Has implementing a NSW Early Access to Stroke Thrombolysis program increased the rate of thrombolysis in the Murrumbidgee Local Health District (MLHD)?

Katherine Mohr

Stroke Care Coordinator

Wagga Wagga Health Service

Wagga Wagga NSW 2650

Address for correspondence

P.O Box 5492

Wagga Wagga NSW 2650

Email: Katherine.mohr@gsahs.health.nsw.gov.au

Phone: 02 69386144

Fax: 02 69386527

ACKNOWLEDGEMENTS:

I would like to thank the following people for their help and support

- David Schmidt, Emma Webster and Kerith Duncanson Rural Research Capacity Building Program
- A/Professor Martin Jude, Latitia Kernaghan for their ongoing support and advice
- Members of the Acute Stroke Team Wagga Wagga Rural Referral Hospital for their support
- David Buckley Senior Health Statistician Murrumbidgee Local Health District

List of Abbreviations and frequently used terms.

Rt-pa: Recombinant tissue plasminogen activator

MHLD: Murrumbidgee Local Health District

ED: Emergency Department

NIHSS: National Institute of Health Stroke Scale

ASU: Acute Stroke Unit

FAST: Face weakness, Arm weakness, Speech Slurred, Time Ring 000

Local: Patients who arrive at the Wagga Wagga Health Service who have no hospital to bypass.

Outlier: Patients arriving by ambulance who have bypassed a local hospital and are transported to the Wagga Wagga Health Service.

THROMBOLYTIC CENTRE: A hospital that provides: 1.24/7 Imaging Department, 2. 24/7 Neurology Service; 3. 24/7 Emergency Department with staff trained to administer Stroke Thrombolysis; 4. 24/7 acute Stroke Unit with collocated monitored beds and a multidisciplinary team trained to care for patient with an acute stroke unit.

EARLY ACCESS TO STROKE THROMBOLYSIS: Aim To improve access to Stroke Thrombolysis by shortening the patient journey from onset of acute stroke symptoms.

NSW REPERFUSION PROJECT: Interchangeable with Early Access to Stroke Thrombolysis.

Table of Contents

Has implementing a NSW Early Access to Stroke Thrombolysis program increased the rate of thrombolysis in the Murrumbidgee Local Health District (MLHD)?

Aim: This research was to determine if the implementation of a program designed to provide Early Access to Stroke Thrombolysis, including an ambulance diversion system increased the utilisation of thrombolysis for ischaemic stroke patients in the MHLD and to examine the barriers to thrombolysis (including awareness of FAST).

Background: There is limited access to thrombolysis for patients living in rural and remote areas of the MHLD, this in part, is due to the ambulance protocol to transport patients to the closest hospital and the distance to travel to access a thrombolytic centre. The Early Access to Stroke Thrombolysis recognises this is a major barrier to thrombolysis and has introduced an ambulance diversion protocol. This diversion enables ambulance paramedics when recognising signs of stroke transport the patient to WWHS for assessment and stroke unit care.

For patients to treat stroke as an emergency, they must be able to recognise signs of stroke. This awareness directly correlates to their action at symptom onset and arrival at hospital in thrombolysis treatment time.

Method: Data was collected by the Acute Stroke Unit (ASU) for both the 12month pre-implementation period from January 2011 to January 2012 and the post implementation period from January 2012 to January 2013.

The database recorded patient demographics of age, sex and Indigenous status, together with patient risk factors such as Atrial Fibrillation, Diabetes, Hypertension, Ischaemic heart Disease, previous stroke and smoking status.

Patient recognition of stroke symptoms was documented as awareness of the National Stroke Foundations campaign of stroke signs and symptoms called FAST.

A component of the early access to thrombolysis project was the training of paramedics in the FAST tool and protocol was revised to authorise transfer of FAST +ve patients to the nearest thrombolytic centre. The effectiveness of this was determined by the patients calling the ambulance and arriving at ASU within treatment time.

Results: The thrombolysis rate for the 12 month period prior to the implementation was 3% and this rate increased to 8% post implementation of the reperfusion program. This showed an increase in the rate of thrombolysis and in the number of patients presenting within the thrombolysis window. The majority of this increase was accounted for by an increased number of patients from outlying areas who received thrombolysis.

Knowledge of FAST was 2% in 2012 and 9% in 2013 this may reflect why patients with stroke signs do not seek urgent medical care.

Conclusion:

The introduction of the NSW Reperfusion Program has led to an increase in the number and rate of patients receiving thrombolysis in the Murrumbidgee Local Health District. This program has addressed one of the pre hospital barriers however the major factor still remains that patients do not recognise the signs of stroke and need to seek urgent medical advice.

Future directions: Further research is required to examine the reasons why patients present to hospital later than 4.5 hours given this remains the primary barrier to effective stroke care.

EXECUTIVE SUMMARY

Stroke is the most common cause of adult disability in Australia with approximately 60,000 new and reoccurring strokes each year. One third of patients who have a stroke will die within the first year, another third will survive with a disability and the remaining third will completely recover.

A stroke is caused by the sudden interruption of the blood supply to the brain, this is usually because of either a ruptured blood vessel or a blood vessel that is blocked by a clot. This results in a lack of oxygen and nutrients supply to the brain causing damage to the brain tissue. The most common symptoms of a stroke include sudden weakness of the face, arm or leg, usually on one side of the body, or difficulty speaking or understanding speech. .

Thrombolysis is an intravenous drug treatment that is proven to reduce death and disability, in ischaemic stroke. The therapy works by dissolving clots in blood vessels in the brain and must be commenced within 4.5 hours of stroke symptom onset. There is a strict protocol for eligibility that must be adhered to. Thrombolysis is the only hyper-acute management for ischaemic stroke that is a highly efficient and cost effective therapy.

The major disadvantage with the use of thrombolysis, is the risk of increased early symptomatic and fatal intracranial hemorrhage. Such risk, however is offset by reduction in the proportion of patients who die or are dependent post stroke.

The National Stroke Foundation Acute Stroke Audit is conducted every 2 years and in 2011 the audit revealed that the thrombolysis rate not only within the MLHD but across most stroke units both metropolitan and rural was well below National Stroke Foundation benchmark.

Thrombolysis rates for ischaemic stroke vary within rural NSW from 0-5%, with the WWHS rate at 4-5%, these rates are low compared to metropolitan sites, with some sites reporting thrombolysis rates of 20%. Although it has been well documented that thrombolysis is the only proven treatment for acute ischaemic stroke a number of barriers to eligible patients receiving the therapy have been identified. The most consistent barriers are patients or carers not recognising the stroke signs and urgency for treatment; not ringing 000 or calling an ambulance at symptom onset or ambulance transferring the patients to the closest hospital rather than to the WWHS, the only thrombolytic centre in the MHLD. This delay often results in patients presenting to the WWHS outside the thrombolysis window of 4.5 hours.

As well as pre-hospital delays to Thrombolysis there are a number of in-hospital delays that impact on the delivery of Thrombolysis. The emergency department staff regularly assess stroke patients in the ED and for them to provide an efficient thrombolysis service they must recognise the signs and symptoms of stroke, treat stroke as a medical emergency and limit time delays to thrombolysis but appropriate triage, minimising delay’s to CT and to the “golden hour” of door to needle time for thrombolysis.

The Ministry of Health recognised from the results of the National Stroke Foundation clinical audits in 2008 and 2011 that the rate of thrombolysis for acute ischaemic stroke was 3%, much lower than best practise benchmarks of 20%. With this information collaboratively with the NSW Ambulance and the Agency for Clinical Innovation developed and implemented a program called the Early Access to Stroke Thrombolysis, also known as the NSW

Reperfusion Project, aimed to reduce the time of stroke symptom onset to definitive treatment.

The aim of this research was to confirm an improvement in thrombolysis rates in the MHLD following the implementation of the NSW Reperfusion Project. It also aimed to identify pre-hospital barriers of patient and ambulance service and in-hospital barriers.

With the introduction of the NSW Stroke Reperfusion Program, the rate of patients receiving thrombolysis has increased in the Murrumbidgee Local Health District, but the results show the number of patients who present to the WWHS within the thrombolysis time window of 4.5 remains low.

Early initial recognition of stroke signs and symptoms is crucial for an early presentation to the emergency department to enable access to the most appropriate treatment and management for stroke, every effort must be made to increase public awareness of the signs and symptoms of stroke and to seek urgent medical treatment.

A positive result of this study is the increased number of patients who are transferred directly from rural sites (stat?), who not only receive thrombolysis but then have immediate access to stroke unit care, improving outcomes for all stroke patients.

This study revealed that a number of patients who ring the ambulance at stroke onset and are transported to their local hospital and with arrival at WWHS outside the thrombolysis window. Although transfer to a thrombolysis centre is the protocol, it is not always current practice, which highlights the need to provide ongoing education and training to Ambulance NSW to eliminate protocol violation. To provide an appropriate and efficient thrombolysis service there must be education and training for all staff involved in the process to limit delays to thrombolysis.

The development of a MHLD wide stroke transfer protocol would assist staff in rural sites to appropriately triage patients and initiate urgent transfer for patients who present to a rural hospital either by private transport or ambulance.

INTRODUCTION:

A stroke occurs when a blood vessel that carries oxygen and nutrients to the brain is either blocked by a clot, ischaemic stroke or when a blood vessel ruptures in the brain, a haemorrhagic stroke. Approximately 70% of strokes are ischaemic and 15% are haemorrhagic (National Stroke Foundation, 2010).

As a result, the area of the brain supplied by that blood vessel is damaged or dies. The severity and consequence of a stroke will vary dramatically, from a limited episode known as a transient ischaemic attack (TIA) which has no ongoing deficit to a severe incident that causes death or permanent disability. (National Stroke Foundation, 2010)

When a stroke occurs, brain cells in the immediate area die because they are no longer receiving the oxygen and nutrients they need to function. This area of dead cells is called an infarct, these cells usually die within minutes to a few hours after stroke onset. These cells can either recover or die depending on what happens in the minutes or hours that follow.

Although ischaemic and haemorrhagic stroke have the same symptoms management and treatment is clinically distinct, e.g, anticoagulation drugs that reduce clotting ability are appropriate treatment for ischaemic stroke but will increase the risk of further bleeding in haemorrhagic stroke.

The financial cost of stroke in Australia is as high as $2.14 billion dollars per year, although this cost is high in financial terms, it is the cost to the stroke survivor and their carers that are the greatest, with residual disability and ongoing care needs. Up to 75% of stroke survivors have a residual disability that makes returning to their previous employment and lifestyle difficult or unachievable. (National Stroke Foundation, 2010)

It is therefore important to identify and implement cost effective projects that improve outcomes and decrease the burden not only on the health system but on individuals and their carers. The personal cost both to patients and their family is immeasurable. (Deloitte Access Economics, 13 March 2013) (National Stroke Foundation, 2010)

Stroke mortality in rural and regional Australia is 20-30% higher compared to metropolitan areas, this is due in part to insufficient and inaccessible rural stroke units, that are able to provide effective treatments, including thrombolysis. This discrepancy indicates a need to identify and to improve stroke services in rural and regional NSW. (AIHW, 2007; Leira, Hess, Torner, & Adams, 2008)

There is overwhelming evidence that patients admitted to an ASU with coordinated services managed by a multidisciplinary team who specialise in stroke are more likely to be alive, with less disability and living at home one year after a stroke than patients managed on a general ward. (Indredavik, 2009; Langhorne, de Villiers, & Pandian, 2012;)

This study evaluated the outcome of a NSW state wide Early Access to Stroke Thrombolysis program initiated by the Ministry of Health, Ambulance Service NSW and Agency for Clinical Innovation to increase the utilisation of thrombolysis at the WWHS by reducing the time of the onset of stroke symptoms to access to a thrombolytic centre. This program included the training of paramedics in stroke signs and symptoms and ambulance diversion to a thrombolysis centre for patients with symptoms within 3 hours.

BACKGROUND/RATIONALE

To increase the number of ischaemic stroke patients receiving thrombolysis, the NSW the Ministry of Health, the Ambulance Service of NSW together with Stroke Services NSW initiated the state wide Early Access to Stroke Thrombolysis program (also referred to as the NSW Reperfusion project) which had the objective of reducing the time of acute stroke symptoms to accessing a 24/7 stroke thrombolytic centre.

When a thromboembolic arterial occlusion occurs, there is a brief therapeutic window during which time intravenous thrombolytic reperfusion can be provided. Thrombolysis is an intravenous drug treatment that that works by dissolving clots in the blood vessels in the brain, it has been proven to reduce death and disability in ischaemic stroke patients. Thrombolysis is a time dependent therapy and therapy must be commenced within 4.5 hours of stroke symptom onset. (Tsivgoulis, Katsanos, & Alexandrov, 2014). Therapy within this time window has been proven to be a safe and effective treatment but recent studies had shown that the earlier treatment commences the greater neurological improvement and associated lower mortality.

Intravenous administration of tissue plasminogen activator (tPA) is recommended by the Clinical Guidelines for Stroke Management National Stroke Foundation for the early treatment of acute ischaemic stroke. However only 1% of all stroke patients receive thrombolytic therapy, this is despite the Clinical Guidelines for Stroke Management suggesting 20% of ischaemic stroke patients may be eligible for thrombolysis. With the rate of thrombolysis being so low it is suggested numerous barriers exist both pre-hospital and in hospital.

Thrombolysis, also known as thrombolytic therapy, has been proven to have a substantial net benefit in selected ischaemic stroke patients. Thrombolytic therapy has been shown to improve the outcome for ischaemic stroke patients by reducing death and disability. (Grupke, Hall, Dobbs, Bix, & Fraser, 2015)The drug licensed for thrombolysis in Australia is Alteplase which is an intravenous drug treatment that works to dissolve clots in blood vessels in the brain, improve blood flow, and prevent damage to tissues and organs. It must be given within 4.5 hours of stroke symptom onset and has a clear set of guidelines. (National Stroke Foundation, 2010)

The average duration of an acute ischemic infarct from onset to completion differs widely from patient to patient. For a non-lacunar stroke, the duration of evolution may extend from 8 to 12 hours (Saver, 2006). The individual differences is influenced by location of vessel occlusion, levels of collaterals, and several other factors including blood sugar, blood pressure and volume of blood (Kidwell, Alger, & Saver, 2003)., 2006).

The main treatment objective for an individual who has suffered an ischemic stroke is to reinstate the cerebral blood flow as quickly as possible after an arterial occlusion, in order to decrease damage to viable brain tissue, resulting in lifelong disability and poor functional outcomes.(Tai & Yan, 2013)

To qualify as a thrombolytic centre stroke clinicians must have experience and education in the management of stroke and thrombolysis. The emergency department will have systems

in place that allow for the rapid triage, diagnosis, with expedited brain imaging and assessment for suitability for thrombolysis.(Brewer, Arize, McCormack, & Williams, 2014)

A major component of the Early Access to Stroke Thrombolysis program is the training of paramedics in the recognition of stroke symptoms. The National Stroke Foundation has a community awareness campaign called FAST. The FAST tool recognises the most common signs of stroke involving Face, Arm, Speech and Time to ring 000.

Facial weakness - can the person smile? Has their mouth or eye drooped?

Arm weakness - can the person raise both arms?

Speech difficulty - can the person speak clearly and understand what you say?

Time to act fast - seek medical attention immediately

(2006 National Stroke Foundation, FAST Campaign)

When paramedics assess a patient as having signs of stroke as per the FAST tool they then transfer the patient directly to a thrombolytic centre with arrival within 3 hours of symptom onset, this is a change from current protocol of transferring patients to their nearest hospital.

The Reperfusion program recognises the importance of involving the ambulance service as an essential strategy to reduce the time of acute stroke symptom to intervention. Pre hospital factors play a significant role in the overall time to presentation of a stroke patient at a thrombolytic centre. With the window for thrombolysis increasing from 3 to 4.5 hours, this should not be viewed as an opportunity to slow the assessment and transfer of patients rather management and planning should continue to focus on reducing the time of symptom onset to arrival for definitive treatment.

Although recognising and diagnosing stroke can often be challenging and complex, it is important that that patients with signs of stroke be identified and appropriate action initiated this also includes notification to the thrombolytic centre. There have been many tools developed to assist the paramedics to increase the accuracy of diagnosis of stroke and to differentiate patients with other diagnosis. The Los Angeles Pre-Hospital Stroke Screen (LAPPS), the Cincinnatti Pre Hospital Stroke Scale and the Melbourne ambulance Stroke Screen (MASS) and the Hunter NIHSS 8 are all ambulance screening tools validated through prospective studies.(Garnett et al., 2010) The NSW Reperfusion program initiated ambulance training using the FAST tool.

The most important element of using a stroke screen is that the tool assists the person assessing the patient to rapidly identify a potential stroke and take the appropriate steps to rapidly initiate transfer to a thrombolytic centre to improve patient outcome.

Recent advances in stroke management and treatment clearly demonstrates that early recognition of stroke symptoms by paramedics, as they are generally the first medical contact for stroke patients, has a pivotal role to play in the treatment of acute stroke. Organisation of ambulance services can reduce delay for patients by transporting patients to a facility that offers access to thrombolysis, rather than the nearest hospital.(Garnett et al., 2010)

Early ambulance coordination and communication with the thrombolytic centre has become a critical component to reducing delays to definitive care for patients with stroke, with research clearly stating poorer outcomes are directly related to increased time to thrombolysis. (McKinney, 2011)

Stroke Statistics

Stroke in Australia is currently the 2nd leading cause of death and the leading cause of disability. In 2014 it was estimated that there were 60,000 new or recurring strokes in Australia, with an estimated 30% of patients dying and a further 30% living with a disability. (National Stroke Foundation, 2010)

Stroke Units

The establishment of acute stroke units in rural and metropolitan hospitals has improved the outcomes for stroke patients by reducing death and disability. (Cadilhac et al., 2013; Indredavik, 2009) The Wagga Wagga acute stroke unit was opened in 2008, this was several years after stroke units in metropolitan areas. Many of these acute stroke units in rural and metropolitan centres now have the capacity to deliver acute thrombolytic therapy 24/7. Wagga Wagga became a 24/7 thrombolytic centre in December 2009. (Indredavik, 2009; Joubert et al., 2008)

The description for a stroke unit is for the unit to be situated in a geographically discrete ward that provides multidisciplinary care to stroke patients. It includes rapid assessment by medical, nursing and allied health staff, appropriate management of stroke as per National Guidelines and to facilitate timely investigations. A stroke unit must have rapid access to Computed Tomography (CT) imaging, carotid Doppler scanning, Magnetic Resonance Imaging (MRI) and pathology services. Other important functions of an acute stroke unit is to facilitate the introduction of new therapies and to be participate in stroke research. (Chan et al., 2012; Indredavik, 2009)

Stroke units provide high-dependency care including physiological and neurological monitoring, rapid treatment of stroke and associated complications, early rehabilitation and palliative care if appropriate.

The development of acute stroke units has shown to improve the outcome for stroke patients by reducing mortality, death and disability. The average length of stay has been reduced and more patients are discharged home with less disability and there has been a reduction of patients requiring transfer for nursing home care. (Indredavik, 2009)

The development of acute stroke units in New South Wales began in metropolitan sites in 2002, with the first rural stroke units opening in 2008. (Tai & Yan, 2013; Tsivgoulis et al., 2014) A number of these ASU's have now commenced a thrombolysis service with a total of thirty 24/7 thrombolytic centres now functioning in NSW. The ASU at Wagga commenced a 24/7 thrombolysis service in December 2009 and we now have thrombolysed 50 patients.

Local problem

The WWHS thrombolysis rate in 2011 was 4%, although this is disappointingly low it is similar to rates for other Australian hospitals including some metropolitan sites who are below 1%. The National Stroke foundation 2013 Clinical Audit determined that 976 patients presented to hospital within the thrombolysis window but the thrombolysis rate was 7% with only 45% of patients were assessed for thrombolysis. Recent evidence suggests that up to 24% of ischaemic stroke patients could be eligible for thrombolysis, if pre-hospital delay could be avoided (Boode, et al., 2007).

Approximately 6.5 million people or one-third of the Australian population live outside major cities. Stroke mortality in rural and regional Australia is approximately 20% and 25-30% higher compared to major cities in men and women respectively, due to limited access to effective treatments such as intravenous thrombolysis. (AIHW, 2007) Within many countries and world regions a geographic disparity in stroke incidence and mortality exists. (AIHW, 2007) This discrepancy indicates the growing need to identify the barriers to stroke thrombolysis within these rural and regional areas to allow tailored interventions to be developed.

Controversy surrounding the use of thrombolysis for Acute Ischaemic Stroke in Australia and in other countries around the world has been primarily due to a large number of multicentre randomised placebo controlled trials that have shown an overall benefit for early treatment with rt-PA, despite an increased risk of early haemorrhage. The largest and most statistically significant trial was a randomised controlled study which was conducted with dedicated stroke teams by the National Institute of Neurological Disorders and Stroke (NINDS) this was the first study to show benefit using rt-PA. (Lees et al., 2010)

The NINDS trial was the first thrombolysis trial that had a strict criteria for its use. This criteria allowed for the selection of patients most likely to benefit from thrombolysis and this criteria is used as guidelines for delivery of thrombolysis within the WWHS and as per the Clinical Guidelines for Stroke Management 2010. (Clark et al., 1999; W. Hacke et al., 1998)

Methodology used in the NINDS trial has been discussed, the group of patients with the better outcomes were patients treated within 90 minutes of stroke onset, with the longer treatment times showing less benefit. This raised bias with data suggesting patients rarely present to hospital within this timeframe and as this would be the smaller group it would be difficult to make this assumption. The other issue raised from the trial was that the stroke severity in the placebo group was higher than the treated group and this was suggested to bias the results.(Lees et al., 2010)

The results of other trials have failed to produce the same findings as the NINDS trial and this could be accounted for in the design and timeframes for treatment, as well as higher doses for administration of rt-PA.(Lees et al., 2010)

Extension of Thrombolytic treatment from 3 to 4.5 hours

The European Cooperative Acute Stroke Study (ECASS III) investigators conducted their third clinical trial to test the efficacy and safety of rt-PA treatment between 3 to 4.5 hours. Results demonstrated a modest but significant improvement in the clinical outcome of patients who received rt-PA between 3 to 4.5 hours as evidenced by a Modified Rankin score of 1 or less. Although the rate of intracranial haemorrhage was higher in the treatment group than with the placebo group mortality between the two groups was not significantly difference. Unlike the NINDS trial, patients with severe strokes were excluded from this trial. This could be the possible explanation of improved outcomes in both placebo and treatment groups of the ECASS III trial, as patients enrolled initially had less severe of stroke symptoms.(Werner Hacke et al., 1995)

BARRIERS-Pre hospital

Although the benefits of early stroke thrombolysis and timely administration of tPA have been demonstrated, only a small amount of patients actually receive thrombolytic treatment. This in part due to the delays that occur from symptom onset to arrival at a thrombolytic centre, together with the narrow time window of 4.5 hours for effective thrombolytic therapy.

Training paramedics and organising ambulance services to transport patients with signs of stroke are a fundamental change in organising management of pre hospital services. The factor consistently recognised as the largest prehospital barrier to arrival hospital within thrombolysis timeframe is public awareness, not only of the FAST signs of stroke but also the need to treat stroke as an emergency and ring the ambulance rather than ringing a relative or making a GP appointment, resulting in some stroke patients not accessing medical care for more than 24 hours after symptom onset. (McKinney et al., 2013)

The National Stroke Foundation launched their stroke awareness campaign FAST in 2006, this campaign in our region lacks effectiveness for creating awareness and behavioural change in the general public, this is evidenced by only ?% of patients been aware of the FAST campaign and % phoning the ambulance, this is the major contributor to our low thrombolysis rate (Bray, O'Connell, Gilligan, & Livingston, 2010).

The rural locations of patients means time is an important factor with many patients unable to access a thrombolytic centre within 3 hours. The ambulance protocol is that patients are to be transferred to the nearest hospital from pick-up.(Brewer et al., 2014)

There have been numerous barriers to stroke thrombolysis identified, not only in the MHLD but worldwide. A review of the pre-hospital barriers to thrombolysis show the:

- Community lack of awareness to stroke signs and symptoms, particularly in high risk patient groups.
- Patient action at stroke onset (Garnett 2010) and failure to call 000
- There is no efficient education in the media for the FAST message to create awareness and behavioural change in the community, particularly in the rural and regional areas
- A lack of pre-assessment tools (Johnson, & Bakas, 2010)
- Lack of knowledge of thrombolysis protocol

- A lack of by-pass protocols for the ambulance service (Nagao & Yan, 2011;
- Patient location for distance to a stroke centre (Nagao & Yan, 2011;

In-hospital Delays to Early Stroke Thrombolysis

Though delayed presentation to the emergency room after the onset of stroke symptoms has been identified as the major limiting factor to utilization of tPA, several in-hospital factors have also been identified in a review of the literature including:

- Delay in medical assessment: This may be related to incorrect triaging of a stroke emergency and thereby delay in alerting the acute stroke team, delay in initial medical assessment, and delay in neurologist's assessment. (Sreedharan & Ravindran, 2011)
- Delay in neuroimaging: This can occur due to delay in ordering a CT scan, delay in transporting the patient to radiology department, delay in scanning in patient and reporting of the results by the radiologist. (Lindsberg, Häppölä, Kallela, Valanne, Kuisma, & Kaste, 2006).
- Delay in obtaining consent for thrombolysis: This delay occurs from difficulty in obtaining consent from patients due to their decreased level of consciousness or speech impairment associated with acute ischemic stroke or staff are unable to contact the next of kin to obtain a history. (White-Bateman, Schumacher, Sacco, & Appelbaum, 2007).
- Delay from physician uncertainty regarding treatment with tPA: This delay arises from physician uncertainty regarding diagnosis of acute stroke, difficulty in initiating treatment within 4.5 hours and some staff are reluctant to commence tPA due to lack of confidence in tPA treatment or trial results.
- Delay from inefficient process of emergency stroke care. This delay has been attributed from delays in assessment, transfers and lack of collaboration. The lack of an expedited stroke triage pathway involving close collaboration between emergency personnel, emergency physicians, nurses, neurologist, and radiologist, can further contribute to in-hospital delay. (Lau, Soo, Graham, Woo, et al., 2010).
- There has been doubt by the emergency physicians regarding the efficacy and safety of rtPA and this has resulted in hesitancy by the emergency physicians to facilitate rtPA for patients due the unjustified perception of the risk of Intracerebral Haemorrhage (ICH).(Bentley 2009)

RESEARCH AIM:

This research aimed to measure the effectiveness of the NSW Reperfusion project developed by NSW Health in conjunction with Agency for Clinical Innovation (ACI) and the Ambulance Service of NSW, which had the primary focus to reduce to reduce the time of acute onset of stroke symptoms to arrival to a stroke unit, with access to 24/7 Thrombolysis and door to needle time for ischaemic stroke patients to receive assessment for thrombolysis.

The program also aimed to improve some of the known in-hospital barriers of lack of recognition of stroke signs, lack of physician knowledge and the lack of urgency for door to needle time to be as minimal as possible for optimum patient outcome.

METHODS:

ETHICS APPROVAL:

Ethics approval for this research was received from the Greater Western Human Research Ethics Committee (HREC).

HREC Project No. LNR/14/GWAHS/17

Funding for this research was provided by: Health Education and Training Unit

STUDY DESIGN:

A repeat cross sectional observational single centre cohort study reviewing the database of prospectively collected data of the Acute Stroke Unit (ASU) at the WWHS from the program pre- implementation period from the 19 January 2012 to 19 January 2013 to the post implementation period of 19 January 2013 to 19 January 2014.

This early access to Thrombolysis program included training every paramedic working in NSW to recognise the signs and symptoms of stroke according to the National Stroke Foundation FAST campaign and subsequently transport them to the nearest acute stroke unit hospital that offers a 24/7 stroke thrombolysis within 3 hours of symptom onset.

The ambulance paramedic provides advance hospital notification allowing the ED to prepare for the arrival of the patients and ensure that the CT scanner, when appropriate, will be freed up for the arrival and use of the stroke patient.

When the ED triage nurse receives a call from the paramedic they then activate the stroke page. This system is a single central page that alerts the Medical Registrar, Advanced Neurology Trainee and the acute stroke team that a FAST +ve patient will be arriving and an estimated time of arrival is given. When the patient arrives there is rapid triage and a repeated stroke page for stroke team notification.

When a stroke alert is called, a pre-prepared stroke package is used consisting of NIHSS scale, thrombolysis protocol, medication administration guidelines, inclusion/exclusion criteria, stroke specific order sets and the nursing care of the thrombolysed patient. The Neurologist/Physician is responsible for the rapid interpretation of the CT brain imaging, pathology results and the decision to thrombolyse.

In this study a quantitative methodology, using the FAST +ve program will be utilised to investigate whether the rates of Thrombolysis have increased since the program

commenced in January 2013. The data will be used to determine which patients have been transferred to the WWHS under the FAST +ve project, who were subsequently thrombolysed. Patients, who were transferred under the FAST + ve protocol and did not receive thrombolysis, will also be examined to determine the barriers which may have influenced this outcome.

The data base information was recorded as a routine best practice and was collected primarily by the Stroke Care Coordinator with each patient admission being recorded via information from electronic medical records, patient charts and patient interviews.

The database recorded patient demographics of age, sex and Indigenous status, together with patient risk factors such as Atrial Fibrillation, Diabetes, Hypertension, Ischaemic heart Disease, previous stroke and smoking status. Data was cleansed and cross-checked to ensure its accuracy. Missing data was retrieved from electronic records or hand written in patient progress notes.

To determine pre-hospital or in-hospital barriers to thrombolysis de-identified data, regarding patient presentation time, patient action at stroke onset, patient characteristics, rates of thrombolysis and reasons patient were not thrombolysed was reviewed.

Pre-hospital barriers were deemed to be present when the patient arrival exceeded 4.5 hours from stroke onset, and in-hospital barriers considered to be present when arrive at the WWHS within the thrombolysis timeframe but did not receive thrombolysis.

The time a stroke patient arrived at the WWHS is recorded as <4.5 hours or >4.5 hours, this determines if the patient is within the time frame to be assessed for thrombolysis.

Patient location was also recorded and will be discussed as either local or outlier, this is determined if the ambulance transfer has bypassed a rural hospital and transferred patients directly to the WWHS, local is patients who have a stroke within the Wagga Wagga area who do not by pass a hospital.

To determine these barriers to thrombolysis all patients have Action at stroke onset recorded, the options are recorded as: Called Ambulance, No action in the initial hour, GP appointment, phoned non-medical person, drove self to hospital or the stroke has occurred as an in-patient.

The reason a patient is not eligible for thrombolysis is entered into the database and recorded as: Time presented to hospital, delay in transfer from outlying hospital, National Institute of Health Scale (NIHSS) as <4 or >22, age, Intercerebral haemorrhage or other.

All appropriate patients were asked “Have you heard of the National Stroke Foundations campaign called FAST to recognise stroke signs” to determine their awareness of the FAST campaign. The response is classed as yes if patients can name all FAST signs.

Results:

A total of 280 patients were admitted to the ASU between 19th of January 2012and 19th January 2013. Of these, 133 patients presented with acute ischaemic stroke and were included in the data analysis, and 149 patients were excluded from data analysis for the following reasons 32 with transient ischaemic attack (TIA), 19 with intracranial haemorrhage, 96 patients presented with stroke mimic conditions and 2 were inpatients.

During the implementation period 19th January 2013 and 19th January 2014 there was a total of 302 patients admitted to the ASU. Of these 132 patients presented with acute ischaemic stroke and were included in the data analysis and 173 patients were excluded for the following reasons 32 presented as TIA, 15 with intracranial haemorrhage and 123 presented as stroke mimics

Figure 1: Characteristics of patients admitted to the ASU at WWBH

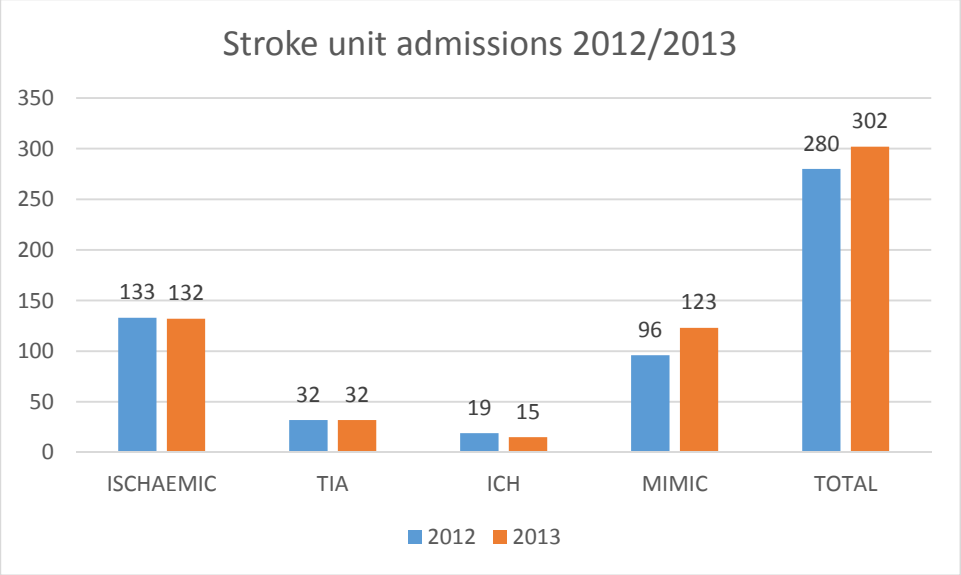


Figure 2: Characteristics of patients admitted to the ASU at WWHS.

Demographics		
Age – mean	73	76
Female	55	47
Male	76	80
Aboriginal or Torres Strait Islander	6	3
Risk Factors		
Atrial Fibrillation	46 (35%)	38 (28%)
Hypercholesterolemia	78 (59%)	69 (52%)
Hypertension	107 (81%)	106 (80%)
Diabetes	41 (31%)	31 (23%)
Ischaemic heart disease	34 (25%)	31 (23%)
Previous stroke	29 (22%)	25 (18%)
Current smoker	28 (22%)	26 (26%)
Previous smoker	44 (33%)	48 (36%)

Figure 3: Patient location prior to Stroke

The proportion of patient's thrombolysed increased from 3.8% (95%CI 1.2% to 8.7%) in 2012 to 9.5% (95%CI 5.0% to 16.0%) in 2013. This increase was not statistically significant (Fishers exact P=0.0805).

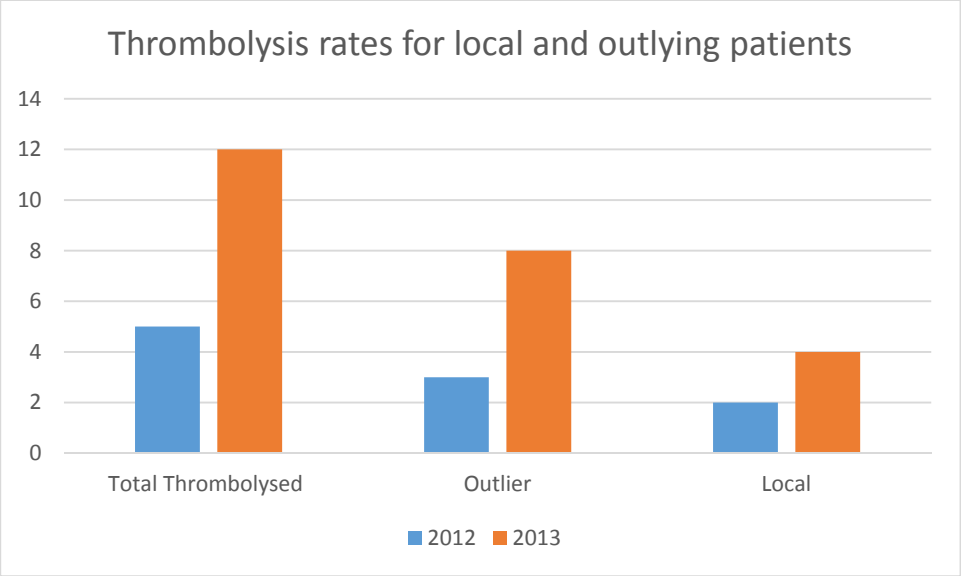
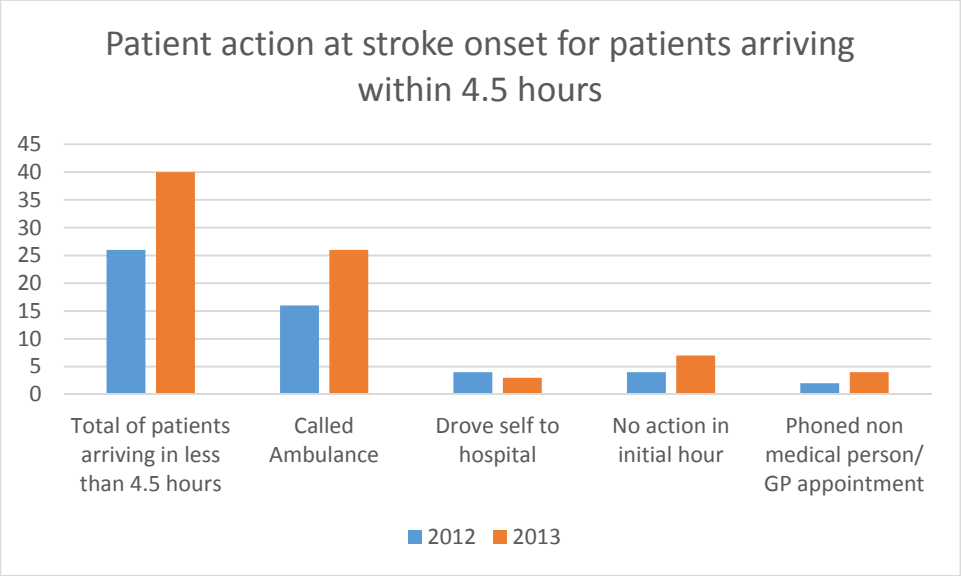


Figure 4: Patient action at stroke onset arriving within 4.5 hours



A significantly higher (p=0.002) proportion of patients (12.7%) were thrombolysed when they had called an ambulance as their first action compared to those that initiated other action (0.6%)

Those patients who called an ambulance at stroke onset were significantly more likely to arrive at hospital within the <4.5 hour timeframe as opposed to those patients who drove themselves to hospital, had a GP appointment or phoned a non-medical person or did not act on their symptoms at stroke onset.

Figure 5: Patient action at stroke onset for patients arriving greater than 4.5 hours.

104 patients (78%) in the 2012 patient sample and in 2013 85 (67%) patient sample arrived after 4.5 hours, although this is an improvement there is still a significant barrier.

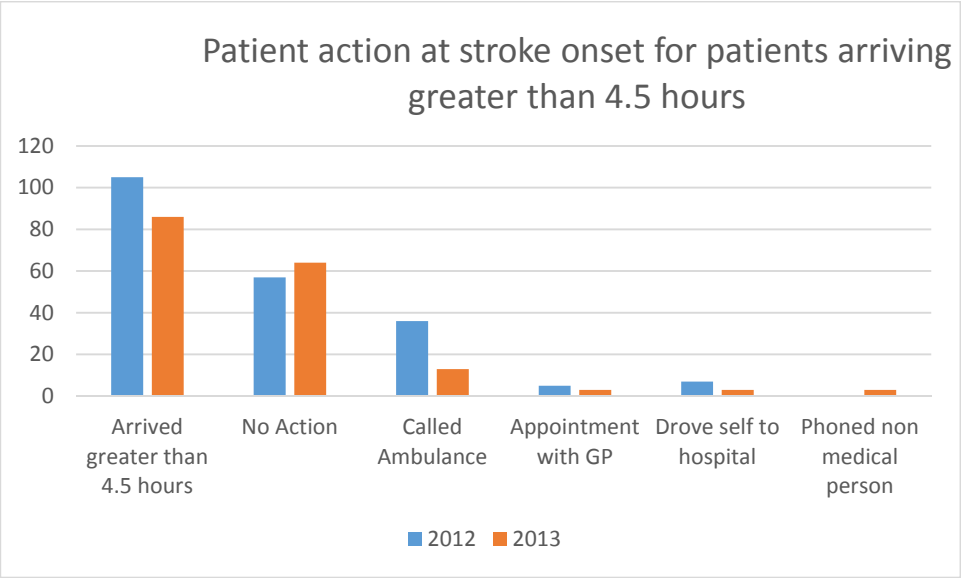


Figure 6: FAST Awareness

Only 5.9% of stroke patients had heard of FAST. The proportion of patients that had heard of FAST rose from 2.65% in 2012 to 9.2% in 2013. Knowledge of the NSF FAST campaign was minimal as illustrated in Table 6.

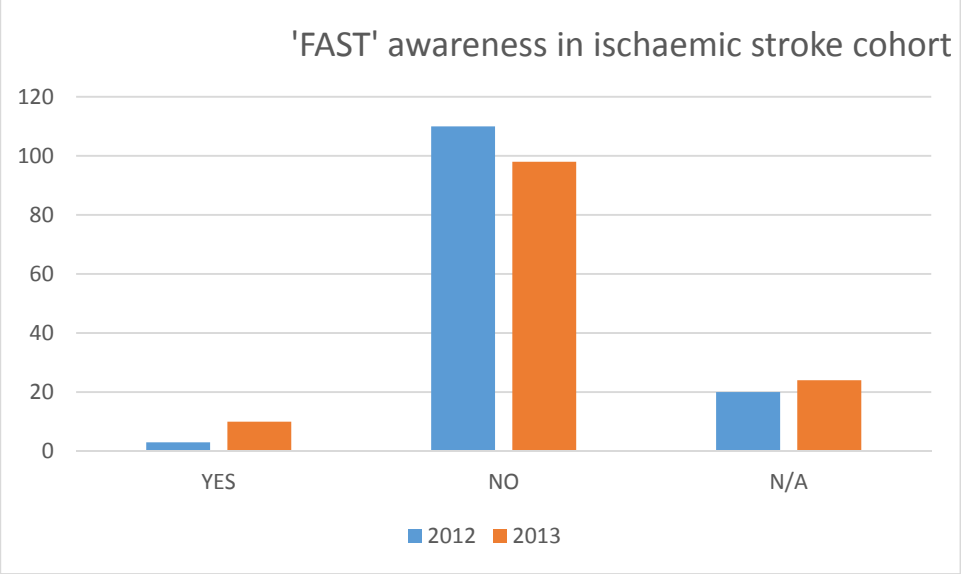
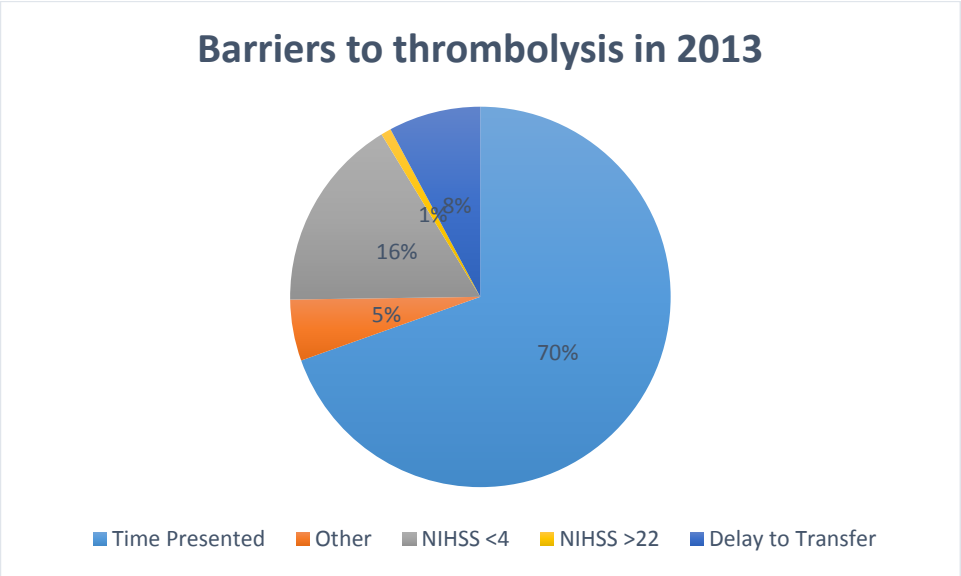


Figure 7: **Barriers to thrombolysis in 2013**



Whilst 67.4% of local patients had a delay that prevented thrombolysis this rose to 81.8% fo patients from outlying areas. This difference was statistically significant (Fishers exact test, P=0.0163).

DISCUSSION

With the introduction of the NSW Stroke Reperfusion Program the proportion of patient's thrombolysed increased from 5 patients 3.8% (95%CI 1.2% to 8.7%) in 2012 to 12 patients 9.5% (95%CI 5.0% to 16.0%) in 2013. This increase was not statistically significant (Fishers exact P=0.0805). The NSF determined from the 2011 Clinical Audit the national thrombolysis rate to be 7% which was higher than the WWHS 2012 rate, the rate in 2013 was 9.5%. The number of patient's thrombolysed remains disappointingly low, although there is an increase in the post implementation period there are significant barriers within the thrombolysis pathway.

Although a significant proportion of patients 41 (31%) arrived at the hospital in time to be eligible for thrombolysis the increase in the portion of patients thrombolyed was not statistically significant (P=0.0805). This could well be due to the small sample size. Although patients may arrive in time not all patients will be eligible for thrombolysis, this is due to the exact criteria for thrombolysis and the relatively small sample it was not possible to statistically adjust for the case variability between years. However, given the definitive evidence of improved timeliness increasing patient potentially eligible for thrombolysis it is likely that further accumulation of data with time will add to the statistical power and the clinical improvement in the proportion of patients being thrombolysed will become statistically significant.

The benefits of early stroke thrombolysis and timely administration of tPA have been demonstrated, only a small number of potentially eligible patients actually receive thrombolytic treatment. In 2013 41(31%) of patients arrived within 4.5 hours, all patients were assessed for thrombolysis and there were no in hospital barriers to patients receiving thrombolysis.

Among the patients in 2013 who presented with stroke 87 (65%) presented to the ED outside of the thrombolysis window, a further 29 patients presented within the window but were ineligible for thrombolysis for the following reason NIHSS of <4 and 10 patients also presented within time but were ineligible for other reasons including INR >1.1, recent surgery, premorbid function and NIHSS >22.

The significant factor in this study has been the recognition of stroke by paramedics and rapid transport to the WWHS for assessment for thrombolysis. In 2013 37% of patients who presented in less than 4.5 hours were outliers, this indicates the education on FAST and the initiation of patient transport to WWHS has been successful.

Early ambulance coordination and communication with the thrombolytic centre has become a critical component to reducing delays to definitive care for patients with stroke, with research clearly stating poorer outcomes are directly related to increased time to thrombolysis. In 2013 there were 9 patients who at stroke symptom onset rang the ambulance but were transported to their local health facility and ongoing transfer time arriving outside the thrombolysis window. This study was unable to determine if these cases there had been no paramedic training or paramedics didn't recognise the FAST tool and

divert the patient. This occurred at multiple sites, rather than at a specific site within the MHLD.

Patient location at stroke onset remains a barrier to thrombolysis with the proportion of patients who are ineligible for thrombolysis because of the delay to access treatment. This has resulted 67.4% of local patients having a barrier to thrombolysis that rises to 81.8% for patients that are outside the local area.

However early initial recognition of stroke signs and symptoms is crucial for an early presentation to the emergency department to access the most appropriate treatment and management for stroke. The NSF stroke symptom awareness campaign of FAST knowledge was poor within our ischaemic stroke cohort. In 2012, 2.65% of patients had heard of FAST and 9.2% in 2013. 18 patients in 2012 and 2013 20 patients were either not asked about their FAST knowledge or were unable to answer due to stroke severity or stroke type.(Figure 6)

In 2013 the greater majority of patients 70% arrived outside the thrombolysis timeframe of 4.5 hours, this indicates that the prehospital barrier is the most significant barrier to thrombolysis. (Figure 7) As the data shows, (Figure 7), patients who were admitted with an ischaemic stroke and may have been eligible for thrombolysis continue to recognize the signs of stroke and seek urgent medical treatment.

In hospital barriers are often given as an explanation why patients do not receive thrombolysis but during the time period of this research there were no patients who arrived in the emergency department within 4.5 hours that were not assessed for thrombolsysis

This study has not reviewed the door to needle time for thrombolysis but a measure of the reperfusion program was to improve the in hospital response, assessment and management of stroke which aims to improve thrombolysis time. The following areas based on best practice strategies of the program were reviewed.

The advance hospital notification by the ambulance service was a trigger for the Triage Nurse to initiate a stroke page to the stroke team with the message “FAST +ve patient with approximate arrival time. The ambulance notification also generates a phone call to medical imaging to provide notification of an expected urgent CT brain requirement, the expectation is that CT will be available as soon as the patient arrives.

With the patient arrival in the emergency department the stroke page is reactivated stating the patient has arrived rapid triage is attended including blood collection. Medical imaging is alerted that the patient is on their way and the patient is generally escorted to medical imaging by paramedics.

Once a stroke alert is called, a pre-prepared stroke packet is used consisting of NIHSS scale, medication guidelines, inclusion/exclusion criteria, stroke pathway, and Nursing care of the thrombolysed patient.

A prompt CT brain scan and interpretation of brain image and the immediate notification of by the radiologist to the Neurologist/Physician has not caused any delay to thrombolysis.

This study has confirmed the most recognised barrier to thrombolysis is the time between symptom onset and the time a patient reaches medical care accounts for the greatest contributor to prehospital delay. In 2012 only 2% of patients admitted to the ASU had any knowledge of FAST. This marginally increased to 9% in 2013.Evidence has suggested that continuous advertising of the FAST campaign is required to build and sustain public awareness of the signs of stroke.(Figure 6)

Patient/carer recognition of the signs of acute stroke and early presentation to hospital is the most important factor in the use of thrombolysis, the majority of ischaemic stroke patients arrived in ED in greater than 4.5 hours.

There have been many significant advances made in the treatment of stroke in recent times, with this study determining improvement in the prehospital and in hospital care. Although research acknowledges that the timing of thrombolysis has the greatest outcome for stroke patients. The window for administration of thrombolysis has increased from 3 to 4.5 hours, but the reality remains that the sooner therapy is commenced the better the outcome for the patient. Recent research supports the belief that the prehospital care of the patient can improve the symptom onset to definitive treatment time. The ambulance identification, reducing scene time and rapid transport to a thrombolytic centre all help to reduce the symptom onset to treatment time. Early notification to the thrombolytic centre has been shown to reduce delay to assessment and therapy, but the early arrival of patients to a thrombolytic centre should not be seen as an opportunity to delay therapy.

Furthermore, in-services and education of ER and other pertinent staff need to be conducted so they perceive a stroke alert with the same sense of urgency as assigned to a cardiac alert or trauma alert. They need to realize that with each passing minute and activity, the brain is dying and irrevocable damage is being done to millions of brain cells. It is also important to acknowledge the fact that door to needle time of less than 60 minutes may not be achievable in all patients presenting with acute ischemic stroke symptoms. Quality, safety and outcome data needs to be regularly and closely monitored for any possible unintended consequences from rushed assessments, dosing errors or complications.

The urgent treatment of acute ischemic stroke must be of the same priority as the treatment of acute myocardial infarction. The rule, lost time equals lost brain, must predominate in the thoughts of all who are involved in the transfer, receipt and treatment of stroke patients. This is why specific networks must be established to ensure rapid transfer of stroke patients to designated hospitals that have the ideal resources in place, bypassing those that do not.

DIRECTIONS FOR FUTURE RESEARCH:

Future research exploring patient action at stroke onset or lack of action as we know that this is the most significant barrier for patients accessing immediate stroke assessment and treatment. The present study provides an opportunity for continued evaluation of quality improvement and performance measures to ensure that acute ischemic stroke patients are treated in a timely manner.

Reviewing the Wagga Wagga Health Service door to needle time for stroke thrombolysis would be a worthwhile evaluation to ensure the service is within the “Golden Hour” for thrombolysis.

STRENGTHS AND LIMITATIONS OF THIS STUDY:

One of the strengths of this study was to enable the review of the thrombolysis service at the hospital that provides the only thrombolytic service within a health district with 14 spoke sites.

A limitation of the study was when analysing patient action at stroke symptom onset was not able to determine why the patient took no action or if there were reasons such as living alone.

This study was not able to determine the reason why ambulance diversion did not occur in 8 of the cases were patients at stroke onset rang the ambulance and were transported to their nearest hospital.

A limitations of this research is that using only a single centre for the study the findings may not be transferrable.

CONCLUSION:

This study examined the implications of the NSW Early Access to Stroke Thrombolysis and have found that the rate of thrombolysis has improved in the MHLD.

This study has shown that implementing a system of training paramedics in the FAST +ve tool, pre-notification and transporting patients to the WWHS has increased the number of patients presenting to the WWHS within the thrombolysis timeframe.

This study also highlighted the well-known pre-hospital barrier of stroke recognition by the community. Every effort needs to be made to increase community awareness of the signs and symptoms of stroke using the FAST message and understand the need to urgently ring the ambulance to access immediate medical care is essential.

Continual community education remains the major basis to any program aimed at reducing pre-hospital delays.

This study highlights the importance of ongoing education and training for paramedics to support their decision making with stroke diagnosis and transfer of patients to the WWHS. Supporting the training will empower the paramedics in stroke diagnosis and will be supported in their decision to immediately transfer patients to WWHS

REFERENCES:

AIHW. (2007). Rural, regional and remote health: a study on mortality. In AIHW (Ed.). Canberra.

Bray, J., O'Connell, B., Gilligan, A., & Livingston, C. (2010). Is FAST stroke smart? Do the content and language used in awareness campaigns describe the experience of stroke symptoms. *International Journal of Stroke, 5*(6), 440-446.

Brewer, L., Arize, C., McCormack, J., & Williams, D. (2014). Delays in the stroke thrombolysis pathway--identifying areas for improvement. *Ir Med J, 107*(5), 143-146.

Cadilhac, D. A., Purvis, T., Kilkenny, M. F., Longworth, M., Mohr, K., Pollack, M., & Levi, C. R. (2013). Evaluation of Rural Stroke Services: Does Implementation of Coordinators and Pathways Improve Care in Rural Hospitals? *Stroke, 44*(10), 2848-2853. doi:10.1161/strokeaha.113.001258

Chan, D., Cordato, D., O'Rourke, F., Chan, D. L., Pollack, M., Middleton, S., & Levi, C. (2012). Comprehensive stroke units: a review of comparitive evidence and experience. *International Journal of Stroke, 8*(4), 260-264.

Clark, W. M., Wissman, S., Albers, G. W., Jhamandas, J. H., Madden, K. P., & Hamilton, S. (1999). Recombinant tissue-type plasminogen activator (Alteplase) for ischemic stroke 3 to 5 hours after symptom onset. The ATLANTIS Study: a randomized controlled trial. Alteplase Thrombolysis for Acute Noninterventional Therapy in Ischemic Stroke. *JAMA, 282*(21), 2019-2026.

Deloitte Access Economics. (13 March 2013). The economic impact of stroke in Australia: National Stroke Foundation.

Garnett, A. R., Marsden, D. L., Parsons, M. W., Quain, D. A., Spratt, N. J., Loudfoot, A. R., . . . Levi, C. R. (2010). The rural Prehospital Acute Stroke Triage (PAST) trial protocol: a controlled trial for rapid facilitated transport of rural acute stroke patients to a regional stroke centre. *Int J Stroke, 5*(6), 506-513. doi:10.1111/j.1747-4949.2010.00522.x

Grupke, S., Hall, J., Dobbs, M., Bix, G. J., & Fraser, J. F. (2015). Understanding history, and not repeating it. Neuroprotection for acute ischemic stroke: From review to preview. *Clin Neurol Neurosurg, 129C*, 1-9. doi:10.1016/j.clineuro.2014.11.013

Hacke, W., Kaste, M., Fieschi, C., Von Kummer, R., Davalos, A., Meier, D., . . . Trouillas, P. (1998). Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II). *Lancet, 352*(9136), 1245-1251.

Hacke, W., Von Kummer, R., Kaste, M., Fieschi, C., Toni, D., Lesaffre, E., . . . Hennerici, M. (1995). Intravenous thrombolysis with recombinant tissue plasminogen activator for acute hemispheric stroke: The European Cooperative Acute Stroke Study (ECASS). *Journal of the American Medical Association, 274*(13), 1017-1025. doi:10.1001/jama.274.13.1017

Indredavik, B. (2009). Editorial: Stroke Unit Care is Beneficial Both for the Patient and for the Health Service and Should Be Widely Implemented. *Stroke, 40*, 1-2.

Joubert, J., Prentice, L. F., Moulin, T., Liaw, S. T., Joubert, L. B., Preux, P. M., . . . McLean, A. (2008). Stroke in rural areas and small communities. *Stroke, 39*(6), 1920-1928.

Langhorne, P., de Villiers, L., & Pandian, J. D. (2012). Applicability of stroke-unit care to low-income and middle-income countries. *Lancet Neurol, 11*(4), 341-348. doi:10.1016/S1474-4422(12)70024-8

Lees, K. R., Bluhmki, E., von Kummer, R., Brott, T. G., Toni, D., Grotta, J. C., . . . ECASS, A. T. L., N. I. N.DS and EPITHET rt-PA Study Group. (2010). Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials. *Lancet, 375*(9727), 1695-1703. doi:10.1016/S0140-6736(10)60491-6

Leira, E., Hess, D., Torner, J., & Adams, H. (2008). Rural - Urban differences in Acute Stroke Management practices. *Arch Neurology, 65*(7), 887-891.

McKinney, J. S., Mylavarapu, K., Lane, J., Roberts, V., Ohman-Strickland, P., & Merlin, M. A. (2013). Hospital prenotification of stroke patients by emergency medical services

improves stroke time targets. *J Stroke Cerebrovasc Dis, 22*(2), 113-118. doi:10.1016/j.jstrokecerebrovasdis.2011.06.018

National Stroke Foundation. (2010). *Clinical Guidelines for Stroke Management*: Stroke Foundation.

Organised inpatient (stroke unit) care for stroke. (2007). *Cochrane Database Syst Rev*(4), Cd000197. doi:10.1002/14651858.CD000197.pub2

Tai, Y. J., & Yan, B. (2013). Minimizing Time to Treatment: Targeted Strategies to Minimize Time to Thrombolysis for Acute Ischaemic Stroke. *Intern Med J*. doi:10.1111/imj.12204

Tsivgoulis, G., Katsanos, A. H., & Alexandrov, A. V. (2014). Reperfusion Therapies of Acute Ischemic Stroke: Potentials and Failures. *Front Neurol, 5*. doi:10.3389/fneur.2014.00215