision algorithms decision criteria are applied concurrently rather than sequentially (see figure 1).

Risk category assignment directly translates into a preferred referral destination. ‘High risk’ triggers the recommendation to refer to hospital immediately. ‘Low risk’ recommends outpatient TIA clinic referral or community management if this is achievable within seven days. In situations where the diagnosis is uncertain the tool provides a variety of management options including the suggestion to contact a specialist for further advice. If a general practitioner does not agree with a certain
recommendation he/she can choose to override the recommendation although they have to provide a reason if choosing to manage a ‘high risk’ patient using a ‘low risk’ management pathway. If there is diagnostic uncertainty due to one or more atypical features the community work-up option does not appear on the triage screen to ensure that these patients receive specialist input before being subjected to long term medication therapy or other potentially harmful interventions.

If general practitioner users pursue a referral to another health care provider the tool automatically generates a printable referral form that includes relevant information and is addressed to the closest or preferred facility. If an e-referral system is available then one of these referrals can also be lodged electronically. General practitioners have to approve the forms and can manually edit all entries.
Figure 1: Summary of the TIA diagnostic and triage algorithm

Any Typical TIA symptoms?

YES

High Risk: ABCD2>3, atrial fibrillation, on anticoagulation, or one or more events over past 7 days

No Atypical Features

TIA High Risk with community work-up override option

Atypical Features: Onset: Not sudden
Symptoms of:
Visual scotoma
Unilateral visual obscuration
Seizure
Syncope/Light-headedness/Pre-syncope
Acute memory Loss
Severe Headache
Bilaterally blurred vision
Agitation/Confusion/Inappropriate Behaviour/Apathy
Isolated vertigo/loss of balance/or ataxia
Somnolence
Other

TIA Low Risk without community work-up option and list atypical symptoms

Without unilateral weakness

“Some symptoms not consistent with TIA” list Atypical Features
TIA work-up option but no community work-up option

No Atypical Features

Low Risk: ABCD2<4 or event >7 days ago

TIA Low Risk with community work-up option

With unilateral weakness

Typical Features: Unilateral weakness including facial droop
Unilateral numbness
Unilateral vision loss/Amurosis Fugax
Visual field loss/Hemianopia/Quadrantinopia
Binocular Diplopia (‘double vision’) Dysarthria (‘slurred speech’) Dysphagia
Dysphasia (‘problems finding words’/’problems understanding words’) Dyspraxia/’clumsy hand’ Anosognosia/ hemi-neglect

Any Atypical Features

TIA High Risk without community work-up override option list atypical features

“Non-straight forward neurological presentation”
2.2.2. TIA/stroke electronic decision support management recommendations

TIA Management has four components: investigations, medical therapy, surgical therapy, and counselling. The TIA/Stroke electronic decision support deals with each component in the following ways:

2.2.2.1. Investigation

If general practitioners refer patients to secondary care all further investigations become the responsibility of the secondary care team. If, however, general practitioners choose to manage a patient in the community they must arrange a head CT, ECG, laboratory tests, and in some cases carotid imaging within seven days of first presentation. Use of the tool provides general practitioners with access to all of these investigations if the tool’s diagnosis and triage advice support comprehensive community management. The tool also screens for appropriateness of carotid imaging by classifying symptoms attributable to posterior or anterior circulatory compromise. If patients presented exclusively with posterior circulatory symptoms general practitioners do not receive the option to request a carotid ultrasound. The tool automatically generates imaging and laboratory referrals that specify the preferred tests/modalities, incorporate relevant information for the testing centre, and as with the referral letters, default to the address of the closest or preferred facility.

In addition to diagnostic access the tool also provides guidance with test result interpretation.

2.2.2.2. Medical Therapy recommendations

Patients with a likely diagnosis of TIA require immediate initiation of antiplatelet therapy and the tool provides guidance on medication selection. If specialist assessment is delayed by several days the tool also recommends initiation of an anti-hypertensive and a statin and provides information on choosing a drug and possible contraindications to consider. A detailed discussion on anticoagulation offers guidance on risks and benefits of initiation and/or continuation of these medications. The tool offers pre-
populated prescriptions at usual dosages, which doctors can edit, print, and hand to patients.

2.2.3. Surgical Therapy recommendations

Following completion of carotid imaging general practitioners can access information about imaging interpretation and appropriate surgical management options depending on imaging findings. The tool stresses the urgency of a referral to a vascular surgeon, if appropriate, in accordance with guideline recommendations.

2.2.4. Behavioural Counselling

If specialist access is delayed the tool advises general practitioners to provide patients with counselling on smoking cessation, driving restrictions, and information about what to do should symptoms recur. If general practitioners elect to manage patients entirely in the community, management advice also prompts them to counsel on diet and exercise. The tool offers patient information leaflets, which doctors can print and hand to patients along with referrals and prescriptions.

2.2.3. Other features of the TIA/stroke electronic decision support

The electronic decision support tool incorporates features that enable learning opportunities for general practitioners using the tool, minimise impact on workflow and consultation duration, and reduce the risk of automation bias.

2.2.3.1. Educational Features

Educational features include readily accessible definitions of neurological symptoms, physical examination tips, help for interpreting diagnostic test results, and advice with medication choice. Information icons and blue hyperlinks indicate educational aids. Next to each main menu item an icon appears that provides a list of sub-menu items by hovering over the icon with a mouse cursor. After opening a sub-menu
additional icons appear next to each symptom with a similar hover function to describe a symptom and offer physical examination suggestions. For example if the user hovers over the icon next to ‘binocular diplopia’ the following messages is displayed: “i.e. ‘double vision’ that resolves if closing or covering either eye – a posterior circulation symptom.” Hovering over words in blue font activates popup boxes with additional information on items such as appropriate criteria for requesting further diagnostic tests, New Zealand Transport Agency Guidelines on driving after TIA, and help with interpreting test results. Underlined blue text acts as hyperlinks to printable forms such as referral forms, prescriptions, or patient information leaflets.

2.2.3.2. Reducing impact on work-flow

To minimise the effect on workflow and consultation duration data entry fields focus on only essential clinical information and incorporate drop down menus to allow for a single page data entry form. The tool requires few transitions between different screens, reducing between screen wait times, and integrates fully into general practitioners’ practice management system or electronic health record to auto-populate fields with information that is already on record, such as vascular risk factors. The tool allows for all data entry to be saved back into the practice management system to improve and automate record keeping. Automatically generated referrals, imaging requests, and prescriptions help to shorten the consultation duration.

2.2.3.3. Reducing automation bias

Automation bias refers to over-reliance by a health care provider on an electronic aid (section 1.2.6). If the tool is to be used, it is important for general practitioners to understand that it does not replace their clinical judgment - only seeks to enhance it. Each outcome screen offers at least two choices requiring doctors to participate in the decision making process. This ensures that doctors take ownership of the final decisions regarding patient care. This also helps to avoid undermining clinicians’ autonomy and ensures that doctors are fully engaged in the process, providing additional patient safety.
In addition, an alert box appears on the final screen reminding doctors that the tool does not replace their clinical judgment and that all final treatment decisions are their own.

2.2.3.4. Built-in incentives

In New Zealand generally only specialists may request publicly funded head CTs. This can create a problem when barriers to specialist access exist, causing a degree of frustration among general practitioners. As an incentive to using the electronic decision support tool general practitioners using the tool may access rapid diagnostic testing, including head CT scans and carotid ultrasound, within seven days of request without prior specialist approval. As a gate keeping function and to prevent oversubscription, general practitioners have to refer patients using the TIA/Stroke electronic decision support generated referral form, which is only possible if the tool supports the decision to obtain these investigations.

In the MidCentral district, the initial launching site for the tool (see Section 2.4), the District Health Board Funding and Planning Division has supported this special access. For roll out in other districts as part of the FASTEST trial (Chapter 3) the trial budget funded some of these investigations, but the bulk of the funding came also from the respective District Health Boards.

2.2.3.5. Ethnic considerations

New Zealand Māori and Pacific Islanders experience stroke on average 10 to 15 years earlier than people of European descent.\textsuperscript{105} Previously discussed risk stratification tools do not take into account this ethnic difference. In an effort to address this disparity the age cut off used in the ABCD2 score as part of the TIA/Stroke electronic decision support tool risk stratification process is set at 50 years of age for Māori and Pacific Islanders in contrast to the usual age cut off of 60 years of age.
2.2.4. Sample Screenshots

Figure 2: Single page data entry form with sub-menu for ‘Communication/speech problems’
If general practitioners elect to manage patients in the community without specialist review the blue ‘Management’ tab can be clicked, displaying more comprehensive management options.
Figure 5: Sample outcome page with ‘community Management’ option selected
Figure 6: High risk TIA patient triage page

Figure 7: Outcome page if the only selected symptom is ‘syncope.’
Figure 8: Sample outcome page in a patient with both unilateral weakness and syncope

Additional variations to outcome screens occur if patients have specific risk factors such as anticoagulant therapy which has immediate management implications, have other health conditions that may negate the appropriateness of an aggressive work-up, or are atypically young for a TIA or stroke presentation.

Figure 9: Example of special advice box added to triage page

If a diagnosis of ‘stroke’ is more likely than a TIA diagnosis then management advice is provided in accordance with the New Zealand Stroke Guideline,\textsuperscript{103} and an overriding recommendation advises immediate referral of the patient to hospital (figure 10).
Figure 10: Advice for a patient with persistent right sided weakness

If initial management will take place in a small community hospital or ambulance transport will be delayed the tool provides further stroke management guidance (figure 11)

Figure 11: Extended community stroke management while awaiting ambulance
2.3. Validation of the electronic decision support tool

2.3.1. Overview

Software testing prior to use in clinical practice used a number of different methods. A very large number, many hundreds, of hypothetical cases were entered into the tool to identify problems requiring resolution before clinical use. These cases were created by the candidate and Jason Hall in an effort to simulate as many different clinical scenarios as possible. The tool then underwent clinical evaluation that compared the electronic decision support tool’s diagnostic accuracy and management advice to clinicians. Clinician groups included stroke experts, general physicians, and general practitioners. The outcomes for this evaluation assessed expert concordance with one another, diagnosis and management appropriateness of generalists compared with experts, and electronic decision support tool diagnosis and management compared with all three clinician groups (Appendix I).

2.3.2. Method of the validation study

Thirty five clinicians participated in the validation studies. There were twelve physicians with expertise in stroke care comprised of neurologists and physicians or geriatricians with special training or expertise in stroke care, twelve general physicians without special interest in stroke, and eleven general practitioners.

All participants assessed seven hypothetical cases based on actual referrals to the MidCentral stroke/TIA service. All seven cases were also entered into the electronic decision support tool by the candidate and two volunteers with no medical background.

Clinicians had to make a diagnosis, recommend a triage destination, and design a management plan. ‘Correct diagnosis’ was based on real life patient final diagnoses or when this was not available, on majority expert opinion. Subsequent management plans were deemed appropriate if they followed New Zealand TIA Guidelines. 27
2.3.3. Results

2.3.3.1. Diagnostic Accuracy

All experts arrived at the same diagnosis in four out of the seven cases: Case 1 = ‘non-TIA/stroke,’ Case 2 = ‘TIA,’ Case 3 = ‘TIA,’ Case 7 = ‘non-TIA.’ In Case 4 10/12 (83%) experts diagnosed ‘stroke’ and 2/12 (17%) diagnosed ‘TIA.’ In Case 5 11/12 (92%) diagnosed ‘stroke’ and 1/12 (8%) ‘TIA,’ and in Case 6 9/12 (75%) diagnosed ‘non-TIA/stroke’ and 3/12 (25%) diagnosed ‘stroke.’ Expert majority opinions matched real life diagnoses where available. Localisation was possible in five cases. Experts unanimously localised cerebrovascular lesions to the same vascular territory (anterior versus posterior) in four of these cases. In Case 2 1/12 (8%) experts failed to provide a localisation. The remaining 11 experts agreed that symptoms localise to the posterior vascular system. Overall, 78/84 (93%) rendered expert opinions arrived at the same diagnoses and 59/60 (98%) the same localisation.

General practitioner diagnoses matched expert majority opinion in 59/77 (76%) of responses and general physician diagnoses matched expert opinion in 66/84 (79%). Expert concordant localisation was achieved in 5/55 (9%) general practitioner responses and 35/60 (58%) general physician responses. When the seven cases were entered appropriately into the electronic decision support tool the tool’s diagnoses and localisations matched expert opinion in 7/7 (100%) and 5/5 (100%) instances respectively.

2.3.3.2. Triage

Patient triage to in- versus outpatient assessments were guideline adherent in 74/84 (88%) of expert triage decisions. Only ten out of the eleven general practitioners provided triage advice. Of the triage decisions made by general practitioners 56/70 (80%) were guideline adherent. General physicians made guideline adherent triage decisions in 54/84 (64%) situations. The electronic decision support tool rendered guideline adherent triage advice in 7/7 (100%) of cases.
2.3.3. Management

Two of the seven cases were TIAs requiring rapid initiation of best medical therapy (antiplatelet(s), statin, and anti-hypertensive). Expert responses addressed all three medications in 22/24 (92%) rendered management plans. General practitioner and general physician responses included best medical therapy in 6/22 (27%) and 9/24 (37%) of management plans respectively. The electronic decision support tool suggested initiation of best medical therapy in 2/2 (100%) of cases.

Smoking cessation, life-style counselling, and driving advice were covered in only a minority of management plans regardless of clinician group. By contrast, the electronic decision support tool suggested these interventions in every case (figure 12).

Figure 12: Management consistency with NZ TIA Guidelines: general practitioners, general physicians, stroke experts, and electronic decision support software

![Figure 12](image)

*BMT = best medical therapy. The n for this was different than non-medical advice: general practitioner n=22, general physician and stroke expert n=24. ‘n’ refers to the maximum number of appropriate responses that could have been rendered by each clinician group.

2.3.4. Non-medic use of the tool

Two research participants who were not medically qualified entered the seven cases into the tool producing 14 diagnoses and management plans. In 1/14 (7%) instances of tool use the participant entered incorrect clinical data and as a result the tool made an
incorrect diagnosis. This situation resulted in the tool triaging the patient to acute inpatient hospital care rather than outpatient care. Other aspects of tool rendered advice were not different otherwise.

2.3.5. Interpretation

In this validation study stroke expert diagnosis and management were concordant between stroke experts and generally, although not universally, New Zealand guideline adherent. General practitioners and general physicians did not consistently match expert diagnoses and their management was less guideline adherent with frequent omission of early best medical management initiation. These results are similar to other research\textsuperscript{30,36} which suggests that generalists may not adequately implement the secondary preventive measures that are best practice care for patients with TIA and stroke. In this study both generalists and stroke specialists frequently omitted non-medical preventive strategies.

The performance of the TIA/Stroke electronic decision support tool achieved diagnostic accuracy comparable with experts and closely mimicked expert triage and medication management advice. The ‘check-list’ nature of the electronic tool is the likely explanation for its superior performance as regards the more comprehensive inclusion of non-medical management provision and highlights a potential strength of such tools in general.

The error made by one of the lay participants underscores the importance of accurate data entry, which may heavily depend on the medical experience of the user. The tool can be calibrated to lower the threshold for urgent referrals to reduce risk associated with data entry errors, however, the optimal use of the tool may still depend on careful clinician oversight of the suggested diagnosis, triage, and management.

In summary, this validation study indicated that the tool could mimic initial expert TIA and stroke care and would likely add value to routine care provided by general practitioners.
2.4. Feasibility of the electronic decision support tool

2.4.1. Introduction

Electronic decision support tool implementation initially occurred in a single New Zealand district, MidCentral, and in a staged approach. A feasibility study was the first step. The aim of the feasibility study was to identify potential problems related to the tool in the real-life setting, receive active end user feedback to advise further software updates, and to gauge training needs before district wide roll-out (Appendix II).

2.4.2. Method of the feasibility study

An eight week feasibility study was performed between 27/7/2009 and 25/9/2009 including eight general practices. A pre-study educational session provided education about TIA management principles and about how to use the electronic decision support tool. Participating clinicians received a ‘Frequently Asked Questions’ leaflet to provide further guidance. At the end of the eight week period relevant patient data were collected from general practice and hospital records and participating general practitioners provided feedback via face-to-face 30 minute interviews using a semi-structured interview schedule.

2.4.3. Results

During the study period eight general practitioners entered eleven patients into the electronic decision support tool. In nine of these patients the advice from the electronic decision support tool was followed by the treating general practitioners. This resulted in two emergency department referrals, three TIA clinic referrals, and community work-ups for four patients. In all nine cases the initial diagnosis made by the electronic decision support was later confirmed as appropriate by a stroke specialist and TIA management occurred in accordance with New Zealand TIA Guidelines. None of these patients experienced any adverse outcomes relating to electronic decision support use.

In two cases general practitioners did not use the electronic decision support tool appropriately and subsequent management was not in accordance with New Zealand TIA and stroke guidelines. In one instance the general practitioner started to use the
tool, but aborted use before reaching the ‘advice’ screen. The general practitioner
diagnosis of TIA was not confirmed by subsequent specialist assessment. Following
through with the electronic decision support tool use would have given advice that a
diagnosis of TIA was unlikely and led to a more accurate diagnostic pathway. The
second instance was of a patient whose details were appropriately entered into the
electronic decision support tool leading to advice that the diagnosis was stroke rather
than a TIA and that the patient should receive triage to acute hospital. Instead the
general practitioner managed the patient in the community. This potentially led to
delays in diagnostic testing and access to rehabilitation services.
In post-pilot interviews all participating general practitioners were satisfied with the
TIA/Stroke electronic decision support software and had no major concerns regarding
user friendliness, time required to enter data, or the overall advice given by the tool.
Several general practitioners offered valuable suggestions. One of these was a request
to allow general practitioners more override options if the advice given by the tool
appeared inappropriate to them. Another offered the suggestion to provide a ‘free text’
box to enter additional information included on the referral forms. Some general
practitioners were concerned that emergency department staff may decline referrals for
TIA if they felt patients did not need urgent care enough for acute hospital assessment.
However, most clinicians felt that an electronic decision support generated emergency
department referral would enhance the referral process as it lends extra credence to the
general practitioner's assessment.

2.4.4. Interpretation of the feasibility study

The feasibility study identified some areas for improvement of the electronic decision
support tool but no major issues. General practitioner feedback was positive and
suggested that the tool was useful and would improve clinical care. The tool was
updated to incorporate user feedback including the option to override management
advice as long as the general practitioner enters a reason for this decision. The pilot
study did not identify any areas of risk associated with TIA/Stroke electronic decision
support tool use that would have precluded wider implementation.
2.5. Post-Implementation Safety Audit

2.5.1. Introduction

The electronic decision support tool was launched for district wide use in the MidCentral district on 29 October 2009 to coincide with World Stroke Day. A retrospective patient record review was carried out in January 2011 to assess if there were adverse health events related to electronic decision support tool use (Appendix III).

2.5.2. Method of the post-implementation audit

The audit assessed major patient morbidity or mortality attributable to electronic decision support within three months of the use of the tool. All patients for whom the TIA/Stroke electronic decision support tool was used to guide management from its availability in July 2009 until October 2010 were included in the audit. Retrospective review of hospital records aimed to identify acute hospital admission following use of the electronic decision support tool as well as acute hospital admission for possible adverse health events linked to electronic decision support tool use.

2.5.3. Results of the post-implementation audit

A total of 79 patients were entered into the electronic decision support tool between August 2009 and October 2010 and 22/79 (28%) had an acute hospital admissions. Eleven admissions were related to a diagnosis of TIA or ischaemic stroke and eleven were due to other causes. There were no identified cases of intracranial or systemic haemorrhage requiring hospitalisation (table 5).
Table 5: Patients admitted following electronic decision support use

<table>
<thead>
<tr>
<th>Reason for Hospital Admission</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transient Ischaemic Attacks</td>
<td>10</td>
</tr>
<tr>
<td>Ischaemic Stroke</td>
<td>1</td>
</tr>
<tr>
<td>Elective Surgery</td>
<td>2</td>
</tr>
<tr>
<td>Loss of Consciousness secondary to Diltiazem*</td>
<td>1</td>
</tr>
<tr>
<td>Fast Atrial Fibrillation due to non compliance</td>
<td>1</td>
</tr>
<tr>
<td>Falls/social concerns**</td>
<td>2</td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>1</td>
</tr>
<tr>
<td>Confusional State with no trigger**</td>
<td>1</td>
</tr>
<tr>
<td>ST elevation Myocardial Infarction</td>
<td>1</td>
</tr>
<tr>
<td>Elective admission for investigation of Multiple Sclerosis</td>
<td>1</td>
</tr>
<tr>
<td>Transfer for rehab post Coronary artery bypass graft</td>
<td>1</td>
</tr>
<tr>
<td>Intracranial Haemorrhage</td>
<td>0</td>
</tr>
<tr>
<td>Systemic Haemorrhage</td>
<td>0</td>
</tr>
</tbody>
</table>

* Diltiazem was started prior to the use of the tool. ** No evidence in medical record that these admissions were related to medication side effects or on the basis of cerebrovascular disease.

Eight of the eleven (73%) admissions for TIA or stroke were admitted immediately from general practice prompted by electronic decision support advice based on the patients’ high risk profiles. Three additional patients (3/79 (3.8%)), originally assigned ‘low risk’ status by the tool and referred for less urgent assessment in the outpatient TIA clinic subsequently re-presented with a second potential TIA prompting immediate admission. No patient in this series developed permanent disability due to subsequent stroke or other adverse events relating to electronic decision support use and all 11 patients were triaged in accordance with New Zealand TIA guidelines. There were also no TIA or stroke admissions within three months of electronic decision support use in any patient in which the electronic decision support initially rejected TIA or stroke as a likely diagnosis.

For the eleven patients admitted to hospital for reasons other than TIA or stroke four patient admissions had a potential link to electronic decision support tool use: they either related to symptoms of potential cerebrovascular origin or possible medication side effects. Careful review of patient records did not find a link between the hospital admission and the use of the electronic decision support tool. Two deaths occurred in...
the audit population. In the first case the tool correctly identified a stroke and in accordance with the rendered advice the general practitioner promptly referred the patient to hospital for immediate specialist advice and hospital admissions. Despite best practice care the patient eventually died from the stroke during this hospitalisation. The second patient died of a myocardial infarction with ventricular fibrillation six months after tool use for a low-risk TIA. TIA and stroke management was entirely guideline adherent in both cases. There was no causative link to electronic decision support use.

2.5.4. Interpretation

The retrospective safety audit found no evidence of harm related to the triage, assessment or initial management as recommended by the TIA/Stroke electronic decision support tool.

2.6. Cohort study of electronic decision support tool use

2.6.1. Introduction

A cohort study assessed the effect of the electronic decision support tool on TIA management processes within the MidCentral district (Appendix IV).

2.6.2. Method of the cohort study

This cohort study included all patients referred to the MidCentral Health stroke services with a referral diagnosis of ‘TIA’ between January 1 and June 30 2009, before the electronic decision support tool was implemented and then again January 1 and June 30 2011, after electronic decision support tool implementation. All patients in the study were identified prospectively. Measurements of the process of care included: time from first point of healthcare contact to specialist review, time from first point of contact to relevant diagnostic testing, the proportion of patients who received best medical therapy within 24 hours of the first assessment by any health care provider, and diagnostic accuracy of the referring doctor. Time to event data were evaluated using survival analysis and the log rank statistic for differences between cohort study periods. Dichotomous variables and differences in proportions were evaluated using relative risks and associated Chi-square tests.
2.6.3. Results of the cohort study

The stroke service received 130 TIA referrals during the 2009 study period and 136 during the 2011 period. In 2009 63/130 (48.5%) of patients received a final specialist diagnosis of either TIA or stroke compared to 79/136 (58.1%) in 2011: Relative risk (RR) 1.21; 95% CI 0.95 to 1.54, \( P=0.12 \).

Based on Kaplan-Meyer survival curve estimates, in 2009 the median time to see a specialist was 10 days (IQR 2-13), which dropped to 3 days (IQR 1-11) in 2011: Hazard ratio (HR) 1.45; 95% CI 1.13-1.86; \( p=0.001 \).

In 2009 51/119 (43%) of patients achieved best medical therapy within 24 hours of first point of contact and in 2011 71/130 (57%): RR 1.33; 95% CI 1.02 to 1.7; \( p=0.04 \).

In 2009 51/129 (40%) and in 2011 77/126 (66%) of patients received behavioural counselling: RR 1.68; 95% CI 1.31-2.16; \( p<0.001 \).

The proportion of patients who had a CT head scan was 93/130 (71.5%) in 2009 and 117/136 (86.0%) in 2011: RR 1.64; 95% CI 1.12 to 2.41, \( p=0.012 \). The median time until a CT scan was performed was 19 days (IQR 2-42) in 2009 and 6 days (IQR 1-26) in 2011: HR 1.34; 95% CI 1.16-1.78; \( p=0.002 \).

In 2009 40/130 (30.8%) and in 2011 71/136 (52.2%) patients underwent carotid imaging: RR 1.53; 95% CI 1.21 to 1.92, \( p<0.001 \). The Kaplan Meyer estimated median time to carotid imaging reduced from 33 days (IQR 6 to 54) in 2009 to 7 days (IQR 2-21) in 2011: HR 1.52; 95% CI 1.02-2.26, \( p = 0.003 \). Table 6 and figure 13 summarise results.
Table 6: Binary outcomes before (2009) and after (2011) the introduction of a TIA/Stroke decision support tool.

<table>
<thead>
<tr>
<th>Variable</th>
<th>2009</th>
<th>2011</th>
<th>Relative risk (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed TIA or stroke</td>
<td>63/130 (48.5%)</td>
<td>79/136 (58.1%)</td>
<td>1.21 (0.95-1.54)</td>
<td>0.12</td>
</tr>
<tr>
<td>Best medical therapy within 24 hours</td>
<td>51/119 (43)†</td>
<td>71/130 (57)§</td>
<td>1.33 (1.02 - 1.71)</td>
<td>0.04</td>
</tr>
<tr>
<td>Behavioural counselling</td>
<td>51/129 (40)*</td>
<td>77/116 (66)‡</td>
<td>1.68 (1.31 - 2.16)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CT scan</td>
<td>93 (72)</td>
<td>117 (86)</td>
<td>1.64 (1.11 – 2.41)</td>
<td>0.012</td>
</tr>
<tr>
<td>Carotid imaging</td>
<td>40 (31)</td>
<td>71 (52)</td>
<td>1.53 (1.21 – 1.92)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data missing for †11, ‡6, *1, and §20 patients.

Figure 13: Time to event Kaplan-Meyer Graph

FPC=First point of contact with a health care professional
2.6.4. Interpretation of the cohort study

This cohort study assessing changes in TIA service provision following the MidCentral district wide implementation of the electronic decision support tool found marked improvements in the process of care that were not obviously related to patient characteristics. However, such a study cannot rule out an unrelated change over time in the way TIA and stroke were managed in the region that was independent of the electronic decision support tool use. Furthermore, while processes of care may have improved these data provide no information about actual patient outcomes or service cost. Chapter 3 describes the study designed to address these knowledge gaps.
Chapter 3: FASTEST Trial

3.1. Introduction

Sections 2.3 through 2.6 of chapter 2 report results that favour use of the electronic decision support tool to improve guideline adherence but do not give estimates of the effect of tool use on patient health outcomes and treatment costs.

The Efficacy and Safety of a TIA Electronic Support Tool (FASTEST) trial aimed to provide robust estimates of the efficacy, safety, and cost implications of TIA/Stroke electronic decision support assisted diagnosis and management of patients presenting in general practice with symptoms of TIA or minor stroke, compared to usual care.

The trial aimed to allow individual general practitioners and specialists to make evidence-based decisions about whether to use the tool. Nationally, District Health Boards and the Ministry of Health could also use the results to inform decision making about national implementation of the tool to reduce the burden of stroke in New Zealand.

3.2. Hypotheses

General practitioners’ use of the electronic decision support tool (described in section 2.2) for diagnosis and management of TIA and minor stroke improves New Zealand TIA Guideline 27 adherence, reduces risk of early recurrent stroke, cerebrovascular and vascular events, and death, favourably affects treatment costs, does not increase adverse events, and receives clinician support.

3.3. Methods

3.3.1. Trial design

The trial design was a multi-centre, parallel-group, single-blind, cluster randomised controlled trial in New Zealand. The clusters were general practices randomised one-to-one to intervention and control groups. Follow-up period was 90 days.
3.3.2. Participants

Eligibility criteria for general practices were: Use of electronic health records compatible with the decision support tool, no prior use of the tool, and access to an organised TIA pathway consistent with the New Zealand TIA Guideline. Guideline consistency requires that local secondary services promote and facilitate the admission to their local inpatient stroke service within 24 hours for specialist assessment for ‘high risk’ (see section 1.1.7) patients and facilitates ‘low risk’ patients to be seen in a specialist TIA clinic within 7 days of referral. The study requirements were not that patients were always seen within these time frames but that there was a commitment to aim to achieve these targets. In addition practices had to be willing to be randomised and at least one clinician from each participating practice had to attend a training session at the start of the trial. Secondary referral centres for participating practices whose general practitioners agreed to participate in the study had to also agree to trial participation.

Eligible patients were those who presented to a participating general practice as their first point of health care contact after experiencing symptoms interpreted as a TIA or stroke by the general practitioner at the time of that initial consultation. Patients who first presented to a secondary level centre, a non-participating general practice, or who were never suspected of having suffered a TIA or stroke by the initial treating doctor were not eligible.

3.3.3. Intervention

The intervention was the TIA/Stroke electronic decision support tool described in chapter 2, section 2.2. All general practitioners in practices allocated to the intervention group could access the tool from the day after randomisation. General practitioners used instructions provided by the research team to create a shortcut icon on their computer desktop tool bar that, if clicked, linked them to the web-based tool.

General practitioners in practices allocated to the control group received the same instructions to create the same desktop icon shortcut. However when they clicked the icon it resulted in the appearance of a pop-up window indicating that they had successfully registered the patient into the trial. There was an option to de-register the patient in case the icon was clicked accidentally. After control group general
practitioners closed the pop-up window they returned to their usual patient care without seeing the electronic decision support tool. Control group doctors were not restricted in any way from accessing other information including the New Zealand TIA Guidelines available on the Stroke Foundation website.27

3.3.4. Outcomes

All outcomes were measured at the individual patient level except for user feedback.

3.3.4.1. Main Outcomes

The two main outcome measures were (1) the proportion of patients receiving primary care management in accordance with New Zealand TIA Guideline recommendations and (2) the proportion of patients experiencing a recurrent stroke within 90 days of initial presentation.

The tool’s stated goal is to improve best practice care through improved guideline adherence (Section 2.2) so that this is a natural primary outcome. Naturally, the ultimate aim of improving guideline adherence is to improve health status, which is in this case achieved through the reduction of subsequent stroke and other vascular events. Likewise, a reduction in stroke risk is a more relevant outcome to patients and health systems. However, this can only be achieved through the electronic decision support tool if improved guideline adherence actually results in stroke risk reduction. For the purposes of this research the efficacy of Guideline adherence is assumed, but not asserted. Therefore, cerebrovascular risk reduction represents a meaningful but indirect measure of the efficacy of the electronic decision support tool. If despite the use of the tool stroke rates are not reduced, it may simply mean that the guidelines are not effective in reducing stroke risk rather than indicate a deficiency in the tool. With these considerations in mind, both outcomes are considered relevant to the project and important for appropriate interpretation of the results.

3.3.4.1.1. Main Outcome 1: Guideline Adherence

To achieve ‘guideline adherence’ a given patient had to be triaged and managed appropriately in accordance with New Zealand TIA Guidelines. For triage to be appropriate, ‘high risk’ (as defined in section 1.1.7) TIA or stroke patients had to be
referred to hospital for immediate stroke team review, and ‘low risk’ patients had to be immediately started on anti-platelet medication and referred to an outpatient TIA clinic or comprehensively managed in the community within seven days of presentation. Comprehensive community investigation required a head CT and ECG for all patients.

The guidelines suggest carotid imaging is not required for all patients. Patients who are either not suitable for surgery because of co-morbidities or who have symptoms consistent with posterior circulation vascular disease may not require carotid imaging. In this study all patients were reviewed for symptoms indicative of isolated posterior circulation vascular compromise as part of the assessment for whether carotid imaging was needed. Assessment for suitability for surgery based on co-morbidities was not possible with the available data and was unable to be used to determine suitability for carotid imaging. Patients with significant carotid stenosis appropriate to the symptoms were to be referred for carotid endarterectomy within two weeks of presentation.

The guidelines state that community managed patients should also start or (as appropriate) continue antiplatelet medication(s) within 24 hours of first presentation unless contraindicated (section 1.1.7). The time frame for initiation of a statin, anti-hypertensive, or anticoagulant is less prescriptive in the guidelines and for this analysis ‘as soon as clinically indicated and deemed safe’ was defined as within seven days of presentation for all of these medications, unless contraindicated, with the caveat that patients started or continued on anticoagulation required CT imaging beforehand.

The guidelines state that diabetes management following TIA should be ‘in line with national guidelines for diabetes’ and because no further specific guidance is provided in the TIA guideline, diabetes management was not considered as a component of guideline adherence.

Although the guideline states that patient counselling should occur this was not measured as part of the main outcome as to guideline adherence but is addressed as a secondary outcome. Guideline adherence as defined for the trial is a complex composite outcome so addition of further components to the composite variable made interpretation difficult. Counselling is an important and frequently omitted management step, but for clarity was addressed as a separate outcome in this study.

Individual components of the ‘guideline adherence’ composite are also presented as part of the supplementary data analysis described in Sections 3.3.4.4. and 3.4.8.
3.3.4.2. **Main Outcome 2: Stroke within 90 days**

*Stroke* is defined in this study as a new presentation with sudden focal neurologic deterioration of ≥24 hour duration attributable to a vascular cause. All events were confirmed both by the treating physician and the candidate, a neurologist who was blinded to the study group of general practices and patients entered into the study.

3.3.4.2. **Secondary Outcome Measures**

3.3.4.2.1. **Cerebrovascular events (TIA or stroke) within 90 days**

This is a composite outcome that includes multiple possible outcome events. Stroke is defined in section 3.3.4.1.2. TIA was defined as a recurrence of a focal neurologic deficit lasting less than 24 hours, attributable to a vascular cause and confirmed by a stroke specialist.

3.3.4.2.2. **Any relevant vascular event or death within 90 days**

This composite measure included stroke, TIA, myocardial infarction, and death. Myocardial infarction was defined as a hospital presentation documenting a specialist confirmed acute myocardial infarction in the clinical records. ‘Angina’ or ‘chest pain’ without documented infarction was not included. Major bleeding was defined as acute bleeding that resulted in hospital presentation.

3.3.4.2.3. **Comprehensive non-medical treatment plan**

Implementation of a comprehensive non-medical treatments required documentation of smoking cessation advice or non-smoking status, diet and exercise advice, and driving advice.

3.3.4.2.4. **Treatment Costs**

Cost measurements were at the individual patient level and included both direct costs relating to the treatment of the index event and cost of any related events during the 90 day follow-up period. Treatment costs included: Costs of outpatient physician visits, ambulance transport, emergency department visits (unless admitted), hospital admission, general practice visits, relevant medications, relevant investigations (ECG,
CT head, MRI brain, prolonged cardiac monitoring, echocardiogram, and carotid imaging by modality), carotid endarterectomy, admissions related to outcome events if any occurred, and the licence fee for the electronic decision support tool. All costs exclude New Zealand’s Goods and Services tax of 15%, and were adjusted to January-June 2012 New Zealand dollars. Costs include any government health care subsidies and patients' co-payment contributions. Costs incurred by patients after the 90 day follow-up period were not included even if related to the index event.

Human Resource Costs were derived from derived from Pharmac’s Cost Resource Manual for Prescription for Pharmacoeconomic Analysis version 2.1. The most common standard costs incurred in this trial are listed in table 7.

Emergency department attendance fees vary depending on the level of service provided and different levels are available at different hospitals. These figures are not available for individual assessments from the medical records. The 2012 listed emergency department services costs ranged from $249 to $313. To achieve consistency this cost analysis used the standard cost of a Level 3/4 Emergency Department consultation which amounts to $249 per attendance. Level 3 and 4 costs are both $249 and all participating hospitals offer this service level.

Hospital admission costs were determined by first identifying the admission diagnosis-related group (DRG) codes assigned by the hospital’s coding team for every individual hospital admission. Coders assign DRG codes after review of clinical records and matching physician diagnoses and related complications using clinical coding criteria as outlined in the 6th edition of the International Statistical Classification of Diseases and Related Health Problems Tenth Revision, Australian Modifications or ICD-10-AM 6th edition medical coding manual and the Australian Refined Diagnosis-Related Groups v5.0 of AR-DRG v5.0. The 2011 Weighted Inlier Equivalent Separations with amendments for New Zealand then provides a comprehensive listing of standard costs for each DRG code.

Medication costs were calculated for each individual patient for all relevant medications prescribed, excluding diabetes medications. Daily costs per drug were taken from Pharmac listing and supplemented by listings in the Monthly Index of Medical Specialties or MIMS formulary. Costs were calculated for a 90 day supply to account for the duration of the follow-up period.
The decision support licensing cost per individual patient was calculated by dividing the estimated total practice annual licensing cost for the entire study population by the number of patients registered during the study adjusted to a 12 month period.\textsuperscript{113}

**Table 7: Service costs**

<table>
<thead>
<tr>
<th>Service</th>
<th>Unit Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Practice Consultation</td>
<td>$69.46</td>
</tr>
<tr>
<td>Specialist Consultation</td>
<td>$292.80</td>
</tr>
<tr>
<td>Emergency Department Consultation</td>
<td>$249.26</td>
</tr>
<tr>
<td>Ambulance Transportation</td>
<td>$478.78</td>
</tr>
<tr>
<td>Hospital Admission</td>
<td></td>
</tr>
<tr>
<td>Transient Ischaemic Attack without catastrophic or severe complication (B69A)</td>
<td>$2,676.09</td>
</tr>
<tr>
<td>Stroke with catastrophic complication (B70A)</td>
<td>$12,338.16</td>
</tr>
<tr>
<td>Stroke with severe complication (B70B)</td>
<td>$7,228.97</td>
</tr>
<tr>
<td>Stroke without catastrophic or severe complication (B70C)</td>
<td>$4,763.44</td>
</tr>
<tr>
<td>Stroke, died or transferred within 5 days (B70D)</td>
<td>$2,507.10</td>
</tr>
<tr>
<td>Extracranial Vascular Procedure without catastrophic complication (B04B)</td>
<td>$11,046.47</td>
</tr>
<tr>
<td>Head Computed Tomography (CT)</td>
<td>$516.57</td>
</tr>
<tr>
<td>Brain Magnetic Resonance (MR) Image</td>
<td>$1,143.11</td>
</tr>
<tr>
<td>Carotid Ultrasound</td>
<td>$334.09</td>
</tr>
<tr>
<td>CT Angiogram</td>
<td>$727.31</td>
</tr>
<tr>
<td>MR Angiogram</td>
<td>$987.22</td>
</tr>
<tr>
<td>Electrocardiogram (ECG)</td>
<td>$79.27</td>
</tr>
<tr>
<td>Holter Monitor</td>
<td>$227.90</td>
</tr>
<tr>
<td>Transthoracic Echocardiogram</td>
<td>$212.13</td>
</tr>
<tr>
<td>Electronic Decision Support Licensing Fee (per patient)</td>
<td>$55.00</td>
</tr>
</tbody>
</table>
3.3.4.2.5. **Adverse Events**

Adverse events were any documented health care presentations relating to treatment side effects. Cerebrovascular and vascular events are outcomes in the trial, but they could also represent adverse events resulting directly from use of the electronic decision support tool. All intervention group outcome events were screened for a possible link to electronic decision support use. Management in the control group (without the use of the tool) may also have adversely affected patient care resulting in cerebrovascular or vascular events, however, these were not included in ‘adverse events.’ This may create a mild imbalance in favour of the control group, but provides a conservative estimate of tool safety.

3.3.4.2.6. **General Practitioner Feedback**

Feedback was recruited from participating GPs through a mailed questionnaire at the end of the study. Responses were made as free text or on a five-point scale from 1=’not at all’ to 5=’all of the time.’ Intervention practices received a questionnaire asking five questions relating to the impact of the tool. Control practices answered just one question relating to the perceived utility of such a tool. In addition, intervention practices reported the time it took them to complete aspects of the tool and their preferred mode of training prior to using the tool.

3.3.4.2.7. **Specialist Feedback**

Stroke specialists from all four secondary referral centres involved in the study underwent a structured telephone interview after study completion. This interview consisted of eleven questions about their impression of the tool’s impact on practice referral patterns and overall patient care eliciting free text answers. Specific questions are listed in the results section.
3.3.4.3. Sub-Group Analysis

A pre-specified sub-group analysis excluded patients later determined by a stroke specialist to have a diagnosis other than TIA or stroke. The published data on stroke risk after TIA reports results for both undifferentiated as well as confirmed TIA patients.\textsuperscript{30,49}

3.3.4.4. Supplementary Data

Additional data summaries relevant to outcomes listed in sections 3.3.4.1 to 3.3.4.3 are also shown without formal statistical analysis.

(1) guideline adherence across the patient journey i.e. including both primary and secondary care sites,
(2) recurrence rates of individual outcomes reported as composites under secondary outcomes,
(3) cost data stratified into doctors’ visits, hospital admissions, investigations, and medications,
(4) percent of patients who achieved various investigations, medications, and counselling,
(5) time to investigations and medication initiation.

3.3.4.5. Exploratory Analyses

The following analyses were not pre-specified and are shown as exploratory analyses:

(1) stroke risk by risk stratification and ABCD2 score,
(2) diagnostic accuracy of electronic decision support,
(3) impact of pre-trial general practitioner training,
(4) ethnic comparisons
(5) general practitioner imaging request patterns.

3.3.5. Sample size

The study was designed to detect a reduction in \textit{90-day Stroke Rate} from 10\% in the control group to 2\% in the intervention group. This is based on stroke rates in published
Unadjusted for the cluster design, this required a total sample size of 274 at 80% power with alpha 0.05. Assuming 40 practices (clusters) and a kappa for association of outcome within the control group of 0.01, similar to the median intra-class correlation in the paper of Adams, the adjusted sample size needed is 292 TIA/stroke patients, or about seven patients per practice over the course of 12 months. This was felt to be feasible and assumes 2.5 general practitioner full-time equivalents per practice and an average of between two and three patients with TIA or minor stroke per general practitioner per year. This takes into account general practitioner diagnostic accuracy of between 50 and 80%. In other words the sample size calculation anticipates between four and five patients registered in the study per general practitioner over 12 months but that between two and three actually have TIA or minor strokes.

For the other main outcome, guideline adherence, a much lower sample size is needed. We estimated based on published research that guideline adherent care would occur in 33% of the patients of usual care clinics and over 90% in the intervention group. Unadjusted for the cluster design a sample size of 20 patients is sufficient to detect this difference. The intra-class correlation coefficient for this outcome was assumed to be much higher (0.4). The planned recruitment of 292 was therefore adequately powered for this outcome.

3.3.6. Randomisation

Randomisation was according to a computer-generated random allocation sequence that did not use stratification or matching. A third-party (Professor Mark Weatherall) created this allocation sequence. Randomisation occurred at the cluster rather than the individual patient level.

The candidate provided all general practice TIA training sessions to achieve a maximum level of consistency. At the conclusion of each training session doctors were invited to participate and complete a consent form – one form per participating practice was signed by a representative or several representatives of each practice. The candidate applied the randomisation sequence in the exact order in which practice representatives handed back the signed consent forms and hid upcoming group assignments on the schedule from view with a blank sheet of paper. After the study group assignment was made everyone present was aware of their group assignment so that there was no further
concealment at the time of randomisation. Each practice received a unique study practice identification number that allowed for later concealment of group assignment during the analysis phase.

Individual patients received study assignment based on their clinic enrolment status: patients enrolled in intervention practices were assigned to the intervention group and patients enrolled in control practices were assigned to the control group. Individual patient consent was not sought as the target of the intervention was general practitioners and not patients. Outcome measurements, however, occurred at the individual patient level and to protect patient rights all patient data were completely de-identified during analysis. In addition, all practices displayed study posters in their rooms to inform patients of the study and providing a free telephone line number that patients could ring for more information.

3.3.7. Blinding
Blinding occurred only during the analysis phase. All participating general practitioners and patients were aware of treatment group allocation. The candidate was aware of treatment group allocation at the time of randomisation. Subsequently, all practices and patients were de-identified and study assignment was concealed during data cleaning and analysis.

3.3.8. Data collection
All registered patients were logged centrally via BPAC Inc into a secure registry. Two research assistants reviewed all general practitioner and hospital records for registered patients and entered relevant data into a de-identified database with patients listed by unique study identification number. Where data were not retrievable from the medical records, participating general practitioners and specialists were contacted who, in some cases, contacted individual patients. Members of the study team had no direct contact with individual patients. After the databases were completed the de-identified information was transferred to the candidate for analysis. Research assistants did not engage in any data interpretation. They simply transcribed information from the medical records. All specific diagnoses (and especially if such were not clearly stated) were supplemented with details of the clinical presentation and investigation reports copied verbatim for later interpretation by the candidate, blinded to the study group of patients.
In one practice the general practitioners did not feel comfortable with research assistants accessing patient medical records and completed data collection themselves. This was a control group practice and no outcome events were reported. All other patient data were collected independently of the treating clinicians.

Research assistants mailed end of study surveys to all participating general practices. All lead stroke physicians at secondary referral hospitals underwent a structured telephone interview eliciting free text responses (section 3.3.4.2.6 and 3.3.4.2.7). Results from surveys were collated by the candidate.

3.3.9. Data cleaning

Data cleaning was performed by the candidate blinded to treatment arm. The candidate explored all patient registrations for eligibility criteria and excluded patients not meeting inclusion criteria (see Section 3.3.2). Exclusions occurred if the registering general practitioner did not suspect a TIA or stroke, a patient presented to secondary services or a non-participating practice before the assessment at the registering site, a patient did not present during the active enrolment period, or general practitioners registered the same patient twice. All patients were counted only once. If patients re-presented during the 90 day follow-up period these events were counted as outcome events. If they re-presented beyond 90 days the second presentation was excluded from analysis. The reason for excluding late re-presentation is that management implementation for the prior presentations might have influenced subsequent management making guideline adherence more challenging to interpret.

When the study dataset was clearly defined each record was checked for completeness, data entry errors (e.g. negative time frames), and appropriateness of outcome assignments. Missing data were filled in by contacting individual clinicians directly and suspicious data were explored by having research assistants review the medical records a second time. Outcome events were explored in detail for relevance and accuracy.
3.3.10. Statistical methods

Simple data description is used to describe the patients recruited for the study. In case of missing data, frequencies were calculated based on total number of patients for whom data were available (i.e. excluding patients with missing data).

Mixed effects generalised linear models are used to estimate the effect of randomised treatment on dichotomous outcome variables. In these models the binary outcome is fitted using a binomial distribution and the logistic link function with the randomly allocated treatment group as a fixed effect. The clusters are accounted for in these models by fitting them as normal random effects. The random effects are fitted by restricted maximum likelihood using an iterative algorithm. This allocates variability into that due to clusters and remaining variability related to the assumed distribution of the outcome variable, in this case related to the binomial distribution. The degree to which outcomes for patients within clusters are similar is summarised by the intra-class correlation coefficient which is the ratio of variability due to clusters divided by total variability. An important issue with using these techniques is that the iterative process can fail, particularly if there are a small number of events. This happens when during iteration the variance component due to clusters develops a value less than zero. Typically in these situations the software implementation of these methods sets the variance component for the cluster to zero, equivalently setting the intra-class correlation coefficient to zero also. The analysis then produced is one that ignores the cluster randomisation and is usually inappropriately precise for the particular comparison. This was the case for the main outcome variable of stroke where there were few outcome events. For this analysis the cluster random effect and intra-class correlation coefficient could not be estimated.

For the single continuous variable, cost, the pre-specified analysis plan was a normal mixed linear model with an identity link function adjusting for clustering with a normal random effect by cluster. In the event the cost data had a skewed distribution and normality assumptions were better met on the logarithm transformed scale. The exponent of the coefficients of the cost data are interpreted as the ratio of mean costs for the intervention and control treatments. Another illustrative method to account for clustering is to analyse average costs per cluster rather than averages for individuals and subsequently accounting for cluster. Employing both methods gave similar results.
When average costs per practice were assessed the distribution was also skewed and also required natural log transformation.

For both the main dichotomous and the continuous variables the intra-cluster correlation coefficients are reported to assist future research in similar settings.

Survey responses were collated and average response scores are presented for general practitioner surveys in addition to individual clinician comments.

All statistical analyses were performed by the candidate in Stata 12.1., guided by Professor Mark Weatherall.

3.4. Results

3.4.1. Numbers randomised, recruited, and analysed

The active study period occurred from 24 February 2012 to 15 May 2013 plus a 90-day follow-up period. The initial practice recruitment target was 40 practices from three New Zealand districts: Hawke’s Bay, Whanganui, and Southern. These districts were chosen because their secondary care lead stroke physicians agreed to participate, current TIA pathways used in these districts were consistent with New Zealand TIA guidelines, they included areas from both the North and the South Island, they included both secondary and tertiary level centres, all three districts have a substantial rural population who may struggle with service access, and two districts have a substantial Māori population.

The 44 recruited practices from these three districts registered fewer patients than anticipated and six months into the trial a fourth district, Taranaki, and 12 additional practices were recruited.

In total 56 practices were enrolled with 29 randomised to the intervention group and 27 to the control group. These practices registered a total of 362 patients. Of these, 291 individual patients met eligibility criteria for trial participation and inclusion in the analysis. Figure 14 shows the participant flow diagram.

Seventy-one patients were excluded from the final analysis. The majority (n=45) were unintentional registrations and either did not present to primary or secondary care
during the study period (n=26) or presented without any neurologic/ophthalmologic symptoms (n=19): orthopaedic problems (n=4), cardiac complaints, mostly chest pain (n=4), psychiatric problems (n=3), acne (n=2), immunisations (n=2), routine follow-up (n=2), other (n=2). This problem was unanticipated and not discovered until the end of the trial. All excluded patients were scrutinised for eligibility by two study clinicians, one of whom was blinded to study arm. In cases of uncertainty the treating general practitioner was contacted for clarification. None of these excluded patients suffered outcome events.

Three patients in the intervention and ten patients in the control group initially presented to a secondary care level emergency department. Seven additional patients were accidentally registered a second time for the same event. One patient in each study group presented before the trial started and one patient in the control group underwent evaluation at a non-participating practice under the care of a general practitioner who also worked at a participating practice where he subsequently registered this patient. All of these patients were also excluded from analysis because they did not meet eligible criteria.

Two patients, one in the intervention and one in the control group, experienced a second ‘TIA’ event beyond the 90 day follow-up period but within the 14 month study period. Because these events did not occur within 90 days of initial presentation they did not qualify as ‘outcome events.’ Both these second events were excluded from analysis as per protocol.
Figure 14: Trial Profile: Number of general practices enrolled and randomised and number of patients registered and included in analysis

56 General practices enrolled

56 Underwent randomisation

29 Intervention practices
27 Control practices

223 Patients registered
139 Patients registered

51 Were excluded from analysis:
- 39 Registered unintentionally
- 5 Duplicate registrations for same event
- 6 GP not first point of contact
- 1 Second registration

20 Were excluded from analysis:
- 6 Registered unintentionally
- 3 Duplicate registrations for same event
- 7 GP not first point of contact
- 1 Patient not from trial practice
- 2 Presented prior to trial
- 1 Second registration

172 Intervention group patients met trial criteria for inclusion
119 Control group patients met trial criteria for inclusion
### 3.4.2. Baseline data

#### 3.4.2.1. Practices

Table 8: General practice characteristics by region and randomisation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>Intervention</th>
<th>Combined/Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total eligible trial patients n/n (%)</td>
<td>119/291 (40.9)</td>
<td>172/291 (59.1)</td>
<td>291/291 (100)</td>
</tr>
<tr>
<td>Total trial practices n/n (%)</td>
<td>27/56 (48.2)</td>
<td>29/56 (51.8)</td>
<td>56/56 (100)</td>
</tr>
<tr>
<td>Mean population/practice (SD)</td>
<td>5202 (4555)</td>
<td>4611 (4652)</td>
<td>4897 (4573)</td>
</tr>
<tr>
<td>Mean registrations/practice (SD)</td>
<td>4.2 (4.1)</td>
<td>5.9 (5.6)</td>
<td>5.1 (4.9)</td>
</tr>
</tbody>
</table>

**By District**

**Whanganui (Population 69,211)**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Intervention</th>
<th>Combined/Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial Patients n/n (%)</td>
<td>7/30 (23.3)</td>
<td>23/30 (76.7)</td>
<td>30/291 (10.3)</td>
</tr>
<tr>
<td>Trial Practices n/n (%)</td>
<td>3/9 (33.3)</td>
<td>6 (66.7)</td>
<td>9/56 (16.1)</td>
</tr>
<tr>
<td>Population/trial practice: Mean (SD)</td>
<td>4697 (3920)</td>
<td>3966 (3294)</td>
<td>4210 (3280)</td>
</tr>
<tr>
<td>Patients per trial practice: Mean (SD)</td>
<td>2.3 (1.2)</td>
<td>3.7 (1.0)</td>
<td>3.2 (0.8)</td>
</tr>
</tbody>
</table>

**Hawke’s Bay (Population 148,248)**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Intervention</th>
<th>Combined/Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial patients n/n (%)</td>
<td>31/86 (36.1)</td>
<td>55/86 (63.9)</td>
<td>86 (29.6)</td>
</tr>
<tr>
<td>Trial practices n/n (%)</td>
<td>10/14 (71.4)</td>
<td>4/28.6</td>
<td>14/6 (25.1)</td>
</tr>
<tr>
<td>Mean population/trial practice n/n (SD)</td>
<td>7124 (5379)</td>
<td>9236 (10370)</td>
<td>7725 (6768)</td>
</tr>
<tr>
<td>Mean trial patients/trial practice n/n (SD)</td>
<td>3.1 (3.3)</td>
<td>14 (9.0)</td>
<td>6.2 (7.2)</td>
</tr>
</tbody>
</table>

**Southern (Population 286,224)**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Intervention</th>
<th>Combined/Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial patients n/n (%)</td>
<td>69/145 (47.6)</td>
<td>76/145 (53.4)</td>
<td>145/291 (49.8)</td>
</tr>
<tr>
<td>Trial practices n/n (%)</td>
<td>11/25 (44.0)</td>
<td>14/25 (56.0)</td>
<td>25/56 (44.6)</td>
</tr>
<tr>
<td>Mean population/trial practice (SD)</td>
<td>4496 (4134)</td>
<td>3167 (1661)</td>
<td>3752 (3011)</td>
</tr>
<tr>
<td>Mean trial patients/practice (SD)</td>
<td>5.8 (1.4)</td>
<td>5.3 (1.1)</td>
<td>5.5 (0.9)</td>
</tr>
</tbody>
</table>

**Taranaki (Population 104,277)**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Intervention</th>
<th>Combined/Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial Patients n/n (%)</td>
<td>12/30 (40.0)</td>
<td>18 (60.0)</td>
<td>30 (10.3)</td>
</tr>
<tr>
<td>Trial Practices n/n (%)</td>
<td>3/8 (37.5)</td>
<td>5/8 (62.5)</td>
<td>8/56 (14.3)</td>
</tr>
<tr>
<td>Mean population/ trial practice (SD)</td>
<td>1898 (843)</td>
<td>5728 (4177)</td>
<td>4292 (3755)</td>
</tr>
<tr>
<td>Mean trial patients/practice (SD)</td>
<td>4 (3.1)</td>
<td>3.6 (1.5)</td>
<td>3.8 (1.3)</td>
</tr>
</tbody>
</table>
### 3.4.2.2. Study Patients

**Table 9: Characteristics of patients by study group**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Study Group</th>
<th>Intervention</th>
<th>Control</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, Mean (SD)</td>
<td></td>
<td>69.8 (13.3)</td>
<td>72.3 (14.0)</td>
<td>70.8 (13.6)</td>
</tr>
<tr>
<td>Sex (M) (%)</td>
<td></td>
<td>67/172 (39.0)</td>
<td>55/119 (46.2)</td>
<td>122/291 (41.9)</td>
</tr>
<tr>
<td>Ethnicity† (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>European</td>
<td></td>
<td>156/172 (90.7)</td>
<td>101/117 (86.3)</td>
<td>259/289 (89.6)</td>
</tr>
<tr>
<td>Māori</td>
<td></td>
<td>10/172 (5.8)</td>
<td>14/117 (11.9)</td>
<td>24/289 (8.3)</td>
</tr>
<tr>
<td>Pacific</td>
<td></td>
<td>1/172 (0.58)</td>
<td>1/117 (0.8)</td>
<td>2/289 (0.7)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>5/172 (2.91)</td>
<td>1/117 (0.8)</td>
<td>6/289 (2.1)</td>
</tr>
<tr>
<td>Tobacco use (%)</td>
<td></td>
<td>45/172 (26.2)</td>
<td>43/119 (36.1)</td>
<td>88/289 (32.7)</td>
</tr>
<tr>
<td>Atrial Fibrillation (%)</td>
<td></td>
<td>18/172 (10.5)</td>
<td>16/119 (13.5)</td>
<td>34/291 (11.7)</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td></td>
<td>93/172 (54.1)</td>
<td>59/119 (49.6)</td>
<td>152/291 (52.2)</td>
</tr>
<tr>
<td>Ischaemic Heart Disease (%)</td>
<td></td>
<td>28/172 (16.3)</td>
<td>22/119 (18.5)</td>
<td>50/291 (17.2)</td>
</tr>
<tr>
<td>Rheumatic Heart Disease (%)</td>
<td></td>
<td>1/172 (0.58)</td>
<td>1/119 (0.84)</td>
<td>2/291 (0.69)</td>
</tr>
<tr>
<td>Prior TIA or stroke (%)</td>
<td></td>
<td>46/172 (26.7)</td>
<td>37/119 (31.1)</td>
<td>83/291 (28.5)</td>
</tr>
<tr>
<td>Diabetes Mellitus (%)</td>
<td></td>
<td>24/172 (14.0)</td>
<td>22/119 (18.5)</td>
<td>46/291 (15.8)</td>
</tr>
<tr>
<td>Dyslipidemia (%)</td>
<td></td>
<td>63/172 (36.6)</td>
<td>47/119 (39.5)</td>
<td>110/291 (37.8)</td>
</tr>
<tr>
<td>On Antiplatelet pre-event (%)</td>
<td></td>
<td>72/172 (41.9)</td>
<td>47/119 (39.5)</td>
<td>119/291 (40.9)</td>
</tr>
<tr>
<td>On Anticoagulant pre-event (%)</td>
<td></td>
<td>7/172 (4.1)</td>
<td>13/119 (10.9)</td>
<td>20/291 (6.9)</td>
</tr>
<tr>
<td>On Statin pre-event (%)</td>
<td></td>
<td>72/172 (41.9)</td>
<td>56/119 (47.1)</td>
<td>128/291 (44.0)</td>
</tr>
<tr>
<td>On Antihypertensive pre-event (%)</td>
<td></td>
<td>90/172 (52.3)</td>
<td>63/119 (52.9)</td>
<td>153/291 (52.6)</td>
</tr>
<tr>
<td>Risk Category (high)§ (%)</td>
<td></td>
<td>116/172 (67.4%)</td>
<td>76/119 (63.9%)</td>
<td>192/291 (66.0)</td>
</tr>
</tbody>
</table>

There were no significant differences between groups with adjusted p values all >0.05. †Ethnicity data were not available on two patients in the control group. §High risk is defined if the patient has any of the following: ongoing symptoms at time of presentation (i.e. possible stroke), ABCD2 score >3, >1 event preceding 7 days, is currently taking an Anticoagulant agent, or carries a diagnosis of atrial fibrillation. In addition, the presenting event has to have occurred ≤7 days prior to presentation.
3.4.3. Efficacy outcomes

More patients received guideline adherent care in the intervention group 131/172 (76.2%), compared to control, 49/119 (41.2%); adjusted odds ratio (OR) 4.57; 95% confidence interval (CI) 2.39-8.71; p<0.0001). The difference between study groups in 90-day stroke rate was not statistically significant although the stroke rate was lower in the intervention group, 2/172 (1.2%) compared to 5/119 (4.2%) in control; OR 0.27, 95% CI 0.05-1.41; p=0.098. It was not possible to estimate the cluster random effect for this outcome. If cluster effect could be estimated it is likely that the adjusted confidence interval would be wider and the p value higher. The intervention group had fewer 90-day vascular events or deaths 6/172 (3.5%) compared to control, 14/119 (11.9%; adjusted OR 0.27; 95% CI 0.09-0.78; p=0.016. Table 10 shows all efficacy outcome measure comparisons between Intervention and Control groups.

Table 10: Outcome measure comparisons by randomised group

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention (n=172)</th>
<th>Control (n=119)</th>
<th>Unadjusted for Cluster</th>
<th>Adjusted for Cluster</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke at 90 days</td>
<td>2 (1.2)</td>
<td>5 (4.2)</td>
<td>0.27 (0.05-1.41)</td>
<td>0.098 n/a†</td>
</tr>
<tr>
<td>Guideline adherence</td>
<td>131 (76.2)</td>
<td>49 (41.2)</td>
<td>4.56 (2.75-7.57)</td>
<td>&lt;0.0001 4.57 (2.39-8.71) &lt;0.0001</td>
</tr>
<tr>
<td>TIA or stroke at 90 days</td>
<td>4 (2.0)</td>
<td>10 (8.5)</td>
<td>0.26 (0.56-0.85)</td>
<td>0.026 0.26 (0.70-0.97) 0.045</td>
</tr>
<tr>
<td>Vascular event* or death</td>
<td>6 (3.5)</td>
<td>14 (11.9)</td>
<td>0.27 (0.10-0.73)</td>
<td>0.006 0.27 (0.09-0.78) 0.016</td>
</tr>
<tr>
<td>Comprehensive counselling</td>
<td>68 (39.5)</td>
<td>19 (16.0)</td>
<td>3.44 (1.93-6.13)</td>
<td>&lt;0.0001 3.44 (1.89-6.27) 0.0001</td>
</tr>
</tbody>
</table>

†For this outcome it was not possible to determine the odds ratio adjusted for cluster due to the small number of events. *Stroke, TIA, myocardial infarction, major bleeding (requiring hospitalisation), or death

The intra-class correlation coefficient for 90-day stroke rate could not be calculated due to the small number of events. The intra-class correlation coefficient for 90-day vascular events or death was 0.01 and this provides an estimate for where the coefficient for stroke might be. The intra-class correlation coefficient for guideline adherence was 0.1.
3.4.4. Safety outcome

There were 14 adverse events: nine (5.2%) in the intervention group and five (4.2%) in the control group (cluster-design adjusted OR 1.25; 95% CI 0.48 to 3.24; p=0.70). Thirteen adverse events were medication side effects and all were reversible without major sequelae.

The final patient was a patient who may have suffered an adverse event relating to advice rendered by the electronic decision support tool. The patient was an 82 year old male who presented with ‘bilateral blurred vision’ and ‘left arm paresthesias.’ Blood pressure was normal, ABCD2 score was two, and no other high risk indicators were identified.

The tool indicated that the presentation was not entirely typical for TIA, because he had an atypical symptom, ‘bilaterally blurred vision,’ and no high risk indicators. He also had a potentially typical symptom, ‘upper limb paresthesias,’ which the general practitioner entered into the tool under ‘upper limb numbness.’ When an atypical and a typical symptom occur concurrently in an otherwise low risk patient the tool highlights the atypical features and encourages the clinician to reconsider the diagnosis although it also offers the option to continue with TIA management and outpatient TIA clinic referral. The general practitioner took on board the tool’s doubts about a TIA diagnosis, documented the diagnosis as probable non-TIA in the medical record, but remained concerned about the patient, felt that urgent specialist review was still warranted, and referred the patient to the outpatient TIA clinic. The general practitioner did not initiate antiplatelet medication because the patient had suffered a significant gastro-intestinal bleed only a few weeks prior, prompting discontinuation of Aspirin at that time. The hospital specialist received and reviewed the referral and scheduled the patient for an outpatient TIA clinic appointment to be seen within seven days. The patient suffered a large right middle cerebral artery stroke six days after seeing the general practitioner and just prior to the scheduled TIA clinic appointment.

In retrospect it is likely that the patient had a ‘homonymous hemianopia’ misinterpreted as ‘bilateral blurred vision.’ Homonymous hemianopia describes vision loss in one visual field, which is a typical TIA or stroke symptom. This is experienced by the patient as an inability to see one half or one quarter of the environment toward one side with clear vision in the other direction. Vision is not typically ‘blurred,’ although could
potentially be described as such if the patient struggles to clearly define the problem. This is further compounded if the clinician is unfamiliar with this presentation and does not ask appropriate questions that could help clarify the symptom constellation.

Based on risk stratification and co-morbidities all actions taken were in accordance with the guidelines and it is unclear whether more urgent specialist assessment would have prevented this adverse outcome. However, the possibility that the tool contributed to the adverse patient outcome cannot be excluded and this occurrence offers insights into some potential limitations of the electronic decision support tool.

3.4.5. Economic analysis

3.4.5.1. Treatment cost comparison

All costs are reported in New Zealand dollars. On the raw scale median per patient treatment costs were $1209 (inter-quartile range (IQR): $378 to 3777) in the intervention and $1998 (IQR: $612 to 5580) in the control group. The mean per patient treatment cost was $2,373 (SD $2850) in the intervention group and $3,852 (SD $4784) in the control group with an average per patient cost difference of $1479. Treatment cost was not normally distributed. Raw and natural log transformed costs and residuals, unadjusted for cluster design, are shown in figures 15 and 16.
After natural log transformation a cost ratio of 0.65 favoured the intervention group with an unadjusted 95% CI of 0.49-0.87; p = 0.004. After adjustment for cluster effect the 95% CI was 0.47 to 0.91; p=0.01.

Alternatively, costs can be compared by performing the analysis at the cluster level. Patient cost averaged across practices had a mean of $3638 (SD $2355) in the control and $2224 (SD 1471) in the intervention group with an average difference of $1414 favouring the intervention group. Medians and inter-quartile ranges were $3484 ($1858 to $4375) for control practices and $1981 ($1150 to $2839) for intervention practices. Distributions at the cluster level were also not normally distributed and are shown both raw and after natural log transformation in figures 17 and 18.
The cost ratio was 0.68: 95%CI 0.41 to 0.95; p=0.02.
The intra-class correlation coefficient for this outcome was 0.05.

3.4.5.2. Outliers

Before performing the natural log transformation and adjusting for cluster effect studentised residuals were explored for outliers. Individuals with residuals >2.5 or <-2.5 were explored. Ten such outliers were identified: four in the intervention and six in the control group. All ten patients were admitted to hospital, underwent multiple investigations and seven underwent surgery (six carotid endarterectomies and one evacuation for a subdural haematoma). One of the three non-surgical patients represented with a second severe stroke and the remaining two non-surgical patients initially presented with severe stroke and underwent MRI scanning. Because of the legitimacy of these treatment costs it was decided not to remove these outliers from the analysis.
3.4.6. Sub-group analysis

The analysis above includes all eligible patients registered for the trial regardless of their final diagnosis. As anticipated a proportion of these patients received a final diagnosis other than TIA or stroke by the end of their work-up. In some cases the general practitioners themselves changed the diagnosis even before referring the patient to a specialist. More detail on general practitioner diagnostic accuracy and electronic decision support impact on diagnosis will be presented in section 3.5.2. A pre-specified sub-group analysis looked at outcome events in only those patients who received a final specialist diagnosis of definite or possible TIA or stroke. Table 11 describes final specialist diagnoses and table 12 the 90-day stroke, TIA/stroke, and vascular event/death rates for the sub-group of patients with final specialist diagnosis of definite or possible TIA or stroke.

Table 11: Final specialist diagnosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention n=172</th>
<th>Control n=119</th>
<th>Combined n=291</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/n (%)</td>
<td>n/n (%)</td>
<td>n/n (%)</td>
</tr>
<tr>
<td>Final (Specialist) Diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIA</td>
<td>68/172 (39.5)</td>
<td>37/119 (31.1)</td>
<td>105/291 (36.1)</td>
</tr>
<tr>
<td>Stroke</td>
<td>24/172 (14.0)</td>
<td>24/119 (20.2)</td>
<td>48/291 (16.5)</td>
</tr>
<tr>
<td>Possible TIA/stroke</td>
<td>7/172 (4.1)</td>
<td>8/119 (6.7)</td>
<td>15/291 (5.2)</td>
</tr>
<tr>
<td>TIA and Stroke (including possible TIA/stroke)</td>
<td>99/172 (57.6)</td>
<td>69/119 (58.0)</td>
<td>168/291 (57.7)</td>
</tr>
<tr>
<td>Migraine</td>
<td>8/172 (4.7)</td>
<td>6/119 (5.0)</td>
<td>14/291 (4.8)</td>
</tr>
<tr>
<td>Seizure</td>
<td>1/172 (0.58)</td>
<td>1/119 (0.84)</td>
<td>2/291 (0.69)</td>
</tr>
<tr>
<td>Other</td>
<td>64/172 (37.2)</td>
<td>43/119 (36.1)</td>
<td>107/291 (36.7)</td>
</tr>
</tbody>
</table>
Table 12: Outcomes calculated for sub-group of patients with TIA/Stroke

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention</th>
<th>Control</th>
<th>Unadjusted</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/n (%)</td>
<td>n/n (%)</td>
<td>OR</td>
<td>p</td>
</tr>
<tr>
<td>Final diagnosis TIA or stroke*</td>
<td>99/172 (57.6)</td>
<td>69/119 (58.0)</td>
<td>0.98 (0.61-1.58)</td>
<td>0.94</td>
</tr>
<tr>
<td>Stroke at 90 days</td>
<td>2/99 (2.2)</td>
<td>5/69 (7.3)</td>
<td>0.26(0.05-1.4)</td>
<td>0.097</td>
</tr>
<tr>
<td>Stroke or TIA at 90 days</td>
<td>4/99 (4.0)</td>
<td>10/69 (14.5)</td>
<td>0.25(0.07-0.83)</td>
<td>0.016</td>
</tr>
<tr>
<td>Vascular event or death at 90 days</td>
<td>4/99 (5.9)</td>
<td>8/69 (21.6)</td>
<td>0.23(0.06-0.81)</td>
<td>0.018</td>
</tr>
</tbody>
</table>

*This refers to patients whose initial presentation judged to represent a TIA or stroke by their general practitioner was eventually confirmed as likely representing a true TIA or stroke by a stroke specialist
†For this outcome it was not possible to determine the odds ratio adjusted for cluster due to the small number of events.

3.4.7. User feedback

3.4.7.1. General practitioner feedback

Study patients were registered by 183 general practitioners from 56 practices. A minimum of one completed questionnaire per practice was requested from each participating practice with 63 questionnaires returned.

The survey captured the following general practitioner demographic data: the mean (SD) age of general practitioners in the control group was 47.3 years (8.3) and in intervention group 50.6 years (7.2). The mean (SD) number of general practitioners per practice was 5.0 (SD 4.1) in the control and 5.3 (SD 5.2) in the intervention group.

The summary of responses of the intervention group users to the five question written questionnaire about the use of the electronic decision support tool are shown in table 13.
Table 13: Intervention general practitioner questionnaire responses

<table>
<thead>
<tr>
<th></th>
<th>Number of responses</th>
<th>Mean Score (SD)</th>
<th>Median (IQR)</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>I found the tool easy to use</td>
<td>30</td>
<td>3.2 (0.7)</td>
<td>3 (3-4)</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>I found the tool improved my efficiency</td>
<td>28</td>
<td>2.5 (1.0)</td>
<td>2.5 (2-3.5)</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>I found the tool improved patient care</td>
<td>32</td>
<td>3.2 (0.9)</td>
<td>3 (3-4)</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>If available, I would use the tool on my patients</td>
<td>31</td>
<td>3.5 (0.6)</td>
<td>4 (3-4)</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>I have had problems with patients relating to the tool</td>
<td>30</td>
<td>1.2 (0.4)</td>
<td>1 (1-1)</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Scores were between 1 and 4 (1= Not at all; 2= Some of the time; 3= Most of the time; 4= All of the time).

Another way of reporting the information displayed in table 13 (above) is by stating that feedback from general practitioners indicated that 31/31 (100%) would use the tool at least some of the time if available, 29/31 (94%) at least most of the time, and 17/31 (55%) all of the time.

Table 14: Examples of intervention general practitioner free text questionnaire responses about the electronic decision support tool

**Positive Comments:**

‘Very well laid out’ – ‘Good pathway’ – ‘Clear and sequential’ – ‘Easy to use’ – ‘Good prompts’

‘Allows quick evidence based decision making in a short consultation and no need to duplicate notes or letter’

‘Better care, because CT scan and dopplers were done in 24 hours avoiding hospital admission’

‘Gave me more confidence in ordering outpatient CT heads and carotid doppler exam’

‘Helped speed up borderline admissions by making it clearer when urgent review needed’

‘Especially good for situations where diagnosis unclear’

‘It was useful to reassure patients who thought they had had a TIA [when] in fact [this] was highly unlikely. There is potential here to develop more tools for this purpose’

‘Very easy to use. Good advice’

**Negative Comments:**

‘Occasionally a bit hard to fit symptoms into choices.’

‘Navigation from section to section can be clunky.’

‘Difficult to change if realised made an error’

‘Very long winded to get to where I would have got anyway; the history section is especially inefficient’
Table 15: Intervention general practitioner questionnaire responses about the time it took them to complete the initial screen to reach a triage decision and the time it took to implement a management plan using the tool

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Number of responses</th>
<th>Mean Score (SD)</th>
<th>Median (IQR)</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time taken to complete the software to reach diagnosis/triage advice</td>
<td>28</td>
<td>6.8 (2.9)</td>
<td>7.5 (7.5-7.5)</td>
<td>2.5</td>
<td>&gt;15</td>
</tr>
<tr>
<td>Time taken to complete referral process to secondary care and indicated interventions using the tool</td>
<td>28</td>
<td>9.6 (5.2)</td>
<td>7.5 (7.5-15)</td>
<td>2.5</td>
<td>&gt;15</td>
</tr>
<tr>
<td>Time taken to complete items in the 'Management' when choosing TIA work-up in the community</td>
<td>23</td>
<td>7.1 (4.8)</td>
<td>4.5 (2.5-7.5)</td>
<td>2.5</td>
<td>&gt;15</td>
</tr>
</tbody>
</table>

Table 16: Examples of intervention general practitioner free test responses about the time it took them to use tool and implement management

Positive:
- ‘Straight forward’
- ‘Made referral letter faster’
- ‘Gets faster’
- ‘Speeds up referral letter’

Negative:
- ‘This is still too long - to get good history, perform exam, plan treatment and discuss treatment plan with patient/relatives’
- ‘Our internet is incredibly slow after 15-30 seconds per page.’
- ‘Too slow (?me ?tool)’

When asked what type of education surrounding use of the tool general practitioners would prefer, 7/28 (25%) felt they needed no instructions, 11/28 (32%) thought written instructions only would be preferable, and 10/28 (36%) preferred face-to-face instructions.

Table 17: Free text comments about training/instructions on tool use

- ‘I liked the face to face but experience only way really got good at it’
- ‘One page ’map' of the process would be useful for noticeboard’
- ‘Pretty self explanatory’
- ‘A 'you tube' style video with animation of form being filled might help’
- ‘More 'model' patients like Minnie - with varying scenarios - I think it would be better if we were more familiar with all the "i" tabs. A printed quick guide as accompanied with 'i’ tab info’
- ‘refresh could be good if not used often’
- ‘CME session’
Final overall intervention general practitioner free text comments included statements such as ‘All in all a useful clinical tool and will remain on my patient management system tool bar’ and ‘Of all the things looked at this is the most professionally developed.’

Table 18: Control group general practitioners single scored question responses

<table>
<thead>
<tr>
<th>Do you feel that access to an electronic support tool for TIA management would be of value?</th>
<th>Number of responses</th>
<th>Mean Score (SD)</th>
<th>Median (IQR)</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>31</td>
<td>2.9 (0.8)</td>
<td>3 (2-3)</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 19: Control general practitioner free text comments about perceived tool utility

| ‘TIA not that common and to have to cover correct process prompt really useful’ |
| ‘We confront acute TIAs relatively infrequently - an electronic support tool to provide current management advice would be very useful’ |
| ‘Overabundance of pathology undermines usefulness.’ |
| ‘Risk of perception [general practitioners] is about tick box for those outside the profession.’ |
| ‘In rural hospitals run by [general practitioners] more data gathered at emergency department] than [general practitioner] surgeries |
| ‘Current TIA referral guidelines are on the Southern DHB website fulfil the same purpose, but would be better integrated into the [practice management system].’ |

3.4.7.2. Stroke specialist feedback

After completion of the enrolment and follow-up periods the four lead stroke specialists running the TIA clinics at the four participating secondary hospitals participated in a structured telephone interview.

Overall specialists felt that neither the number of hospital referrals nor telephone calls had changed significantly from before to after the study. However, they noted an overall improvement in quality of referrals especially when the electronic decision support tool was used. Two specialists commented as follows:

“I found these referrals to be of good quality and the GP using the tool seemed to have more confidence in starting medications at first point of contact. Using risk
stratification more appropriately. Pursuing appropriate investigations more confidently.”

“[Use of the electronic decision support] improved standard of referrals because of added core information.”

Overall specialists stated the speed of receiving referrals from general practitioners did not change. One specialist felt that the use of the electronic decision support tool sped up the process compared with routinely typed letters. Another specialist expressed concern about a separate referral process for other patients as part of a nearly simultaneously rolled-out e-referral system. The forms looked similar but were processed differently. This caused some confusion for clinicians initially.

All specialists reported improved general practitioner management prior to patient arrival in TIA clinic. Examples of comments include:

“[Patients] are more likely to be on secondary preventative medications. [It is] very seldom now that I get anyone who is not on anything at all.”

“Most people are arriving with Aspirin and Statin and [there is] some improved awareness about driving.”

“Overall, participating GPs seemed more aware of TIA’s now and the time factor. I noticed this in both groups and I think it was because of the education that was provided at the start of the trial.”

Specialists noted a particular benefit in patients who had received care using the electronic decision support tool:

“For those managed with the tool it was very unusual to come in without antiplatelets and [there are] fewer rubbish referrals.”

“Increased referrer confidence.”

“People who used the tool seemed to implement more comprehensive care although on one occasion driving box was ticked but patient and wife adamantly denied being told.”

No one had received any complaints about the tool from patients nor expressed any negative impacts of the tool on their workflow.
All four specialists voiced support for the use of the tool in their districts:

“I think the advice about the secondary preventative measures to start them straight away and reminding GPs what they should prescribe is very good. It also helps them to identify true TIAs and sending referrals in a timely fashion.”

Specialists supported direct CT and ultrasound access although felt more comfortable in the context of a decision tool:

“I think if they have an appropriate decision making tool to guide them I don’t have a problem with it – not sure if radiology services would agree.”

“No problem with [general practitioners] using diagnostics directly especially if they use the tool then no concerns whatever.”

NB: ‘GP’ in above quotes refers to ‘general practitioner.’

3.4.8. Supplementary data

Additional data of potential interest are reported in tables below to supplement the prior data and provide additional detail on the above composite outcomes. It is important to view these data within the framework of the results reported in sections 3.4.3 and 3.4.5 rather than in isolation. They were not pre-specified individual outcomes and hence statistical significance values are not reported.

Guideline adherence is a complex outcome that depends on diagnosis, risk stratification, referral destination, achievement of investigations, and implementation of secondary prevention. Some of these were linked to required time frames depending on risk category. To achieve guideline adherence all aspects of care in an individual patient had to align with the guideline recommendations. Tables 20 and 21 show rates and average times for sub-categories. These figures did not directly inform the outcome discussed in section 3.4.3 because guideline adherence was assessed for each individual patient rather than being based on averages across the entire study population.
Table 20: Interventions achieved

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention N=172</th>
<th>Control N=119</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigations</td>
<td>n/n (%)</td>
<td>n/n(%)</td>
</tr>
<tr>
<td>CT/MRI</td>
<td>119/172 (69.2)</td>
<td>76/119 (63.4)</td>
</tr>
<tr>
<td>Carotid Imaging</td>
<td>104/172 (60.5)</td>
<td>81/119 (68.1)</td>
</tr>
<tr>
<td>ECG</td>
<td>69/172 (40.1)</td>
<td>43/119 (36.1)</td>
</tr>
<tr>
<td>Medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>126/172 (73.3)</td>
<td>70/119 (58.8)</td>
</tr>
<tr>
<td>Anti-hypertensive</td>
<td>87/172 (50.6)</td>
<td>41/119 (34.5)</td>
</tr>
<tr>
<td>Statin</td>
<td>93/172 (54.1)</td>
<td>47/119 (39.5)</td>
</tr>
<tr>
<td>Counseling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>148/119 (86.4)</td>
<td>85/119 (71.4)</td>
</tr>
<tr>
<td>Driving</td>
<td>91/119 (52.9)</td>
<td>37/119 (31.1)</td>
</tr>
<tr>
<td>Lifestyle</td>
<td>68/119 (39.5)</td>
<td>20/119 (16.8)</td>
</tr>
</tbody>
</table>

Table 21: Time to investigations and medication initiation (days)

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>IQR</td>
</tr>
<tr>
<td>general practitioner to CT</td>
<td>2</td>
<td>0-9</td>
</tr>
<tr>
<td>general practitioner to carotid imaging</td>
<td>4</td>
<td>2-15</td>
</tr>
<tr>
<td>general practitioner to ECG</td>
<td>0</td>
<td>0-1.5</td>
</tr>
<tr>
<td>general practitioner to Antiplatelet Rx</td>
<td>0</td>
<td>0-0.5</td>
</tr>
<tr>
<td>general practitioner to anticoagulant Rx</td>
<td>4</td>
<td>0-5</td>
</tr>
<tr>
<td>general practitioner to Statin Rx</td>
<td>2</td>
<td>0-7</td>
</tr>
<tr>
<td>general practitioner to antihypertensive Rx</td>
<td>3</td>
<td>0-8</td>
</tr>
</tbody>
</table>

Time to investigation only includes patients who actually underwent investigations; time to medication refers to initiation of a new prescription except for anticoagulants where delay is often caused by stopping the Rx to await CT so all patients were included in this.

General practitioners did not always follow the management advice rendered by the electronic decision support tool. Had general practitioners consistently followed the tool’s advice guideline adherence rate in the intervention group would have risen to 140/172 (81.4%). The pre-specified composite outcome of guideline adherence was limited to primary care management. When looking at the entire patient journey, inclusive of the secondary care management phase, the overall guideline adherence drops to 29/172 (16.9%) in the intervention group and 3/119 (2.5%) in the control group.
The secondary efficacy outcomes looked at composites of several vascular events grouped into two composite outcomes. Table 22 shows the frequency of events stratified by individual diagnosis. In cases where an individual experienced multiple outcome events they were only counted once in the composite outcomes, which explains why the figures in table 22 do not exactly add up to figures presented in section 3.4.3.

Table 22: Individual outcomes in cerebrovascular and vascular composites

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/n (%)</td>
<td>n/n (%)</td>
</tr>
<tr>
<td>TIA at 90 days</td>
<td>2/172 (3.0)</td>
<td>6/119 (5.1)</td>
</tr>
<tr>
<td>MI at 90 days</td>
<td>0/172 (0.0)</td>
<td>1/119 (0.84)</td>
</tr>
<tr>
<td>Major bleed at 90 days</td>
<td>0/172 (0.0)</td>
<td>1/119 (0.84)</td>
</tr>
<tr>
<td>Death at 90 days</td>
<td>2/172 (1.2)</td>
<td>3/172 (2.5)</td>
</tr>
</tbody>
</table>

Treatment cost is a further composite outcome that was assessed per individual patient. Table 23 shows components of this cost analysis that provide insight into which components of treatment costs differed most between treatment groups. Again, overall treatment costs are not based on summation of averages across treatment categories, but instead were micro-costed at individual patient level. The averages presented in the table 23 were not pre-specified outcomes. They are intended as supplementary information and not suited to draw firm conclusions.
### Table 23: Cost data stratified by category

<table>
<thead>
<tr>
<th>Category</th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean(SD)</td>
<td>Median (IQR)</td>
</tr>
<tr>
<td>Electronic decision support tool</td>
<td>55 (0)</td>
<td>55 (55-55)</td>
</tr>
<tr>
<td>General practitioner consultation</td>
<td>131 (68)</td>
<td>139 (69-208)</td>
</tr>
<tr>
<td>Ambulance</td>
<td>58 (157)</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Emergency department attendance</td>
<td>38 (90)</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Stroke specialist consultation</td>
<td>73 (125)</td>
<td>0 (0-275)</td>
</tr>
<tr>
<td>Hospital admissions</td>
<td>1295 (2018)</td>
<td>0 (0-2644)</td>
</tr>
<tr>
<td>Investigations</td>
<td>537 (530)</td>
<td>517 (0-930)</td>
</tr>
<tr>
<td>Medications</td>
<td>58 (81)</td>
<td>43 (20-70)</td>
</tr>
<tr>
<td>Total</td>
<td>2374 (2851)</td>
<td>1209 (378-3777)</td>
</tr>
</tbody>
</table>

Hospital costs consisted primarily of hospitalisation costs related to the index event with a mean (SD) of 1168 (2018) in the intervention group and 1914 (3220) in the control group. Significant other hospital cost contributions came from subsequent carotid endarterectomies and hospitalisations related to recurrent stroke and other vascular events that occurred during the 3 month follow-up period. These costs were also greater in the control group with mean (SD) carotid endartectomy related costs of 129 (1188) in the intervention and 464 (2226) in the control group and the mean (SD) costs related to outcome events during the follow-up period was 128 (653) in the intervention and 512 (1580) in the control group.

### 3.5. Exploratory analyses

#### 3.5.1. Introduction

The results reported in Section 3.4 report on pre-specified outcomes as described in the FASTEST study protocol (HRC 11/261) and represent the main body of knowledge gained from the trial. In addition, the collected data can be mined for other information that may be of interest to stroke and health services researchers. Section 3.5 presents the results of exploratory analyses conducted to generate hypotheses. Statistical
significance has not been assessed to prevent type I error (i.e. the inappropriate rejection of a true null hypothesis).

3.5.2. Diagnostic accuracy

One of the intended functions of the TIA/Stroke electronic decision support tool is to improve the diagnostic accuracy of general practitioners. The intention is to reduce unnecessary referrals to specialists and heighten the sense of urgency in patients with a definite TIA diagnosis, especially if they are at high risk of experiencing early stroke.

While an assessment of the tool’s ability to achieve this goal was not a pre-specified trial outcome it is nonetheless relevant to explore whether this feature does indeed add diagnostic value. If the diagnostic algorithm does not add diagnostic value to general practitioners’ assessments then it represents an unnecessary feature that simply wastes general practitioner time. If it worsens general practitioner diagnostic accuracy then it exposes patients to undue risk.

Unfortunately, assessing the diagnostic accuracy of the tool is not entirely straightforward because of at least three reasons: (1) the tool does not make any definite diagnoses; it merely indicates whether a diagnosis of TIA is more or less likely; (2) the tool is not intended as a stand-alone diagnostic tool, but is intended for use by general practitioners who add their own diagnostic expertise; and (3) in some instances the tool may indicate that the diagnosis of TIA or stroke is unlikely, but if certain high risk factors such as atrial fibrillation are present it still recommends urgent specialist review.

Table 24 provides details of potential triage outcomes that indicate a degree of diagnostic uncertainty.
Table 24: Diagnostic/triage outcomes rendered by the tool if the diagnosis of TIA or stroke is uncertain

<table>
<thead>
<tr>
<th>Clinical situation</th>
<th>Tool Triage Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>In patients who either had no typical TIA symptoms or had non-sudden symptom onset.</td>
<td><strong>Non-straightforward neurological presentation</strong>&lt;br&gt;Your patient’s symptoms are not entirely typical for a TIA or acute stroke. It is suggested that you consider an alternative diagnosis. If you still suspect that a serious neurological problem is at hand and/or more specialist dependent work-up such as an MRI is required you should consider contacting the neurologist/physician at the hospital to discuss the case. If the patient is acutely ill please consider referral to ED for urgent medical assessment. You may contact the neurologists/physicians at the hospital for advice or refer the patient to the medical team at the hospital if the patient is acutely ill.</td>
</tr>
<tr>
<td>In patients who are low risk and have at least one typical (unless this is weakness) and one atypical feature.</td>
<td><strong>Symptoms not consistent with TIA</strong>&lt;br&gt;In addition to some typical TIA features you also report:&lt;br&gt;Seizure and Syncope&lt;br&gt;This is an atypical presentation for TIA/Stroke and may suggest that the primary diagnosis is not in fact TIA/Stroke. Alternative diagnoses should be considered and discussion with a specialist before proceeding with further management is suggested.&lt;br&gt;I will reconsider the diagnosis and exit the programme (select ‘Continue’ below to generate summary).&lt;br&gt;Refer to Neurology/General Medicine/other specialist as appropriate:&lt;br&gt;Generate Specialist Referral&lt;br&gt;c) Ignore above comment and proceed with TIA/stroke care (select checkbox to view TIA/stroke advice)</td>
</tr>
<tr>
<td>In patients who have high risk factors or unilateral weakness AND have at least on typical (unilateral weakness or other) and one atypical feature.</td>
<td><strong>Your patient may have suffered from a TIA and the estimated seven day stroke risk is High</strong>&lt;br&gt;Administer Aspirin 300mg (UNLESS patient is on Warfarin or Dabigatran) and refer patient to ED for urgent specialist assessment and consideration of hospital admission for urgent inpatient workup.&lt;br&gt;Generate ED Referral&lt;br&gt;In addition to some typical TIA features you also report:&lt;br&gt;Seizure&lt;br&gt;Syncope&lt;br&gt;This is an atypical presentation for TIA/Stroke. However, you also report other features that are either highly suggestive of a TIA/Stroke or indicate a potentially high risk situation. All of these factors have been taken into consideration when generating the above management advice. Nonetheless, please be aware that the diagnosis is somewhat uncertain and thus alternative diagnoses should be considered and specialist input is strongly recommended.</td>
</tr>
</tbody>
</table>

In an attempt to provide some indication of the utility of the tool in regards to diagnostic contribution and potential risk, table 25 provides proportions of patients with final specialist diagnosis (TIA/stroke or not) over initial diagnoses made by control group general practitioners, intervention group general practitioners, electronic decision support alone, and cases in which the GP final diagnosis matched the tool diagnosis.
Table 25: Proportions of patients with final specialist diagnosis (TIA/stroke or non-TIA/stroke) over generalist/tool diagnoses by treatment arm

<table>
<thead>
<tr>
<th>Generalist/tool diagnosis by treatment arm</th>
<th>Final specialist diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TIA/stroke</td>
</tr>
<tr>
<td><strong>CONTROL</strong></td>
<td></td>
</tr>
<tr>
<td>General practitioner diagnosis (%)</td>
<td>TIA/stroke</td>
</tr>
<tr>
<td>N=94</td>
<td>54/94 (57)</td>
</tr>
<tr>
<td>N=25</td>
<td>15/25 (60)</td>
</tr>
<tr>
<td><strong>INTERVENTION</strong></td>
<td></td>
</tr>
<tr>
<td>General practitioner diagnosis (%)</td>
<td>TIA/stroke</td>
</tr>
<tr>
<td>N=134</td>
<td>89/134 (66)</td>
</tr>
<tr>
<td>N=38</td>
<td>10/38 (26)</td>
</tr>
<tr>
<td><strong>INTERVENTION</strong></td>
<td></td>
</tr>
<tr>
<td>Tool diagnosis* (%)</td>
<td>TIA/stroke</td>
</tr>
<tr>
<td>N=97</td>
<td>60/97 (62)</td>
</tr>
<tr>
<td>N=49</td>
<td>10/49 (20)</td>
</tr>
<tr>
<td><strong>INTERVENTION</strong></td>
<td></td>
</tr>
<tr>
<td>Cases where tool &amp; GP diagnosis agreed (%)</td>
<td>TIA/stroke</td>
</tr>
<tr>
<td>N=90</td>
<td>62/90 (69)</td>
</tr>
<tr>
<td>N=23</td>
<td>2/23 (9)</td>
</tr>
</tbody>
</table>

*final electronic decision support diagnosis was only available in 146 patients. Bolded figures are positive predictive value (left column) and negative predictive value (right column).

Table 26 shows clinical details on the ten patients in the intervention group in whom the tool incorrectly questioned the diagnosis of TIA and stroke. This exploration helps to advise potential tool adjustments that may improve the tool’s diagnostic utility.
Table 26: Features of ten patients with tool identified atypical features who received a final specialist diagnosis of TIA or stroke

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Symptoms (GP notes)</th>
<th>resolved</th>
<th>BP</th>
<th>ABCD 2</th>
<th>High Risk</th>
<th>Symptoms (tool)</th>
<th>Tool Diagnosis</th>
<th>Tool Triage</th>
<th>Triage destination by GP</th>
<th>Final Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>66</td>
<td>M</td>
<td>“Blurred speech”</td>
<td>no</td>
<td>142/92</td>
<td>4</td>
<td>1</td>
<td>left arm numbness - non sudden - AF</td>
<td>non-straight forward</td>
<td>ED**</td>
<td>GP</td>
<td>TIA</td>
</tr>
<tr>
<td>75</td>
<td>M</td>
<td>“He felt weak”</td>
<td>no</td>
<td>220/84</td>
<td>6</td>
<td>1</td>
<td>right arm weakness - non sudden - AF</td>
<td>non-straight forward</td>
<td>ED</td>
<td>ED</td>
<td>TIA</td>
</tr>
<tr>
<td>70</td>
<td>F</td>
<td>“Shaking, nausea, loss of balance, feeling of impending doom”</td>
<td>no</td>
<td>140/80</td>
<td>4</td>
<td>1</td>
<td>loss of balance</td>
<td>non-straight forward</td>
<td>Other**</td>
<td>TIA Clinic</td>
<td>TIA</td>
</tr>
<tr>
<td>71</td>
<td>M</td>
<td>“R arm feel numb”</td>
<td>no</td>
<td>140/70</td>
<td>4</td>
<td>1</td>
<td>right arm numbness - non sudden</td>
<td>non-straight forward</td>
<td>ED</td>
<td>ED</td>
<td>TIA</td>
</tr>
<tr>
<td>82</td>
<td>M</td>
<td>“Left numbness, blurred vision, history of migraine, recent change in BP meds, bleeding gastric ulcer”</td>
<td>yes</td>
<td>110/64</td>
<td>2</td>
<td>0</td>
<td>bilateral blurred vision and left numbness</td>
<td>Symptoms not consistent with TIA</td>
<td>other</td>
<td>TIA Clinic</td>
<td>Stroke</td>
</tr>
<tr>
<td>84</td>
<td>M</td>
<td>“Short term memory problems”</td>
<td>yes</td>
<td>130/80</td>
<td>4</td>
<td>0</td>
<td>confusion, memory loss, ataxia, loss of balance - 2 months ago</td>
<td>Symptoms not consistent with TIA</td>
<td>Other</td>
<td>TIA Clinic</td>
<td>Stroke</td>
</tr>
<tr>
<td>83</td>
<td>F</td>
<td>“Shimmering visual aura both eyes, jaggedly lines, then large whole and headache”</td>
<td>yes</td>
<td>148/80</td>
<td>3</td>
<td>0</td>
<td>scintillating scotoma and ataxia</td>
<td>Symptoms not consistent with TIA</td>
<td>Other</td>
<td>TIA Clinic</td>
<td>TIA</td>
</tr>
<tr>
<td>79</td>
<td>F</td>
<td>“Felt heady, no control over legs; they felt tingly, like jelly in legs - felt to floor, giddy and blurry vision”</td>
<td>yes</td>
<td>190/92</td>
<td>6</td>
<td>1</td>
<td>left weakness, presyncope</td>
<td>TIA with unusual symptoms</td>
<td>ED</td>
<td>ED</td>
<td>TIA</td>
</tr>
<tr>
<td>78</td>
<td>F</td>
<td>“Right leg didn’t feel right”</td>
<td>yes</td>
<td>148/80</td>
<td>6</td>
<td>1</td>
<td>right weakness, presyncope</td>
<td>TIA with unusual symptoms</td>
<td>ED</td>
<td>GP</td>
<td>TIA</td>
</tr>
<tr>
<td>49</td>
<td>F</td>
<td>“Difficulty finding words and identifying family, associated/fuzzy vision, followed by headache”</td>
<td>yes</td>
<td>142/78</td>
<td>4</td>
<td>1</td>
<td>bilateral blurred vision, left numbness</td>
<td>TIA with unusual symptoms</td>
<td>ED</td>
<td>TIA Clinic</td>
<td>TIA</td>
</tr>
</tbody>
</table>

§GP=general practitioner; *’Other’ indicates multiple options for general practitioner to choose from based on their best diagnosis. **ED=emergency department – and indicates that the tool recommended emergency department referral due to presence of high risk factors despite atypical features.

General practitioner diagnostic accuracy is particularly relevant when the general practitioner decides not to refer the patient for a specialist opinion. Because the electronic decision support tool offers general practitioners in the intervention group the option to manage TIA patients in the community it is of particular concern to know that these patients did indeed suffer a TIA. Similarly, some patients who receive a final general practitioner diagnosis of non-TIA are never referred to a specialist and if this diagnosis is incorrect the patient is at risk of developing a stroke. Table 27 focuses on patients never referred for specialist review.
Table 27: Patients who underwent community work-up without specialist input

<table>
<thead>
<tr>
<th>General practitioner final diagnosis</th>
<th>Final specialist diagnosis</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TIA/stroke</td>
<td>NON TIA/stroke</td>
<td></td>
</tr>
<tr>
<td>Control N=24</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIA/Stroke N=0</td>
<td>0/0 (n/a)</td>
<td>0/0 (n/a)</td>
<td></td>
</tr>
<tr>
<td>Non-TIA/Stroke N=24</td>
<td>14/24 (58)</td>
<td>10/24 (42)</td>
<td></td>
</tr>
<tr>
<td>Intervention N=44</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIA/Stroke N=29</td>
<td>23/29 (79)</td>
<td>6/29 (21)</td>
<td></td>
</tr>
<tr>
<td>Non-TIA/Stroke N=15</td>
<td>1/15 (7)</td>
<td>14/15 (93)</td>
<td></td>
</tr>
</tbody>
</table>

*Numbers in bold represent positive (left column) and negative (right column) predictive value of general practitioner diagnosis with the aid of electronic decision support (control) and with support (intervention).

3.5.3. Impact of general practitioner training

Prior to begin of the trial enrollment period all participating general practitioners were invited to attend an education session on TIA management.

Of the 181 general practitioners who enrolled patients into the study 79 (43.7%) attended the training session. Of the 291 patients included in the analysis 140 (48.1%) received care from general practitioners who attended training sessions. Guideline adherence was not overall greater among general practitioners who had attended training (61/140, 44%) compared with those who did not (85/151, 56.3%). Outcome events were slightly more common in patients managed by general practitioners without training (table 28).
Table 28: Guideline adherence and 90-day cerebrovascular/vascular risk in patients managed by general practitioners who attended a pre-trial TIA training session compared with those managed by general practitioners who did not attend the training session

<table>
<thead>
<tr>
<th></th>
<th>Training N=140</th>
<th>No Training N=151</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline adherence</td>
<td>61/140 (43.6)</td>
<td>85/151 (56.3)</td>
</tr>
<tr>
<td>Stroke at 90 days</td>
<td>2/140 (1.4)</td>
<td>5/151 (3.3)</td>
</tr>
<tr>
<td>TIA or stroke at 90 days</td>
<td>6/151 (4.3)</td>
<td>8/140 (5.3)</td>
</tr>
<tr>
<td>Vascular event or death at 90 days</td>
<td>9/140 (6.4)</td>
<td>11/151 (7.3)</td>
</tr>
</tbody>
</table>

Training and electronic decision support may convey an additive effect and relevant figures are displayed in table 29.

Table 29: Guideline adherence and efficacy outcome event rates stratified by training plus/minus electronic decision support use

<table>
<thead>
<tr>
<th></th>
<th>Intervention N=172</th>
<th>Control N=119</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Training plus tool N=71</td>
<td>Tool without training N=101</td>
</tr>
<tr>
<td>Guideline adherence</td>
<td>38/71 (53.5)</td>
<td>65/101 (64.4)</td>
</tr>
<tr>
<td>Stroke at 90 days</td>
<td>0/71 (0%)</td>
<td>2/101 (2.0)</td>
</tr>
<tr>
<td>TIA or stroke at 90 days</td>
<td>0/71 (0%)</td>
<td>4/101 (4.0)</td>
</tr>
<tr>
<td>Vascular event or death at 90 days</td>
<td>1/71 (1.4%)</td>
<td>6/101 (5.9)</td>
</tr>
</tbody>
</table>

3.5.4. Risk stratification to predict stroke recurrence

3.5.4.1. Introduction

The New Zealand TIA Guidelines²⁷ in part rely on the ABCD2 risk score for risk assignment. In addition to the score the guideline incorporates several other factors indicating high risk: atrial fibrillation, anticoagulation, crescendo TIAs (more than one even over past seven days), and ongoing symptoms (i.e. possible stroke). This risk particular approach not been previously validated.

Although the ABCD2 score has been validated it has also been criticised because in some settings it does not reliably predict early stroke recurrence.¹¹⁶,¹¹⁷ The FASTEST trial was not designed to assess the validity of the ABCD2 score or the enhanced risk
stratification promoted by the guideline however this issue can be explored in the dataset.

3.5.4.2. **Guideline Risk Stratification**

In the total study group 192/291 (66.0%) were classed as ‘high risk’ and 99/291 (34.0%) as ‘low risk’ by New Zealand TIA Guideline criteria (see section 1.1.7). Of the seven total stroke recurrences that occurred within 90 days of first point of contact six were classed as ‘high risk’ resulting in a ‘high risk’ 90-day stroke rate of 3.1% (95% CI 1.1-6.7) and one patient was ‘low risk’ resulting in a ‘low-risk’ 90 day stroke rate of 1.0% (95% CI 0.02-5.5). The patients classed as ‘high risk’ received this category for the following reasons: atrial fibrillation (n=2), isolated high ABCD2 score (n=1), high ABCD2 and ongoing symptoms (n=3). The one ‘low risk’ patient who suffered a stroke had an ABCD2 score of 2 (for age and duration) and suffered a stroke within six days of initial assessment while awaiting outpatient TIA clinic review. This patient has previously been discussed (section 3.4.4). This patient’s risk was further increased because he had a recent gastrointestinal bleed and thus could not tolerate antiplatelet medications – something not captured in either risk stratification system. Whether his stroke could have been prevented through earlier specialist assessment is not known.

3.5.4.3. **ABCD2 Risk Stratification**

An ABCD2 score could be calculated for 252 patients. In 39 patients either the initial blood pressure or the symptom duration was not clearly documented. Using the ABCD2 score to divide patients into ‘high’ and ‘low risk’ results in 113/252 (38.8%) ‘low risk’ (ABCD2 0 to 3) and 139/252 (55.2%) ‘high risk’ (ABCD2 4 to 7) patients.

Of the 7/291 FASTEST patients having strokes during the 90 day follow-up period four had a high ABCD2 and three a low ABCD2 score. No stroke occurred between 0 and 48 hours of initial presentation. One stroke occurred between 48 hours and 7 days of presentation (a ‘low risk’ patient) and six strokes occurred between 7 and 90 days of initial presentation.
In this study the seven day stroke risk for low risk patients was 1/113 (0.9%; 95% CI 0.2-4.8) and 90 day stroke risk is 3/113 (2.7%; 95% CI 0.6-7.6). This compares to published figures for these two groups of respectively 1.2% and 3.1%. The seven day stroke risk for ‘high risk’, ABCD2 scores of >3, patients is 0/139 (0%; one-sided 97.5% CI 3.0%) and 90 day stroke risk 4/139 (2.9%; 95% CI 0.8-7.2).

Tables 30 and 31 show risk by individual score and a comparison between the ABCD2 score published prediction and actual figures from the FASTEST trial stratified by ABCD2 score alone and the enhanced stratification recommended by the New Zealand TIA Guideline stratification system.

**Table 30: 90-Day Stroke Risk by ABCD2 score in FASTEST patients**

<table>
<thead>
<tr>
<th>ABCD2 score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>n/a</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>5</td>
<td>11</td>
<td>42</td>
<td>55</td>
<td>57</td>
<td>44</td>
<td>30</td>
<td>8</td>
<td>39</td>
<td>291</td>
</tr>
<tr>
<td>Stroke at 90 days (n)</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>90 day stroke risk</td>
<td>0%</td>
<td>0%</td>
<td>4.8%</td>
<td>1.8%</td>
<td>3.5%</td>
<td>0%</td>
<td>6.7%</td>
<td>0%</td>
<td>0%</td>
<td>2.4%</td>
</tr>
</tbody>
</table>

**Table 31: 90-Day Stroke Risk by Risk Category comparing ABCD2 score alone with New Zealand Guideline criteria**

<table>
<thead>
<tr>
<th></th>
<th>Low risk (ABCD2 0-3)</th>
<th>Medium Risk* (ABCD2 4-5)</th>
<th>High Risk (ABCD2 6-7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of total in respective risk category</td>
<td>34%</td>
<td>45%</td>
<td>21%</td>
</tr>
<tr>
<td>ABCD2 Predicted Stroke Risk</td>
<td>3.1%</td>
<td>9.8%</td>
<td>17.8%</td>
</tr>
<tr>
<td>% of total (FASTEST) in respective risk category</td>
<td>45%</td>
<td>44%</td>
<td>15%</td>
</tr>
<tr>
<td>FASTEST Observed (ABCD2 only) (95% CI)</td>
<td>2.7% (0.6-7.6)</td>
<td>2.0% (0.2-6.9)</td>
<td>5.3% (0.6-17.8)</td>
</tr>
<tr>
<td>FASTEST Observed (ABCD2 only)* (95% CI)</td>
<td>2.7% (0.6-7.5)</td>
<td>2.9% (0.8-7.2)</td>
<td></td>
</tr>
<tr>
<td>FASTEST Observed (Guideline Criteria) (95% CI)</td>
<td>1.0% (0.02-5.5%)</td>
<td>3.1% (1.1-6.7%)</td>
<td></td>
</tr>
</tbody>
</table>

*In the validation studies a ‘medium risk’ group is included and data for a combined ‘high risk’ group is not provided. For comparison purposes data is shown both separated into two and three groups in the table above.
Some previously discussed TIA trials (section 1.1.5.) compared their 90-day stroke rates to those predicted by the ABCD2 validation score. In the FASTEST study it was possible to calculate an ABCD2 score for 129 patients in the intervention group. Based on ABCD2 score prediction 9.3 of these 129 patients should have experienced a stroke within 90 days (7.2%). This compares to 2/129 (1.6%) of actual strokes observed in the intervention group. Calculating the 90-day stroke risk for all patients for whom an ABCD2 score could be calculated (n=252) the predicted stroke risk for the FASTEST population would have been 20/252 (7.9%). There were fewer high risk TIAs in the FASTEST sample (38/252; 15%) than were reported in the ABCD2 validation study (21%). Had the distribution of scores been the same in both study populations the overall stroke rate in the FASTEST study, based on ABCD2 score alone would have been expected to be 23/252 or 9.2%.

3.5.5. Ethnicity

3.5.5.1. Introduction

Stroke and TIA has been reported to occur at a younger age in Māori and Pacific Islander residing in the greater Auckland region. Data from outside of the greater Auckland region on ethnic differences in TIA and stroke are lacking.

The FASTEST trial protocol included an adjustment of the ABCD2 score to account for the reported age disparity in stroke incidence. If patients of Māori and Pacific Island origin were entered into the tool they scored an ‘age’ point on the ABCD2 risk stratification system if they were 50 and older in contrast to the published criteria of 60 and older.

Sections 3.5.5.2 and 3.5.4.3 describe FASTEST trial results stratified by ethnicity and findings relating to the adjusted ABCD2 score.
3.5.5.2. Ethnic Stratification

Ethnic data were available for 289 out of 291 patients. Mean age differed between groups with Māori and Pacific patients presenting at a younger age than European patients (table 32). Patients’ of other ethnic origin had ‘other’ listed in their medical records without any further description. There were no patients of confirmed Asian, African, or American descent in this data set. Table 32 also shows study outcomes stratified by ethnic origin.

Table 32: Study outcomes stratified by ethnic origin

<table>
<thead>
<tr>
<th></th>
<th>European</th>
<th>Māori</th>
<th>Pacifika</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number enrolled</td>
<td>257</td>
<td>24</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Mean Age (SD)</td>
<td>72.2 (12.8)</td>
<td>57.1 (15.3)</td>
<td>59 (1.4)</td>
<td>65 (1.4)</td>
</tr>
<tr>
<td>TIA/stroke confirmed n/n (%)</td>
<td>152/257 (59.1%)</td>
<td>10/24 (41.7%)</td>
<td>2/2 (100%)</td>
<td>3/6 (50%)</td>
</tr>
<tr>
<td>High Risk n/n (%)</td>
<td>167/257 (65.0%)</td>
<td>17/24 (70.1%)</td>
<td>1/2 (50%)</td>
<td>6/6 (100%)</td>
</tr>
<tr>
<td>Guideline Adherence n/n (%)</td>
<td>132/257 (51.4%)</td>
<td>12/24 (50%)</td>
<td>0/2 (0%)</td>
<td>1/6 (16.7%)</td>
</tr>
<tr>
<td>Behavioural Counseling n/n (%)</td>
<td>77/257 (30%)</td>
<td>6/18 (25%)</td>
<td>1/2 (50%)</td>
<td>2/6 (33.3%)</td>
</tr>
<tr>
<td>Mean Treatment cost (SD)</td>
<td>$3033 (3953)</td>
<td>$2537 (2339)</td>
<td>$5807 (6552)</td>
<td>$2761 (2659)</td>
</tr>
<tr>
<td>90 day stroke n/n (%)</td>
<td>5/257 (2.7%)</td>
<td>0/24 (0%)</td>
<td>0/2 (0%)</td>
<td>0/6 (0%)</td>
</tr>
<tr>
<td>90 day vascular event n/n (%)</td>
<td>19/257 (7.4%)</td>
<td>0/24 (0%)</td>
<td>1/2 (50%)</td>
<td>0/6 (0%)</td>
</tr>
</tbody>
</table>

3.5.5.3. Ethnic adjusted ABCD2 score

Out of the 26 enrolled Māori or Pacific patients eleven were in the intervention group and three of these were aged between 50 and 60 years. Two had an increase in score from 2 to 3 although one was already classed as ‘high risk’ because of ongoing symptoms. Neither of these two patients received a final specialist diagnosis of TIA or stroke. The third patient's score increased from 3 to 4 and thus would have experienced a change in triage category (ABCD2 ≥4 = ‘high risk’) except that he also had ongoing symptoms and was already classed as ‘high risk’ on that basis. This patient was urgently referred to the emergency department, did receive a final diagnosis of TIA and underwent urgent carotid endarterectomy without suffering any further event. In other words, the adjusted scoring system in the tool did not cause any change in advice or management in this data set. None of these patients experienced an outcome event.
Of the 15 Maori/Pacific control patients two were aged between 50 and 60 years. If applying the adjusted ABCD2 score retrospectively to these two patients they would have moved from 0 to 1 and 6 to 7. Neither of these changes would have caused a change in management per the guidelines.

3.5.6. General practitioner imaging access

3.5.6.1. Introduction

As an incentive for general practitioner uptake the electronic decision support tool offers general practitioners rapid access to head CT and carotid imaging if they complete the tool and the tool recommends these investigations.

Giving general practitioners access to investigations generally reserved to specialists risks oversubscription potentially resulting in reduced access to these investigations by specialists. The next section describes pattern of use of this privilege within the FASTEST data set.

3.5.6.2. Imaging utilisation

General practitioners requested carotid ultrasound for 15/291 patients (5.2%) and head CT in 19/291 (6.5%) of study patients. Not all requests came from intervention practices: 5/15 (33%) ultrasound and 1/19 (5%) head CT requests came from control group general practitioners. Carotid ultrasound is accessible to general practitioners in some of the participating districts although it is unclear how the one head CT request was actioned from within a control practice without clear specialist approval.

3.5.6.3. Appropriateness of requests

Of the 15 patients referred for ultrasound 14 (93%) had a final diagnosis of cerebrovascular disease and 12 (80%) had symptoms consistent with anterior circulation pathology.

Of the five control patients two had clear posterior circulation symptoms (40%) and probably did not require an ultrasound for this reason. Of the 10 intervention patients one (10%) had pure posterior circulation symptoms.
All 19 patients sent for head CT were reasonable candidates for CT based on the initial general practitioner documented symptoms and 14/19 (74%) received a final diagnosis of TIA or stroke from a specialist.

3.6. Trial registration
ACTRN12611000792921

3.7. Funding
New Zealand Health Research Council 11/268 (Appendix VI)

3.8. Ethics
New Zealand Health and Disability Ethic Committee
URA/11/08/048 (Appendix VII)
Chapter 4: Discussion

4.1. FASTEST trial

Section 4.1 discusses the results of the FASTEST trial presented in chapter 3, sections 3.4 and 3.5.

4.1.1. Efficacy

Section 4.1.1 discusses results presented in section 3.4.3.

4.1.1.1. Guideline adherence

The FASTEST trial provides firm evidence that the TIA/Stroke electronic decision support tool increases adherence of general practitioners to New Zealand TIA Guidelines. Effective implementation of the New Zealand TIA Guidelines in primary care is the main purpose of the tool (section 2.2) and this trial shows that the tool effectively delivers on this aim.

That being said, while the difference between groups was profound, the observed guideline adherence of 41% in the control group exceeded the anticipated rate of 33% and the observed rate of 76% in the intervention group did not quite reach the anticipated 90%. The anticipated figures were based on earlier simulated exercises conducted as part of the validation study (see section 2.3) comparing TIA management among several clinician groups and the tool. The higher than expected rate of guideline adherence in the control group might have been attributed to the training session conducted at the beginning of the study, but no association between training attendance and control group guideline adherence (section 3.5.3) was observed making this assertion an unlikely explanation. Another possible explanation is that in a simulated patient encounter doctors may be less engaged than during a real-life consultation and so more thought and effort may go into actual clinical decision making. There may also have been an overall improvement in general practitioner TIA guideline awareness and management skills over the time frame between the validation study and the FASTEST trial. Lastly, the Hawthorne effect (i.e. better performance because of the knowledge that one is being observed) may have played a role.

The lower than expected rate of guideline adherence in the intervention group may be explained by the following. General practitioners did not always follow the advice
provided by the tool and adherence would have been greater (81%) if they had, as shown in section 3.4.8. Inappropriate advice by the tool is possible and section 3.5.2 showed that the diagnostic assistant component of the tool did not always result in accurate general practitioner diagnoses, which in rare cases affected subsequent management. General practitioners also did not always correctly enter clinical information into the tool so the derived advice was then inaccurate. Lastly, in some cases it may in fact be more appropriate not to follow clinical guidelines. Clinical guidelines are intended to assist and not replace clinical judgement and they may not be applicable to all real life clinical situations.

Guideline adherence is a complex outcome (defined in section 3.3.4). Section 3.4.8 presents more information about the components of the guideline adherence composite outcome. Exploration of individual components may provide insights into which measures may be most important (e.g. achievement of particular investigations or initiation of individual preventive medications and/or the time frame to achieving these measures).

This trial was not designed to detect clinically significant differences in the proportions of achieving individual components of the guideline adherence composite outcome nor the differences in time to diagnostic testing or initiation of medication. In addition, it is not clear how the size of clinically relevant differences could be defined. Nevertheless, the proportions of participants who achieved appropriate investigations were similar between randomised groups. The proportions of participants who received optimum medical and non-medical treatments were higher in the intervention group. The intervention group also had faster access to carotid imaging and earlier initiation of cholesterol lowering and anti-hypertensive medications than the control group. However, the intervention group had a slightly longer delay to CT head scans and anticoagulant therapy was more delayed compared to the control group. The delay in anticoagulation therapy may be related to the tool’s guideline based recommendation that brain imaging occurs before continuation or initiation of these drugs. This is intended to reduce the risk of bleeding complications. Overall, differences in individual components were too small to identify one or two interventions that could readily explain any differences in patient outcome events.
Although the analysis of the primary stroke outcome variable lacked statistical power to detect a difference between the intervention and control groups because of the unexpected low rate of stroke, all secondary vascular outcome assessments favoured the intervention group. If this improvement is the result of improved guideline adherence then the benefit gained could be due to a combination of factors or, alternatively it could suggest that an intervention threshold has to be reached through improvement in a number of ways. For example, antiplatelet medication may have been started sooner in some patients with a positive effect on outcomes but in other patients earlier carotid imaging may have achieved a positive outcome through a different mechanism. This means differences in the efficacy of individual components of the New Zealand TIA Guideline may not be meaningful or detectable as it is the guideline adherence as a whole that is beneficial.

In comparison to the control group of the EXPRESS study\textsuperscript{30} the FASTEST trial shows better and faster attainment of investigations and implementation of medications. This supports the assertion that TIA care overall has improved over the past seven years. Improvements are probably in response to studies like EXPRESS and the publication of the New Zealand and other international TIA guidelines\textsuperscript{27,101} that promote early secondary prevention to reduce recurrent stroke. This in turn may have affected the results discussed in section 4.1.1.3.

In section 3.4.8 an assessment of guideline adherence using different criteria is reported. The main study outcome focussed on guideline adherence in primary care because this is the target audience of the tool. Overall guideline adherence across the primary/secondary patient care continuum is less relevant to the tool but provides insight into current overall TIA Guideline adherence in New Zealand. When secondary care guideline adherence was included, the intervention group still performed better than the control group. However, overall guideline adherence was relatively poor, at less than 20% in both groups. Of the variables presented in table 23, limited access to rapid carotid imaging was a major barrier to achieving guideline adherence. This is less relevant to primary care guideline adherence because patients managed in the community were, by definition, ‘low risk’ and thus allowing carotid imaging within 7 days. This was achieved on average. The majority of patients managed in secondary care were ‘high risk’ patients who require imaging within 48 hours. Other urgent interventions were more reliably achieved and, in light of the finding that 90-day stroke
rates were low despite the inability to consistently achieve rapid carotid imaging, this may mean that rapid carotid imaging is less important than previously thought.

4.1.1.2. Comprehensive counselling

Section 3.4.3 also shows that implementation of comprehensive counselling (non-medical treatments) occurred more frequently in the intervention group. This area of patient management is often neglected by both generalists and specialists. Apart from smoking cessation the benefit from lifestyle counselling has not yet been clearly quantified in robust research. The effect of the other elements of comprehensive counselling on short-term patient outcomes is uncertain. Nonetheless, a healthy lifestyle is associated with overall better cardiovascular health outcomes and so lifestyle recommendations are an important aspect of secondary stroke prevention. Poor implementation of these measures may relate to the uncertainty about their effectiveness, concerns about poor patient compliance, and the time required to provide patient counselling compared with medication prescription. Counselling can be streamlined and this is a particular area where electronic tools can help by providing reminders and outlining counselling techniques for doctors. They can also offer printed patient information for reinforcement.

4.1.1.3. Early recurrent stroke risk

The second main hypothesis of the FASTEST trial was that electronic decision support associated improvement in New Zealand TIA Guideline adherence is associated with improved stroke-related patient outcomes, specifically a reduction in 90-day stroke recurrence. The point estimate for the difference in proportions of participants who had 90-day stroke recurrence favoured the intervention group, but with wide confidence intervals and a p-value of >0.05.

This can be interpreted in several ways. It may be that, in fact, adherence to the New Zealand TIA Guideline does not effectively reduce stroke recurrence, which would indicate a limitation of the Guideline rather than the tool. This is one of the reasons why direct process measures (e.g. ‘guideline adherence’) are generally favoured over more indirect patient health outcome measures (‘90-day stroke rate’) in research.
assessing the impact of interventions aimed to improve health service quality. Alternatively, the degree or nature of improved guideline adherence in the intervention study population may not have sufficed to actualise the expected guideline effect. It seems most likely, however, that because of the unexpectedly low occurrence of stroke in the control group, the failure to detect a statistically significant effect for the primary outcome variable represents a Type II error (i.e. inappropriate acceptance of the null hypothesis due to methodological factors).

At the time when the FASTEST protocol was devised the only prospectively collected study data on baseline 90-day stroke risk following TIA came from the EXPRESS and ABCD2 validation studies. Both indicated a 90-day stroke risk of around 10%. Proposed rapid specialist access TIA service models reported varying figures between 1.3-2.2% depending on their definition of ‘TIA’. Most prior studies included all potential TIA/stroke patients (akin to FASTEST ‘per protocol’ population), but some authors limited their analysis to confirmed TIA/stroke patients. These 90-day stroke estimates informed FASTEST trial sample size calculations.

The 90-day stroke rates in the FASTEST trial were 1.2% in the intervention and 4.2% in the control arm in the ‘per protocol’ analysis and 2.2% in the intervention and 7.3% in the control arm in patients with confirmed TIA/stroke. Both figures are presented to allow comparison to all relevant prior studies listed in table 3 (section 1.1.5). Comparing results to prior studies shows that the 90-day stroke rate in the FASTEST trial intervention group is similar to rates observed in the setting of TIA services that offer more urgent specialist and/or imaging access for all potential TIA patients through such mechanisms as daily open access specialist TIA walk-in clinics. What differs is the stroke rate in the control group, which was substantially lower than predicted. This indicates that the electronic decisions support tool associated improvement in guideline adherence resulted in a clinically relevant improvement in 90-day stroke rate, but that the sample size was too small to detect a significant difference because sample size calculations were based on an overestimate of 90-day stroke rate in the control group.

Had the FASTEST intervention data been merely compared to predicted stroke rates based on the ABCD2 score akin to prior assessments of TIA service models the 90-day stroke risk reduction would have seemed more dramatic. As discussed in section 3.5.4 a reliable ABCD2 score could be calculated on 129 intervention participants of whom two suffered a stroke (1.6%). The anticipated number of participants in the ‘per-
protocol’ population who should have had a stroke based on the ABCD2 adjusted stroke risk was 7.2%. The difference between this anticipated rate of 7.2% compared to the observed rate of 1.6%, is similar to that reported in the SOS-TIA study, which proposed 24/7 rapid access stroke clinics staffed by stroke neurologists around the clock, and would have achieved a p-value of 0.02.

The lower than expected stroke rate in the control group could be related to an overall improvement in primary care stroke and vascular disease prevention. Table 9 (section 3.4.2) describes patient baseline characteristics and shows that many patients in the study sample were already taking relevant medications for secondary prevention. Widespread dissemination and availability of studies such as EXPRESS and the New Zealand TIA Guidelines in 2007 and 2008 may also have contributed to improved background knowledge and practice in the control group, even without the use of an electronic decision support tool. Both of these prior reports promote implementation of early secondary prevention. This was already present then before randomisation in the study sample.

It is possible also that the randomisation may not have been particularly effective in producing two clearly separated sets of clinician practice. In particular the control group may have had superior performance than might otherwise be anticipated because of training or knowledge that their performance in stroke prevention was monitored, as a form of the ‘Hawthorne’ effect. An exploratory analysis stratifying the control group by whether training had been attended (see section 3.5.3) did, however, not find an association.

Regardless of the reason for the control group’s 90 day stroke risk being lower than anticipated, the intervention group’s 90-day stroke rate in confirmed TIA/stroke patients was 2.2%, nearly identical to the 2.1% rate reported with same day open access specialist TIA clinics. This suggests that primary care physician initiated management with the aid of the TIA/Stroke decision support tool may achieve a similar 90-day stroke rate to daily specialist clinics.

4.1.1.4. Risk of recurrent cerebrovascular and vascular events

All secondary outcomes favoured the intervention group. The reduced cerebrovascular and vascular event rates indicate that the TIA/Stroke electronic decision support tool
positively affects patient outcomes and underscores the assertion in section 4.1.1.3 that
the tool probably does provide important benefit as regards stroke risk reduction, but
not to the degree that was anticipated when the study’s sample size was planned.

4.1.2. Safety

This section discusses results presented in section 3.4.4.

The adverse event rate was similar between the two groups. Most adverse events
related to medication side effects. The similarity in adverse event rate between study
groups provides reassurance that use of the tool did not trigger excessive introduction of
medical therapies that resulted in poor patient outcomes due to adverse medication
effects. In general, none of the observed adverse reactions were serious in nature and
they were all reversed upon discontinuation of the medication.

One adverse event in the intervention group described an unfavourable patient outcome
that may have been related to the use of the tool and was not medication related. The
incident, a fatal stroke, raises several issues.

Firstly, it highlights that low ABCD2 scores can miss high risk patients. Others have
made similar observations.\textsuperscript{116,117,123} No predictive tool can be expected to be perfect and
the overall rate of stroke in patients with a low ABCD2 score was only 2.4\% - too low
to justify hospital admission for all of these patients based on cost-effectiveness
data.\textsuperscript{47,48} With the additional New Zealand TIA Guideline criteria, the 90 day stroke
risk of ‘low risk’ patients was only 1.0\%. Although the population risk is low a death is
still an important outcome for affected individuals, their families, and their health
practitioners. Translating population and cost-effectiveness data to individual patient
treatment decisions is challenging. That many other patients benefit from health care
based on the average patient often provides little comfort in this situation. This signifies
an obligation to continually improve prioritisation techniques to optimise them as much
as possible. However, it has to be kept in mind that the prioritisation ‘error’ was in
accordance with current best practice guidelines and was therefore not a failure of the
TIA/Stroke tool, which merely aims to apply these guidelines, but rather a failure of the
guidelines themselves. Appropriateness of risk stratification is further discussed in
section 4.1.5.3.

Secondly, this case highlights the challenges of interpreting TIA symptoms and
neurological complaints in general. The GP did misinterpret one of the presenting
complaints and while this is unlikely to have significantly affected the outcome it has offered an area for potential improvement in the tool algorithm. This information has already informed software updates. Diagnostic aspects of the tool are further discussed in section 4.1.5.1 and software updates in section 4.4.

For the FASTEST trial, recurrent strokes or other vascular events in the control group that were unrelated to medication side effects were not included under adverse patient outcomes. Most participants in the control group did not receive guideline adherent care and sub-optimal general practitioner management decisions may well have contributed to some of the control group 90-day stroke and vascular events. And despite the previously discussed death the overall the death rate was higher in the control group (2.5%) than the intervention group (1.2%) (table 22; section 3.4.8). However, the purpose of adverse event reporting was neither to re-report the rate of recurrent stroke, vascular, or death events nor to re-report degree of guideline adherence. Instead this safety outcome examined additional adverse events and focused on any potential harm that the tool may have inflicted. As there was no tool exposure in the control group there was also no risk of contribution of the tool to adverse patient outcomes.

### 4.1.3. Treatment cost

This section discusses results presented in section 3.4.5.

Cost data analysis indicates that use of the electronic decision support tool is associated with reduced average per patient treatment cost. The cost stratification analysis is presented as supplementary information (table 23; section 3.4.8) and shows that hospitalisation related costs constitute the main difference between the study groups. Most hospitalisation costs were due to the index events with lesser contribution from subsequent hospitalisation due to outcome events or carotid endarterectomies. In all of these categories the control group patients incurred higher costs. By contrast, general practitioner visits and, of course, electronic support tool costs were higher in the intervention group.

The higher initial hospital cost is explained by a higher proportion of patients referred urgently to secondary care than was necessary based on risk indicators. The overall proportion of high risk patients was the same in both groups. All high risk patients should be admitted to hospital. If all admissions were appropriate the average initial
hospitalisation cost in both study groups should be similar. If it is not it suggests that either some low risk or non-TIA patients in the control group were unnecessarily admitted or that some high risk patients in the intervention group were inappropriately managed as outpatients. There was a lower risk of recurrent strokes and vascular events and higher rate of guideline adherence in the intervention group so it is reasonable to assume that the higher initial hospitalisation costs in the control group represent inappropriate admissions rather than the reverse.

The high costs due to ‘outcome related’ hospitalisations are explained by a beneficial effect of the tool in reducing recurrence rates unless the difference in recurrence rate was due purely to chance or other unknown factors.

The higher cost related to endarterectomy in the control group without an associated drop in outcome events could indicate that some of these interventions were inappropriate, that the risk of surgery outweighed any benefits, or that there was a chance imbalance between treatment arms that is too small to draw firm conclusions. The carotid ultrasound findings of the seven patients who underwent carotid endarterectomy showed that five had high-grade (70-99%) and five had moderate (50-69%) carotid stenosis. All seven had a final diagnosis of TIA or stroke. One surgery was performed late (49 days after the event) and one patient suffered a complication. The evidence to support the utility of carotid endarterectomy in light of ever increasing efficacy of medical treatments is a current topic of debate. The overall low rate of carotid endarterectomy in the FASTEST trial makes it difficult to draw firm conclusions, but also makes it unlikely that the contribution of this potential imbalance markedly impacted on overall average treatment costs. To assess the impact of carotid endarterectomy, average costs were compared removing this item and the intervention group average expenses remained significantly lower.

In summary, the observed cost savings in both initial and recurrent outcome event related hospitalisations can be explained by a positive effect of the TIA/Stroke electronic decision support tool. The cost savings related to fewer carotid endarterectomies in the intervention group did not significantly impact the overall results and could either be due to chance or could indicate that carotid endarterectomy was not the most cost-effective management choice in some of these patients. Exploring clinical details around New Zealand patients undergoing carotid
endarterectomy to assess cost-effectiveness in a larger sample could form a useful future project.

4.1.4. User feedback

This section discusses results presented in section 3.4.7. Specialist and general practitioner feedback was positive. The feedback about the potential utility of the tool was very favourable among doctors who had used the tool. All indicated that they would use the tool again, if it was available after the study was completed, and most indicated that they would use it ‘all the time.’ By contrast enthusiasm about potential utility among control practice general practitioners who were not familiar with the tool was more guarded. This suggests a potential barrier to initial uptake.

Most users felt that the tool improved patient care, but the effect on work efficiency was seen as neutral. Use of the tool frequently triggers a more comprehensive management plan than would otherwise be pursued. While this is good for the patient it will inadvertently reduce the general practitioners’ speed in managing their total workload. This may explain some of the reported reduction in efficiency. Some users felt that, despite the development team’s efforts, work flow could be improved. In response to this feedback further software updates are currently underway. In particular, the next update will require fewer screen transitions and enhanced functionality and speed when moving between screens.

Specialists were all supportive of the tool and noted improved general practitioner management when the tool was used. No patient complaints were received and no other problems were encountered. The specialists welcomed greater general practitioner involvement and thought that the use of the tool facilitated this. They also supported general practitioner direct access to diagnostics including head CT and seemed more comfortable with this in the setting of the tool which could help as a gate keeper.

4.1.5. Exploratory analyses

This section discusses the exploratory analyses presented in section 3.5. Intended goals of the FASTEST trial are comprehensively discussed in section 4.1. The discussion in this present section centres on additional knowledge that was gained from the trial data.
This information may serve to generate future hypotheses relating to TIA electronic decision support, TIA management in general, and also aspects of general practice policy in more general terms.

4.1.5.1. Diagnostic accuracy

This section discusses information presented in section 3.5.2.

One of the intended features of the electronic decision support tool is to help general practitioners make an accurate diagnosis for TIA/stroke versus non-TIA/stroke. Diagnostic accuracy is important to ensure that patients access the care they need in a timely fashion. Patients incorrectly diagnosed with a TIA/stroke may be exposed to investigations and treatments that are unnecessary and may even be harmful. At the same time implementation of more appropriate interventions aimed at the true diagnosis may be delayed. In addition, referral of non-TIAs/strokes to stroke services unnecessarily burdens these services, potentially impacting the care of true TIA/stroke patients. Conversely, patients inappropriately diagnosed as non-TIA/stroke may experience delays or even complete omission of appropriate stroke preventive therapies and might suffer a subsequent recurrent stroke, other vascular event, or even death.

However, as discussed in section 1.1.5 diagnosing TIA and stroke is difficult and some have argued that all patients referred with potential TIA/stroke should be referred to a specialist because missing a TIA poses significantly greater harm than referring a non-TIA patient. This is the approach endorsed by cardiologists in the setting of acute chest pain. As a result the evaluation of chest pain has become a substantial burden on the health sector and this is despite the fact that the associated risk of myocardial infarction is lower than the risk of stroke following a TIA.

Specialists who promote universal hospital referral for certain symptoms may not fully appreciate that general practitioners make diagnostic and risk stratification decisions every day and tables 25 and 27 (section 3.5.2) demonstrate that this occurs whether they have access to a decision support tool or not. The reality of general practice is that referral of everyone with discomfort in the upper torso or a ‘funny turn’ is simply not appropriate. Making these types of decisions is exactly what general practitioners do all the time. Tables 25 and 27 (section 3.5.2) also show that the TIA/Stroke electronic decision support tool can help to improve general practitioner diagnostic accuracy and
thereby improve optimum patient triage. Diagnostic support goes both ways: it not only reduces referral of TIA mimics, but can also increase referral of actual TIAs.

Exploration of the 5.8% of patients with a final diagnosis of TIA/stroke in whom the tool indicated atypical features has provided insight into areas of potential tool improvement. This has resulted in three subtle changes during a post-FASTEST trial software update discussed in detail section 4.4 below.

4.1.5.2. Impact of general practitioner training

This section discusses information presented in section 3.5.3.

As part of the trial design general practitioners were invited to attend a training session on ‘TIA Management in Primary Care.’ The candidate offered centralised training in Hastings, New Plymouth, and Dunedin. General practitioners practicing in remote areas found it difficult to attend these centralised training sessions. Therefore, the candidate also travelled to Wairoa, Stratford, Patea, Balclutha, Alexandra, Wanaka, and Queenstown to offer training sessions in individual practices.

While it was anticipated that these training sessions may impact the study power by contributing in itself to an overall reduced stroke rate, an analysis of this impact was not one of the pre-specified study outcomes.

The exploratory analysis indicates that training sessions alone did not have a major impact on either guideline adherence or outcome events. However, there appears to have been an additive effect when general practitioners used the electronic decision support tool AND attended the training session. This suggests that the information communicated in the training session may have required subsequent reinforcement through the tool in order to achieve maximal impact. This is an assertion that will have to be explored further in a properly designed study and to this end it would be valuable to pre-specify the impact of training on the effect of electronic decision support tools in future clinical trials. Because a significant impact of training on the FASTEST trial results cannot be excluded, further roll-out of the tool should probably be combined with training sessions routinely wherever possible.
4.1.5.3. Risk stratification

This section discusses information presented in section 3.5.4.

The ABCD2 score has been criticised and the New Zealand TIA Guideline criteria have not been subjected to rigorous evidence testing. The FASTEST trial analysis of these risk indicators can be interpreted in two ways. The overall risk of stroke was very low in the intervention group where guideline adherence was high. This suggests that the currently used scoring systems provide a reasonable aid in the effort to reduce recurrent stroke following a TIA. Alternatively, one could argue that especially the ABCD2 score, but also the New Zealand TIA Guidelines, are imperfect at predicting early stroke recurrence and require further refinement.

Such refinement has been attempted and new scores are now available including the ABCD3, ABCD3-I, and other scores. The ABCD3 incorporates ‘dual events,’ a feature already covered by the New Zealand TIA Guideline criteria. The other scores all include early imaging and their predictive value is only minimally improved over the ABCD2 or ABCD3 scores. Obtaining imaging at first point of contact to allow triaging to take place requires hyper-urgent hospital level care, which in the candidate’s mind obviates the need for a triage score. One consideration may be the addition of auscultation for a carotid bruit, which can help to predict critical carotid stenosis, as a further indicator for high risk patients. Ongoing work will be required to further optimise TIA triage in the New Zealand health setting although it has to be said that while there is always room for improvement overall the New Zealand TIA Guidelines have performed very well.

4.1.5.4. Ethnic differences

This section discusses information presented in section 3.5.5.

In general terms ethnic differences in cerebrovascular disease occur worldwide. Auckland researchers have shown that Māori and Pacific patients experience stroke at a younger age. Non-urban New Zealand data, from outside the greater Auckland region, are not available. The FASTEST trial results confirm that Māori and Pacific patients outside of the greater Auckland region present at a younger age. Equity of access is an ongoing concern. It is encouraging that the 90-day stroke risk in Māori and
Pacific people in the FASTEST sample was zero, suggesting that care is not inferior. Guideline adherence was also similar and the higher rate of patients with a final diagnosis of non-TIA/stroke suggests that the threshold for concern is not lower in the non-Pakeha population. In general, due to the small number of Māori and Pacific people in the study findings have to be interpreted with caution. Further work in assessing stroke and TIA patterns in the Māori and Pacific population, including those residing in more rural areas is needed.

The electronic decision support tool utilised a Māori/Pacific adjusted ABCD2 risk score. While this score adjustment did not lead to any changes in patient management it also did not categorise patients inappropriately to high risk categories and may thus be worth considering for further use.

4.1.5.5. General practitioner imaging access

This section discusses information presented in section 3.5.6. As part of the trial, use of the tool allowed general practitioners imaging access in select cases. This was arranged in different ways in the four participating district health boards. In some areas general practitioners accessed public services, fully funded by the hospital (Hawke’s Bay and Whanganui). In another they accessed a private provider with partial funding through their primary health organisation (Southern), and one district health board contracts a private provider for all imaging and trial-associated radiological investigations were exclusively funded through the trial budget (Taranaki). In districts where other health organisations contributed each organisation was keen to set an upper limit of somewhere between two to four scans per month before financial support from the trial budget would kick in because there was concern about potential over utilisation. Assessment of the volume of requests and their appropriateness was not a formal pre-specified outcome of the study, but because this aspect of the tool had raised concerns among specialists and health care managers, the degree of utilisation and appropriateness of requests was explored. These results may also help health service managers to decide whether adopting this feature is sensible as part of future implementation.
It is encouraging that the number of general practitioner requests was low and that when the tool was used the test requests were generally appropriate. Overall numbers were small, but the higher rate of inappropriate test requests in the control group does suggest that there may well be a role for electronic decision support in assisting generalists with test selection. The overall similar cost of diagnostics between groups (table 23; section 3.4.6.3) supports the notion that general practitioner access did not drive up health care costs.

In light of the low frequency of requests, high degree of appropriateness of requests, and no increase of overall treatment cost it appears reasonable to continue inclusion of this feature with future roll-out of the tool. Ongoing support from local health organisations will have to be negotiated for each district and intermittent audits of utilisation rate could provide further evidence for or against continuation of this service arrangement.

4.1.6. Limitations

This section discusses overall limitations relating to the FASTEST trial described and reported in sections 3.1 to 3.4.

The trial may not be fully generalisable to all of New Zealand. Patients and practices were recruited in districts with secondary and tertiary university level hospitals but did not include either of New Zealand’s two major metropolitan areas (Auckland and Christchurch). Hospitals from both areas were invited to participate, but stated technological compatibility issues and/or use of different TIA pathways already in use as reasons for choosing not to participate. It could be argued that the tool is of greatest utility in more rural areas where specialist access might be more challenging and the study’s focus on such areas allows firm conclusions to be drawn relating to that treatment setting. A second limitation is the study’s focus on New Zealand. While this helps to establish validity about the tool’s impact on New Zealand health care it affects generalisability to other health care systems.

The lower number of registrations in the control group likely relates to three factors: first, overall there were two more practices in the intervention group (this was a chance occurrence based on the randomisation schedule and total number of practices enrolled); second, a single participating practice was very large, consisting of 21 GPs, and this
practice was randomised to the intervention group; and third, control group GPs appeared to be more prone to ‘forget’ about trial participation and may have failed to register some control patients because they did not do anything differently from usual care. It is unlikely that the imbalance was due to other hidden biases and this is supported by the well balanced baseline characteristics of individual patients in the two groups. Potential bias due to differences between practices was mitigated by fitting ‘practice’ (i.e. ‘cluster’) as a random effect during the analysis.

A further limitation is the high number of unintentional registrations in the study population. This was an unforeseen problem not discovered until the end of the data collection period as no interim analysis was planned or performed. Unintentional registrations could have led to selection bias for recruitment into the two study arms. To minimise this risk each patient deemed ineligible by the research assistants was reviewed by the candidate blinded as to study group allocation. This careful review indicated that most of the patients who were unintentionally registered were not even seen by their general practitioner during the study period and the few that were seen had no documented presentations in either general practice or hospital records for any type of neurological or ophthalmological symptom during the study period. Among this group of patients were toddlers presenting for immunisations and even a patient who had died before the registration. When there was any doubt, the relevant general practitioner was consulted by the candidate and if there was any suggestion that the registration may have been intentional the patient remained in the sample. The reason for these accidental registrations remains unclear. One possibility is that some general practitioners simply wanted to trial the tool and opened it while they were logged into the record of a randomly selected patient in their medical record database. Another possibility is that general practitioners may, on occasion, have clicked an incorrect desk top icon and thus inadvertently registered a patient into the study. The study icon was located near a number of other icons including a button to open an ‘Accident Compensation Commission’ application and the ‘BPAC Acne tool,’ which may explain why orthopaedic and acne diagnoses appeared in the list of patients who were inadvertently registered (see section 3.4.1). To safeguard against accidental registrations the doctor was always asked to confirm the registration after the initial desk top button click. But it appears that some doctors accidentally clicked the button and then also accidentally confirmed the registration.
An ‘intention-to-treat’ analysis capturing all registrations was considered but it was felt inappropriate and was not part of the study plans. Unlike a usual intention-to-treat analysis that includes patients appropriately randomised to a study group who then either did not undergo the intervention or were lost to follow-up, these patients were (a) not the unit of randomisation (all randomised general practices were included in the analysis regardless whether individual intervention group general practitioners used the tool or not in their management) and (b) these patients were never intended and/or eligible for participation. Furthermore, because most of these patients were also never seen during the study period, the available medical records could not provide the required data for analysis. For example, guideline adherence and 90-day stroke risk cannot be assessed without a date of initial presentation. Including these individuals would also skew baseline characteristics by lowering the average age, number of risk factors, and lowering proportions of high risk patients in the intervention group complicating interpretation. Lastly, given that patients who were registered unintentionally had no evidence of TIA or stroke during the study period it is not surprising that none of these patients suffered a 90-day outcome event. The majority of these registrations occurred in the intervention group and thus inclusion of these results would have likely resulted in significant 90-day stroke outcome that would have inappropriately over-estimated the tools impact. To maximise transparency the numbers of excluded patients are included in the participant flow diagram and it is hoped that discussion of this issue will assist with optimisation of future study designs.

The study reports two main outcome variables. This risks inflating Type I error rates. An informal Bonferroni adjustment, setting a threshold for statistical significance of 0.025, is still consistent with guideline adherence being better in the intervention group.

One of the main outcomes underwent a change of definition between the original trial protocol submitted to the Health Research Council and the final analysis. The original Health Research Council funding application defined the second main outcome as ‘Stroke or TIA’ within 90 days. The subsequent trial registration (ANZCTR: 12611000792921) and published protocol paper defined this outcome as ‘Stroke’ only. This reflected a different emphasis on which was a clinically relevant definition between primary care and secondary care clinicians in the research team. General practitioners felt that TIA should be included because the decision support tool was designed to assist in the diagnosis of TIA. The stroke physicians felt that TIA was less
relevant as a patient centred outcome because of its transient nature compared to completed stroke. To facilitate comparison to prior research and because ‘stroke’ was listed in both the trial registration (completed by the candidate without input from other members of the study team) and the protocol paper\textsuperscript{115} ‘stroke’ was chosen for the final analysis. Both outcomes are presented although that of ‘Stroke and/or TIA’ was left as a secondary outcome.

The cluster design, also discussed under strengths below, increased the complexity of the analysis. Stroke events were too few to successfully fit ‘cluster’ as a random effect and thus calculate an intra-class correlation coefficient. This means that the confidence intervals reported for the 90-day stroke outcomes are likely to be too narrow. This issue has to be kept in mind during interpretation and its occurrence may help to advise future study design.

4.1.7. Strengths

This section discusses overall strengths of the FASTEST trial described and reported in sections 3.1 to 3.4.

Strengths of this study include its pragmatic real world location with inclusion of rural areas where specialist access is especially challenging and its cluster design, which increases its clinical relevance and takes into account practice related factors. The cluster design was planned to prevent contamination. The tool is inherently educational and if randomisation had occurred at the patient level then individual doctors would have managed some of their own and potentially their colleague’s patients with and others without the tool. The learning effect from the tool would likely have affected (i.e. contaminated) management of subsequent control patients.

Additional strengths are that data collection was almost complete (i.e. very few missing values) and there was complete 90 day follow-up case ascertainment. Furthermore, great care was taken to minimise assessment bias. The measurement of guideline adherence was masked as to study arm and assigning ‘adherence’ to each management category followed a strict protocol, exactly according to what is described in the guidelines. One area that was anticipated to be prone to reviewer interpretation was adequacy of diabetic care because this can be handled via medications or lifestyle changes and the New Zealand TIA Guidelines are not clear on specific criteria. For this
reason diabetes care was excluded a priori from guideline adherence assessments. Final specialist diagnoses and outcome event confirmation was also masked to study arm. If a disagreement occurred between reported specialist diagnoses and the blinded specialist assessment a third clinician was consulted for a further opinion.

The estimated intra-cluster correlation coefficient, for those variables where it could be calculated, was similar to that anticipated in the sample size calculation based on the intra-cluster correlation coefficient that was published by Adams et al. Their reported coefficient of 0.01 matches exactly the coefficient that was found in vascular event outcomes in this study. Presenting additional coefficients for other outcomes should be of benefit to future researchers running similar studies.

The cluster randomisation increased the risk of significant differences of important co-variates between study groups because of potential differences between practices. It is reassuring that the distribution of potentially influential co-variates appeared similar in the two groups. While it is recommended that the distribution of co-variates between randomised groups is not formally tested, due to the cluster design baseline characteristics were formally compared between groups and this confirmed that there were no statistically significant differences.

4.1.8. Overall FASTEST conclusion

In conclusion the results of the FASTEST trial show that an integrated approach to TIA management using the general practice based FASTEST TIA/Stroke electronic decision support tool results in greater guideline adherence, more efficient health resource utilisation, with better outcomes and lower treatment costs, than usual clinical care. It represents a viable less expensive alternative to referring all potential TIA patients for rapid (within 48 hours) specialist assessments.
4.2. FASTEST trial results in the context of prior studies

This section discusses FASTEST trial results in the context of prior literature discussed in Chapters 1 and 2.

4.2.1. In the context of prior TIA/Stroke electronic decision support research

This section discusses FASTEST trial results in the context of studies discussed in Chapter 2.

The validation study (section 2.3) indicated that the use of the tool achieves a greater level of guideline adherence than general practitioners working in isolation. This finding was confirmed by the FASTEST trial.

The feasibility evaluation (section 2.4) suggested good user-uptake, which the FASTEST trial results reiterate on a larger scale. In addition to individual general practitioner feedback the trial also examined buy-in from secondary care clinicians strengthening the assertion that uptake of the tool across both primary and secondary care is achievable.

The FASTEST trial adds safety data on 172 patients to the previously conducted safety audit on 79 patients (section 2.5). Of these 251 patients one patient suffered a serious adverse event that could potentially be linked to the tool resulting in an overall rate of 1/251 or 0.4%. As discussed before, the event was more a failure of the guideline to identify a high risk patient than the use of the tool and has to be weighed against the observed treatment benefit.

Results of the cohort study (section 2.6) are also supported by the trial results and suggest that some of the observed benefits in the cohort study were indeed related to the implementation of the tool rather than purely on the basis of other possible changes to TIA management during the study period.

In summary, FASTEST trial results echo findings from prior observational studies assessing the utility of the TIA/Stroke electronic decisions support tool.
4.2.2. In the context of prior TIA service research

This section discusses FASTEST trial results in the context of studies presented in Chapter 1, section 1.3.

Section 4.1.1.3 discusses FASTEST trial stroke rates compared with stroke rates reported in other TIA service models described in section 1.1.5. Implementation of TIA/Stroke electronic decision support appears to achieve similar stroke recurrence rates as other service models that require faster and more ubiquitous access to hospital level and/or stroke specialist care.

Comparing other FASTEST trial outcomes to the available literature is more challenging. None of the five reported studies on service models\textsuperscript{30,36,49-51} reported quantitative impact of their service models on guideline adherence, user-feedback, treatment cost, or safety aside from reporting recurrence of stroke and vascular events.

In 2005 Nguyen-Huynh and Johnston published cost data assessing the cost-effectiveness of hospitalisation for TIA on the basis of access to thrombolysis treatment in case of early stroke recurrence. They concluded that 24-hour hospitalisation is cost effective for patients with 24-hour stroke risks of >5\%.\textsuperscript{47} In 2011 Joshi and colleagues found in their cost-effectiveness analysis that hospitalisation was no more cost-effective than urgent-access TIA clinics regardless of degree of early stroke risk. The urgent-access TIA models they used for comparison were models three and four discussed in section 1.1.5, both advocating same day specialist review albeit in the outpatient setting. Neither of these two cost-effectiveness studies compared real life costs, but instead developed cost models using published rates of thrombolysis administration and early stroke risk after TIA. What can be concluded is that results of the FASTEST trial match prior projections that indicate that hospital admission for all TIA patients is unlikely to be cost-effective and that admitting some may be cost-effective. The new information gained from the FASTEST trial is that improving primary care guideline adherence through the use of an electronic decision support tool reduces overall treatment costs even if some specialist assessments are delayed without increasing overall stroke risk. Future studies assessing different TIA service models should routinely include a cost analysis to allow further comparisons and provide quantitative real life cost data that can help drive health service decision making.
The only literature reference to an improvement in TIA guideline adherence comes from Brown and colleagues\textsuperscript{90} who demonstrated that an emergency department based partially electronic decision support tool can improve guideline adherence (see section 1.3.2). In contrast to the FASTEST trial their data includes no information about behavioural counselling or diagnostic accuracy. However, their results do match FASTEST trial observations related to the positive impact of electronic decision support on guideline adherence and underscore the potential utility of electronic decision support beyond primary care, encompassing the entire patient care continuum.

User-feedback was provided by Weir et al. after trialling a decision support tool assisting hospital based clinicians with choosing antiplatelet therapy (section 1.3.2). They received feedback from only nine clinicians, four of whom did not positively endorse the tool. By contrast the FASTEST tool feedback from general practitioners indicated that 31/31 (100%) would use the tool at least some of the time if available, 29/31 (94%) at least most of the time, and 17/31 (55%) all of the time. All interviewed specialists (4/4) endorsed the use of the tool in primary care.

In summary, the FASTEST trial results align with prior TIA service and TIA/Stroke electronic decision support research findings and add further information in areas where prior published data were scarce. In addition, the FASTEST trial is the first assessment of different TIA service models in New Zealand and the first randomised controlled trial assessing different TIA service models worldwide. These features alone indicate the substantial contribution that the FASTEST trial results add to national and international knowledge.

\textbf{4.2.3. In the context of prior electronic decision support research}

This section discusses FASTEST trial results in the context of studies presented in Chapter 1, section 1.2.

Previous data indicate that electronic decision support systems can effectively improve guideline adherence.\textsuperscript{66,69,74-77} The FASTEST trials results indicate that the same is true for the TIA/Stroke electronic decision support tool. Results of the impact on patient outcomes and treatment costs have been reported less frequently and are inconsistent.\textsuperscript{66,74} The results of the FASTEST trial show improved patients outcomes
and reduced treatment costs in the setting of its electronic decision support tool thereby contributing to the growing body of evidence underlying electronic decision support tools in general.

Findings from prior studies surrounding user-feedback and implementation,\textsuperscript{73,84-86} can also be endorsed by results from the FASTEST trial. For example, the collaborative approach involving both specialists and generalists early in the development process and throughout the research project, has likely contributed to its success. Furthermore, training prior to use appears to have enhanced outcomes. Lastly, perceptions of impeded practitioner autonomy were encountered, as others have reported.\textsuperscript{85} Concerns about practitioner autonomy were more common among clinicians without exposure to the tool than among those who had actually used it (section 3.4.7) highlighting the importance of addressing this barrier before implementing such a tool to reduce the risk of limited end-user uptake.

In summary, FASTEST trial results add to the current body of evidence on electronic decision support tools in general and particularly in the areas of patient outcomes and treatment cost. As evidence supporting the use of such tools continues to increase it can be expected that their uses become more widespread over time. Because of their heterogeneity it will likely remain important to test each new tool to assess its specific impact on health services and individual patients similar to new pharmaceuticals or surgical devices.

4.3. TIA/Stroke electronic decision support in the broader context

This section discusses the TIA/Stroke electronic decision support tool in the broader context of the current health care environment.

Health care is growing ever more complex with rapidly increasing knowledge and treatment options, and an ageing patient population. More knowledge and therapies are of clear benefit to patients and populations, but leave doctors struggling with information overload and the challenge of staying up to date. On the one hand this development encourages sub-specialisation. On the other hand more treatments raise health care costs and because specialists are expensive there is a competing drive to shift more and more care back into primary care. Matters are further complicated if
populations are dispersed making reliance on generalists even more important because geographic distances impede timely specialist access.

In this modern health care climate there is increasing pressure to find ways to help clinicians cope with the available information, ensure patient safety, and maximise patient outcomes. Checklists and electronic decision tools have emerged as potential aids borrowing in part from other industries facing similar issues of increasing complexity.89

TIAs are a good example of a health care condition that is connected to a common and serious cause of adult mortality and disability (i.e. stroke), but in and of itself represents an infrequent diagnosis encountered by general practitioners, with a high general practitioner false positive diagnostic rate.52,64 Because of its urgency and complexity TIA has traditionally been viewed as a condition requiring specialist input and often routine hospital admission. However, when competing with other acute illnesses it is more difficult to justify urgent hospital care because in and of themselves TIAs are not disabling at all. They are simply indicators of potential risk. So the important issue is urgent implementation of secondary prevention rather than urgent round the clock nursing care. The former should be accomplishable without hospital admissions and as reviewed in section 1.1.5 a number of models have been proposed (table 3).

The New Zealand TIA Guidelines27 have taken devolution of care one step further by shifting even more responsibility into the primary care sector. This is in line with general New Zealand health care policy as a measure to produce cost savings, reduce wait times, and ‘provide care closer to home.’132 For this shift to work effectively guidelines require adherence and general practitioners who see TIAs only a few times each year are challenged to be sufficiently familiar with the latest treatment guidelines.

Some clinicians may be concerned by an implication that this decision support tool can replace clinical judgment with ‘tick box medicine.’ However, previous data indicate that this tool in the hands of lay people does not achieve similar results.64 The tool is designed for use by qualified clinicians and requires all final treatment decisions to be made by a doctor. It does not replace clinical decision making, it enhances it. Further, the TIA/Stroke decision support tool generally encourages specialist review for good reasons. TIA and stroke are complex conditions best managed by experienced specialists.52,64 The tool is primarily designed to appropriately prioritise urgent
specialist management for high risk patients and to reduce referral of clear TIA mimickers for stroke specialist management. This allows specialists to focus on those patients in greatest need of expert care at a time that is most efficient from a health delivery perspective. The tool therefore integrates primary and secondary services across the patient journey to more effectively and efficiently improve patient outcomes. Such collaboration is especially important in areas where immediate access to specialist services is challenging to provide due to limited resource or geographic distance, patients are reluctant to engage with specialist services, or health resource constraints dictate exploration of alternative service models.\textsuperscript{132,133}

The results of the FASTEST trial indicate that primary care guideline adherence is improved with the availability of the electronic decision support tool and that this in turn effectively reduced cerebrovascular and vascular event recurrence. The risk to patients is minimal and there is a beneficial effect on health resource utilisation. On top of this users seem to like the tool and are willing to use it.

In summary, the TIA electronic decision support tool is an effective measure to help address modern pressures on TIA services. In more general terms these study results provide evidence that use of electronic decision support tools can effectively support primary/secondary integration to promote more efficient and effective health care provision in New Zealand for acute low incidence conditions in addition to the more traditional use of electronic decision support in the setting of chronic disease management.

4.4. Next steps

All previous evidence surrounding TIA service delivery comes from case series and cohort studies. The FASTEST trial is the only randomised controlled trial on TIA service delivery in the world to date. It will be difficult to argue superiority of other treatment models at least in New Zealand and possibly worldwide.

The next step is to ensure the tool can be made available to as many general practitioners as possible to harness the benefits that this tool provides to patients. In order to achieve this goal results of this work have been communicated to the New Zealand Ministry of Health who has approved a business case to fund nationwide roll
out of the TIA/stroke electronic decision support tool. Many electronic tools are appearing throughout New Zealand and compatibility issues are arising, requiring consideration. The TIA stroke tool could serve as a pilot for exploring the successful integration of primary care practice management systems, independent management modules, additional more generic electronic guideline resources, and e-referral systems to secondary care. Such integration appears to be the way of the future and work needs to progress collaboratively to make this transition efficient and effective. The New Zealand Health Information Technology Board is aware of these issues and is actively working to address these challenges. In addition to New Zealand wide implementation the tool has also stirred interest in the United Kingdom and discussions of overseas adaptations are currently underway.

The tool itself appears to be safe. However, the New Zealand TIA Guideline criteria failed to identify one at risk patient (1/291 (0.4%)) who suffered an early recurrent stroke that may have been preventable had this individual been admitted to hospital. Admitting all TIA patients to hospital may have prevented this early recurrent stroke. Whether such a risk is acceptable and justifiable is a health care policy decision and not dependent on the candidate’s personal view. This data should be helpful for policy makers to make informed future decisions.

One way to attempt further reduction of preventable stroke is ongoing refinement of the tool as well as the guidelines and several valuable lessons were learned from this trial. While it appears that direct attributable damage because of the tool was minimal some mistakes in data entry and management decisions did occur that could potentially be addressed by subtle changes in the tool. The following changes have already been made in response to FASTEST trial observations:

1. The wording around atypical symptoms in a low risk patient now puts more emphasis on the possibility of a TIA despite presence of atypical symptoms.
2. The importance of ‘non-sudden onset’ has been downgraded and is now treated like any other atypical feature.
3. All patients with a high risk profile, regardless of symptom presentation, are diagnosed as a TIA in the first instance.
(4) If ‘bilateral blurred vision’ is selected a warning box appears asking the doctor to screen for diplopia and visual field disturbance and if either is possible to select these items instead.

Updates to the New Zealand TIA Guidelines are a more cumbersome matter. When the next update takes place the authors will be encouraged to consider findings from this trial. The electronic decision support tool will be updated on an ongoing basis as additional data becomes available.

4.5. Future studies

Ongoing audit of TIA electronic decisions support tool use is advisable with adjustments if and when problems arise. Other future studies should further evaluate cultural aspects of TIA care and electronic decision support tools, general practitioner imaging utilisation, and TIA triage scores. Furthermore, an expansion of the TIA/Stroke electronic decision support tool to emergency medical services and even individual patient use should be explored. Similar tools for use in stroke care beyond TIA (e.g. acute stroke care and even rehabilitation) require consideration. Other areas of primary and secondary care interface could likely stand to gain from improved guideline adherence through the use of electronic decisions support as well.

4.6. Final conclusion

TIA is a medical emergency and requires urgent implementation of secondary prevention. With increasing health care complexity inter-sectorial collaboration and exploration of new management strategies are important to pursue. The TIA/Stroke electronic decisions support tool is an example of such collaboration and innovation. The journey from inspiration through implementation and rigorous scientific evaluation has been successful in demonstrating the utility of this tool for New Zealanders and perhaps beyond.
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Appendices

Appendix I: Validation Study

Who should manage transient ischemic attacks? A comparison between stroke experts, generalists, and electronic decision support

Annemarii Ranta, Pietro Cariga

Abstract

Aims Rapid expert management of transient ischemic attacks (TIA) has been shown to reduce the incidence of stroke, but is not always achievable. This study aims to demonstrate that TIA management by stroke experts is indeed more guideline adherent than that of generalists and that a TIA/stroke electronic decision support (EDS) tool closely mimics expert advice and improves guideline adherence.

Methods 11 general practitioners (GPs), 12 general physicians, and 12 stroke specialists assessed and provided management plans for 7 hypothetical patients with potential TIAs. Responses were compared with the advice provided when patient data was entered into a TIA/stroke EDS programme.

Results Diagnosis and medical management was highly consistent and guideline adherent amongst stroke experts. Diagnostic accuracy was lower in the GP and general physician groups (76% and 79% respectively) and only one-third of generalists initiated best medical therapy when indicated. The TIA/stroke EDS consistently agreed with expert diagnosis, investigations, and medical management and provided most comprehensive lifestyle advice.

Conclusion This study (a) confirms that stroke expert care achieves higher guideline adherence and (b) provides validation that the TIA/stroke EDS tool is able to mimic expert advice and can reliably apply best practice guidelines.

Transient ischaemic attacks (TIAs) identify people at high risk of stroke. The key intervention that reduces subsequent stroke is rapid initiation of best medical therapy via urgent (<24 hour) specialist review. Care following this model has been associated with an 80% reduction in 90 day stroke risk from 10.3% to 2.1% (adjusted hazard ratio 0.20, 95% CI 0.08-0.49, p=0.0001).

In New Zealand, providing a 24 hour, 7 days a week, rapid access stroke specialist run TIA service is challenging. Involving other, less specialised clinicians is often the only alternative. However, the quality of care provided by such clinicians is uncertain and generally assumed to be inferior.

Electronic decision support (EDS) has been used in a variety of health care settings, but has not been widely used in the management of TIA or stroke.

In 2009 the MidCentral stroke service in collaboration with BPAC (Inc) launched a TIA/Stroke EDS tool after completion of a small pilot.

This tool consists of a web-based single page data entry form (Figure 1) and a computer algorithm that utilises criteria from the New Zealand TIA guidelines to (a)
confirm a diagnosis of TIA or stroke and (b) recommend an evidenced based management plan which can, depending on risk stratification, range from immediate hospital referral to community management by the GP with access to relevant diagnostics.

Figure 1. TIA/stroke EDS data entry form with sample case
This study aimed to (a) confirm the notion that stroke specialist care is indeed superior to both general practitioners (GPs) and general physicians without special expertise in stroke and to (b) assess whether this novel TIA/Stroke electronic decision support (EDS) tool can help to enhance the management skills of generalists to more closely mimic management provided by experts and improve overall guideline adherence.

Methods

Twelve physicians with expertise in stroke care (neurologists and physicians/geriatricians with special training/experience in stroke care), ten GPs, and 12 general physicians without special training or experience in stroke care were recruited via various methods.

Stroke experts were identified through an informal New Zealand stroke doctor network and contacted via email with an 86% response rate. General physicians were recruited from the investigators’ home institution during a regular medical grand rounds lecture with a 71% response rate. These physicians all participate in the general medicine roster and are actively involved in the management of patients with stroke and TIAs.

GPs were recruited from the authors’ home DHB by contacting all GPs via email for whom an email address was on file in the department of neurology with a 27% response rate.

All participants were asked to assess seven hypothetical cases based on real life referrals to the MidCentral Stroke/TIA Service. Subsequently, all seven cases were entered into the EDS tool by the primary investigator for comparison to clinician responses.

To ensure that EDS advice was not strongly dependent on the degree of expertise of the individual entering the data, two volunteers with no medical background were also asked to enter these same seven cases into the TIA/stroke EDS tool.

The seven cases consisted of two patients with transient symptoms not typical of TIA (Case 1 & 7), one with a posterior circulation TIA (Case 2), one with an anterior circulation TIA (Case 3), one with a subtle posterior circulation stroke with delayed presentation (Case 4), one with a hyperacute anterior circulation stroke (Case 5), and one with progressive cranial nerve signs and symptoms developing over 48 hours and no vascular risk factors based on a real life patient with Miller-Fisher variant of Guillain-Barre syndrome (Case 6).

Clinicians were asked to make a diagnosis, triage the patient, and design a management plan. Answers were generally recruited in free text format to limit prompting.

Parameters assessed included: diagnosis (including anatomic localisation i.e. anterior versus posterior circulation), medication initiation (which and when), investigations requested and patient counselling (smoking cessation, diet advice, driving restrictions).

All cases were in part hypothetical and even when they closely approximated a real life patient a definite final diagnosis was not always possible. Thus in most cases the majority opinion of the stroke experts was considered to represent the ‘best possible diagnosis.’

Management appropriateness as regards triage, diagnostic work-up and medication/counselling was assessed by comparison with expert majority opinion and best practice guideline recommendations.

Diagnostic cost was estimated using MidCentral DHB public hospital prices. An appropriateness score was calculated by adding 10 points for each appropriate investigation and subtracting 10 points for each inappropriate or omitted investigation.

Investigations considered include MRI, CT, carotid imaging, electrocardiogram, echocardiogram, and Holter monitor/24 hour telemetry. When more than one option was suggested the cheapest option was used in calculations. Laboratory cost, other investigations, and hospitalisation costs were not considered.

Results

Diagnosis and localisation was highly consistent amongst stroke experts. Stroke experts concurred with one another as regards diagnosis and anatomic localisation.
(anterior versus posterior circulation) in 93% (range: 75–100% depending on the case) and 98% (93–100%) of cases respectively. Where a definite diagnosis was known (Cases 3–6) all 12 experts arrived at the correct diagnosis.

GPs and general physicians demonstrated diagnostic accuracy of 76% (45–100%) and 79% (33–100%) respectively. Accurate localisation was achieved by GPs in only 9% (0–27%) and by general physicians in 58% (33–77%) of cases (Figure 2).

By contrast when appropriate patient data was entered into the TIA/Stroke EDS expert diagnosis and localisation were matched 100% of the time.

**Figure 2. GP and general physicians (%) achieving diagnostic and localisation consistency with expert majority opinion**

Triage advice was more consistent across all groups although with this variable GPs outperformed general physicians; 84% (60–100%) of GPs achieved appropriate triage advice compared with only 59% (39–100%) of general physicians; by contrast the software achieved this in 100% of cases.

When appropriate (as determined by both expert majority opinion and best practice guidelines) 92% of stroke experts recommended immediate initiation of best medical therapy (BMT) consisting of antiplatelet(s), statin, and an antihypertensive.

In comparison only 27% of GPs and 31% of internists initiated BMT immediately when indicated. The software recommended BMT initiation at first point of contact in every case where appropriate.

All three clinician groups significantly underperformed when it came to additional management advice including counselling on diet, smoking cessation, and driving restrictions.

By contrast, these items were consistently addressed by advice generated by the automated software (Figure 3).
Figure 3. Management consistency with New Zealand TIA Guidelines: GPs, general physicians, stroke experts, and EDS software

BMT=Best Medical Therapy; ‘smoking,’ ‘lifestyle,’ and ‘driving’ refers to whether need for counselling was mentioned.

Overall the estimated management costs were highest amongst stroke experts and lowest amongst GPs and appropriateness of investigation amongst clinicians was highest in the expert group and generally inversely proportional to cost (Figure 4).

Figure 4. Investigation appropriateness and cost by clinician group

*Score is calculated by adding 10 points for each investigation ordered in accordance with New Zealand guidelines and subtracting 10 points for each omitted or inappropriate investigation ordered.
When two non-doctors were asked to enter the seven cases into the TIA/stroke EDS tool the same answers were elicited as when entered by a stroke expert except on a single occasion when a volunteer accidentally entered incorrect clinical data. The resultant diagnosis over-estimated the acuity of the problem prompting hospital level rather than outpatient care, however, other advice rendered remained appropriate.

Discussion

Unsurprisingly and quite reassuringly, stroke expert management was highly concordant with one another and generally guideline based. As expected diagnostic and localisation skills were poorer in the generalist groups with general physicians out performing GPs.

The frequent omission of initiation of best medical management by generalists compared with experts echoes previous findings and strongly supports the notion that generalists in isolation do not adequately implement secondary preventive measures. However, it is noteworthy that even experts frequently omitted implementing non-medical preventive strategies.

Diagnostic cost increased with level of expertise and the appropriateness of the diagnostics requested did as well. This is not surprising and further highlights that while expert care is probably more expensive than generalist care it is also more comprehensive and appropriate.

The performance of the TIA/Stroke EDS tool was superior to that of generalists, achieved diagnostic accuracy comparable with experts and closely mimicked expert triage and medication management advice.

The ‘check-list’ nature of an electronic tool is the likely explanation for its superior performance as regards the more comprehensive inclusion of otherwise often neglected non-medical management provision and highlights one of the clear strengths of such tools.

While cost effectiveness of investigation of the EDS tool appeared superior to both generalists and experts this finding has to be interpreted with caution. Firstly, the appropriateness score did not take into account potential variations amongst investigations as regards degree of importance, secondly cost assessment was solely based on investigation and specifically did not consider the cost of the EDS tool itself, and finally the EDS never advises to obtain MRI scanning as it is a primary care based tool and thereby will almost by definition incur a lower management cost than experts.

Whether an MRI is ever the most appropriate first investigation in the management of a probable stroke or TIA patient is debatable and beyond the scope of this paper. Nonetheless, the findings suggest that some degree of standardisation may in fact offer potential cost savings. The perhaps somewhat surprisingly lower ‘indication score’ amongst experts compared with the EDS was primarily related to frequent omission to request ECGs amongst the experts.

While the software can add value to generalist driven TIA care it is important to note that accuracy of data entry is paramount. Some precautions can be set to ensure that if in doubt the software errs on ‘over-estimating’ rather than ‘under-estimating’ clinical
risk ensuring adequate patient safety at the potential expense of optimum resource utilisation. However, on top of that it appears important that the individual using the software tool has some medical expertise so that overt errors are readily recognised and all management decisions are sanctioned by a clinician before being implemented.

This is a small, observational study limiting the conclusions that can be drawn. However, the close concordance with expert advice does provide a degree of validation of this tool and several outcome measures strongly suggest that there is a role for an electronic decision support tool in aiding general doctors with the management of TIAs especially when experts are not readily available.

A large randomised controlled trial (FASTEST Trial: ACTRN12611000792921) is currently underway to conclusively ascertain the safety, efficacy, and cost effectiveness of this tool in clinical practice.

**Competing interests:** Nil.

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Appendix II: Feasibility Study

Title: Transient ischaemic attack and stroke risk: pilot of a primary care electronic decision support tool

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Abstract

Introduction: Transient ischaemic attacks (TIA) are a high-risk condition with stroke and rapid management reduces the risk. Rapid specialist access to initiate timely management is often challenging to achieve.

Aim: To assess the feasibility of implementing a TIA/Stroke electronic decision support (EDS) tool intended to aid general practitioners (GPs) in the timely management of TIAs.

Methods: An eight-week pilot provided access to the TIA/Stroke EDS to selected GPs in the MidCentral district, with subsequent patient record review and a post-pilot user satisfaction survey.

Results: Eleven patients from eight practices were entered into the tool and when EDS-recommended advice was followed, diagnosis was accurate and management was in accordance with New Zealand TIA guidelines. No adverse outcomes resulted, and user feedback was positive.

Discussion: Results indicate that wider implementation of the TIA/Stroke EDS tool is feasible.

Keywords: Decision support systems; primary health care; software; stroke; transient ischaemic attack

Introduction

Stroke is the second most common cause of death worldwide and the most common cause of long-term adult disability in developed countries. Transient ischaemic attacks (TIA) identify people at high risk of stroke. This risk is greatest in the first 48 hours and then decreases over time. The key intervention that reduces subsequent stroke is same-day specialist review and initiation of best medical therapy at first point of contact, which has been shown to have an 80% reduction in 90-day stroke risk from 10.3% to 2.1%.

Providing 24-hour, seven-days-a-week rapid access to stroke specialists is a challenge throughout New Zealand and in particular in the smaller, smaller district health boards (DHBs). To circumvent the problem of limited or delayed access to hospital specialist assessment, the MidCentral Stroke Service, in collaboration with the MidCentral DHB, and the Best Practice Advocacy Centre Inc. (BPAC Inc.), developed a novel electronic decision support (EDS) tool to aid general practitioners (GPs) in diagnosing, triaging, and treating patients appropriately and expediently. The tool is based primarily on the New Zealand Guidelines for the Assessment and Management of People with Recent Transient Ischaemic Attack and its main objective is to prompt initiation of best medical therapy at first point of contact in the community, rather than awaiting potentially delayed specialist review at the hospital. In order to support rapid work-up in the community, GPs also gain access to relevant diagnostics (e.g., head CT and carotid ultrasound) if deemed appropriate by the EDS tool. The tool is web-based, maintained by BPAC Inc., and requires access to the MedTech32 practice management system.

The purpose of this pilot was to assess the feasibility of implementing the TIA/Stroke EDS in the MidCentral DHB primary care sector prior to a district-wide launch.

Methods

At the time of the pilot, there were 32 practices in the MidCentral District using MedTech32. This pilot involved eight (25%) of the 32 eligible GPs.
practices and pilot practices were chosen based on three factors: adequate numbers of GPs, current capability to access best practice EDS modules, and an overall representative patient mix of the MidCentral population. Practices were located in the provincial centre of Palmerston North and the smaller nearby town of Feilding. One practice serves a predominantly Maori population. Practices were of median size ranging from two to five GPs per practice.

The tool itself consists of a web-based data entry form requesting information about the presenting symptoms and a brief examination. Some entry fields are self-populated through data extraction from the practice management system, entering patient data takes approximately three to five minutes.

The tool then runs the information through an algorithm with three main possible diagnostic outcomes: (a) stroke, (b) TIA, or (c) 'non-straight forward neurological presentation.'

The first two are further subdivided by risk category and anatomic localisation. Lastly, several additional stipulations to ‘diagnosis and triage’ advice are provided if (a) the patient is young (460 years), (b) presentation includes atypical symptoms, or (c) the patient is either terminally ill or severely demented.

Triage advice is given in accordance with the New Zealand TIA guidelines and depends on the diagnosis, localisation, and risk category. If several management options are acceptable, then the GP is presented with options varying in degree of specialist support.

Two weeks prior to the pilot period, an educational session was offered to participating GPs and their practice nurses covering TIA management principles and instructions as to how to use the tool. The EDS was made available to participating practices for a total of eight weeks (27/7/09-25/9/09). Participating GPs were asked to enter all potential TIA/stroke patients during the eight-week pilot period. At the end of the eight-week period, relevant patient data was reviewed through access to centralised records captured by BPACInc. as well as by review of relevant GP and hospital records. In addition, participating GPs were interviewed using a standardised questionnaire.

National Ethics Committee research ethics approval was not required for the evaluation of the TIA/Stroke EDS roll-out in the MidCentral District. This non-experimental observational ‘study’ was classed as a clinical audit.

Results

Throughout the pilot period eight GPs entered 11 patients into the EDS tool seeking management advice.

In nine of these patients, the advice rendered by the EDS was followed by the treating GPs and this resulted in two emergency department referrals, three TIA clinic referrals, and four community ‘work-ups’ by GPs. In all nine cases, the initial diagnosis made by the EDS was later confirmed as appropriate by a stroke specialist and TIA triage and management occurred in accordance with the New Zealand TIA guidelines. None of the patients experienced any adverse outcomes relating to EDS use.

In two cases, GPs did not utilise the EDS tool appropriately and subsequent management was not in accordance with New Zealand TIA guidelines. In the first, the GP started to use the EDS tool but aborted use before reaching the ‘advice’ screen. Thus the GP managed the patient ‘on his own’ without benefiting from EDS use. This patient was diagnosed by the GP as having a TIA; however, this diagnosis was later deemed incorrect by a specialist. Had the GP continued on to the EDS advice screen, the EDS tool would
have informed the GP that a diagnosis of TIA was in fact unlikely, which may have led to arriving at the correct diagnosis sooner. The second patient’s data was entered correctly into the EDS tool and was correctly diagnosed by the tool as having suffered a stroke rather than a TIA. However, despite the EDS advising the GP to refer the patient to the Accident & Emergency Department (A&E) for urgent specialist review, general practitioner-based management continued. This led to inappropriate delays in diagnostics and precluded timely access to rehabilitation services. The author is aware of one additional TIA patient who presented to this cohort of GPs during the pilot period who was not entered into the EDS because of local IT difficulties.

According to the post-pilot questionnaire, all participating GPs who had used the tool were satisfied with the TIA/Stroke EDS software and had no major concerns regarding user-friendliness, time required to enter data, or the overall advice given by the tool. A few minor issues were raised, including a request to allow the GP more override options if the advice given by the tool appeared to be inappropriate. Other comments included a mention that some medications were not recognised by the EDS and a request to add a free-text box to enter additional information on the referral form. In addition, some GPs voiced concerns that A&E staff might turn down referrals for patients with TIA as they would not be deemed urgent enough by frontline hospital staff. However, those GPs who in fact used an EDS-generated A&E referral to send a patient to the A&E reported that having used the tool actually helped the A&E referral process because it lent extra credence to the GP’s assessment.

Discussion

TIAs are medical emergencies requiring urgent intervention in high-risk patients and this novel TIA/Stroke EDS tool is intended to improve appropriateness and urgency of care. However, prior to launching this tool it was important to ensure that there were no significant risks to patients associated with software use.

Overall, this pilot did not identify any areas of unacceptable risk associated with TIA/Stroke EDS use that would preclude wider implementation. In addition, participant feedback was positive and suggested that the tool was user-friendly and seen as potentially beneficial by treating GPs.

The request to allow GPs more override options is a slightly difficult one. On the one hand, if sufficient flexibility is not allowed, clinicians may see the tool as impinging on their autonomy and may simply not use it. On the other hand, the pilot data indicated that when GPs did not follow the advice given by the EDS, management was less appropriate. To compromise, some additional override options were added to the EDS following the pilot; however, diagnostic access continues to be available only for patients deemed to require them by the EDS tool. In addition, GPs have to enter a reason for overriding the advice and are continuously reminded that they are veering away from the suggested and guideline-based treatment plan.

In conclusion, this pilot was judged sufficient to indicate acceptable usability and safety and the TIA/Stroke EDS has been launched in the Mid-Central District. Based on this pilot and preliminary results from district-wide post-implementation evaluations, the Health Research Council has funded a randomised controlled trial comparing EDS versus non-EDS assisted TIA management in a number of New Zealand DHBs. This trial (FASTEST Trial: ACTRN12611000792921) is currently underway to assess feasibility of a nationwide launch of this software tool and results will be available next year.

References

Appendix III: Safety Audit

Transient Ischemic Attack/Stroke Electronic Decision Support: A 14-Month Safety Audit

Timothy L. Lavin, MBBS,* and Annemarie Ranta, MD††

Background: To assess the safety of a Transient Ischemic Attack (TIA)/Stroke Electronic Decision Support (EDS) tool in the primary care setting intended to aid general practitioners in the timely management of transient ischemic attacks (TIAs). Methods: A 14-month safety audit reviewing all patients managed with the help of the TIA/Stroke EDS tool. Major morbidity and mortality were assessed by screening patients for subsequent hospital admissions and investigating potential links to EDS use. Results: Seventy-nine patients were managed with the aid of the TIA/Stroke EDS. EDS use resulted in 8 appropriate immediate hospital admissions because of patients being at high risk of stroke. Three patients had delayed admission, but care was fully guideline-based and patients had no adverse outcome. Eleven admissions were unrelated to EDS use. Two deaths occurred; these did not result from inappropriate EDS advice. Conclusions: Results suggest that TIA/Stroke EDS use is not associated with major morbidity or mortality. Larger studies are needed to draw more definite conclusions regarding the utility of this TIA/Stroke EDS in preventing strokes. Key Words: Stroke—Transient Ischemic Attack (TIA)—decision support tools—computer-assisted—delivery of health care—integrated.

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Introduction

Stroke is a significant burden on patients, society, and health care systems.1,2 Overall, it constitutes the second highest cause of death worldwide and the most common cause of long-term disability.3,4 Transient ischemic attacks (TIAs) or ministrokes often herald an imminent disabling or fatal stroke,5,6 and early investigation and initiation of secondary prevention via rapid access specialist clinics have shown to substantially reduce the risk of subsequent stroke and other adverse events.6,8,9

In New Zealand, many rural and smaller urban areas cannot offer rapid (<24 hours) access to specialist TIA clinics, and admitting all potential TIA patients to the hospital is not only costly but also often inappropriate because of a high rate of misdiagnosis.10 To address this challenge, a Transient Ischemic Attack (TIA)/Stroke Electronic Decision Support (EDS) tool was designed to improve the diagnostic accuracy of general practitioners (GPs), limit emergency department referrals to high-risk patients, and prompt GPs to initiate secondary prevention immediately if specialist review is anticipated to be delayed by more than 24 hours. Throughout the process, the treating GP has ready access to phone advice from a hospital specialist with expertise in stroke care if backup is required.

This tool consists of a web-based single-page data entry form that is completed by the GP (Fig 1). The computer algorithm incorporates diagnostic criteria and risk stratification in accordance with the New Zealand TIA guideline which includes but is not limited to the ABCD2 score.10 If a diagnosis of TIA or stroke is confirmed, a management recommendation is rendered including preferred triage destination, urgency of investigations, and...
medical/risk factor management. Strategies to encourage GPs’ utilization of the tool include automatically generated referrals and prescriptions, tailored patient information leaflets, links to additional educational materials, and in some instances direct GP access to relevant investigations. To facilitate rapid data entry, the tool integrates with the GP’s medical record system allowing fields to self-populate if relevant information has previously been documented (e.g., medical history of atrial fibrillation and demographic data). All these features have been listed as favorable by surveyed GPs contributing to general end user uptake.19

To ensure that the tool sufficiently mimics expert advice, a study was conducted comparing expert, generalist,
and software management of a number of hypothetical cases that demonstrated a high concordance rate between majority expert opinion and software advice.\textsuperscript{14}

The purpose of this study was to monitor for major morbidity and mortality potentially attributable to TIA/Stroke EDS use after its launch in a single New Zealand district before more widespread implementation.

Methods

We defined "major morbidity or mortality attributable to EDS use" as events resulting in hospital admission within 3 months of EDS use relating to inappropriate management based on a recommendation made by the EDS tool. We were particularly concerned about (1) medication side effects such as antiplatelet/anticoagulant-induced hemorrhages or antihypertensive-induced presyncope/syncope because of overprescription in cases where the EDS tool may have false positively diagnosed a TIA or stroke and (2) delayed admissions for preventable stroke in cases where the EDS either falsely negatively diagnosed a non-TIA or incorrectly assigned "low-risk category" leading to an inappropriate delay in management.

All patients for whom the TIA/Stroke EDS was used to guide management since being made available in July 2009 and up to October 2010 were included in this safety audit. Hospital records were retrospectively reviewed for hospital admissions after entry into the EDS tool up to January 2011. Any admission because of potential iatrogenic causes secondary to management initiated by the EDS were followed up with review of the clinical records and primary care notes to ascertain if the event could somehow be linked to the use of the TIA EDS tool. If a linkage was identified, we aimed to ascertain whether the adverse event leading to hospital admission was because of inappropriate advice (defined as "non-guideline based") rendered by the EDS tool and whether it might have been prevented had the EDS tool not been used.

As per the National Ethics Committee research, ethics approval was not required as this non-experimental and observational "study" was classed as a clinical audit.

Results

A total of 79 patients were entered into the EDS tool between August 2009 and October 2010. Among this patient group, there were a total of 22 (28%) admissions. Eleven of these patients were related to a diagnosis of TIA or ischemic stroke and 11 patients because of other causes. There were no incidences of intra- or extracranial hemorrhages (Table 1).

Among the 11 TIA/Stroke-related admissions, 8 were admitted immediately from the GP's surgery prompted by EDS advice based on the patients' high-risk profiles. Three additional patients, originally triaged by the EDS to less urgent "outpatient" assessment because of a low-risk profile, subsequently re-presented with a second TIA prompting immediate admission at that stage. None of these patients developed subsequent strokes or other adverse events relating to EDS use, and all 11 patients were triaged in accordance with the New Zealand TIA guideline.\textsuperscript{31} There were no TIA or stroke admissions within 3 months of EDS use in any patient in which the EDS initially rejected TIA or stroke as a likely diagnosis.

Among the 11 patients admitted for non-TIA or stroke, 4 patients had a potential link to EDS use and their records were closely scrutinized. However, the patient admitted for loss of consciousness attributed to Diltiazem was noted to have been started on this medication for cardiac problems before any assessment by the TIA/Stroke EDS tool. The patient admitted with acute confusion was not found to have a vascular cause for this presentation nor had there been any medications initiated as part of EDS use. Of the 2 patients admitted with falls, no link to EDS use could be found: the first being related to alcohol intoxication and the second because of urinary tract infection (UTI) and Parkinson disease.

There were 2 deaths in this population. The first was caused by a posterior circulation stroke in an 87-year-old patient referred immediately and appropriately to hospital by his GP following advice of the EDS tool. The second was a 91-year-old woman admitted 6 months after attendance to her GP with a TIA. EDS use at that time indicated a diagnosis of low-risk TIA, and the patient was appropriately managed in an outpatient specialist TIA clinic. After 6 months, she was admitted with a myocardial infarction and ventricular fibrillation, which did not respond to resuscitation. No apparent link between EDS use and cause of death was identified.

In summary, no patients were identified with serious morbidity or mortality directly related to the triage,
assessment, or initial management as recommended by the TIA/Stroke EDS tool.

Discussion

EDS use throughout the health sector is gaining in popularity, but data regarding its utility and safety are limited and often equivocal. This study of a TIA/Stroke EDS aimed to assess the safety of such a tool in clinical practice and found no evidence to indicate any serious associated risk.

Specifically, there was no evidence to indicate any serious preventable harm due to mis-diagnosis, inappropriate triage, or over/under-medication prompted by the EDS. It is noteworthy that while no patients diagnosed by the EDS as ‘non-TIAs’ had symptom recurrence, three patients diagnosed by EDS as TIA, but triaged to the ‘low risk’ group suffered subsequent TIAs. None of these patients came to lasting harm, but this observation could still suggest that the tool may be better at diagnosing than triaging TIAs. However, all three triaging decisions where strictly in accordance with NZ TIA guidelines. The guidelines, which employ the ABCD2 score, clearly specify which patients require rapid assessments and none of the three patients met these criteria. This highlights that any clinical decision, whether an electronic tool is used or not, is only as good as the evidence base that it is built upon and further refinement of current guideline endorsed risk stratification criteria in NZ may be required.

This study has limitations. First, it was limited by the review of hospital discharge summaries in most of the cases. This limits our assessment of safety to major morbidity or mortality within the hospital setting only. Any other less significant morbidity managed in primary care such as minor medication side effects, for example, would not have been noted within this study. Also the study was retrospective and uncontrolled. To more conclusively assess the safety of this tool and EDS utility, in general, it will require larger patient numbers, and a prospective randomized controlled study (FASTEST Trial ACTRN12611000792921) is now underway.

Nonetheless, overall, these findings are reassuring and suggest that use of the TIA/Stroke EDS does not pose any major risks to patients.

References

Utility of a primary care based transient ischaemic attack electronic decision support tool: a prospective sequential comparison

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Abstract

Background

Stroke is a major cause of death and disability worldwide. Reducing the incidence of stroke has the potential to not only improve health outcomes, but also lead to significant cost savings for health services. Transient ischaemic attacks (TIA) can herald an imminent stroke and following a TIA early initiation of best medical therapy significantly reduces the risk of subsequent stroke. To achieve time targets rapid access stroke specialist services have been promoted; however, a number of resource related barriers can impede specialist access and cause unnecessary time delays. Cross sector collaboration led to the development of a primary care based TIA/Stroke electronic decision support (EDS) tool. This study aimed to assess the impact of this tool on improving access and reducing management delays.
Methods

This is a prospective before (2009) versus after (2011) study of the effect on process of care following the implementation of EDS assisted TIA management in primary care. All patients presenting with TIA to secondary services were included. Outcomes assessed were TIA Guideline adherence and patient safety.

Results

Over the study period 266 patients presented for TIA assessment (130 in 2009 and 136 in 2011). Following EDS implementation the median delay to specialist assessment fell from 10 days in 2009 to three days in 2011 (HR 1.45; 95% CI 1.13-1.86; p = 0.001), the number of patients achieving optimal medical therapy within 24 hours rose from 43% to 57% (RR 1.33; 95% CI 1.02-1.71; p = 0.04), carotid and CT imaging were achieved significantly faster (HR 1.52 (1.02-2.26) p = 0.003 and HR 1.34 (1.16-1.78 p = 0.002) respectively), and there were no adverse events associated with EDS use.

Conclusion

The availability of TIA/Stroke electronic decision support in the primary care setting was associated with reductions in management delays without compromising patient safety.

Keywords

Health service delivery, Electronic decision support, Transient ischaemic attack, Stroke, Stroke care, Secondary prevention

Background

Stroke is the third most common cause of death worldwide, the most common cause of long term adult disability in developed countries and represents a major burden on society both in terms of human and health services costs [1,2]. Ischaemic stroke is caused by an interruption of blood flow to the brain. This is typically caused by a blood clot, or thrombus, lodged in and blocking flow through cerebral arteries. Transient ischaemic attacks (TIAs) often herald an imminent disabling or fatal stroke [3-5] and early investigation and initiation of secondary prevention via rapid access specialist clinics has been shown to substantially reduce this risk [3,6,7]. However, most TIA and stroke studies come from tertiary university centres and many areas around the world struggle to mimic service models as proposed by the SOS-TIA [7] or EXPRESS [6] trials due to a variety of resource limitations.

In New Zealand, a low population density country, many rural and smaller urban areas lack the requisite patient volumes and health resources to make rapid (<24 hours) access outpatient specialist TIA clinics a feasible option and admitting all potential TIA patients to the hospital is too costly and often inappropriate due to a high rate of TIA mimics [8]. Other barriers to specialist access include geographical distances, patient financial constraints, as well as patient preference to be managed by their family doctor. In settings such as these innovative alternative models of care require exploration to
achieve similar patient outcomes. Shifting some of the responsibility of caring for these patients back into the primary care sector is attractive from an access perspective, however, general practitioner (GPs) see TIA patients infrequently and may lack the confidence to initiate management without expert input [9]. The utilisation of new technologies such as computerised decision support tools offer an opportunity to provide generalists with additional support that goes beyond referencing a guideline. These tools are gaining in popularity throughout the health sector not only to improve access, but also to improve overall quality of care and cost-effectiveness [10].

To address the challenge of limited specialist access in rural and provincial New Zealand MidCentral Health neurologists collaborated with the primary care driven Best Practice Advocacy Centre (bpac) to design a TIA/Stroke Electronic Decision Support (EDS) tool intended to improve general practitioners’ (GPs) diagnostic accuracy, limit emergency department referrals to high risk patients, and prompt GPs to initiate secondary prevention immediately if specialist review is anticipated to be delayed or not achievable.

To ensure that the tool sufficiently mimics expert advice we conducted a study comparing expert, generalist, and software management of a number of hypothetical cases which demonstrated a high concordance rate between majority stroke expert opinion and software advice [9]. In addition, prior to launching the tool we conducted an eight week pilot [11] and subsequent to the launch a 14-month safety audit [12], both of which demonstrated high user satisfaction and no patient safety concerns. The aim of this study was to assess if the implementation of a TIA/Stroke EDS in the primary care setting would be associated with a reduction of avoidable TIA management delays without incurring additional patient risk.

**Methods**

**Intervention**

The EDS tool consists of a web based single page data entry form that is completed by the GP (Figure 1). The computer algorithm incorporates diagnostic criteria and risk stratification in accordance with the New Zealand TIA guideline [13] as well as expert clinician experience. Unlike most electronic pathways the algorithm does not simply follow a vertical electronic flow-chart, but instead considers and carefully weighs specific clinical information provided concurrently to render a decision. This process aims to more closely mimic the decision making process of an experienced clinician, which is, in the case of TIA and many other medical conditions, considerably more complex than following a flow chart. For example, if three symptoms are listed one of which is typical for TIA and two are not clinical judgement has to be applied to weigh each individual symptoms in order to decide whether there is enough evidence to make TIA a likely diagnosis or not. In general, the computer algorithm errs on the side of over- rather than under-diagnosing TIAs to minimise risk and in the rare instance where a patient has no typical symptoms, but is still classed as ‘high risk’ applying the above criteria the tool still recommends urgent management. When a diagnosis of TIA or stroke is deemed likely a management recommendation is rendered based on risk stratification (Figure 2). A simplified diagnostic algorithm is shown in Supplementary...
Figure 1 and additional screenshots showing possible outcome pages can be viewed in prior publications [14].

Figure 1: TIA/Stroke electronic decision support data entry form depicting a sample case.

*PMS = Practice Management System i.e. GP electronic patient records
Several strategies are in place to encourage GP utilisation of the tool. Firstly, the tool fully integrates into the GP electronic medical record system. This allows automatic population of a number of data entry fields with information previously documented (e.g. past medical history of atrial fibrillation or diabetes and demographic data). This avoids duplication and facilitates rapid data entry. Furthermore, the tool automatically generates specialist and investigation referrals, pre-populates prescriptions, prints...
tailored patient information leaflets, and provides links to additional educational materials. The tool is also inherently educational by providing the GP with definitions for neurological symptoms, guiding them into obtaining a focused history and examination, and providing them with immediate diagnostic feedback. Lastly, by using the tool the GP may choose to manage the patient entirely on their own in the community. If the GP chooses to self manage and the tool supports a diagnosis of TIA the GP has rapid (<48 hour) access to head computed tomography (CT) and carotid ultrasound (if anatomic localisation supports a carotid territory TIA). Head CT access is otherwise generally limited to secondary care physicians in New Zealand and therefore the use of the tool offers GPs more autonomy when required. All of these features have been listed as favourable by surveyed GPs contributing to general end user uptake [11].

Setting, design, and participants

The TIA/Stroke EDS was assessed in the MidCentral District Health Board (MDHB) after its launch in late 2009. MDHB provides public health services to approximately 170,000 people on New Zealand’s central North Island. In New Zealand’s public health system all hospital services, including investigations, are publicly funded and free of charge to patients. GP visits and prescription payments are subsidised, but require a co-payment. Some private specialist services are available although there were no private stroke service or neurology providers in the MDHB area during the study periods.

From January 2009 onward we prospectively identified all patients referred with a diagnosis of ‘TIA’ to the MidCentral outpatient TIA Clinic or the inpatient Acute Stroke Service. The study periods were from 1 January 2009 to 30 June 2009 (‘before’ EDS launch) and from 1 January 2011 to 30 June 2011 (‘after’ EDS launch) with 90 day follow-up periods.

Patients who were managed using the EDS, whether referred to secondary services or not, were independently identified via bpac’s central database and in addition underwent detailed primary care record review to screen for any adverse events that could potentially be linked to EDS use.

The New Zealand National Ethics Committee was consulted on the project and exempted the study from a formal ethics review because they considered this project an audit of an institutional service change.

Study outcomes

There were four binary outcomes: 1) achievement of initiation of best medical therapy (BMT) within 24 hours of first presentation to a doctor; 2) documentation of behavioural counseling (including smoking cessation, diet/exercise, and driving advice); 3) achievement of CT scan; 4) achievement of carotid imaging. In addition there were three time-to event outcomes: 1) time to specialist, 2) time to brain computed tomography (CT), and 3) time to carotid imaging.

BMT looked at achievement of either anticoagulation for patients with atrial fibrillation (AF) or implementation of the combination of: 1) an antiplatelet or antiplatelet combination (Aspirin monotherapy was considered acceptable); 2) a statin, and 3) an anti-hypertensive. If a particular contraindication was listed the drug class was not
required to achieve BMT. Patients who were already on BMT at the time of presentation were considered to have achieved BMT within 24 hours.

In addition, EDS safety was assessed by GP and hospital record review for any GP or hospital presentations that could possibly relate to the use of the EDS tool (e.g. due to a medication initiated based on EDS advice, or a mis-diagnosis or incorrect triage advice rendered by the EDS).

**Data analysis**

All categorical data are presented as counts and percentages stratified by study period (2009/2011) and relative risks were calculated. The significance of association was assessed using the Chi-squared or the Fisher exact when the expected or actual cell count was less than five. Standard methods of survival analysis were used to investigate time to event outcomes. The unconditional association between this measure and the time period was assessed using the log-rank statistic. Multi-variate modeling was performed to assess for the impact of differences in baseline characteristics (smoking and ischaemic heart disease). All statistical tests were performed using R 2.15.

**Results**

**Efficacy**

In total 236 patients were included in the study: 130 in 2009 and 136 in 2011. All patients carried a referral diagnosis of ‘TIA’ and were eventually reviewed by a specialist who rendered a final diagnosis. Table 1 describes the baseline characteristics of patients at the initial presentation. A greater percentage of patients had ischaemic heart disease in 2009 (47% vs 29%; p = 0.001) and a greater number of patients had a history of tobacco use in 2011 (22% vs 49%; p < 0.001). However, including these parameters in multi-variate modelling did not impact the significance of the following results.

**Table 2 Primary outcomes before (2009) and after (2011) the introduction of a TIA/Stroke decision support tool**

<table>
<thead>
<tr>
<th>Variable</th>
<th>2009 (n = 130)</th>
<th>2011 (n = 136)</th>
<th>Relative risk (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMT within 24 hours</td>
<td>51 (43)†</td>
<td>71 (57)§</td>
<td>1.33 (1.02 - 1.71)</td>
<td>0.04</td>
</tr>
<tr>
<td>Behavioural counseling</td>
<td>51 (40)‡</td>
<td>77 (66)§</td>
<td>1.68 (1.31 - 2.16)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CT scan</td>
<td>93 (72)</td>
<td>117 (86)</td>
<td>1.3 (1.07 - 1.59)</td>
<td>0.006</td>
</tr>
<tr>
<td>Carotid imaging</td>
<td>40 (31)</td>
<td>71 (52)</td>
<td>1.7 (1.25 - 2.3)</td>
<td>0.0006</td>
</tr>
</tbody>
</table>

Data are number and percentage. Data missing for 11, 16, 1, and 20 patients.
Best medical therapy was achieved by 43% of patients in 2009 and 57% in 2011 (Relative Risk (RR) 1.33; 95% Confidence Interval (CI) 1.02-1.7; $p = 0.04$) and behavioural counseling was provided to 40% of patients in 2009 and 66% of patients in 2011 (RR 1.68; 95% CI 1.31-2.16; $p < 0.0001$) (Table 2).

### Table 1: Baseline characteristics in patients who presented to the MidCentral Stroke Service before (2009) and after (2011) the introduction of a TIA/Stroke decision support tool

<table>
<thead>
<tr>
<th>Variable</th>
<th>2009</th>
<th>2011</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 130)</td>
<td>(n = 136)</td>
<td></td>
</tr>
<tr>
<td>Male gender</td>
<td>57 (44)</td>
<td>69 (51)</td>
<td>0.26</td>
</tr>
<tr>
<td>Hypertension</td>
<td>88 (69)*</td>
<td>90 (66)</td>
<td>0.68</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>23 (18)†</td>
<td>18 (13)</td>
<td>0.34</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>34 (27)†</td>
<td>29 (21)</td>
<td>0.28</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>61 (48)†</td>
<td>39 (29)</td>
<td>0.002</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>82 (65)†</td>
<td>74 (54)</td>
<td>0.34</td>
</tr>
<tr>
<td>Current or ex-smoker</td>
<td>28 (29)‡</td>
<td>67 (56)§</td>
<td>0.0002</td>
</tr>
<tr>
<td>Stroke risk classified as high†</td>
<td>88 (68)</td>
<td>103 (76)</td>
<td>0.19</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td>0.69</td>
</tr>
<tr>
<td>&lt;60</td>
<td>26 (20)</td>
<td>33 (24)</td>
<td></td>
</tr>
<tr>
<td>60-79</td>
<td>68 (52)</td>
<td>66 (49)</td>
<td></td>
</tr>
<tr>
<td>&gt;=80</td>
<td>36 (28)</td>
<td>37 (27)</td>
<td></td>
</tr>
<tr>
<td>Best medical therapy at initial presentation</td>
<td>47 (36)</td>
<td>43 (32)</td>
<td>0.51</td>
</tr>
</tbody>
</table>

Data are number and percentage. Data missing for *3, †4, ‡35, and §11 patients. †Patients are classed as ‘high risk’ if they have ongoing stroke symptoms, an ABCD2 score ≥4, ≥2 events over preceding 7 days, atrial fibrillation, and/or receive anticoagulation therapy.

The time from first point of contact (FPC) until stroke specialist review was significantly shorter in 2011 than 2009 ($p = 0.001$; Figure 3). In 2011 the median time from FPC to specialist was 10 days which decreased to three days in 2011 (Hazard ratio (HR) 1.45; 95% CI 1.13-1.86).
Patients seen in 2011 were 1.3 times (95% CI 1.07 - 1.59) more likely to have a CT scan than those seen in 2009 (p = 0.006; Table 1) and the median time till a CT scan was performed reduced from 2 days in 2009 to 1 day in 2011 (HR 1.34; 95% CI 1.16-1.78; p
Similarly patients seen in 2011 were 1.7 (95% CI 1.25 - 2.3) more likely than patients seen in 2009 to have carotid imaging (p = 0.0006) and time to carotid imaging reduced from 24 days in 2009 to 7 days in 2011 (HR 1.52; 95% CI 1.02-2.26; p-value = 0.003; Figure 3).

Safety

During the 2011 study period, five patients represented to hospital within 90 days of receiving EDS assisted management. Admission diagnoses included: hip fracture due to falls attributed to postural hypotension (unrelated to recent medication initiation), elective management of a patent foramen ovale (without recurrent TIA/Stroke), bronchitis, astrocytoma, and migraine. While some of these diagnoses were related to the patients’ original ‘TIA’ presentation in no instance were these admissions adversely related to misdiagnosis or inappropriate management recommendations by the TIA EDS. There were no instances of even minor medication related adverse events or treatment delays due to EDS misdiagnosis or inappropriate triage advice. There were no cases of recurrent TIA or stroke amongst patients triaged as ‘low risk’ while awaiting outpatient specialist review. Similarly patients diagnosed as ‘non-TIA’ by the tool did not present with any subsequent cerebrovascular events.

Discussion

We describe the first application of an electronic decision support tool in the primary care setting to aid in the management of TIA and minor strokes. This ‘Before and After’ study suggests that the implementation of this tool was associated with a significant improvement in the rate of rapid initiation of best medical TIA therapy, which has previously been shown to significantly reduce recurrent stroke [8]. In addition to earlier medication initiation we also observed a reduction in time delays to specialist review and relevant imaging. Furthermore, behavioural counseling and overall rate of diagnostic imaging acquisition improved after the tool was implemented.

Our data also suggest that this tool is safe. There were no cases of inappropriate diagnosis, triage, or management advice resulting in adverse events. Patients diagnosed as ‘non-TIAs’ did not experience any later recurrent TIAs or strokes and patients triaged as ‘low risk’ did not experience any recurrent TIAs or strokes while awaiting specialist review.

This study has clear limitations given its non-randomised observational design. While our comparison groups were identified prospectively and included all patients presenting to stroke specialists in the entire study population there remains a potential that some patients were missed because they were never referred to secondary care. There were also some baseline differences between groups: there was a higher prevalence of ischaemic heart disease in the 2009 and tobacco use in 2011. However, results remained significant even after adjusting for these potential confounders. As regards other potential service related confounders it is important to note that there were no changes relating to referral processing, admission criteria, appointment booking, diagnostic access, or neurology and radiology staff numbers between the two study periods. Nonetheless, despite our efforts to control for any changes other than the introduction of the TIA/Stroke EDS between study periods unrecognised confounders
cannot, of course, be excluded in this type of study. For example, the promotion of the tool itself and wide dissemination of national TIA best practice guideline may have progressively raised TIA awareness throughout the district resulting in a general improvement in TIA care over time. A final limitation is that this study does not provide information about the impact of the tool on actual patient outcomes such as 90-day stroke risk. Complete 90-day follow-up data was not available for this sample and the study was not adequately powered to assess the tool’s impact on stroke recurrence. However, results from a multi-centre cluster randomised controlled trial, specifically designed to assess the tool’s impact on patient outcomes, will be available later this year and will provide further information [14].

**Conclusion**

This cross-sectoral collaborative implementation of a TIA/Stroke EDS was associated with an improvement in TIA guideline adherence and a reduction in avoidable management delays, which have previously been linked to improved stroke outcomes and reduced health care costs. While our study design precludes us from asserting a clear causative link the findings nonetheless suggest that this type of health service provision may represent a feasible option to improve primary/secondary integration and improve overall TIA management and stroke prevention especially. This model would be particularly applicable in areas where more traditional models of care are difficult to replicate due to health resource limitations or geographical/cultural barriers impeding rapid specialist access. Results from a more definitive randomised controlled trial testing the efficacy and safety of this tool will be forthcoming later this year (FASTEST Trial ACTRN1261100079292).

**Abbreviations**

TIA, Transient ischaemic attack; EDS, Electronic decision support; GP, General practitioner; BMT, Best medical therapy; FPC, First point of contact (with a doctor); CT, Computed tomography; RR, Relative risk; CI, Confidence interval; HR, Hazard ratio

**Competing interests**

The authors declare that they have no competing interests.

**Authors’ contributions**

AR developed the TIA/Stroke EDS, designed the study, had overall oversight of study and final analysis/interpretation of data, and drafted the manuscript. CY: Led efficacy outcome data collection, participated in efficacy data analysis, and contributed to manuscript preparation. MF: Led safety data collection, analysed safety data, and contributed to manuscript preparation. PC: contributed to study conception and design, identified study patients for data collection, and assisted with manuscript preparation. CM: Assisted with data collection and manuscript preparation. NC: assisted with study
design, performed statistical analysis, and assisted with manuscript preparation. All authors read and approved the final manuscript.

Acknowledgement

The authors wish to thank the Best Practice Advocacy Centre for their contribution to the development of the EDS tool, Drs Jonathon Morton and David Ayling who provided invaluable primary care input during the development and implementation phase, and the Palmerston North Medical Research Foundation who supported this project with a research grant.

References


Efficacy and safety of a TIA/stroke electronic support tool (FASTEST) trial: Study protocol

Anremarei Ranta, Susan Dovey, Mark Weatherall and Dea O’Dea

Abstract

Background: Strokes are a common cause of adult disability and mortality worldwide. Transient ischaemic attacks (TIAs) are associated with a high risk of subsequent stroke, and rapid intervention has the potential to reduce stroke burden. This study will assess a novel electronic decision support (EDS) tool to allow general practitioners (GPs) to implement evidence-based care rapidly without full reliance on specialists.

Methods/design: This is a cluster randomized controlled trial comparing TIA/stroke management of GPs with access to the EDS tool versus usual care. The intervention period is 12 months with a 3-month follow-up period for individual patients. Primary outcomes consist of stroke within 90 days of presenting event and adherence to the New Zealand national TIA guideline.

Discussion: A positive study will provide strong evidence for widespread implementation of this tool in practice and has the potential to improve key outcomes for patients and reduce the burden of stroke.

Trial registration: Australia New Zealand Clinical Trials Registry ACTRN12611007929291

Keywords: Stroke, Ischaemic Attack, Transient (TIA), Electronic Decision Support (EDS), Decision Support Techniques, Decision Making, Computer-Assisted, Delivery of Healthcare, Integrated

Background

Stroke is the second most common cause of death worldwide and the most common cause of long term adult disability in developed countries [1,2]. Stroke costs New Zealand over $450 million every year [3]. If current trends in stroke incidence and mortality continue [4-6], the number of stroke survivors in New Zealand will reach 50,000 by 2015 [7], with overall annual costs of >$700 million. Reducing the burden of stroke is a key goal for health service planning [8].

Transient ischaemic attacks (TIAs) identify people at high risk of stroke. TIA is defined as transient loss of focal cerebral or ocular function lasting <24 hours, attributable to ischaemic vascular disease. TIAs precede stroke in approximately 25% of stroke victims. The 24-hour cut-off point is arbitrary and minor strokes, defined as symptom duration of >24 hours but with subsequent complete or near complete recovery, carry the same high risk of subsequent stroke as TIAs. Both indicate circulatory compromise of brain tissue that is at risk of infarction, but which is yet entirely or nearly entirely salvageable. Transient cerebral ischemia is typically caused by unstable plaques affecting the larger vessels that supply large amounts of brain tissue. As a result, the majority of strokes that follow TIA or minor stroke are severely disabling or fatal, and these are most likely to occur within 48 hours and up to seven days following TIA while the plaque remains 'fresh' [9]. This highlights the importance of urgent intervention to maximize stroke prevention in high-risk patients. A key intervention that reduces subsequent stroke is rapid initiation of best medical therapy via urgent (<24 hour) specialist review [10,11]. Care following this model has been associated with an 80% reduction in 90-day stroke risk from 10.3% to 2.1% (adjusted hazard ratio 0.20, 95% CI 0.08 to 0.49; p = 0.0001) [10].

In New Zealand, providing 24-hour, seven days a week, rapid access specialist TIA clinic is challenging especially in the smaller district health boards (DHBs), where patient numbers cannot support a sufficient number
of neurologists/stroke physicians to staff an around-the-
clock specialist service. A UK study has shown that most
patients experiencing TIA or minor stroke first seek
healthcare from their general practitioner (GP) [12], even
when the event occurs outside normal working hours.
Thus, in a setting of limited specialist access it seems logi-
cal to look for ways that urgent intervention could be
offered at the GP level in order to avoid unnecessary and
potentially life-threatening treatment delays. However, the
scope of clinical conditions managed in general practice is
very broad, and individual GPs will have patients present-
ing to them with TIA/stroke relatively infrequently. Our
analysis of general practice records suggests that, on aver-
age, a GP will be consulted four to five times per year
by a patient presenting with a presumed TIA/minor
stroke. However, GP diagnostic accuracy of TIA/minor
stroke is only 50% to 80% [13], so the actual rate of recog-
nized TIA/minor stroke patients encountered by GPs may
be as few as two to three patients per year.
Electronic clinical decision support systems (EDS) may be
especially valuable for assisting clinical decision-
making in such circumstances, where a condition is both
challenging to diagnose correctly and encountered by
generally clinicians relatively infrequently. New Zealand's
MidCentral Stroke Service, in collaboration with the Best
Practice Advocacy Centre Inc. (BPAC), has developed a
novel TIA/stroke EDS tool. The tool may mitigate the
problem of limited or delayed specialist assessment in a
setting in which many GPs lack the experience necessary
to manage TIA/stroke independently. It aids GPs in
accurately diagnose TIA's, promoting treatment initiation
at first point of contact rather than awaiting specialist
review, and prompts GPs to manage TIA and stroke
patients comprehensively and in accordance with New
Zealand guidelines [13].

One of the benefits of the EDS tool is that it is inher-
ently educational, providing GPs with immediate feed-
back on diagnosis and guideline-based advice, which can
be applied to the management of future patients and
improve diagnostic and management skills over time.

Throughout New Zealand, similar BPAC decision sup-
port modules are used by 76% of general practices and
85% of GPs. The TIA/stroke module differs from other
existing modules because it focuses on the management of
an acute medical problem rather than chronic care or
disease prevention. However, in its operation it mirrors
other existing tools. The TIA/stroke tool is a new module
that has so far been used only in the MidCentral DHB.
National implementation of the TIA/stroke decision sup-
port module has the potential to significantly reduce
the burden of stroke throughout New Zealand. However,
its use may also involve two main possible threats to
patient safety; patients may be erroneously diagnosed as
not having a TIA and miss out on early treatment and/or
specialist referral and patients may be erroneously diag-
nosed with a TIA and placed needlessly on potentially
harmful medications such as aspirin.

There has been no research investigating impacts of any
BPAC EDS modules on clinical behavior and patient out-
comes in New Zealand. International evidence on whether
point-of-care decision support improves patient care has
been equivocal [4,15]. Decision support tools are becom-
ing ubiquitous throughout New Zealand primary care and
their utility should be carefully evaluated. In particular, do
they assist clinicians to make evidence-based clinical deci-
sions? In a literature review, we identified 175 published
eports of research into EDS use in primary care settings,
but no tool that addresses the complex clinical care needed
for initial presentation of TIA/stroke. Systematic reviews of
the decision support literature conclude that there is a
shortage of well-designed randomized controlled trials of
EDS that provide assessments of its effectiveness in chang-
ing patient outcomes, as well as in changing clinician be-
havior [16-21].

To date, we have conducted four studies to assess the
TIA/stroke decision support tool. A pre-launch commu-
nity-based pilot indicated a high degree of GP satisfaction,
excellent guideline adherence when the tool's management
advice was followed closely, and no adverse patient out-
comes [22]. A second study comparing stroke experts, GPs,
and decision support management in seven small cases
found that management was guideline adherent 88% among
GPs without EDS, 92% among specialists, and 100% when
the decision support tool was used [23]. Data from a
before-and-after study in the MidCentral DHB showed that
best medical therapy was in place within 24 hours in 31%
of patients before introduction of the EDS system and 52%
after its introduction [24]. Finally, a recent unpublished
audit of all patients managed using the EDS for the 9
months following its launch has not found any significant
adverse events associated with its use. Although re-
assuring and promising these small non-experimental
studies support the need for a well-designed randomized
controlled trial to assess this novel treatment approach.

The aim of the FASTEST trial is to formally test the effi-
cacy and safety of New Zealand's TIA/stroke decision sup-
port tool compared with usual care. This study has received
funding from the Health Research Council of New
Zealand (grant 11/268), ethics approval from the Ministry
of Health Multi-region Ethics Committee (URA/11/08/048)
and has been under way since November 2011.

Methods/Design
Design
Cluster randomized controlled trial of general practices
with and without TIA/stroke EDS, comparing TIA and
stroke management strategies, outcomes, and cost in
each arm.
Intervention

The decision support tool is an internet-based module provided and maintained by BPAC. GPs access this tool by clicking a menu button situated on the navigation bar of their practice management software that links them to the BPAC module site. From there they select the TIA/stroke tool from a menu. Once selected, a single page of tick boxes opens up for GPs to complete covering items such as relevant aspects of presenting illness history and a brief focused physical examination. Fields for relevant past medical history (e.g., diabetes and smoking history) are automatically populated by extracting data directly from the practice management system (Figure 1).

Completing the page of background and clinical presentation data takes approximately two to five minutes depending on the GP’s familiarity with the tool. Based on this information, the software confirms or rejects TIA/stroke as the likely diagnosis. If TIA or stroke is...
confirmed, a triage recommendation is generated based on the validated ABCD2 risk score [25] supplemented by several other variables taken from the New Zealand TIA guidelines [13] (Figure 2). If patients are triaged into the 'low risk' category, GPs are offered the option of either referring them to a TIA clinic for specialist review within seven days or of managing the patients themselves in the community. If community management is selected, a step-by-step outline is provided with links to pre-populated relevant prescriptions, radiology referral forms, and a variety of patient information leaflets (Figure 3). If patients are triaged into the 'high risk' category, GPs are advised to refer them to hospital immediately for specialist assessment and diagnostic work-up to be achieved within 24 hours, and GPs are not offered the community management option. However, if a GP feels that urgent hospital referral is not appropriate in any given situation (e.g. the patient refuses to attend the Emergency Department), then GPs have the option to override this recommendation and refer patients to an outpatient specialist TIA clinic instead, as long as a reason for overriding the recommendation is specified. Hospital referral forms are automatically generated and contain all information needed for specialists to prioritize patients appropriately. In the case of a hyper-acute stroke with unresolved symptoms that started within the preceding 45 hours (i.e., within the thrombolyis window) the tool is immediately shorted and the GP is advised to call 111 for emergent hospital transfer to a centre where stroke thrombolysis is available.

To preserve patient confidentiality, all patient data for the study generated by the decision support tool are transmitted in an encrypted format to BPAC and from there to the research team.

** Outcome measures **

The two primary outcome measures are recurrent stroke within 90 days of initial presentation with TIA or stroke and management in accordance with New Zealand TIA guidelines with regard to treatment with anti-platelet therapy being achieved within 24 hours of presentation; treatment with statin, anti-hypertensive, and/or warfarin (if applicable and not contraindicated) being achieved as soon as clinically indicated and deemed safe and receipt of appropriate diagnostic investigations within 24 hours or seven days based on risk stratification.

Secondary outcomes include: adverse events (including, but not limited to, medication side effects, diagnostic delays, and misdiagnoses); occurrence of recurrent TIA, myocardial infarction, major bleeding, and/or death within 90 days; implementation of a comprehensive adjuvant treatment plan (smoking cessation counseling, exercise/diet advice, communication of driving restrictions, and education on thrombolysis); overall treatment cost (including both direct cost relating to treatment of index event and cost of any events related to presenting complaint during the follow-up period), and GP and TIA clinic specialist satisfaction.

** Sample size calculation **

The primary outcome is the proportion of participants who have recurrent stroke within 90 days of the presenting TIA/ stroke. Based on previous work [9,11,24], we estimate that 10% of those in the control group will have a stroke or TIA compared to 2% of patients in the intervention group.
Unadjusted for the cluster design, a total sample size of 274, one-half in each of two treatment arms, is needed to detect this size difference with 80% power and type I error rate of 5% [26]. We planned to recruit 40 practices, representing clusters, and used an intraclass correlation coefficient of 0.01 similar to the median intra-class correlation in the paper of Adams [27]. Based on an average of seven participants per practice, the adjusted sample size ended up as 292.

This is achievable in 12 months assuming an average of 2.5 GP full-time equivalents per practice and an average of two to three TIA/minor stroke patients per GP per year. The sample size calculation also takes into account an expected 50% to 80% GP diagnostic accuracy. We anticipate that an average of four to five patients will be recruited in the study per GP over 12 months, but with an average of only two to three patients having actually suffered a true TIA or minor stroke.

A pre-specified second primary outcome is the proportion of patients who receive management according to New Zealand TIA guidelines. This outcome is likely to be achieved for around 33% of usual care participants compared to an anticipated 92% in the intervention group [23]. Unadjusted for the cluster design, this requires a total sample size of 20 patients. The intra-class correlation coefficient for this outcome will be much higher. Based on a value of 0.4, the study is likely to have sufficient power to detect this difference.

**Practice engagement**

Three districts (Hawke’s Bay and Whanganui in the North Island and the Southern region in the South Island) were chosen to participate in this study. All practices in these areas have access to a hospital based specialist run TIA clinic for consultations during regular hours. All of their practices will have access to 24 hour/7 day a week acute medical care in the hospital in patient setting.

GPs are eligible to participate in the study if their practices use an electronic practice management system and they agree to be randomized into either the intervention group (using the TIA/Stroke decision support tool) or the control group (who agrees not to use the TIA/Stroke tool) for the 12 months of the intervention phase. All practices in these districts were invited by letter to participate, followed by individual phone calls to promote timely recruitment. GPs were then invited to attend an educational session where the Principle Investigator (PI) reviewed management principles of TIA and stroke and the study’s processes in detail. Representatives
from all interested practices attended one of these sessions, confirmed their willingness to participate, signed consent forms, and were randomized on the spot. Posters were provided for practices to have in their waiting rooms, advising patients of the practice’s involvement in the study. Out of the 136 GP practices in these three regions, 44 practices were successfully recruited by the planned intervention start date of 1 March 2012.

A randomization schedule for participating practices was drawn up by the statistical advisor to the project (MW).

After use of the EDS tool, there are some instances when GPs require rapid access to carotid ultrasound or head computed tomography (CT). This is not currently available in the public health system to most GPs enrolled in the trial and related costs for private provision of carotid ultrasound and head CT will be funded through the study to ensure that all patients have similar access to diagnostic tests in the different regions of the study. GP access to these tests endorsed by EDS is an important aspect of the intervention and has to be assured.

Study data

GPs in both the intervention and control groups will be provided with a menu button situated on the navigation bar of their practice management software (indicate the link to register patients for the study). GPs will click the button when they encounter a patient they believe is suffering from a TIA or stroke. In the control group, the button click will prompt patient clinical details to be registered and stored centrally by BPAC and the GP will be advised to continue with routine care. In the intervention group, clicking the button will open up the TIA/stroke EDS module and the GP will then use the software. For each patient in the intervention group, information about diagnosis, triage advice, and management plan given to the GP by the EDS tool will be recorded and stored centrally at BPAC, in addition to patient clinical details.

Throughout the trial and at the end of the 12-month intervention period, records of all patients entered into the BPAC database via the procedure described above will be reviewed for outcome measures three or more months after being registered. GP records will be scrutinized and all data collected will be verified and supplemented by hospital and coroners’ records when applicable. Data collection will be accomplished by a study clinician via use of an electronic Microsoft Access tick box form to facilitate efficient data analysis.

Specific data collected about patients include: final diagnosis including anatomical localization (confirmed by specialist)—TIA, ischemic stroke, hemorrhagic stroke, or other and anterior versus posterior localization; ABCD2 score if available; initial GP triage destination (community, hospital, or TIA clinic); past medical history of atrial fibrillation, current warfarin use, more than one TIA/stroke event over past seven days (all high risk indications); medical treatment with antiplatelet(s), statin, and/or antihypertensive accomplished in 24 hours, 24 hours to 7 days or >7 days; documentation of counseling/education (smoking, diet/exercise, driving, thrombolysis) and by whom it was provided (GP/practice nurse, hospital physician, hospital nurse); investigations and time frame (< 24 hours, 24 hours to 7 days, > 7 days) for ECG, CT head, MRI, echocardiogram, Holter monitor, and carotid ultrasound if obtained; hospital specialist review ‘yes/no’ in < 24 hours, 24 hours, to 7 days, > 7 hours; hospitalizations related to index event ‘yes/no’ if yes number of days in hospital and discharge location; and TIA, stroke, MI, major bleeding or death within three months of index event, any significant adverse events attributable to medications prescribed after index event, diagnostic delays and/or misdiagnosis (significant event is defined as an event that prompted a GP visit, phone call, hospitalization or death). All identifiable data will be expunged from the final dataset to be analyzed for the study, leaving patients identified only by a unique study code.

In addition, at the end of the study, GPs will be surveyed regarding satisfaction with the tool as regards usability, efficiency, and any patient concerns of which they have been made aware. Specialists providing care through a TIA clinic will be surveyed regarding satisfaction with referral quality and any concerns or observations they have made comparing management with versus without TIA/stroke EDS.

Analysis

This is a single-blinded study with the statistician analyzing the results blinded to the study group of participants. The statistician analyzing the data will be based in a different geographical site from the team managing the study and collecting the data. The analyst will be provided with data file from which all patient, practice, and study group identifying data has been expunged. These variables will be replaced in the analysis file with non-identifiable numeric codes. Before being provided with the data file for analysis, the principal investigator and one other investigator will check the data to ensure that all potentially identifying information has been removed.

The analysis will use a generalized linear mixed model to take account of both the dichotomous outcome variables and the cluster design. These models are more complex than generalized linear models or mixed linear models. The outcomes for individual patients will be the response variables, but we will take account of the
cluster design and plan to fit practice and practice-treatment interaction effects as random effects. We may have to explore if the practice-treatment interaction effect has a non-zero value and fit a simpler model. PROC GLIMMIX in SAS will be used to fit the models [28–30].

Analysis of the outcomes will include all patients registered by the GPs, including those who eventually turn out to have a diagnosis other than TIA/stroke (i.e., intention-to-treat analysis). However, a pre-specified secondary analysis is of the main outcomes for only patients who were confirmed to have suffered an actual TIA or minor stroke by specialist assessment.

Cost comparisons

This study is focused on short-term costs and consequences of the proposed intervention, occurring within three months of the initial TIA or stroke.

All costs will be measured as at a specified date. For example, as ‘dollars in year 2010 prices,’ or ‘year ending in June 2011.’ Costs measured in dollars of another date will be adjusted using appropriate price or cost indices to the chosen base date. The chosen date will be the latest period, at the time of carrying out the analyses, for which the necessary price or cost indices are available. All costs will be measured excluding Goods and Services Tax (GST). This means that any raw data will be clearly identified as either including or excluding GST, and, in the former case, adjusted to remove GST.

The costs associated with using the intervention (purchase of the computer module from Bpac plus any installation, training, and support costs) will be included in the cost analysis. These costs apply of course to the ‘intervention arm’ only. Other costs will be collected in tandem with the collection of clinical information, for both ‘intervention’ and ‘control’ arms of the trial. That is, costs will be collected for every individual reporting to a practice in the trial with a TIA/stroke. The advantage of collecting data at individual level is that standard deviations and confidence intervals for the cost estimates can then be readily calculated [31]. Also, simulation techniques can subsequently be applied, if desired, to assess the robustness of the conclusions reached from the research.

Costs will be collected for the following: GP visit; ambulance/transport cost; specialist consultation; hospital stay; investigations (ECG, CT, carotid ultrasound, MRI, echocardiogram, Holter monitor, laboratory tests); medications (hospital and ex-hospital).

In general the approach to costing will follow that laid down in Pharmac’s latest (2012 edition) *Prescription for Pharmacoeconomic Analysis* [32]. (Pharmac is the New Zealand agency that decides which pharmaceuticals qualify for government subsidy, and the amount of subsidy). Where applicable ‘standard costs’ given in the *Cost Resource Manual* [33] provided by Pharmac, such as the average cost per GP consultation, will be used. For consultations and medications any subsidy to patients will be added back to give total cost pre-subsidy. For hospital admissions (day-patient or in-patient), the appropriate diagnosis-related grouping cost-weight will be used and lengths of stay data will also be collected for collateral information.

Discussion

The study is challenging, and there are a number of important issues we have attempted to address in the study design.

Study results are intended to be widely applicable nationally and internationally. Involving practices from both North and South Island sites ensures that data will be applicable to a wide range of geographical sites throughout New Zealand. All three study regions are DHBs with relatively small, geographically dispersed populations. On the one hand, this makes them representative of areas that may benefit the most from this type of intervention; yet, our focus on smaller centers may limit application of study data to larger urban centers. To offset this, we have included one DHB centered around a tertiary university medical centre (University of Otago, Dunedin School of Medicine). The three largest population centers in New Zealand (Auckland, Christchurch, and Wellington) were excluded from recruitment because they either have other pathways in place that would take significant time and effort to align with the decision support tool or are in the process of restructuring their services that precluded trial involvement.

Secondly, it can be argued that a cluster randomized design may not be appropriate for this study. However, in the study design we felt that randomization should be at the practice level (cluster design) in order to minimize any potential learning effect created by software use. We decided we should not randomize individual patients because the EDS tool educates GPs on guideline based care and this would affect the care of later patients randomized to the placebo arm and considerably dictate any intervention effect should one exist. Even randomizing GPs to different groups within a practice may have lead to potential confounding because colleagues may discuss cases and their management with one another. GPs within a practice may also cover for one another, which risks inconsistency in EDS use should serial visits occur by a single patient. On the other hand, cluster designs carry the risk of confounding because similar GPs may naturally group themselves in collegial practices. This is addressed in the study design by an increase in sample size to offset the cluster effect.

Another issue is that activation of a ‘registration’ button automatically draws GPs' attention to the fact
that they are participating in a study, which may affect patient management. Furthermore, practices volunteering for the study may be generally more motivated than non-volunteers, which may introduce some degree of selection bias. Both of these may dilute measured benefit of the intervention because both sources of bias may improve the level of care in the placebo group compared with average GP care encountered in other practices in the country. Thus, while this may make it more difficult for the study to define a significant difference between intervention and placebo, we feel reassured that a false positive result is unlikely.

With regard to economic assessments because of the short-term focus of the study, the following items were excluded: lost economic contribution (or lost productivity), i.e., the income from employment lost because of either premature mortality or inability to work because of illness (Pharmac [32] recommends the exclusion of these indirect patient costs, and the cost of post-hospital institutionalisation, nursing care, and social services. These, if included, could be expected, would be expected, if the intervention is effective, to favor the intervention. In order to get some indication of the extent, discharge rate (home, hospital level, or residential home-level care) will be recorded during data collection. Furthermore, lost Quality-Adjusted Life-Years (QALYs) will also be included. Strictly speaking, these are a health outcome rather than an economic outcome and will be indirectly captured in the number of strokes occurring in each study arm.

Lastly, the primary outcome of 90-day stroke rate may be difficult to achieve. The study was powered to achieve this outcome, but the only available data on post-TIA stroke rates is now several years old, and the recent more widespread use of secondary preventive medications due to significant efforts toward cardiovascular risk reduction may have had a significant impact on current stroke rates. To account for this potential difficulty, we have selected a second primary outcome in the form of overall guideline adherence.

Overall, we anticipate that information from this study will allow DHBs to decide whether to implement this or similar interventions should go ahead and GPs to decide whether to use the tool. Should the BPAC TIA/stroke EDS tool be found to improve key outcomes for patients then its widespread use has the potential to reduce the burden of stroke in New Zealand.

Abbreviations: TIA = Transient Ischaemic Attack; EDS = Electronic Decision Support; GP = General Practitioner; DHB = District Health Board; BPAC = Best Practice Advocacy Centre; PI = Principal Investigator; CT = Computed Tomography; DCL = Dendroclimatology; MRI = Magnetic Resonance Imaging; GBT = Goods and Services Tax; QALY = Quality-adjusted life-years.

Competing interests: The authors declare that they have no competing interests.

Authors’ contribution: AR designed the EDS tool, conceived of the trial, designed the protocol, coordinated the trial and wrote the manuscript. JD contributed to trial design, trial coordination and manuscript preparation. MR contributed to trial design, oversaw statistical aspects of the protocol and analysis, and contributed to manuscript preparation. DO designed economic aspects of the trial protocol, oversaw analysis and interpretation of economic parameters and helped with relevant sections of the manuscript. All authors read and approved the final manuscript.

Acknowledgements: This study has received funding from the Health Research Council of New Zealand (grant 11/268), ethics approval from the Ministry of Health Multiregion Ethics Committee (FM 11/1168048) and has been under way since November 2011. We would like to acknowledge Prof Murray Tindall, Dr John Connors, Dr John Campbell, and BPAC Inc for their contribution to the design and setup of this project.

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Received: 23 July 2012 Accepted: 25 September 2012
Published: 31 October 2012

References


Appendix VI: FASTEST Trial Protocol (Grant Application)

Research Project Full Application (GA211F)

Applicants are advised to:
1) confirm that they have been invited to submit a full application;
2) confirm which Investment Signal fund they have been approved to apply for;
3) read the Guidelines for definitions and instructions before completing this form;
4) read the HRC Rules for applicant eligibility criteria and budgetary entitlements;
5) confirm the application due date for hardcopies and electronic files;
6) ensure that the correct version of this application form is used.

Incomplete or late applications will not be accepted.
The information contained in this Full Application form must be consistent with that previously provided at the EOI stage, otherwise your Full Application may be disqualified.

Indicate type of computer used to complete this form (X): Windows PC: x or, MAC:

Double-click header, replace “11/xyz” with your application Ref ID #: replace “NI surname” with your surname. Double-click elsewhere on the form to return to main part of form. Enter the Ref ID # in the box at the top of the page.

MODULE 1: GENERAL INFORMATION

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First Named Investigator

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<tr>
<td>Dr</td>
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Organisation

University of Otago

Lay Summary of Research (150 word limit)

Stroke is the second most common cause of death worldwide and represents a significant burden on the health care sector. Transient ischaemic attacks (TIAs) identify high risk patients and rapid best medical management reduces stroke risk by 80%. The TIA/Stroke electronic decision support (EDS) tool is designed to help general practitioners to realise this potential risk reduction. This study aims to test the efficacy of the EDS tool with regard to stroke reduction, assess any risks associated with EDS use, and establish costs of EDS use compared with usual management. The study design is a randomised controlled trial comparing EDS use versus usual care over a 12 month enrolment and a three month follow-up period. This is the first formal evaluation of a TIA/Stroke EDS and, within 3 years of study commencement, its results will inform policy and practice relating to use of this TIA/Stroke EDS in New Zealand.
### List of Named Investigators

Details must be the same as those in the individual CVs in Module 6

Copy and paste table for additional names

**Named Investigator 2**

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<tr>
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<td>Professor</td>
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MODULE 2: RESEARCH

Section 2A – Summary of Proposed Research (1 page limit)

Rationale for Research

Stroke is the second most common cause of death worldwide. If current trends in stroke incidence continue, the number of stroke survivors in New Zealand will reach 50,000 by 2015, with overall annual costs of >$700 million. Reducing the burden of stroke is a key goal for health service planning. Transient ischaemic attacks (TIAs) identify people at high risk of stroke and rapid specialist assessment (within 24 hours) of patients presenting with TIA has been linked with an 80% reduction in 90 day stroke risk. The main specialist intervention that leads to this risk reduction is early initiation of secondary preventive medications.

In New Zealand, providing a 24 hour, seven days a week, rapid access specialist TIA clinic is challenging. To circumvent the problem of limited or delayed specialist assessment a novel electronic decision support (EDS) tool has been developed by the MidCentral District Health Board (DHB) stroke service in collaboration with the Best Practice Advocacy Centre Inc. (BPAC) to aid general practitioners (GPs) in accurately diagnosing TIAs and promoting treatment initiation at first point of contact rather than awaiting specialist review. In addition, the tool prompts GPs to manage the care of TIA and stroke patients comprehensively and in accordance with the New Zealand TIA guidelines.

As EDS for a range of other topics is becoming ubiquitous throughout New Zealand primary care there is some concern to know whether such a tool is doing what it is intended to do: assisting clinicians to make evidence-based clinical decisions. Furthermore, although national implementation of the TIA/Stroke EDS tool has the potential to significantly reduce the burden of stroke throughout New Zealand, its use may also involve two main possible threats to patient safety: (1) patients may be erroneously diagnosed as NOT having a TIA and miss out on early treatment and/or specialist referral; and (2) patients may be erroneously diagnosed WITH a TIA and placed needlessly on potentially harmful medications such as Aspirin. To date, the TIA/Stroke EDS tool has been used only in the MidCentral (DHB).

Aims

To assess the efficacy and safety of the TIA/Stroke EDS tool. The study will focus on the effects of EDS use in the GP setting on stroke prevention, national guideline adherence, potentially associated risks, and cost compared with routine care.

Research Design and Methods

This is a cluster randomised controlled trial of general practices with and without the TIA/Stroke EDS tool. General practices will be randomised to use the EDS tool or manage patient care as usual. Enrolment will be for 12 months with a 3 month follow-up period to assess for 90 day stroke risk. Records will be analysed for diagnosis, triage location, investigations, medical management, adverse events, and cost.

Anticipated Outcomes/Impact on Investment Signal Goals

The New Zealand Health and Disability sector will be able to make informed decisions about using the TIA/Stroke EDS tool within 3 years of the research contract commencing. This study will provide a real-world assessment of the effect of EDS availability on improving clinical
decision making in order to maximise health outcomes. The TIA/Stroke EDS tool is an innovative new technology that is intended to improve quality, safety, and access to services while at the same time decreasing demand on costly hospital care and thus producing a higher degree of productivity and sustainability for the future. The main focus is on primary/secondary integration by offering GPs the opportunity to proactively and safely manage their own patients in the community with the assurance of full specialist back-up when required. This project is about real-time, action orientated and multidisciplinary research with a new collaboration between neurologists/stroke physicians and GPs.
Rationale for Research

Stroke is the second most common cause of death worldwide and the most common cause of long term adult disability in developed countries.\textsuperscript{1,2} Stroke costs New Zealand over $450 million every year.\textsuperscript{3} If current trends in stroke incidence and mortality continue,\textsuperscript{4,6} the number of stroke survivors will reach 50,000 by 2015,\textsuperscript{7} with overall annual costs of >$700 million. Reducing the burden of stroke is a key goal for health service planning.\textsuperscript{8}

Transient ischaemic attacks (TIAs) identify people at high risk of stroke. TIA is a transient loss of focal cerebral or ocular function lasting <24 hours, attributable to ischaemic vascular disease and precedes a full stroke in approximately 25% of stroke victims. The 24 hour cut off point is somewhat arbitrary and minor strokes defined as symptom duration of >24 hours but with subsequent complete or near complete recovery carry a similar risk as TIAs. Both indicate cerebral circulatory compromise with potentially significant tissue at risk that is still entirely or nearly entirely salvageable. Transient cerebral ischaemia tends to be caused by unstable plaques affecting the larger vessels which supply large amounts of brain tissue. As a result the majority of strokes following either TIAs or minor strokes are severely disabling or fatal and are most likely to occur within 48 hours to seven days following a TIA while the plaque remains fresh.\textsuperscript{9} Both these facts highlight the importance of urgent intervention to maximise stroke prevention in high risk patients. The key intervention that reduces subsequent stroke is rapid initiation of best medical therapy via urgent (<24 hour) specialist review.\textsuperscript{10,11} Care following this model has been associated with an 80% reduction in 90 day stroke risk from 10.3% to 2.1% (adjusted hazard ratio 0.20, 95% CI 0.08-0.49; p=0.0001).\textsuperscript{10}

In New Zealand, providing a 24 hour, seven days a week, rapid access specialist TIA clinic is a challenge. This is especially the case in the smaller district health boards (DHBs), where patient numbers cannot support a sufficient number of neurologists/stroke physicians to staff an around-the-clock specialist service. A UK study has shown that most patients experiencing TIA or minor stroke first seek health care from their general practitioner (GP)\textsuperscript{12} even when the event occurs outside normal working hours. Thus, in a setting of limited specialist access it seems logical to look for ways that urgent intervention could be offered at the GP level in order to avoid unnecessary and potentially life threatening treatment delays. However, the scope of clinical conditions managed in general practice is very broad and individual GPs will have patients presenting to them with TIA/Stroke relatively infrequently. Our analysis of general practice records suggests that, on average, a GP will be consulted 4-5 times per year by a patient presenting with a presumed TIA/minor stroke. However, GP diagnostic accuracy of TIA/minor stroke is only 50-80%\textsuperscript{13} dropping the rate of ‘actual’ TIA/minor stroke patients encountered by GPs to only 2-3 patients per year and highlighting the diagnostic challenges associated with the care of these patients.

Electronic clinical decision support systems are especially valuable for assisting clinical decision-making in such circumstances, where a patient’s condition is a) challenging to diagnose correctly and b) not uncommon but relatively infrequent. And thus the MidCentral Stroke Service in collaboration with the Best Practice Advocacy Centre Inc. (BPAC) has developed a novel TIA/Stroke electronic decision support (EDS) tool. The tool’s intention is to
mitigate the problem of limited or delayed specialist assessment in a setting in which a significant percentage of GPs lack the experience necessary to manage TIA/Stroke independently. It aids GPs to accurately diagnose TIAs, promoting treatment initiation at first point of contact rather than awaiting specialist review, and prompting GPs to manage TIA and stroke patients comprehensively and in accordance with the New Zealand TIA guidelines.\(^\text{13}\)

Specifically, the tool is a web based module provided and maintained by BPAC. GPs access this tool by clicking a menu button situated on the navigation bar of their practice management software that links them to the BPAC module site. From there they select the TIA/Stroke EDS tool from a menu. Once selected a single page of tick boxes opens up for GPs to complete covering items such as relevant aspects of history of presenting illness and a brief focused physical examination. Fields for relevant past medical history (e.g. diabetes and smoking history) are automatically populated by extracting data directly from the practice management system. Completing the page of background and clinical presentation data takes approximately 2-5 minutes depending on the GP’s familiarity with the tool. Based on this information the software confirms or rejects TIA/stroke as the likely diagnosis. If TIA or stroke is confirmed a triage recommendation is generated based on a validated risk score\(^\text{14}\) supplemented by several other variables taken from the New Zealand TIA guidelines and clinical experience.\(^\text{13}\) If patients are triaged into the “low risk” category GPs are offered the option of either referring them to a specialist TIA clinic or to manage the patients themselves in the community. If community management is selected a step by step outline is provided with links to pre-populated relevant prescriptions, radiology referral forms, and life-style information leaflets. If patients are triaged into the “high risk” category GPs are advised to refer them to hospital for specialist assessment and diagnostic work-up to be achieved within 24 hours and GPs are not offered the community management option. However, if a GP feels that ED referral is not appropriate in any given situation (e.g. the patient refuses to attend ED) then the GP has the option to override this recommendation and refer patients to an outpatient specialist TIA clinic instead, as long as a reason for overriding the recommendation is specified. Referrals to hospital are automatically generated and contain all required information to allow the specialist to prioritise them appropriately. In the case of a hyper-acute stroke that is within the 4.5 hour thrombolysis window the tool is immediately aborted and the GP is advised to call 111 for emergent hospital transfer to a centre where stroke thrombolysis is available.

The BPAC tools are all web based and all patient related data are transmitted in an encrypted format to preserve patient confidentiality. Data relating to individual patients are stored centrally in Dunedin at the BPAC office in a highly secured facility.

One of the benefits of the EDS tool is that it is inherently educational, providing GPs with immediate feedback on diagnosis and guideline based advice, which can be applied to the management of future patients and sharpen their diagnostic and management skills over time. With time GPs will learn which symptoms are not typical of TIA or Stroke and will defer using the tool initially, considering alternative and more likely diagnoses in the first instance. Additionally, with each use of the tool the GP becomes more proficient and efficient at using it, progressively speeding up the process.

The TIA/Stroke module differs somewhat from other existing modules as it focuses on the management of an acute medical problem rather than chronic care or disease prevention. However, in other ways it mimics other existing tools. Throughout New Zealand such BPAC EDS modules are used by 76% of general practices and 85% of general practitioners. The
TIA/Stroke tool is a new module that has so far been used only in the MidCentral DHB. National implementation of the TIA/Stroke EDS tool has the potential to significantly reduce the burden of stroke throughout New Zealand. However, its use may also involve two main possible threats to patient safety: (1) patients may be erroneously diagnosed as NOT having a TIA and miss out on early treatment and/or specialist referral; and (2) patients may be erroneously diagnosed WITH a TIA and placed needlessly on potentially harmful medications such as aspirin.

Thus far there has been no research investigating impacts of any BPAC EDS modules on clinical behaviours and patient outcomes in New Zealand. Internationally, the evidence that use of EDS improves patient care has been equivocal. As EDS is becoming ubiquitous throughout New Zealand primary care there is some concern to know whether it is doing what it is intended to do: assisting clinicians to make evidence-based clinical decisions. We have identified 175 published reports of research into EDS use in primary care settings but no EDS has yet addressed the complex clinical care needed for initial presentation of TIA/stroke. Five systematic reviews of this literature conclude that there is a shortage of well-designed randomised controlled trials of EDS that provide assessments of EDS effectiveness in changing patient outcomes, as well as in changing clinical behaviour.

To date we have conducted three studies to assess the TIA/Stroke EDS tool. A pre-launch community-based pilot indicated a high degree of GP satisfaction, excellent guideline adherence when EDS management was followed closely, and no adverse patient outcomes. A second study comparing stroke experts, GPs, and EDS management in 7 sample cases found that management was guideline adherent 33% among GPs without EDS, 92% among specialists, and 100% when EDS was used. Preliminary data from an on-going before-and-after study in the MidCentral DHB showed a 27% to 53% increase in Aspirin initiation at first point of contact within 3 months of the launch of the software in the district. Finally, a recent audit of all patients managed using EDS for the 12 months following its launch has not found any significant adverse events associated with EDS use. These pilot studies are promising, but small, uncontrolled, and observational, highlighting the need for a well designed randomised controlled trial to assess this novel treatment approach.

The aim of the proposed study is to formally test the efficacy and safety of the TIA/stroke EDS in comparison with usual care. Information from this study will allow DHBs to decide if wider implementation should go ahead and GPs to decide whether to use the tool. Should the TIA/Stroke EDS tool be found to improve key outcomes for patients then wide-spread implementation of the tool has the potential to reduce the burden of stroke in New Zealand.

Research Design and Methods

**Design:** Cluster randomised controlled trial of general practices with and without TIA/Stroke EDS comparing TIA and stroke management strategies, outcomes, and cost in each arm.

**Outcome measures:** The primary outcome measures are (1) further TIA or stroke within three months of initial presentation with TIA or stroke and (2) ‘management in accordance with NZ TIA guidelines’ as regards (a) treatment with anti-platelet therapy being achieved within 24 hours of presentation (b) treatment with statin, anti-hypertensive, and/or warfarin (if applicable and not contraindicated) being achieved as soon as clinically indicated and deemed safe, (c)
receipt of appropriate diagnostic investigations within 24 hours or 7 days based on risk stratification.

Secondary outcomes include: (1) adverse events (including, but not limited to, medication side effects, diagnostic delays, and misdiagnoses), (2) occurrence of myocardial infarction, major bleeding, and/or death within three months, (3) implementation of a comprehensive adjuvant treatment plan (smoking cessation counselling, exercise/diet advice, communication of driving restrictions, and education on thrombolysis), (4) overall treatment cost (including both direct cost relating to treatment of index event and cost of any events related to presenting complaint during the follow-up period), and (5) GP and TIA clinic specialist satisfaction.

**Sample size calculation:** Our preferred primary outcome is the proportion of participants who have a TIA or stroke within three months of the presenting TIA/stroke. Based on previous work,\(^9\)\(^1\)\(^1\)\(^2\)\(^6\) we estimate that 10% of patients in the control group will have a stroke or TIA compared to 2% of patients in the intervention group.

Unadjusted for the cluster design, this requires a total sample size of 274 at 80% power with alpha 0.05. Assuming 40 practices (clusters) and a kappa for association of outcome within the control group\(^2\)\(^7\) of 0.01, similar to the median intra-class correlation in the paper of Adams,\(^2\)\(^8\) the adjusted sample size needed is 292 TIA/stroke patients, about 7 patients per practice over the course of 12 months, which is achievable, assuming an average of 2.5 GP full-time equivalents (FTEs) per practice and an average of 2-3 TIA/minor stroke patients per GP per year. This is taking into account an expected 50-80%\(^1\)\(^3\) GP diagnostic accuracy, i.e. we in fact anticipate that an average of 4-5 patients will be registered in the study per GP over 12 months, but with an average of only 2-3 of these 4-5 patients representing true TIAs or minor strokes.

The other main outcome is the proportion of patients who receive management according to guidelines. This outcome is likely to be achieved for around 33% of usual care participants compared to an anticipated 92% in the intervention group.\(^2\)\(^4\) Unadjusted for the cluster design this requires a total sample size of 20 patients. The kappa for this outcome will be much higher, 0.4. If a total of 20 practices (clusters) can participate the adjusted sample size remains 20 and thus only one patient per practice is needed to evaluate this outcome. However, if only 10 practices can be used for recruitment, then the cluster adjusted sample size needed is 60 patients, 6 per cluster (practice).

In order to adequately assess both of these main outcomes we aim to recruit 40 GP practices.

**Practice engagement:** All general practices in Hawke’s Bay DHB, Whanganui DHB, and Southern DHB will be invited to participate in the study. These districts were chosen because their relatively smaller size makes them representative of areas that may benefit the most from this type of intervention.

Hawke’s Bay and Whanganui are geographically close to the primary investigator which will help to limit travel cost and facilitate oversight. In addition, it was felt to be important to include at least one site on the South Island and Southern DHB is geographically close to several of the other investigators. All practices in these areas will have access to a hospital based specialist run TIA clinic for consultations during regular hours. All of their practices will have access to 24 hour/7 day a week acute medical care in the hospital inpatient setting.
MidCentral DHB had to be excluded as the software tool is already available to GPs in this district and prior familiarity with the tool is likely to confound results as use of the tool has a learning effect. This learning effect is anticipated to affect future patient care even if the tool is not available later on. Involving practices from both North and South Island sites is intended to ensure that data will be applicable to a wide range of geographical sites throughout New Zealand. All three sites are relatively small DHBs which may limit application of study data to larger centres. However, the three largest centres (Auckland, Christchurch, and Wellington) had to be excluded from recruitment as they are currently either not subscribing to BPAC modules, have other pathways in place that would take time to align with the EDS, or are in the process of restructuring their services that precluded trial involvement.

GPs are eligible to participate if they use an electronic practice management system and agree to be randomised into either the Intervention group (who will use the TIA/Stroke EDS) or the Control group (who agree not to use the TIA/Stroke EDS) for the 12 months of the intervention phase. All practices in these districts will be invited by letter to participate and if recruitment is insufficient follow-up phone calls will be undertaken. There are a total of 136 GP practices in these three DHBs which should readily allow for the recruitment of 30 participating centres. Should the required level of recruitment fail in the proposed DHBs additional DHB recruitment will be considered. Bay of Plenty, Taranaki, Wairarapa, and South Canterbury DHBs have already indicated interest in both participating in the study and in using its results, even if their participation is not needed.

Randomisation will occur at the practice level (cluster design) in order to minimise any potential learning effect created by software use. It is inappropriate to randomise individual patients as EDS educates GPs on guideline based care and this would impact on care of later patients randomised to the placebo arm. Even randomising GPs to different groups within a practice may lead to potential confounding as colleagues may discuss cases and their management with one another and GPs within a practice may cover for one another, which risks inconsistency in EDS use should serial visits occur by a single patient. The research team recognises that the cluster design carries its own risk of confounding as similar practitioners may naturally group themselves in collegial practices. This will be addressed by a corresponding increase in sample size to offset the cluster effect.

A randomisation schedule will be drawn up by Prof Mark Weatherall, statistical advisor to the project, as the identity of the study practices will remain unknown to him. The PI and other researchers will know the name and location of the practices but will refer to them by number (1-30). As practices agree to participate the study’s PI will notify Weatherall and he will advise her as to the study group allocation of the practice (Intervention or Control group). The PI will make these requests in separate phone calls for each practice, not knowing the randomisation schedule in advance.

Practices will initially indicate their willingness to participate in the study via a phone, fax, or email response to a letter of invitation signed by the investigators. GPs, nurses, and administrators of the practices will then be invited to an evening meeting in each DHB where the study’s processes will be explained in detail and practices will be asked to confirm their willingness to participate by signing a Consent Form. Subsequently, a research nurse will visit each practice to initiate study processes. Posters will be provided for practices to have in their waiting rooms, advising patients of the practice’s involvement in the study.
Training on EDS use will be provided to all GPs in Intervention practices. GPs in the placebo arm will be trained in only using the notification system outlined below. Ongoing support will be available to GPs throughout the study period.

In areas where rapid access to carotid ultrasound or head CT is not currently available to GPs this will be funded through the study to ensure that all patients have similar access to diagnostics in the different areas being looked at. GP access to these tests endorsed by EDS triage/ recommendation is an important aspect of the intervention and has to be assured.

**Study data:** GPs in both the Intervention and Control groups will be provided with a menu button situated on the navigation bar of their practice management software that will be labelled “TIA/Stroke Study.” GPs will click the button when they encounter a patient they believe to be suffering from a TIA or stroke. In the Control Group the button click will prompt patient clinical details to be registered and stored centrally by BPAC and the GP will be advised to continue with routine care. In the Intervention group clicking the button will open up the TIA/Stroke EDS module and the GP will then use the software. For each patient in the Intervention group information about diagnosis, triage advice, and management plan given to the GP by the EDS tool will be recorded and stored centrally at BPAC, in addition to patient clinical details.

Activation of such a button automatically draws the practitioner’s attention to the fact that he/she is participating in a study, which may affect patient management. Furthermore, practices volunteering for the study may be generally more motivated and keen than non-volunteers, which potentially introduces some degree of selection bias. It is anticipated that both of these potential sources of bias will, if anything, weaken the measured benefit of the intervention. This is because both sources of threats to external validity (generalise-ability) are expected to improve the level of care in the placebo group compared with average GP care encountered in day to day care across all practices in the country. Thus, while this may make it more difficult to prove a significant difference between intervention and placebo we feel reassured that a resultant false positive trial result is unlikely.

At the end of the 12 month intervention period records of all patients entered into the BPAC database via the procedure described above will be reviewed. GP records will be scrutinised and all data collected will be verified and supplemented by hospital and coroners’ records when applicable. Data collection will be accomplished by the study nurse via use of a tick box form to facilitate efficient data analysis.

Specific data to be collected about patients will include: (a) Final diagnosis including localisation (confirmed by specialist): TIA, Ischaemic stroke, haemorrhagic stroke, or other and anterior versus posterior localisation. (b) ABCD2 score if available, (c) initial GP triage destination (community, hospital, or TIA clinic), (d) past medical history of atrial fibrillation, current warfarin use, more than one TIA/Stroke event over past 7 days (all high risk indicators), (e) medical treatment with antiplatelet, statin, antihypertensive: accomplished in <24 hours, 24 hours to 7 days, >7 days, (f) documentation of counselling/education (smoking, diet, exercise, driving, thrombolysis) and by whom it was provided (GP/practice nurse, hospital physician, hospital nurse) (g) Investigations and time frame (< 24 hours, 24 hours to 7 days, > 7 days) for ECG, CT head, MRI, echocardiogram, Holter monitor, and carotid ultrasound if obtained (f) Hospital specialist review ‘yes/no’ in < 24 hours, 24 hours to 7 days, > 7 hours, (g) hospitalisations related to index event ‘yes/no;’ if yes number of days in hospital and discharge
location, (h) TIA, Stroke, MI, major bleeding or death within 3 months of index event, any
significant adverse events attributable to medications prescribed after index event, diagnostic
delays, and/or misdiagnosis (‘significant event’ is defined as an event that prompted a GP
visit/phone call, hospitalisation or death). All identifiable data will be expunged from the final
dataset to be analysed for the study, leaving patients identified only by a unique study code.

In addition, at the end of the study GPs will be surveyed regarding satisfaction with the tool as
regards usability, efficiency, and any patient concerns of which they have been made aware.
Specialists providing care through a TIA clinic will be surveyed regarding satisfaction with
referral quality and any concerns or observations they have made comparing management with
versus without TIA/Stroke EDS.

**Analysis:** The analysis will be a generalised linear mixed model, to take account of both the
dichotomous outcome variables and the cluster design. Model fitting in these models is more
complex than in generalised linear models or mixed linear models. We plan to fit practice and
practice times treatment effects as random effects, however we may have to explore if the
practice times treatment effect has a non-zero value and fit a simpler model. PROC GLIMMIX
in SAS will be used to fit the models.29-31

The analysis of the outcomes will include all patients registered by the GPs including those who
eventually turn out to have a diagnosis other than TIA/stroke (i.e. ‘intention-to-treat’ analysis).
However, a pre-specified secondary analysis is of the main outcomes for only those patients
who were confirmed to have suffered an actual TIA or minor stroke by the specialist
assessment.

**Cost Comparisons:** This study is focussed on short-term costs and consequences of the
proposed intervention, occurring within 3 months of the initial TIA or stroke.

All costs will be measured as at a specified date. That is as ‘dollars in year 2010 prices’, or ‘year
ending in June 2011’. Costs measured in dollars of another date will be adjusted using
appropriate price or cost indices to the chosen ‘base date’. The chosen date will be the latest
period, at the time of carrying out the analyses, for which the necessary price or cost indices are
available. All costs will be measured excluding Goods and Services Tax (GST). This means that
any raw data will be clearly identified as either including or excluding GST, and, in the former
case, adjusted to remove GST.

The costs associated with using the intervention (purchase of the computer module from BPAC
plus any installation, training, and support costs) will be included in the cost analysis. These
costs apply of course to the ‘intervention arm’ only. Other costs will be collected in tandem with
the collection of clinical information, for both ‘intervention’ and ‘control’ arms of the trial. That
is, costs will be collected for every individual reporting to a practice in the trial with a
TIA/stroke. The advantage of collecting data at individual level is that standard deviations and
confidence intervals for the cost estimates can then be readily calculated.32 Also, simulation
techniques can subsequently be applied, if desired, to assess the robustness of the conclusions
reached from the research.

Costs will be collected for the following: (1) GP visit; (2) Ambulance cost; (2) Specialist
consultation; (3) Hospital stay; (4) Investigations (ECG, CT, carotid ultrasound, MRI,
echocardiogram, holter monitor, laboratory tests; (5) Medications (hospital and ex-hospital).
Where applicable ‘standard costs’, such as the average cost per GP consultation given in Appendix 5 of Pharmac’s Prescription for Pharmacoeconomic Analysis,\(^{33}\) will be used. For medications any subsidy to patients will be added back to give total cost pre-subsidy. For hospital admissions (day-patient or in-patient) the appropriate DRG (Diagnosis related Grouping) cost-weight will be used and length of stay data will also be collected for collateral information.

Because of the short-term focus of the study, the following items are excluded: (1) ‘Lost economic contribution’ (or “Lost Productivity’). That is, the income from employment lost because of either premature mortality or inability to work because of illness. (2) The cost of post-hospital institutionalisation, nursing care and social services. These, if included, could be expected, if the intervention is effective, to favour the intervention. In order to get some indication of this effect discharge location (home, hospital level, or residential home level care) will be recorded during data collection. Furthermore, lost Quality-adjusted Life-Years (QALYs) will also not be included. Strictly speaking these are a ‘health outcome’ rather than an economic cost.

Anticipated Outcomes/Impact on Investment Signal Goals

*This application is made in response to the New Zealand Health Delivery Investment Signal 2011. The main goal of this Investment Signal is to deliver research that informs decisions or valuable changes to policy or practice within 5 years of the contract commencing. This study will be completed within 3 years of the contract commencing and will deliver research that will inform DHB funders and planners who have to make decisions about whether to purchase licences for the TIA/Stroke EDS tool in their region and GPs about changing their practice to use this tool.*

*This study will provide a real-world assessment of the effect of EDS availability on improving clinical decision making in order to maximise health outcomes. This is the most formal assessment proposed to date of an EDS software in widespread use in New Zealand and is about real-time, action-oriented and multidisciplinary research with a new collaboration between neurologists/stroke physicians and GPs.*

The TIA/Stroke EDS tool itself supports the translation of knowledge as outlined in the New Zealand TIA guidelines into front-line clinical best practice by placing the information at GPs’ finger tips and thus more quickly and effectively improving health services, systems and outcomes. It is an innovative new technology that aims to improve quality and efficacy of TIA and stroke care by encouraging rapid intervention starting in the GP surgery and carrying through to the secondary sector when required. It is particularly tailored to serve the New Zealand population with special features such as Maori/Pacific Islander sensitive risk scores.

The tool was designed by specialists in collaboration with GPs for use in the GP setting. It aims to shift some of the traditionally specialist focussed care back to GPs, but ensures readily available specialist backup when required. This empowers GPs to retain “ownership” of “their” patients and represents a more patient focussed treatment paradigm by keeping care as close as possible to the home and whanau, an environment in which patients feel safe and comfortable. It also reduces the demand on specialist clinics and allows specialists to focus on the more complex cases where their input is most needed and facilitates such consultations occurring in a
timely manner. In these ways this innovation aims to create a more integrated and mutually supportive relationship between patient, GP, and specialist than has traditionally been the case.

Aside from the anticipated improvement in health outcomes by reducing the number of strokes in New Zealand it is also anticipated that this trial will produce measured evidence of costs associated with both using and not using the TIA/Stroke EDS tool: this will give a firmer foundation for funding decisions than has previously been possible. Cost savings may eventuate through a combination of reduced long term disability, reduced hospitalisations, reduced inappropriate diagnostics, and reduced number of inappropriate specialist referrals. Health care sustainability may improve through improved productivity, cost effectiveness, and a higher degree of GP and specialist satisfaction due to empowerment, support, and appropriate patient referral processes.

If efficacy of the TIA/Stroke EDS tool as a way to improve guideline adherence and stroke prevention can be established and is nationally implemented we can expect improved TIA/stroke care within as little as three years. We might then logically expect to see a rapid improvement in health care outcomes.

**Knowledge arising from this study will be transferred to DHB managers via a personally addressed study brief detailing the results and to stroke physicians and GPs via publications in New Zealand as well as international scientific journals and presentations at conferences. The Otago University's Maori Consultation Committee will also be advised of the results.**

In addition, the newly established New Zealand Clinical Stroke Network supported by the Ministry of Health and the New Zealand Stroke Foundation will be utilised for information dissemination. Most stroke physicians across New Zealand are aware of the TIA/Stroke EDS tool and are keen to implement the tool locally, but many are awaiting more scientific evidence before proceeding. These physicians will be contacted directly with study results as soon as they become available. Also, GP liaison appointments of DHBs across New Zealand have started communicating with members of the research team regarding local implementation of the tool and these clinicians will be similarly informed personally of updates and results by the primary investigator.

Data from prior studies on the TIA/Stroke EDS tool have been presented nationally and internationally with interest in adapting the tool to local services extending beyond New Zealand. The results of the awaited randomised trial will be disseminated to these interested parties via personal correspondence as well.

**Responsiveness to Māori**

One of the positive attributes of computerised decision support is that by design it is impartial in the guidance it gives clinicians, while at the same time integrating into that advice all the relevant clinical features of an individual patient. As regards the TIA/Stroke EDS in particular the significantly higher risk for Māori to develop strokes at a younger age has been taken into consideration when calculating risk scores and giving triage advice. The main triage tool used by the EDS is the ABCD2 score developed by Rothwell (UK) and Johnston (USA). This score has been adjusted by the research team to give Maori and Pacific Islanders a point (out of a
maximum of 7) for “age” if over 50 years old in comparison with Pakeha who score a point if over 60 years of age.

BPAC has staff specifically employed to identify the aspects of its programme that have different implications for Māori and non-Māori and to “translate” Māori perspectives for clinicians. Being embedded in Māori culture is necessary for these staff members. They will apply the same reviews to this study as they apply to other BPAC activities, to ensure it is responsive to Maori. Additionally the University of Otago researchers are consulting with the University’s Māori Research Consultation group about this project.

Track Record of the Research Team

Dr Anna Ranta is the principal investigator for this study. She is a neurologist and lead stroke physician at MidCentral DHB and an Associate Dean of Undergraduate Medical Studies for the University of Otago, Wellington. She wrote the clinical logic tree underlying the TIA/Stroke EDS and has conducted several smaller studies to assess efficacy and safety of this tool. She has formerly participated as co-investigator in several national and international stroke and neurology randomised controlled and observational clinical trials, has performed several extensive stroke audits in the MidCentral region, and has established a regional stroke network in the lower North Island. She is currently involved with the establishment of a National Clinical Stroke Network supported by the New Zealand Stroke Foundation and the Ministry of Health. Optimising health resource utilisation and aiming for best achievable quality of care within resource constraints have been the focus of her work over the past three years. This is reflected in multiple initiatives she has led across the MidCentral district as regards neurology specialist access and primary/secondary integration as well as on a regional basis facilitating access and appropriate prioritisation for treatment at the tertiary care level. She has been invited to present her multiple innovations at centres and organizations throughout New Zealand and holds several leadership positions within the DHB’s provider as well as funding and planning arms.

She will be supported in her principal investigator role in this study by Dr John Gommans, a general physician/geriatrician and Chief Medical Officer (Hospital) at Hawke’s Bay DHB. Dr Gommans is also the Medical Advisor to the Stroke Foundation, Central Region. He is the lead author of the New Zealand TIA Guideline and has over 15 years experience as a principal investigator in multiple international randomised controlled clinical stroke trials. He will be overseeing most aspects of the trial in the Hawke’s Bay region.

Associate Professor Susan Dovey has had more than 20 years research experience in general practice, including in the USA, the UK, and Australia. She holds a full-time academic post in the Department of General Practice and Rural Health, Dunedin School of Medicine, but has previously worked part-time in the Best Practice Advocacy Centre and is able to translate research processes and findings between academic and applied settings. She has published 120 scientific papers (including five studies reporting general practice randomised controlled trials), made 37 conference presentations and supervised 18 postgraduate thesis students through to completion of their degree. She has collaborated in applied general practice research with Murray Tilyard since 1986, producing over 40 papers together.

Professor Murray Tilyard is professor of general practice at the Dunedin School of Medicine, past Head of the Department of General Practice, and Chief Executive of BPAC Inc.
responsible for the electronic design aspects of the TIA/Stroke EDS. He has a strong track record of innovation and research in New Zealand general practice. He established BPAC in 1997 as a response to evidence of uninformed prescribing practices among GPs in Otago. Since then he has developed the BPAC programme to incorporate a number of internationally innovative activities, including electronic decision support. He also founded the general practice organisation South Link Health Inc., following the successful completion of an HRC research project funded in the early 1990s to investigate the translation of the ‘budget-holding’ idea from the UK to New Zealand. He is a clinically active GP, working 1-2 days per week in his own general practice.

Professor Mark Weatherall is a clinician with a strong bio-statistical background with experience in planning and analysis of randomised trials, meta-analysis, and statistical analysis of other forms of quantitative research. Previous HRC grants for stroke related research for which he is an investigator were a randomised trial of specific social interventions after stroke (‘Improving stroke recovery for Maori and their whanau’) and a feasibility study of a cluster randomised trial for a rehabilitation stroke intervention (‘A feasibility study of a structured means of eliciting goals in rehabilitation’); both submitted or in preparation to submission for publication.

Des O’Dea has worked and taught as a health economist for more than a decade. He has taught the post-graduate Health Economics Diploma in Public Health paper for the last ten years at the University of Otago, Wellington. His research, mainly as an independent consultant, has included reports on the Costs of Skin Cancer, for the Cancer Society, the Costs of Injury, for ACC, and Tobacco Taxation, for the Health Sponsorship Council. He has also carried out cost-effectiveness analyses, for example of the ‘Green Prescription’, and has assisted the Women’s Lifestyle programme at the Department of Primary Health, University of Otago, Wellington, with costing questions.

Professor Alan Barber, stroke neurologist, Auckland DHB/University of Auckland, Professor John Campbell, geriatrician, University of Otago, and Dr John Fink, stroke neurologist, Canterbury DHB, will form the Advisory group for this study.

Timeline

Nov 1 2011 – Dec 31 2011:
Complete approvals, complete recruitment of all relevant staff, adapt software tool to local provider needs as required, visits to participating DHBs to start practice recruitment and determine any particular local needs including set up for GP referred diagnostics.

November 1 2011 – March 31 2012:
GP practice recruitment, randomisation, training, and software installation in individual practices.

March 1 2012 – Feb 28 2013:
Intervention period with active patient registration and software use (in Intervention group). Initiation of data collection on an ongoing basis as patients are registered in the study data base. Data to be collected at time of registration and again after 3 months.

**March 1 – April 30 2013:**
Final data collection for 3 month follow-up data. Initiation of data analysis.

**February 1 – August 31 2013:**
Data cleaning and analysis.

**July 1 – Oct 31 2013:**
Report writing and dissemination of results.
References


Appendix VII: FASTEST Trial Ethics Approval

14 September 2011

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Private Bag 11036
Palmerston North

Cc: A/Prof Susan Dowey

Dear Dr Ranta

Ethics ref: URA/11/08/048 (please quote in all correspondence)
Study title: Efficacy and safety of TIA Electronic Support tool (FASTEST) Trial: A study to assess the benefit of an electronic tool used by GPs to assist in diagnosis and management of transient ischaemic attacks (TIAs). HRC 11/268

Investigators: Dr A Ranta, A/Prof Susan Dowey, Dr J Gommans, Prof M Tilyard, Dr M Weatherall, Mr D O’Dea, Dr J Gregson, Dr B Rae

This study was given ethical approval by the Upper South A Regional Ethics Committee. A list of members of the Committee is attached.

Approved Documents
• Study protocol version 1 dated 28/07/2011
• Information sheet and Consent form version 1 dated 28/07/2011

This approval is valid until 31 October 2013, provided that Annual Progress Reports are submitted (see below).

Access to ACC
For the purposes of section 32 of the Accident Compensation Act 2001, the Committee is satisfied that this study is not being conducted principally for the benefit of the manufacturer or distributor of the medicine or item in respect of which the trial is being carried out. Participants injured as a result of treatment received in this trial will therefore be eligible to be considered for compensation in respect of those injuries under the ACC scheme.

Amendments and Protocol Deviations
All significant amendments to this proposal must receive prior approval from the Committee. Significant amendments include (but are not limited to) changes to:
— the researcher responsible for the conduct of the study at a study site
— the addition of an extra study site
— the design or duration of the study
— the method of recruitment
— information sheets and informed consent procedures.

Significant deviations from the approved protocol must be reported to the Committee as soon as possible.

Annual Progress Reports and Final Reports
The first Annual Progress Report for this study is due to the Committee by 30 September 2012. The Annual Report Form that should be used is available at www.ethicscommittees.health.govt.nz. Please note that if you do not provide a progress report by this date, ethical approval may be withdrawn.

A Final Report is also required at the conclusion of the study. The Final Report Form is also available at www.ethicscommittees.health.govt.nz.

Requirements for the Reporting of Serious Adverse Events (SAEs)
SAEs occurring in this study must be individually reported to the Committee within 7-15 days only where they:

— are unexpected because they are not outlined in the investigator’s brochure, and
— are not defined study endpoints (e.g. death or hospitalisation), and
— occur in patients located in New Zealand, and
— if the study involves blinding, result in a decision to break the study code.

There is no requirement for the individual reporting to ethics committees of SAEs that do not meet all of these criteria. However, if your study is overseen by a data monitoring committee, copies of its letters of recommendation to the Principal Investigator should be forwarded to the Committee as soon as possible.

Please see www.ethicscommittees.health.govt.nz for more information on the reporting of SAEs, and to download the SAE Report Form.

Statement of compliance
The committee is constituted in accordance with its Terms of Reference. It complies with the Operational Standard for Ethics Committees and the principles of international good clinical practice.

The committee is approved by the Health Research Council’s Ethics Committee for the purposes of section 25(1)(c) of the Health Research Council Act 1996.

We wish you all the best with your study.

Yours sincerely

Aliene Hierckx
Administrator
Upper South A Regional Ethics Committee
Uppersoutha_ethicscommittee@mon.govt.nz
List of members of the Upper Region A Ethics Committee, August 2011

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Gender</th>
</tr>
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<tbody>
<tr>
<td>Liz Richards</td>
<td>Consumer Representative, Lay member</td>
<td>Female</td>
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<tr>
<td>Carolyn Bull</td>
<td>Legal Representative, Lay member</td>
<td>Female</td>
</tr>
<tr>
<td>Murray Cameron</td>
<td>Health Researcher, Health Professional Member</td>
<td>Male</td>
</tr>
<tr>
<td>Angelika Frank-Alexander</td>
<td>Community Representative, Lay member</td>
<td>Female</td>
</tr>
<tr>
<td>Allison Franklin</td>
<td>Consumer representative, Lay member</td>
<td>Female</td>
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<tr>
<td>John Horwood</td>
<td>Biostatistician, Lay member</td>
<td>Male</td>
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<tr>
<td>Jane Kerr</td>
<td>Researcher, Health Professional Member</td>
<td>Female</td>
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<tr>
<td>Ellen McCrae</td>
<td>Pharmacist, Health Professional member</td>
<td>Female</td>
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<tr>
<td>Edie Moko</td>
<td>Maori representative, Lay member</td>
<td>Female</td>
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<tr>
<td>Barbara Nicholas</td>
<td>Ethicist, Lay member</td>
<td>Female</td>
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<tr>
<td>Christine Robertson</td>
<td>Health Practitioner, Health Professional member</td>
<td>Female</td>
</tr>
<tr>
<td>Russell Scott</td>
<td>Health Practitioner, Health Professional member</td>
<td>Male</td>
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Carolynn Bull, Barbara Nicholas and Russell Scott were not present at the meeting of 22 August 2011.

Signed: ___________________________  14 September 2011

Aileke Dierckx (Administrator)  Date