Feasibility and criterion validity of The Holistic and Reliable Oral Assessment Tool (THROAT) in acute dysphagic stroke patients

Feasibility and criterion validity of The Holistic and Reliable Oral Assessment Tool (THROAT) in acute dysphagic stroke patients

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IV. List of Abbreviations and Acronyms

AF	Atrial Fibrillation
BOP	Bleeding on Probing
BPE	Basic Periodontal Exam
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
CRF	Case Report Form
CRN	Clinical Research Network
CSC	Comprehensive Stroke Centre
CXR	Chest X-ray (radiograph)
DCP	Dental Care Professional
EPR	Electronic Patient Records
GCP	Good Clinical Practice
GDP	General Dental Practitioner
GCS	Glasgow Coma Scale
IQR	Inter-quartile Range
IRAS	Integrated Research Application System
MRC	Medical Research Council
mRS	modified Rankin Score
NBM	Nil-by-mouth
NHS	National Health Service
NIHSS	National Institutes of Health Stroke Scale
PACS	Picture Archiving System
PICH	Primary Intra-cerebral Haemorrhage
PSC	Primary Stroke Centre
SAP	Stroke-associated Pneumonia
SD	Standard Deviation
SRFT	Salford Royal Foundation Trust

SSNAP	Sentinel Stroke National Audit Programme
THROAT	The Holistic and Reliable Oral Assessment Tool
WBC	White Blood Cell

V. Abstract

The University of Manchester
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Oral Health and Development of Stroke-Associated Pneumonia

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Introduction: Aspiration of oral bacteria is a biologically plausible mechanism in the development of stroke-associated pneumonia (SAP). There are no validated nursing assessment tools for oral health in stroke care or oral hygiene intervention trials. The Holistic and Reliable Oral Assessment Tool (THROAT) has been developed for use in older hospitalised patients and may have value in acute stroke patients. We evaluated the feasibility and concurrent validity of THROAT compared to a detailed dental examination in dysphagic acute stroke patients.

Aims: To assess the feasibility and concurrent validity of a nurse-assessed oral assessment tool (THROAT) compared to a detailed dental examination in dysphagic acute stroke patients. A secondary aim was to assess the predictive validity of the tool for SAP.

Method: A prospective, single-centre cohort observational design based at Salford Royal Foundation Trust. Patients within 24 hour of acute stroke onset, who were nil-by-mouth and expected to remain on the stroke unit >72 hours were screened for inclusion. THROAT was recorded by a research nurse, and a blinded dental care professional undertook a detailed dental examination, both within 24 hours of stroke symptom onset. Follow up every 48 hours until day 10 post-stroke was undertaken to determine acquisition of SAP.

Results: Of 51 eligible patients approached, 33 (65%) consented to participate with one withdrawal (n=32, median age 79y; 56% women; median NIH stroke scale score=10.5). Both oral examinations were successfully completed and well tolerated in all participants. The mean time to complete THROAT was 2.1 minutes, and 5.3 minutes for the dental examination. Correlation between the individual components of THROAT and the dental examination was generally poor, although there was a modest correlation (r=0.48, *p*=0.00519) between the 'Teeth/Denture' score of THROAT and 'percentage of teeth with ≥1 site with plaque present' from the dental examination. 6 patients were diagnosed with SAP (18.8%); those with SAP were significantly associated, $p<0.05$, with being older, being edentulous, having fewer teeth and not being registered with a GDP.

Conclusion: THROAT and detailed dental examination were both feasible in dysphagic acute stroke patients at risk of SAP. Larger studies are required to evaluate concurrent validity of THROAT, and the predictive validity of THROAT and dental examination for SAP and clinical outcomes.

VI. Declaration

That no portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

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1. Introduction

1.1 Definition, epidemiology and aetiology

1.1.1 Definition

A stroke occurs when the blood supply to the brain is interrupted causing acute ischaemia and cell death. The World Health Organization defined stroke as “rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin” (Aho, Harmsen et al. 1980). There are two main types of strokes; ischaemic and haemorrhagic. The former occurs when a cerebral artery becomes partially or fully occluded, often due to a blood clot, and the latter when the vessel ruptures (National Heart Lung and Blood Institute 2014). In the United Kingdom (UK), approximately 85% of strokes are ischaemic (Hinkle and Guanci 2007). Further definitions of cerebral infarction (ischaemic stroke) and intracerebral haemorrhage are outlined in Appendix 1 (Sacco, Kasner et al. 2013).

1.1.2 Epidemiology

In the UK, The Stroke Association estimated that every five minutes someone will have a stroke, which equates to approximately 152,000 people each year (Townsend, Wickramasinghe et al. 2012). Using data from three studies conducted in the UK in the latest available years, stroke incidence can be estimated to range from 125 to 280 cases per 100,000 (Table 1).

Table 1 Incidence of stroke in three studies across the United Kingdom

Study	Setting	Incidence/100,000
Oxford Vascular Study (Rothwell, Coull et al. 2005)	Oxfordshire, 2004	161
National Stroke Audit 2004 (Hippisley-Cox, Pringle et al. 2004)	Great Britain, 2003	125.5
The Scottish Borders Stroke Study (Syme, Byrne et al. 2005)	Scottish Borders, 1999	280

(Scarborough, Peto et al. 2009)

The results also inferred an even distribution of stroke incidence across both sexes, although Scarborough et al. (2009) argue that it is slightly higher in women.

Stroke is by no means a problem limited to western or high-income countries; its incidence has reached epidemic proportions across the world (World Stroke Organisation

2012).WHO estimated that in 2002 there were 15.3 million strokes worldwide (WHO 2002). A recent systematic review that reported on 56 population-based studies found that over the past 40 years, stroke incidence has increased more than 100% in low to middle income countries (Feigin, Lawes et al. 2009). For the first time, this has exceeded the level of stroke incidence seen in high-income countries by 20% (Feigin, Lawes et al. 2009). Furthermore, there is a diminution of stroke incidence in developed countries, mainly due to efforts to control the risk factors for stroke such as high blood pressure and smoking (Guilbert 2003). Nevertheless, the absolute number of strokes continues to increase due to the ageing population (McKay and Mensah 2004).

1.1.3 Important Risk Factors

A table of the stroke risk factors have been summarised in Table 2 and have been categorised into modifiable and non-modifiable risk factors.

Table 2 A Summary of Stroke Risk Factors

Non-modifiable	**Major modifiable**	**Other modifiable**
Advancing age	High blood pressure	Mental health
Atrial fibrillation	Abnormal blood cholesterol	Psychosocial stress
Coronary heart disease	Smoking	Alcohol use
Family history of stroke	Diabetes mellitus	Use of certain medication
Sex	Obesity	– oral contraceptive
Trauma (head injury)	Physical inactivity	- hormone replacements
	Unhealthy diet	

Hypertension (sustained high blood pressure) is the most important risk factor for stroke, contributing to about 50% of all strokes (Lawes, Hoorn et al. 2008). This can be further potentiated when in combination with other factors (World Heart Federation 2014). For example, the risk of suffering a stroke in smokers with high blood pressure is five times higher than that of a smoker with normal blood pressure and 20 times higher compared to a non-smoker (Aldoori and Rahman 1998). In particular, diabetics are at an increased risk of both hypertension and stroke (Stegmayr and Asplund 1995). Diabetes can increase stroke risk due to high levels of blood glucose increasing atherosclerosis-related inflammation. The hypothesis that diabetes may confer excess risk of stroke independently has long been investigated (Barrett-Connor and Khaw 1988). One study conducted in California, found ‘the increased relative risk for stroke in diabetes was still apparent after stratifying for blood pressure’ and after adjustments for other covariates.

The findings were also in concordance with the Framingham Study, the longest running prospective epidemiologic study, which found the incidence of cerebral infarction to be 2.5 to 3.5 times higher in diabetic patients compared with non-diabetic subjects (Kannel and McGee 1979).

Furthermore, the Framingham Study not only demonstrated hypertension as the principal risk factor for stroke (Wolf 2012); but it confirmed that impaired cardiac function also increases stroke risk due to a disturbed blood flow. The incidence of stroke more than doubles in the presence of coronary heart disease; more than quadruples in subjects with cardiac failure and is five times higher when atrial fibrillation (AF) is present (Wolf, Abbott et al. 1991). Lin et al. found that within this population the stroke patients with atrial fibrillation had 'higher mortality, more recurrences, worse severity, and poorer functional status' than those without (Lin, Wolf et al. 1996). The onset of AF can occur at any age, but is more common with increasing age; with a 5% increase in incidence over 65 years and a 10% increase in incidence over 80 years old (National Stroke Association).

Age is the most powerful non-modifiable independent risk factor for stroke and the risk of stroke doubles every decade after age 55 (McKay and Mensah 2004). In 2010, the total number of deaths from stroke in adults over 55 years old in the UK was 47,918, more than 32 times higher than those below the age of 55 (Townsend, Wickramasinghe et al. 2012). This represents a significant problem given the major demographic trends emerging for the future. By 2050, the number of people over the age of sixty will increase from 680 million to 2 billion, an increase from 11 to 22 percent of the world's population since 2009.(Pirkl 2009). At a national level, one in six people in the UK are currently aged 65 and over with this predicted to increase to one in four by 2050 (Cracknell 2010).

Other factors including mental ill-health, alcohol use, psychosocial stress and use of certain medication (some oral contraceptives and hormone replacement therapy) can contribute to stroke risk (Camargo 1989, Sacco, Benjamin et al. 1997, Pan, Sun et al. 2011, Henderson, Clark et al. 2013). Being female therefore increases risk of stroke because many of the risk factors are sex-specific (pregnancy, oral contraceptive use, postmenopausal use) or are more prevalent in women; AF, diabetes mellitus, hypertension, depression, psychosocial stress (Bushnell, McCullough et al. 2014). Two other major, but modifiable, risk factors for stroke are physical inactivity and obesity, both of which are of high prevalence in the UK. Although there is evidence that moderate physical activity (at least 2 hours and 30 minutes every week for adults aged 65 and over) can reduce the risk of stroke by up to 27% (McKay and Mensah 2004) approximately a

third of adults in the UK in 2009 are classified as ‘inactive’ (Scarborough, Bhatnagar et al. 2010).

Healthy lifestyle measures can be taken to prevent the risk of stroke such as eating high amounts of fruit and vegetables; it has been suggested that every extra portion of fruit/vegetable can reduce the incidence of stroke by a further 5% (Dauchet, Amouyel et al. 2006).

1.2 Stroke mortality and morbidity

1.2.1 Stroke mortality and morbidity

Stroke is the second leading cause of death worldwide (WHO 2008) and the leading cause of adult neurological disability (WHO 2004). Of the 15 million strokes occurring worldwide, nearly six million of these cause death and another 5 million cause permanent disability (2014). Stroke accounts for 53,000 deaths every year in the UK, approximately 9% of all deaths (Scarborough, Peto et al. 2009). In England, it is the third most common cause of death, after heart disease and all cancers (Adamson, Beswick et al. 2004).

However, the death rate from stroke has fallen over the last 40 years (Scarborough, Peto et al. 2009). This fall in mortality rate reflects the positive changes made in many countries to reduce stroke risk factors, including smoking rates and drug therapy aimed at reducing blood pressure. Combined with the improvements in acute care and the ageing population, the numbers surviving stroke is likely to increase, potentially increasing the burden of stroke disability (CDC 2003, Scarborough, Peto et al. 2009).

More than half of all stroke survivors are left dependent on others for everyday activities (Intercollegiate Stroke Working Party 2010) with 300,000 currently living with stroke-related disabilities in England alone. This costs the NHS over £2.8 billion a year (National Audit Office 2005).

1.2.2 Presentation and impact of stroke on patients

Stroke presents with sudden loss of focal neurological function, producing a range of neurological impairments. The pattern, extent and severity of the neurological impairments are influenced mainly by the region of the brain affected and the size of the stroke., There are a considerable range of disabilities among the 1.1 million stroke

survivors living in the UK; more than any other condition (Adamson, Beswick et al. 2004).They can be divided into the following categories (National Institutes of Health 2008):

1. paralysis or problems controlling movement (hemiparesis)
2. sensory disturbances including pain (hemi-sensory disturbance)
3. problems with balance/coordination (ataxia)
4. problems using or understanding language (aphasia)
5. problems with articulation (dysarthria)
6. problems with swallowing (dysphagia)
7. problems with visual fields (hemianopia)
8. double vision (diplopia)
9. problems with thinking and memory (cognitive problems)
10. emotional disturbances

Patients often experience several impairments relating to a particular area of the brain affected e.g. aphasia and weakness of the right limbs in a left hemisphere stroke. Paralysis or problems controlling movement are the most common of the disabilities resulting from stroke. This paralysis is usually on the side of the body opposite the side of the brain damaged by the stroke and can affect the face, a limb, or the entire side of the body. As many as 80% of stroke patients have difficulty with general movement and up to 40% are unable to use an arm in the long-term (Intercollegiate Stroke Working Party 2012). If this one-sided paralysis involves the complete inability to move it is referred to as hemiplegia or hemiparesis if it is less than total weakness. These patients have difficulty with daily activities such as walking or grasping objects.

Damage to the lower part of the brain, the cerebellum, can affect the body's ability to coordinate movement, a disability called ataxia. It can be identified by incoordination of limbs, wide and unsteady gait and impaired balance. There is a paucity in the literature regarding this functional impairment. Teasell et al. examined the incidence of ataxia in 85 consecutive admissions of brainstem stroke to be 86% (Teasell, Foley et al. 2002). A brainstem stroke can also result in diplopia. Teasell et al. (2002) found 38% of their patients were affected in this manner.

As many as two-thirds of people experience some change in their vision after stroke, exacerbating other stroke related symptoms (Stroke Association 2012). For example, people with hemianopia (loss of one half of the visual field), have difficulty reading and people with visual processing problems can suffer from prosopagnosia, which interferes

with the recognition of familiar people and objects (Stroke Association 2012). In turn this can lead to further frustration and a multitude of other emotional disturbances. Annoni et al. suggests that emotion complications can impact upon perceptive, motivational, autonomic and motor responses, whilst also affecting cognitive evaluation (Annoni, Staub et al. 2006). It is of upmost important that this is recognised by clinicians in the acute phase as emotion highly influences behaviour which could impact how the person responds to initial assessments. For example, when assessing speech, drowsiness, decreased level of consciousness and dysphagia can make the assessment more challenging.

1.2.3 Dysphagia

Swallowing, is a complicated reflex that involves six cranial nerves stimulating a well-orchestrated sequence of three major phases of muscle contraction; oral, pharyngeal and the oesophageal (Vega 2014). Dysphagia is a frequent and potentially serious complication of stroke (Smithard, O'Neill et al. 1997). A stroke can affect each of the swallowing phases by interrupting neuromuscular function at various levels (brainstem or cerebral hemispheres) (Sandhaus, Zalon et al. 2009). In a systematic review, dysphagia was shown to have an incidence of 37%-78% in acute stroke patients (Martino, Foley et al. 2005). This varying incidence largely relates to differences in definition of dysphagia and the timing and method of assessment. For many patients dysphagia is transient, and resolves spontaneously. Gordon et al. reported that most resolved within 14 days (Gordon, Hewer et al. 1987), with a mean time of 8.5 days. (Smithard, O'Neill et al. 1997).

In the interim, patients with dysphagia can suffer coughing or choking when trying to swallow, change in voice or speech (wet voice), gagging and nasal regurgitation (Morris 2009). Dysphagia can also often increase the patients' risk of developing other medical conditions. Unmanaged, it can reduce stroke sufferers' quality of life and lead to dehydration, malnutrition, respiratory infections and death (Ekberg, Hamdy et al. 2002). Dehydration causes sputum to thicken and patients may be affected by breathing difficulties. The associated malnutrition from dysphagia leads to lethargy and decreased ability to perform personal hygiene, to work and socialise and to be mobile. Dysphagia is a risk factor for aspiration; when oropharyngeal or gastric material passes beyond the true vocal fold and is misdirected into the lower respiratory tract (Hammond and Goldstein 2006). Aspiration occurs in about 40-50% of stroke patients with dysphagia (Marik and Kaplan 2003). Aspiration pneumonia occurs when these inhaled secretions are colonised by pathogens. Due to this chain of events, many studies have inferred a relationship between dysphagia and aspiration pneumonia (Martin, Corlew et al. 1994, Kidd, Lawson

et al. 1995, Langmore, Terpenning et al. 1998). Furthermore, Martino et al. found the presence of confirmed aspiration is strongly associated with pneumonia (RR 11.56; 95% CI 3.36-39.77) in dysphagic stroke patients (Martino, Foley et al. 2005).

1.2.4 Stroke associated pneumonia

Aspiration pneumonia is one of the commonest complications of stroke and has a major impact on outcome. It occurs in around 10% of patients hospitalised with stroke, most frequently during the first week after stroke onset (Westendorp, Nederkoorn et al. 2011), which may reflect the high prevalence of dysphagia during the acute phase. Several studies have highlighted the adverse impact of infections on the outcome of stroke. Stroke-associated pneumonia (SAP) independently increases in-hospital mortality 2-6 fold, and increases hospitalisation costs, length of stay and likelihood of a poor outcome in survivors (Katzan, Cebul et al. 2003); (Ovbiagele, Hills et al. 2006); (Finlayson, Kapral et al. 2011); (Wilson 2012); (Aslanyan, Weir et al. 2004); (Katzan, Dawson et al. 2007); (Tong, Kuklina et al. 2010); (Koennecke, Belz et al. 2011). In one study it was reported that as many as 34% of all stroke deaths were due to acquisition of pneumonia. It represents the third highest cause of mortality in the first month following stroke (Addington, Stephens et al. 1999).

Whilst aspiration is strongly associated with SAP, the pathophysiology of SAP is not fully understood. However, SAP is a clinically important complication and is a potentially preventable cause of significant morbidity and mortality. Better understanding of the pathophysiology of SAP and its risk factors is of fundamental importance when approaching prevention and treatment.

1.3 Clinical management

1.3.1 Clinical management of stroke

Detail on the full spectrum of stroke management is beyond the scope of this thesis. Nonetheless, modern management of stroke is focused around urgent assessment and timely transfer to specialist stroke units for individualised multidisciplinary care. Medical treatments for acute ischaemic stroke include thrombolysis (to disperse occluding thrombus), aspirin (NICE 2008) and strategies to prevent complications or recurrent vascular events. Due to the range of stroke-associated disabilities, post stroke management and rehabilitation encompasses services from a range of health care

professionals: physicians; nurses; physiotherapists; occupational therapist; speech and language therapists and vocational therapists. The importance of a multi-disciplinary approach was highlighted by the National Institute for Health and Care Excellence, who published guidelines in 2008. Following presentation, brain imaging should be performed to determine stroke subtype (ischaemic or haemorrhagic) immediately (within an hour) if thrombolysis is potentially indicated, or as soon as possible (within 24 hours of symptom onset) (NICE 2008).

1.3.2 Clinical and nursing assessments

Basic observations such as oxygen saturation, blood glucose levels and blood pressure, should be carried out by nurses to aid maintenance or restoration of homeostasis. These are carried out at least four hourly on admission depending on the clinical presentation. Determining the Glasgow Coma Scale (GCS) score of stroke patients at initial assessment and during the acute phase is a routine clinical practice in many institutions; it is a neurological scale that assessed the conscious state of the patient (Miah, Hoque et al. 2009). GCS score on admission along with other demographic variables such as cardiac status and severity of neurological dysfunction (National Institutes of Health Stroke Scale, NIHSS) (Appendix 2) can be used as valuable predictors for outcome of stroke patients (Miah, Hoque et al. 2009); (Tsao, Hemphill et al. 2005); (Ebell 2008). Dysphagia can also be an independent predictor of mortality as it has been suggested that it carries a sevenfold increased risk of aspiration pneumonia (Singh and Hamdy 2006), so early detection of dysphagia is vital.

1.3.3 Assessment of swallowing function

It is important that people with acute stroke are screened for dysphagia by an appropriately trained healthcare professional before being given any oral food, fluid or medication (NICE 2008). This should be undertaken within 4 hours of admission (Intercollegiate Stroke Working Party 2012). The most frequently used swallow test is the bedside water swallow screen, which involves stages of dry swallow and sips of different volumes of water. The purpose of this is to provide a method of early detection of dysphagia with the aim of improving timely management and patient outcomes. Bedside tests are safe, relatively straightforward, and easily repeated but are shown to have variable sensitivity (42% to 92%), specificity (59% to 91%), and inter-rater reliability (κ=0 to 1.0) (Ramsey, Smithard et al. 2003). It may be hospital protocol, as with Salford Royal Foundation Trust, that a pre-screening checklist (Appendix 3) is completed before progressing to the initial stroke water swallow screen (SWSS).

If this initial swallow screen identifies a problem it will be followed up by a specialist assessment, by a speech and language therapist, for the implementation of an on-going management plan. This involves re-assessment with texture-modified diets, general dysphagia therapy programs, non-oral (enteral) feeding, monitoring route of medications, and physical and olfactory stimulation. Instrumental assessments of swallowing e.g. videofluoroscopy (VF) may be required to supplement clinical assessment and tailor management. Management of dysphagia largely focuses on strategies to avoid aspiration following stroke. Until then, if the healthcare team conclude an unsafe swallow, 'nil by mouth' is employed (Stroke Association 2012).

It is when these swallowing problems are not assessed early enough that serious complications can arise, as aforementioned; dehydration, malnutrition, aspiration and aspiration pneumonia (Morris 2009).

1.3.4 Avoidance of Stroke Associated Pneumonia

Current guidelines of stroke treatment recommend early antibiotic treatment in case of suspected pneumonia for example, appearance of fever (Adams, Del Zoppo et al. 2007). Although if the underlying cause (e.g. aspiration) of the pneumonia is not identified and treated, it is likely to recur (Langmore, Terpenning et al. 1998). In hospital settings, precautions such as elevating the head of the bed and treating any nausea and vomiting are commonly carried out to prevent aspiration of refluxed material, along with protection of the airway and bedside suctioning (Langmore, Terpenning et al. 1998, Chamorro, Horcajada et al. 2005). However, there is a lack of formal evidence-based data on prevention guidelines and early management of post stroke infections in general.

In a prospective study, Sellars et al. confirmed the multifactorial nature of aspiration pneumonia in acute stroke patients and identified several independent risk factors including failure of the water swallow test (Sellars, Bowie et al. 2007). However, having dysphagia and aspiration are not necessarily sufficient to predict risk of aspiration pneumonia (Langmore, Terpenning et al. 1998). Consistent associations were shown for older age, stroke severity (as measured by the NIHSS), impaired level of consciousness, gastroesophageal reflux or vomiting, and a compromised immune system (Finegold 1991, Perry and Love 2001, Aslanyan, Weir et al. 2004, Sellars, Bowie et al. 2007, Satou, Oguro et al. 2013). Several more recent studies have attempted to derive clinical risk scores for identifying individuals at-risk of developing pneumonia using baseline clinical characteristics. A clinical risk score, ISAN (prestroke Independence, Sex, Age, NIHSS), has recently been suggested to be a promising tool for SAP prediction and is the first

study to include haemorrhagic strokes, but external validation is required (Smith, Bray et al. 2015) The simplest, and best validated is the A^2DS^2 score as a tool for the prediction of post-stroke pneumonia using clinical variables on admission; age 75+, atrial fibrillation, dysphagia, sex (male) and stroke severity (NIHSS) (Hoffmann, Malzahn et al. 2012). There were a number of limitations to this study, including a lack of standardisation for the screen for dysphagia. Keeping dysphagia as a constant would be useful to compare the effect of other risk factors of SAP, especially in regards to the plausibility of aspiration via the oropharynx. It remains uncertain to what degree the aspiration of colonised oropharyngeal contents contributes to pneumonia (Langdon, Lee et al. 2008).

Many studies regarding the bacteriology of aspiration pneumonia infer that a combination of colonisation of the oropharynx with bacterial pathogens and micro aspiration of saliva containing these bacteria may be the most common source of aspiration pneumonia (Mulligan R 1992, Terpenning, Bretz et al. 1993, Langmore, Terpenning et al. 1998, Terpenning, Taylor et al. 2001, Azarpazhooh and Leake 2006, Hassan, Khealani et al. 2006). The oral cavity harbours thousands of species of micro-organisms and may be an important reservoir for aspiration of bacteria which can cause stroke-associated pneumonia in susceptible individuals.

1.4 The importance of oral health in stroke and its sequelae

1.4.1 Role of oral health in stroke

There is evidence for a two-way association between oral health and stroke (Loesche and Lopatin 1998). There are several potential pathophysiological mechanisms to link gingivitis and periodontal disease to stroke (Dörfer, Becher et al. 2004). Gingivitis, inflammation of the gums, is the initial stage of gum disease. If left untreated gingivitis can become periodontitis, which is irreversible damage involving the progressive loss of the alveolar bone around the teeth and eventual tooth loss. Periodontitis is caused by the presence of microorganisms on the tooth's surfaces, along with an exaggerated host response against these microorganisms. The inflamed periodontium may release bacteria and inflammatory markers into the blood stream which could contribute to causation of stroke (Li, Kolltveit et al. 2000, Sfyroeras, Roussas et al. 2012). However, such associations between periodontal disease and incidence of stroke do not imply causation, and may be markers of other pathophysiological processes causing stroke or shared risk factors.

Patients hospitalised with stroke are less likely to have visited a dentist in the preceding year, have greater tooth loss and worse levels of gingivitis and periodontitis than non-stroke controls (Pow, Leung et al. 2005); (Grau, Becher et al. 2004); (Pradeep, Hadge et al. 2010); (Ghizoni, Taveira et al. 2012); (Yoshida, Murakami et al. 2012). One cohort study concluded that men who had ≤24 teeth at baseline were at a higher risk of stroke compared to men with ≥25 teeth (HR=1.57; 95% CI, 1.24 to 1.98) (Joshipura, Hung et al. 2003). Since edentulousness is a common consequence of periodontitis it was found to be independently associated with admission stroke severity (Slowik, Wnuk et al. 2010).

1.4.2 Impact of stroke on oral health

On the contrary, the acute stroke patient is often unable to perform adequate oral care (Clayton 2012). Post-stroke impairments such as paralysis and cognitive problems can lead to problems with manual dexterity and coordination when using a tooth brush, difficulties when rinsing and a diminished awareness when there is food or residue left in the oral cavity (Arai, Sumi et al. 2003); all of which can subsequently lead to caries (tooth decay), gingivitis or periodontal disease. Certain medications prescribed for patients after stroke may further impact their oral health, leading to dry mouth (xerostomia), ulcers and stomatitis (Ghezzi and Ship 2000, Janket, Jones et al. 2003). Xerostomia in stroke patients can also be caused by decreased levels of consciousness, mouth breathing, oxygen therapy and by being nil-by-mouth (Bartels 2005). Dry mouth not only gives rise to an increased incidence of caries, periodontal disease and oral infection (e.g. candida albicans) but can impact denture wearers. Saliva is essential for denture retention and stability, and without it may cause mucosal injury and discomfort. Stroke patients with dentures also have to contend with facial muscle coordination problems and physical changes in the mouth post-stroke, for example facial drooping. This will exacerbate any speech and swallowing difficulties (Monaco, Cattaneo et al. 2012). Research shows that such people have a poorer quality of diet, consume fewer fruits and vegetables and eat a lower variety of foods compared to subjects with some of their own teeth or properly fitting dentures (Sahyoun and Krall 2003). Thus, ill- fitting dentures can directly impact quality of life. As many as 50% of stroke survivors have reported to wear removable dentures (Zhu, McGrath et al. 2008). A prospective study by Iinuma et al. confirmed that overnight denture wearing can potentiate the risk of pneumonia, with a hazard ratio of 2.35 (Iinuma, Arai et al. 2014). Interestingly, the nocturnal denture wearers in this study were also associated with a lower frequency of dental visits and denture cleaning. Therefore, more research is needed to definitively conclude that only the removal of dentures during sleep would be significantly sufficient to reduce the risk of pneumonia.

Those that wear dentures whilst they sleep were more likely to have tongue and denture plaque, gum inflammation, *Candida albicans* prominent culture and higher levels of circulating interleukin-6 (Iinuma, Arai et al. 2014); denture stomatitis can harbour potentially infectious respiratory pathogens.

1.4.3 Role of oral health in SAP

The link between oral health and systemic disease has been documented through several clinical studies and reviews (Shay 2002, Terpenning 2005, Azarpazhooh and Leake 2006). The pathogenesis of aspiration pneumonia occurs if the material aspirated is pathogenic to the lungs and if the host response is impaired. The bacteria in the oropharynx can depend on many varying factors such as malnutrition, inactivity and presence of oral/dental disease (Johanson, Pierce et al. 1969, Verghese and Berk 1983). The latter affects the oral flora composition more directly, including plaque, gingivitis, periodontal disease and tooth decay.

In Marik's review of the bacterial aetiology of aspiration pneumonia he showed that the most frequently isolated microorganisms in the cause of infection were aerobic gram-negative bacilli, AGNB (Marik 2001). However, these microorganisms are not ordinarily part of the 'healthy' oral flora (Marsh, Martin et al. 2009). Oro-pharyngeal carriage of gram-negative organisms (e.g. *Pseudomonas aeruginosa, Porphyromonas gingivalis*), *Staphylococcus aureus* and yeasts (e.g. *Candida albicans*) is present in some patients with acute stroke (Gosney, Martin et al. 2006);(Zhu, McMillan et al. 2008); (Hirota, Konaka et al. 2010), and as high as three-quarters of stroke patients in one study (Lam, McMillan et al. 2013). P*. gingivalis* (found in supragingival plaque) is an important anaerobic pathogen associated with periodontal disease and its relationship as a risk factor for aspiration pneumonia has been previously reported (Scannapieco and Mylotte 1996, Mojon, Budtz-Jørgensen et al. 1997). *S. aureus,* not usually related to the oral flora, was found to be the only bacterial species significantly associated with aspiration pneumonia in *both* the dentate and edentulous patient groups in a prospective study in a veteran population (Terpenning, Taylor et al. 2001). A possible explanation of the increased rate of oral colonisation of AGNB in stroke patients is the 'physical change in the cleansing of the oral cavity, altered epithelial surfaces and changes in the saliva flow and distribution' (Millns, Gosney et al. 2003). However, the relevance of particular classes or species of micro-organisms is unclear, and another study failed to demonstrate an independent association between oral yeasts, coliforms or *S. aureus* and development of pneumonia in stroke patients (Sellars, Bowie et al. 2007). Thick and sticky saliva or xerostomia contributes to a higher concentration of microorganisms and if aspirated or mixed with

food or liquid up to 100,000,000 bacterial/ml salvia could enter the lungs. Dry mouth also increases the risk of plaque development and dental caries (Bartels 2005), however, although a factor, it was not independently related to development of pneumonia (Sellars, Bowie et al. 2007).

It is consistently found that there are many putative oral/dental risk factors significantly associated with aspiration pneumonia. A cohort study of 189 male veterans found significant predictors of aspiration pneumonia included being dependent for feeding, dependent for oral care, number of decayed teeth, tube feeding, more than one medical diagnosis, number of medications and smoking (Langmore, Terpenning et al. 1998).

1.4.4 Interventions to improve oral health

Oral health and oral care are recognised to be important by stroke patients and staff, yet oral care is a relatively neglected part of stroke unit care (Talbot, Brady et al. 2005), (Horne, McCracken et al. 2014). Interventions to improve oral care in the acute phase of stroke could form the basis for reducing pneumonia and improving patient experience and clinical outcomes (Eisenstadt 2010). In a systematic review (van der Maarel-Wierink, Vanobbergen et al. 2011), two studies, one using 40 elderly nursing home patients and the other 358 stroke patients, showed that improvement of oral health care diminished the risk of developing aspiration pneumonia and the risk of dying from aspiration pneumonia directly (Yoshino, Ebihara et al. 2001, Yoneyama, Yoshida et al. 2002). The three remaining studies conferred that adequate oral health care decreased the amount of potential respiratory pathogens and suggested a reduction in the risk of aspiration pneumonia by improving the swallowing reflex and cough reflex sensitivity (Watando, Ebihara et al. 2004, Bassim, Gibson et al. 2008, Ishikawa, Yoneyama et al. 2008). However, the complex neurological impairments encountered in patients with stroke, and lack of staff training pose significant challenges to safe and effective delivery of oral care interventions in stroke patients. Small phase 2 studies have demonstrated that chlorhexidine-based interventions are feasible and reduce indices of plaque/periodontal disease, but have not been powered for pneumonia or clinical outcomes (Lam, McMillan et al. 2013, Kim, Jang et al. 2014).

1.4.5 Need for further research

There are several issues to consider for further development of oral care interventions in acute stroke unit care. Firstly, “proof-of concept” relating poor oral health to the development of stroke-associated pneumonia to support biological plausibility for oral care interventions has yet to be established. Secondly, whilst detailed “gold standard”

dental assessments have previously been undertaken in patients with acute stroke without reported adverse effects (Grau, Becher et al. 2004); (Pradeep, Hadge et al. 2010); (Ghizoni, Taveira et al. 2012), the feasibility of dental assessment in patients at greatest risk of stroke associated pneumonia (advancing age, nil-by-mouth and worse stroke severity, NIHSS score) is uncertain. Thirdly, the availability of trained dental professionals to provide assessments routinely in stroke unit care is very limited and unfeasible. Since nursing staff constitute to the majority of the ward care and daily assessments, there is a need for preventative strategies which are simple, replicable and require a short amount of time to carry out during routine examinations. The British Dietetic Association state that mouth care should be considered when assessing and managing patients with dysphagia (Hughes 2011). Since swallow screen is carried out at regular intervals post-stroke admission, then oral health care should be held in the same regard as an essential component of holistic care (Stout, Goulding et al. 2009).

There have been many publications offering oral assessment tools and guidelines for their use; however no single tool appears to have achieved pre-eminence and there are currently no fully validated nursing oral assessment tools for phase 2/3 studies and clinical practice. Assessments can be hindered by reluctance and nurses' perceptions about oral care (Evans 2001) along with factors such as lack of equipment, poor education and time pressures. The Holistic and Reliable Oral Assessment Tool (THROAT) was derived and evaluated in acutely hospitalised elderly patients, which included recovering stroke patients, and is reliable with established content validity (Dickinson, Watkins et al. 2001). The THROAT (Appendix 4) allows seven areas of the mouth to be assessed using a numeric scale 0-3. However, the THROAT has not been externally validated in patients in the acute phase of stroke, and the criterion validity relating to gold standard dental measures or for predicting stroke associated pneumonia is not known.

2. Aims and Objectives

The aim of this study is, therefore, to assess the feasibility and concurrent validity of a nurse-assessed oral assessment tool (THROAT) in the acute stroke setting. A secondary aim is to to assess predictive validity of the tool for stroke-associated pneumonia (SAP). The objectives were to:

1) Assess the feasibility of undertaking the THROAT (nursing staff) and a dental assessment (research DCP) in acutely dysphagic stroke patients, within 24 hours of onset
2) Evaluate concurrent validity of THROAT using the dental assessment as criterion standard
3) Explore the associations of the THROAT and the dental assessment with the occurrence of SAP

3. Methods

3.1 Study Design

This was a prospective, single-centre cohort observational study to primarily assess the feasibility and concurrent validity of The Holistic and Reliable Oral Assessment Tool (THROAT) in acutely dysphagic stroke patients.

3.2 Study Setting

This study was undertaken at Salford Royal NHS Foundation Trust (SRFT), which provides the Comprehensive Stroke Centre (CSC) for the Greater Manchester Clinical Stroke Network. Stroke services in Greater Manchester are configured to provide hyper-acute stroke care at one of three specialist receiving centres – the CSC at Salford, and two primary stroke centres (PSCs) at Stockport (Stepping Hill Hospital) and Bury (Fairfield General Hospital). Patients who are FAST (Face Arm Speech Time) positive, presenting with symptoms within four hours of onset are brought directly to one of these centres in line with protocols established with the ambulance service. FAST is an easy and rapid way to identify the most commons symptoms of stroke; facial droop, arm weakness and slurred speech. Each centre serves a third of the conurbation during the hours of 0700-1900 Monday-Friday, whilst Salford receives all patients within 4 hours of symptom onset out of hours and at weekends. The term 'hyper-acute stroke care' describes specialist services provided to patients within a short time (usually first 24-72 hours) after stroke. An acute bundle of care is delivered (including brain imaging, thrombolysis where indicated, swallow assessment, administration of aspirin, therapy assessment). Once stable and the care bundle has been given, patients are repatriated to their local stroke unit (district stroke centre or PSC) for ongoing care, investigation and rehabilitation. SRFT therefore only provides ongoing care and rehabilitation to Salford residents and all other patients would be relocated.

3.3 Ethical Considerations

3.3.1 Ethical Approval

Minor amendments were made to the study protocol following an IRAS (integrated research application system) review via teleconference on 18/09/2014.The study (14/WA/1153) was then approved by NRES Wales Research Ethics Committee 5 and received a favourable opinion (Appendix 5).

3.3.2 Participant Confidentiality

Throughout the study it was ensured that the participant's anonymity was maintained. Patients were identified by their initials and a unique participant study number only on any documentation associated with the study. Data was stored in accordance to local data protection guidelines and in keeping with the Medical Research Council's (MRC) Personal Information in Medical Research Guidelines (Medical Research Council 2000).

3.3.3 Declaration of Helsinki

The Principal Investigator ensured the study was conducted in full conformity with the current version of the Declaration of Helsinki (World Medical Association 2013).

3.3.4 Guidelines for Good Clinical Practice (GCP)

The Principal Investigator ensured that the study was conducted in full conformity with Research Governance Framework and Good Clinical Practice.

3.4 Study Procedure

Figure 1 An overview of the study procedure

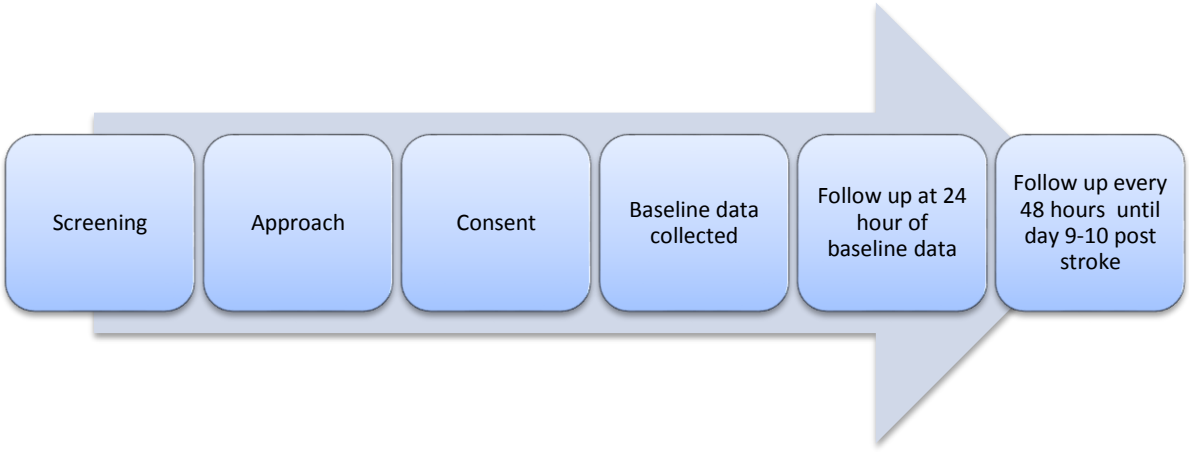


Figure 1 gives a broad overview of the study procedure beginning with screening and approaching of the patients and following through to end of study assessments. An outline of the study schedule was incorporated into the front of each case report form (Appendix 6)

3.4.1 Data Collection

An individual paper case report form (CRF) was completed for each patient recruited into the study to store collated data, in line with Good Clinical Practice guidelines. Any

information was non-identifiable and the list of patients and the respective CRF number was kept in the secure site file at SRFT. The total time spent with each patient was kept at a minimum so as not to disrupt clinical routine care. Most data collection could be done remotely using the hospitals EPR, electronic patient record, systems (Allscripts' Sunrise Clinical Manager). However, it was necessary to visit the patient on the ward to do the oral assessments, to record any adverse events and to confirm the swallowing/nutritional status of the patient.

3.4.2 Screening

All patients who were admitted to Salford Royal Foundation Trust with a suspected stroke were screened for eligibility, by the local Comprehensive Research Network (CRN) stroke research practitioners and the research dental care professional, using the criteria in Table 3.

Table 3 The eligibility criteria for screening potential patients

Inclusion Criteria	**Exclusion Criteria**
Confirmed diagnosis of acute stroke within 24h of symptom onset	Discharge home planned from SRFT stroke services within 72 hours/Rapidly improving symptoms suggestive of transient ischaemic attack
Aged ≥ 18years old	Current treatment for lower respiratory tract infection (LRTI) or confirmed treatment for lower respiratory tract infection in the preceding month
Nil by mouth (NBM) following baseline clinical nurse swallow screen	Receiving or anticipated end-of life care
Able to undergo baseline oral health assessments within 24h of stroke onset	Planned repatriation to a hospital outside of Greater Manchester

The primary diagnosis of ischaemic stroke or intracerebral haemorrhage was based on clinical presentation and baseline brain imaging. The Oxfordshire Community Stroke Project (OSCP) classification, used clinically in assessment of extent of the stroke, the area of the brain that has been affected, the underlying cause, and the prognosis (Appendix 7), was recorded. Nil-by-mouth (NBM) status was determined from clinical

baseline water-swallow assessment, carried out by a member of the stroke nursing team usually within 4 hours of presentation. Patients were also NBM by default if they are unsuitable for a water-swallow assessment, for example if they have impaired consciousness, they cannot sit up or if they are unable to participate sufficiently because of cognitive or language problems.

Should a patient be considered eligible for the study, it was necessary to consider the patient's base hospital. Study assessments would need to continue for patients repatriated to their local hospital until day 10 post-stroke onset (study end). After liaising with Greater Manchester hospitals, the participating repatriation sites were: Stockport NHS Foundation Trust; University Hospital of South Manchester NHS Foundation Trust (Wythenshawe); Pennine Acute Hospitals NHS Trust (Fairfield and Oldham); and Wrightington, Wigan and Leigh NHS Foundation Trust. The appropriate governance and research and development processes were followed to facilitate ongoing data collection after repatriation to these sites.

3.4.3 Consent

Each individual deemed eligible was approached by the CRN stroke research practitioners or the DCP researcher. The whole consent process was in line with Good Clinical Practice (GCP) guidelines. Before a patient's participation in the study was permitted, it was the recruiter's responsibility to obtain written informed consent from the participant (Appendix 8). The patient information sheet and consent forms were produced in an aphasia-friendly format (Appendix 9) in partnership with service users from the North West Stroke Local Research Network Patient and Carer Involvement Group. Adequate explanation of the study was given before any study specific procedures were initiated. An assessment of the patient's capacity was made by the researcher seeking consent. If potential patients were unable to provide written informed consent, then a personal consultee was identified (usually next of kin) who could confirm that the patient would not object to study participation. If a personal consultee was not available, a nominated personal-legal consultee (usually a clinician who is independent of the research team) could be approached.

If the participant regained capacity, they were asked to sign consent to ongoing participation. Should the participant choose not to continue their participation, it was made clear to the consultee that any data collected to the point of withdrawal will be retained by the investigating team and the participant may still be followed up in order to report any adverse events but that they are free to withdraw at any time.

3.4.4 Baseline data

Following consent or declaration by the personal consultee, the baseline data characteristics were recorded within 24 hours of the participant's stroke symptom onset: age, sex, stroke classification and subtype, stroke severity, disability status of the patient (pre and post-stroke admission), vascular risk factors, past medical history, smoking status, medications, vital signs, level of consciousness and nutritional status.

The stroke severity was measured by performing a NIHSS at admission; this was usually done by the attending stroke doctor (Appendix 2). A modified Rankin Scale (mRS) gives an insight of the degree of disability the patient has when carrying out daily activities. The scale ranges from 0-6 (from sound health without symptoms to death). The score was carried out by a stroke nurse who recorded two scores; one relating to the disability status of the patient up to a month prior to admission and the other relating to the disability status of the patient at hospital admission (after suffering a stroke). The Glasgow Coma Score (GCS) measures the patient's level of consciousness. The scale is composed of 3 elements, each with different grades: eye response (grades 1-4), verbal response (grades 1-5), and motor response (grades 1-6). The lowest possible GCS is 3 (indicating deep coma or death) and the highest is 15 (normal).

Other diagnostic tools undertaken as part of clinical care were recorded such as a copy of the ECG, white blood cell count and plasma C-reactive protein concentration. Information from the blood tests was to aid the stroke specialist to make an informed diagnosis for any suspected infection.

3.4.5 THROAT score

The THROAT was carried out within 24 hours of stroke symptom onset by one of the CRN research nurses (Appendix 4). The research nurses were involved in a previous oral hygiene trial in which there was an online training package including mouth anatomy and the THROAT score assessment tool. For this study, they revisited the THROAT prior to commencing study recruitment using oral digital photos of a variety of dental cases (Appendix 10). Individually the CRN research team used the THROAT to assess each of the dental cases. All scores were collected and any rater who fell outside of the average were encouraged to perform the THROAT as well as another rater and then discuss their findings to decrease the discrepancies in the scores.

The time taken for the THROAT assessment was recorded per patient and the THROAT sheet was placed in the back of the respective case report form so the research dental care professional was blinded to the THROAT score results.

3.4.6 Bedside dental examination

The bedside dental examination was also carried out within 24 hours of stroke symptom onset by the research dental care professional, blinded to THROAT. An assessment sheet was developed for the case report form (Appendix 11) to visualise and record the following:

- Dentate status (edentulous, fully dentate, partially dentate)
- Number of remaining teeth
- Presence of dentures (if present, type of denture (full/partial and metal/acrylic and brief description of condition[1])
- Proportion of teeth with at least one periodontal site that bled (at four evenly spaced points around the tooth)
- Proportion of teeth with a site that had plaque present (moderate amounts of visible plaque that can be scraped with a probe)
- Proportion of teeth with a site that had a pocket depth between 3.5mm and 5.5mm (BPE code 3), by recording pocket depth at four points for each tooth
- Proportion of teeth with a site that had a pocket depth greater than 5.5mm (BPE code 4), by recording pocket depth at four points for each tooth
- Proportion of teeth with frankly cavitated carious lesions

Pocket depth (PD) was used as a main measure for the presence of periodontal destruction. A full-mouth assessment for periodontal status was conducted and pocket depth was measured on 4 sites per tooth (mesiobuccal, distobuccal, mesiolingual/palatal and distolingual/palatal). For the examination a single-use mouth mirror and a disposable ball-pointed C-type probe with 2 black bands at 3.5-5.5mm and 8.5-11.5mm were used. According to the Community Periodontal Index for Treatment Needs (CPITN) for pocket depth the following definition for periodontitis was used: PD 0-3 mm as no/mild periodontitis, at least one pocket ≥4 mm and <6 mm as moderate and with at least one pocket ≥6 mm as severe periodontitis (Cutress, Ainamo et al. 1987). Therefore, it was time efficient to record a Basic Periodontal Examination (BPE) code, as shown in Table 4, at each 4 sites per tooth.

[1] This was not undertaken in all denture-wearer subjects. After the first edentulous patient, and therefore yielded no numerical data, it was thought that a brief description of the denture may have added value. However, this was dependent whether the patient had the denture available on the ward.

Table 4 The coding system for Basic Periodontal Exam (BPE)

Code 0	No pockets >3.5 mm, no calculus/overhangs, no bleeding after probing (black band completely visible)
Code 1	No pockets >3.5 mm, no calculus/overhangs, but bleeding after probing (black band completely visible)
Code 2	No pockets >3.5 mm, but supra- or subgingival calculus/overhangs (black band completely visible)
Code 3	Probing depth 3.5-5.5 mm (black band partially visible, indicating pocket of 4-5 mm)
Code 4	Probing depth >5.5 mm (black band entirely within the pocket, indicating pocket of 6 mm or more)

The bleeding sites were measured according to Lang et al. (Lang, Adler et al. 1990). After measuring the pocket depth, the four corresponding sites per tooth were inspected for the presence or absence of bleeding. The absence of bleeding on probing (BOP) can serve as a predictor of periodontal stability. If the percentage of sites with BOP for each person was less than 30% of all probed sites, it was defined as 'local bleeding' only. A percentage of 30% of sites or higher was considered as 'general bleeding' on probing.

For edentulous patients, those with no teeth, the proportion of disease would be recorded as 0. Since no numerical data could be taken, a brief description of the oral health and general state of any dentures was commented on. A Dictaphone was used during this bedside dental assessment to not only reduce the need for a scribe or reduce potential cross contamination when recording measurements, but to keep the time the patient had their mouth open at a minimum. This was imperative as it could be argued that there is an increased risk of aspiration if the patient has their mouth open for a sustained period of time or that the patient may not tolerate the whole examination if it took longer. The use of a Dictaphone also provided the time taken for the examination.

3.4.7 24 hour assessment

The 24-hour assessment would be day 1 or day 2 after stroke onset (depending on when the patient was admitted to hospital). Here the NIHSS score and the swallowing/nutritional status were repeated. The 24-hour NIHSS was performed either by the attending doctor on the ward round for the patients that were thrombolysed, or by the CRN research nurse for those that were not. A comparison of the two NIHSS scores gave an indication to any

early neurological improvement or deterioration made by the patient. A stroke-associated pneumonia (SAP) screening checklist was carried out and antibiotic usage was recorded. The patient would also be visited by either a CRN research nurse or the dental care professional researcher to record any adverse events that may have taken place.

3.4.8 48 hour assessments

The swallowing/nutritional status, SAP screening checklist and antibiotic usage were recorded on alternate days after day 01 up until day 10 post stroke. Follow up to day 10 was implemented mainly because the incidence of SAP tends to be greatest during the first 7-10 days after stroke (Westendorp, Nederkoorn et al. 2011).

3.4.9 Stroke-associated pneumonia (SAP) diagnosis

Since there is no diagnostic clinical criteria validated in stroke-associated pneumonia, diagnosis of SAP was based on a recently proposed Centers for Disease Control and Prevention (CDC) modified criteria (Smith, Kishore et al. 2015). The modified criteria can be found in Appendix 12, which has categorised diagnosis into 'probable SAP' and 'definite SAP', based on whether chest radiograph reports were definitive. The SAP screening checklist data from the patients CRF and the electronic patients records (EPR) clinical, laboratory and prescription data, as well as any chest x-rays and reports on the SRFT Picture Archiving System (PACS) were reviewed by the specialist in stroke medicine to apply the CDC criteria. For repatriated patients, the stroke specialist reviewed all the chest x-ray imaging and reports from the base hospitals via the Greater Manchester PACS.

3.5 Data Analysis

3.5.1 Feasibility

Feasibility of recruitment was determined by the proportion of eligible patients that consented to study participation and exploration of the reasons for non-participation. Feasibility of both the THROAT and dental assessment was assessed by the number who tolerated completion of each assessment and the time taken was also recorded for each assessment. Characteristics of the patients that had participated in the study were relevant also in determining the feasibility of oral assessments in the acute stroke setting. Baseline characteristics have been summarised using descriptive statistics; they were expressed as means and standard deviations *(SD)* or as percentages. Continuous variables with non-normal distributions (such as age, mRs, NIHSS, and GCS) are described as medians and inter-quartile ranges *(IQR).*

3.5.2 Concurrent Validity

The bedside dental examination, carried out by the dental care professional (DCP), was used as the gold standard measurement. Therefore, concurrent validity between the two oral assessments has been assessed by the correlation of the THROAT (individual component scores and the total score) with each element of the detailed dental examination. Linear relationships were investigated using the Pearson Product Moment Correlation. The statistical software used to carry out the analysis of association was R programming software version 3.2.0 (R Development Core Team 2010).

3.5.3 SAP Analysis

The study population was categorised into those without and those with stroke-associated pneumonia (either probable or definite SAP). Participants have been included for all analyses for which their data is available. Where outcome data are missing no imputation has been undertaken. Differences in variables at baseline (prior clinical characteristics, risk factors and stroke details), in-hospital events and discharge status, and oral assessments were compared; categorical variables were compared using the Chi-square test, and continuous variables (parametric and non-parametric) were compared using the student *t*-test and the Mann-Whitney U test. In all analyses, $p<0.05$ indicated statistical significance.

For predictive validity, SAP would be the outcome measure in a logistic regression model. An odds ratio was calculated for inferential univariate analysis with 95% confidence interval. For continuous variables a linear relationship was assumed. The variables and SAP outcome that had a substantial association ($p<0.05$) were then entered into a multivariable model. However, should the study population prove too small for the multivariable analysis, then the known risk factors were also summarised using the A^2DS^2 score (Hoffmann, Malzahn et al. 2012).

3.6 Data Handling and Record Keeping

Study documentation was completed and stored in accordance to the MRC guidelines for Good Clinical Practice in clinical trials (Medical Research Council 1998) and other applicable local guidelines. Study documentation was anonymised as soon as practical and this will be kept in a secure location, accessible to the Principal Investigator and study sponsor only. Study documentation will be retained for a minimum of 5 years after the

date of the last publication. Archiving will be in accordance with the Sponsor's recommendations.

3.7 Financing and Insurance

Funding of this study was provided by the University of Manchester Dental School and SRFT Hyperacute Stroke Research Centre flexibility and sustainability funding. The study was sponsored by the University of Manchester and their liability insurance (Zurich® Municipal) was in place (Appendix 13). The Principal Investigator is a substantive employ of SRFT and since all participants have been recruited there, standard NHS policy will apply regarding non-negligent harm.

3.8 Publication Policy

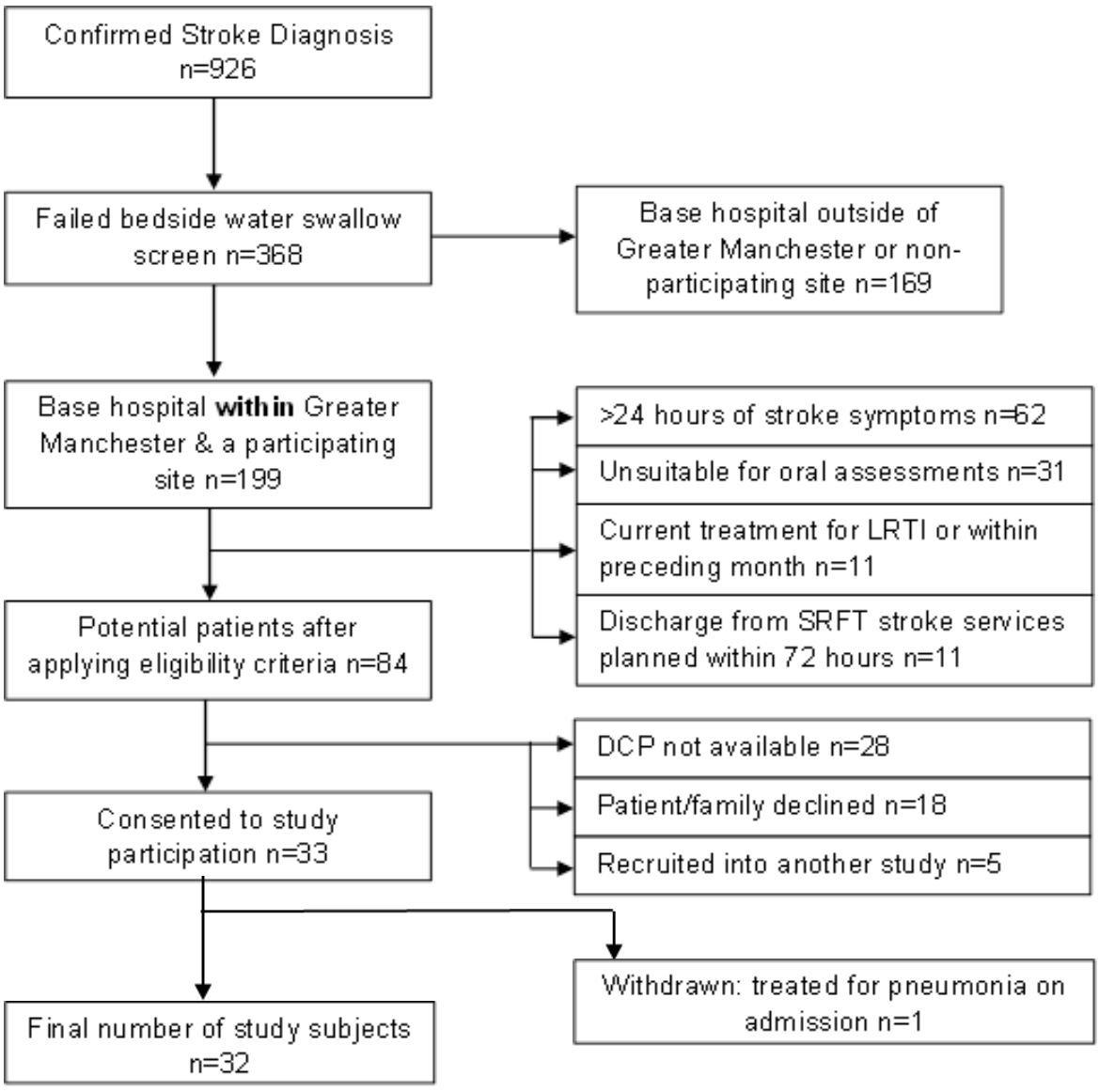
This was a postgraduate research-based study. The dental care professional researcher and Principal Investigator have full access to all the data and final responsibility for the decision to submit the findings of this research for publication. The study results were primarily used for the writing of this MPhil.

4. Results

4.1 Study Recruitment

The screening of patients for this study began on 27/11/2014 and continued for 28 weeks until 12/06/2015 of which included 14 days for the DCP's annual leave. Figure 2 summarises the screening process involved in identifying potential patients.

Figure 2 Flowchart indicating the screening and selection process of study participants



Over this study period, there were 926 confirmed stroke patients admitted to Salford Royal Foundation Trust. 368 (39.7%) of these patients were categorised as being "nil-by-mouth" within 24 hours of hospital admission; those that were not placed NBM were excluded, as per eligibility criteria. Those patients whose base hospital was outside of the

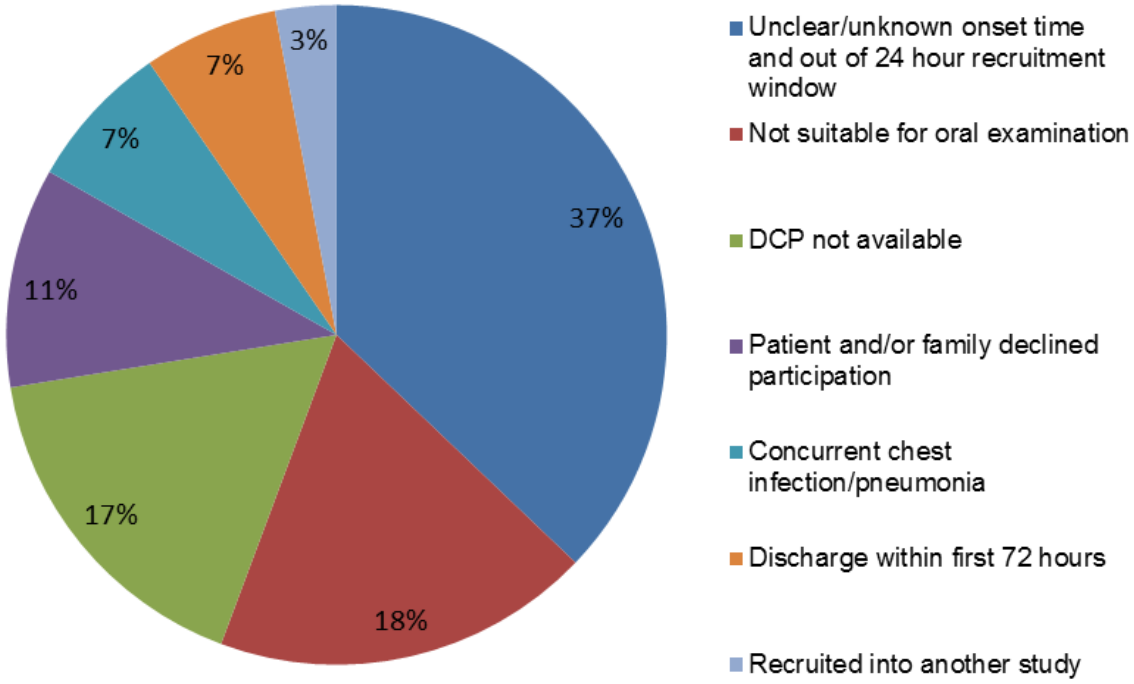
Greater Manchester area or were not a participating site could not be considered for study involvement, leaving 199 potential patients. 115 of these patients were rejected for inclusion after applying the eligibility criteria; not within 24 hour of stroke symptom onset, unsuitable for oral health assessment, current treatment for lower respiratory tract infection (or within the preceding month), discharge planned within 72 hours. Patients that were deemed not suitable for oral examinations included those that were agitated or aggressive, vomiting, contending with other co-morbidities, or receiving (or were anticipated for) palliative care.

Out of the remaining 84 suitable patients, 28 could not be recruited due to the limited weekend availability of the DCP and 5 patients were recruited into another study which was investigating breath sampling for pneumonia. Therefore, 51 patients were approached and 33 consented to study participation (65%). 1 recruited patient was treated for pneumonia on the night they were admitted to hospital and had to be withdrawn from the study, as per exclusion criteria. The final number of study participants was 32.

Figure 3 presents the various reasons for non-recruitment out of the confirmed stroke patients that were NBM and from a participating area, n=167[2] (199 minus the 32 recruited patients).

[2] The 1 patient that was withdrawn because they were treated for pneumonia on the day of admission is therefore included in 'concurrent chest infection/pneumonia'

Figure 3 The distribution of the various reasons for non-recruitment of screened patients (n=167)



The main reason for exclusion was unknown or unclear onset time of stroke (37%) which meant the initial 24 hour period, requirement for the initial assessments to be measured, could not be confirmed.

4.2 Baseline Demographics

4.2.1 Baseline Characteristics of participating patients

Table 4 presents the baseline characteristics of the 32 study participants; 18 females and 14 males. The median age of the patients was 77 years, with a range from 43 years to 94 years. Figure 4 shows the different age groups of the patients; the modal age groups (n=10) were 71-80 years and 81-90 years.

Figure 4 The age range of the participants

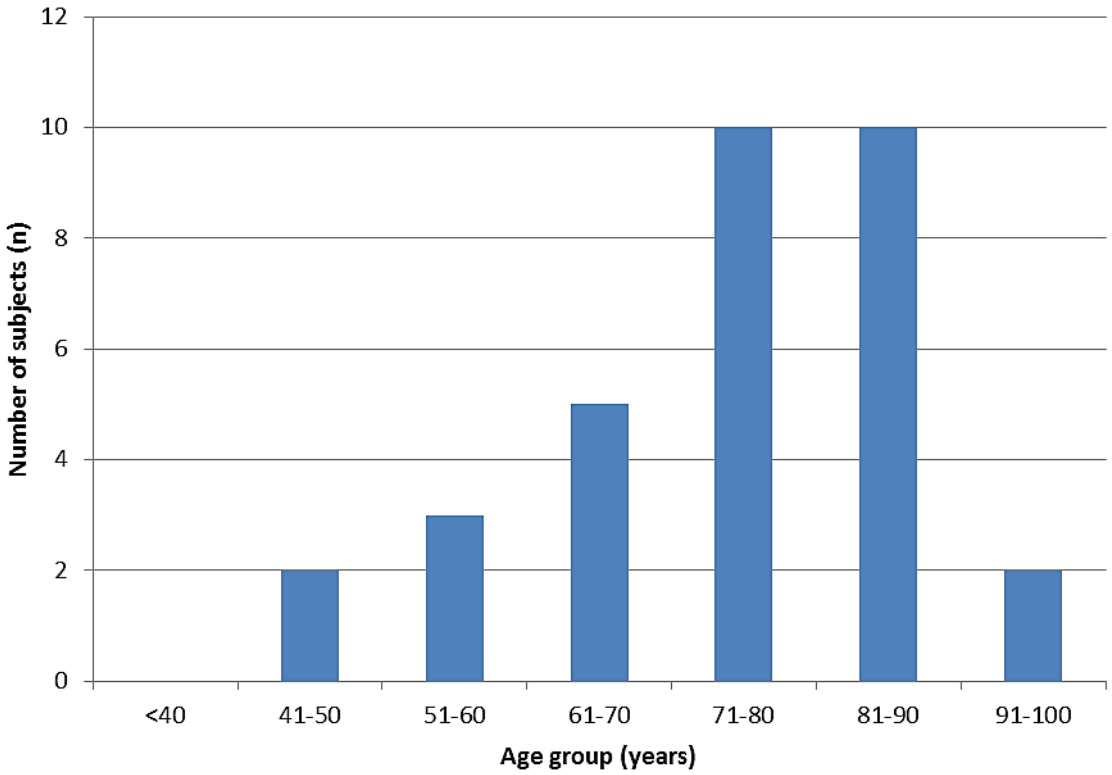


Table 5 summarises the prevalence of prior clinical characteristics and conditions for the study subjects and a univariate analysis for those with and without pneumonia. A thorough medical history was recorded in the individual case report forms (CRF) for each patient using their electronic patient records. A list of pre-hospitalised medical conditions has been displayed in the latter half of Table 5; it summarises 27 of the 32 subjects suffered from at least 1 of the conditions. As expected, the incidence of hypertension was high (59.4%).

Table 5 Demographics and presenting clinical characteristics of the participants

Baseline Indices	**Number of subjects n=32**	**Without pneumonia n=26**	**With pneumonia n=6**	***P*[a]**	**Univariate OR (95%, CI)**
Age, Median *(IQR)*	77 *(20.5)*	76 (18.3)	89 *(12.0)*	0.034[b]*	1.1 (1.0-1.3)
Female, %	56.3	50.0	83.3	0.138	5.0 (0.5-48.9)
Pre-stroke mRS, Median *(IQR)*	0 *(2.3)*	0.5 *(2.0)*	0 *(2.3)*	0.944[b]	1.1 (0.6-2.0)

Disability pre-stroke (mRS 3-5), %		25.0	23.1	33.3	0.601	1.7 (0.2-11.5)
Smoking (including ex-smokers), %		40.6	42.3	33.3	0.687	0.7 (0.1-4.4)
Alcohol use, %		46.9	53.9	16.7	0.010*	0.2 (0.02-1.7)
Blood Pressure (mmHg)	**Systolic, Mean *(SD)***	157.3 *(31.9)*	158.4 *(32.8)*	152.73 *(27.4)*	0.702[c]	1.0 (1.0-1.0)
	Diastolic, Mean *(SD)*	81.7 *(14.8)*	80.1 *(13.4)*	84.7 *(14.6)*	0.477[c]	1.0 (1.0-1.1)
Hypertension, %		59.4	61.5	50.0	0.604	0.6 (0.1-3.7)
Previous stroke/TIA, %		40.6	38.5	50.0	0.604	1.6 (0.3-9.5)
Atrial Fibrillation, %		37.5	30.8	66.7	0.102	4.5 (0.7-29.8)
Coronary Artery Disease, %		31.3	34.6	16.7	0.393	0.4 (0.04-3.8)
Diabetes Mellitus, %		28.1	30.8	16.7	0.489	0.5 (0.05-4.5)
Hypercholesterolemia, %		18.8	19.2	16.7	0.885	0.8 (0.08-8.9)
Hyperlipidaemia, %		15.6	15.4	16.7	0.938	1.1 (0.1-12.1)
Chronic Obstructive Pulmonary Disease, %		12.5	15.4	0.0	0.304	0.0

IQR, interquartile range; SD, standard deviation; TIA, transient ischaemic attack

[a]Chi-square test, unless otherwise indicated. [b]Mann-Whitney U test. [c]Student *t*-test

*Result is significant at p<0.05; OR, Odds Ratio; CI, Confidence Interval

The modified Rankin scale (mRS), as mentioned in the Methods section, records the degree of disability or dependence of patients in everyday activities. The median mRS (pre-stroke) was 0, exhibiting no symptoms at all; and was also zero in both those with and without pneumonia (Table 5). The two scores, pre-stroke mRS and mRS on admission have been summarised in Table 6. 53% of participants had a mRS score of 0 a month before they were hospitalised with a stroke. This can be compared to the mRS recorded on admission, in which no patients scored 0 or 1; the modal mRS score was 4 (n=22). In this study, 'disability' was defined as a mRS score of 3-5; disability for the study population increased from 25% (n=8) before stroke to 87.5% (n=28) post-stroke.

Table 6 The modified Rankin Scale (mRS) score pre-stroke admission and mRS score on admission of study subjects

mRS score description	**Pre-stroke admission mRS** **Number of subjects (n=32)**	**At admission mRS** **Number of subjects (n=32)**
0 - No symptoms	17	0
1 - No significant disability. Able to carry out all usual activities, despite some symptoms	2	0
2 - Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities	5	4
3 -Moderate disability. Requires some help, but able to walk unassisted	7	2
4 -Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted	0	22
5- Severe disability. Requires constant nursing care and attention, bedridden, incontinent	1	4

Lifestyle factors were recorded for every patient. 19 patients had never smoked, 11 were ex-smokers and two were current smokers. 15 of the subjects were noted to have some degree of alcohol intake, including the two current smokers. It was necessary for this information to be collected independently of the data in the patient's computerised notes as there was often a variation in consumption amount. However, an insight to the alcohol

units per week was often not known in those patients who had a personal consultee consent on their behalf.

4.2.2 Stroke Details

Table 7 gives an overview of the stroke diagnosis, admission and discharge status for the patients. 30 patients (94%) were treated for ischaemic strokes and two patients suffered a primary intracerebral haemorrhage (PICH). As per eligibility criteria, all patients were placed nil-by-mouth (NBM) after a bedside water swallow screen within the first 24 hours of stroke symptom onset. By the 24 hour assessment, only 8 patients were NBM; 4 of whom had a nasogastric tube placement. After the day 10 assessment (study end), 5 patients had remained NBM.

Out of the 32 patients, 16 (50.0%) were deemed fit for discharge from hospital before day 10 post stroke and could therefore not be wholly followed up as anticipated (Table 7).

Table 7 Clinical stroke subtypes, in-hospital events and discharge status in study participants

In-hospital Indices		**Number of subjects n=32**	**Without pneumonia n=26**	**With pneumonia n=6**	***P*[a]**	**Univariate OR (95%, CI)**
Ischaemic Stroke – OSCP subtypes (Appendix 7)	**LACS, %**	12.5	11.5	16.7	0.732	1.5 (0.1-18.0)
	TACS, %	31.3	26.9	33.3	0.753	1.4 (0.2-9.1)
	PACS, %	31.3	30.8	50.0	0.371	2.3 (0.4-13.7)
	POCS, %	12.5	15.4	0.0	0.304	0.0
	Other, %	6.3	7.7	0.0	0.483	0.0
Primary Intracerebral Haemorrhage, %		6.3	7.7	0.0	0.483	0.0
Received Thrombolysis, %		9.4	7.7	16.7	0.500	2.4 (0.2-31.9)
Admission to SRFT within 0-4h of stroke		84.4	84.6	83.3	0.938	0.9 (0.08-10.0)

onset, %					
Initial NIHSS score, Median *(IQR)*	10.5 *(14.0)*	10.5 *(15.8)*	8 *(13.3)*	0.480[b]	1.0 (0.9-1.1)
Glasgow Coma scale, Median *(IQR)*	15 *(2.3)*	15 *(2.0)*	15 *(2.3)*	0.425[b]	1.0 (0.6-1.7)
Disability post-stroke (mRS 3-5), %	87.5	88.5	83.3	0.732	0.7 (0.06-7.6)
NGT feeding, %	18.8	15.4	33.3	0.310	2.8 (0.4-20.4)
Discharged before Day 10 post stroke, %	50.0	50.0	50.0	1.00	1 (0.2-5.9)

NIHSS, National Institutes of Health Stroke Scale; IQR, interquartile range; mRS, modified Rankin Scale; NGT, nasogastric tube; TIA, transient ischaemic attack

[a]Chi-square test, unless otherwise indicated. [b]Mann-Whitney U test.

OR, Odds Ratio; CI, Confidence Interval

The stroke severity was measured by performing a NIHSS at admission (Appendix 2). The median initial NIHSS of the patients was 10.5; table 8 shows the distribution of the scores amongst the study participants, the range for the initial NIHSS was from 2 to 30 with an interquartile range of 14. The NIHSS scores of the two PICH patients were 9 and 17. NIHSS score was repeated at 24 hours however, nine patients were discharged home or repatriated to their base hospital before this could be carried out. The median NIHSS at 24 hours was 6, and scores ranged from 0 to 21 with an interquartile range of 9.5. For those that had a repeated NIHSS score at 24 hours (n=23), 15 (65.2%) showed an improvement in stroke severity after 24 hours.

Table 8 The range of the initial NIHSS score and NIHSS score at 24 hours post-stroke of study subjects

NIHSS Score	Initial n=32 (%)	At 24 hours n=23 (%)
No stroke symptoms [score 0-4]	12 (37.5)	11 (47.8)
Minor stroke [score 5-15]	9 (28.1)	7 (30.4)
Moderate stroke [score 16-20]	6 (18.8)	4 (17.4)
Severe stroke [21-42]	5 (15.6)	1 (4.4)

The summary of the baseline data in Table 7 indicates that the median Glasgow Coma Scale (GCS) score was 15, out of a possible 15 (indicating a fully awake person), with an interquartile range of 2.25. The lowest GCS recorded was 9, in a patient that had suffered a severe stroke (NIHSS score of 23). The patients that had capacity to consent to the study for themselves had a mean GCS of 14.7 compared to those that needed a personal consultee was 12.2. 20 of the participants were deemed competent to consent for themselves, 8 of which used the “easy-access” information sheet and consent form due to suffering from aphasia, sight problems or poor literacy skills.

4.3 Oral Health Assessments

4.3.1 Dental History

Table 9 summarises the dental history of the study participants. 28.1% of the patients were not registered with a General Dental Practitioner. Of those that were registered (n=23), 15 had attended an appointment within the last 6 months of whom 2 regularly saw a dental hygienist. 14 (43.8%) of all the patients were denture-wearers and 2 admitted to wearing their dentures at night. 6 of the 7 edentulous (toothless) patients wore dentures. 5 patients (15.6%) required assistance with mouth care and their pre-stroke mRS ranged from 2 to 5. Two study subjects did not use a toothbrush as part of their daily oral care; 1 patient was edentulous and the other had full upper and lower acrylic dentures. Of those that used a toothbrush, 2 (6.7%) favoured a powered brush over a manual.

Table 9 Summary of dental history in study participants

Dental History Indices	Number of subjects n=32	Without pneumonia n=26	With pneumonia n=6	*P*[a]	Univariate OR (95%, CI)
Number of teeth, Mean *(SD)*	14.9 *(9.6)*	16.7 *(8.5)*	6.8 *(9.7)*	0.022[c]*	0.9 (0.8-1.0)
Denture wearers, %	43.8	42.3	50.0	0.732	1.4 (0.2-8.1)
Edentulous, %	21.9	11.5	66.7	0.003*	15.3 (1.9-122.8)
Not registered with GDP, %	28.1	19.2	66.7	0.002*	8.4 (1.2-59.5)
Attended GDP in last 6 months, %	46.8	50.0	33.3	0.461	0.5 (0.08-3.2)

SD, standard deviation; GDP, general dental practitioner

[a]Chi-square test, unless otherwise indicated; [c]Student *t*-test.

*Result is significant at p<0.05; OR, Odds Ratio; CI, Confidence Interval

Since 21.9% (n=7) of the study population were edentulous it was necessary to explore the differences between those with and without teeth (Table 10) by comparing baseline characteristics, known risk factors for oral disease (smoking and alcohol consumption), stroke severity and dental history. The edentulous subjects were significantly older than those with teeth (p<0.01) and, predictably, were significantly associated with wearing dentures (p<0.05). The participants with no teeth were also significantly associated with, at p<0.01, not being registered with a general dental practitioner (GDP).

Table 10 Differences between the dentate and the edentulous study participants

Comparative Indices	Dentate subjects (n=25)	Edentulous subjects (n=7)	*P*[a]
Age, median *(IQR)*	76 *(16.0)*	89 *(2.5)*	0.001[b*]
Female, %	52.0	71.4	0.360
NIHSS, median *(IQR)*	12 *(14.0)*	6 *(11.0)*	0.787[b]
Smoking (including ex-smokers), %	36.0	57.1	0.314
Alcohol use, %	56.0	14.3	0.051
Not registered with GDP, %	8.0	85.7	<0.001*
Denture wearer, %	32.0	85.7	0.011*

IQR, inter-quartile range; NIHSS, National Institutes of Health Stroke Scale, GDP; general dental practitioner

[a]Chi-square test, unless otherwise indicated. [b]Mann-Whitney U test.

*Result is significant at p<0.05

4.3.2 THROAT Results

The THROAT was carried out and completed in all 32 patients. There was only one patient for which two raters carried out a THROAT score, there was a moderate positive correlation (r=0.75). For analysis, a mean of the two scores for each component was taken for this patient. The time taken for completing the score ranged from 1 to 5 minutes, and the mean time taken was 2.1 minutes. The THROAT took 5 minutes for the subjects at the beginning of the study and took less time for the participants recruited thereafter. The number of teeth did not correlate with the time taken for the THROAT score (r=-0.0894, *p*=0.628) (Figure 6)

The final THROAT score for each patient was the sum of the scores (0-3) for each feature (lips, teeth/dentures, gums, mucous membranes, palate, tongue and saliva). The

description of each score for each feature can be found in Appendix 4. Table 11 gives a summary of the frequencies of each component score for all the study participants.

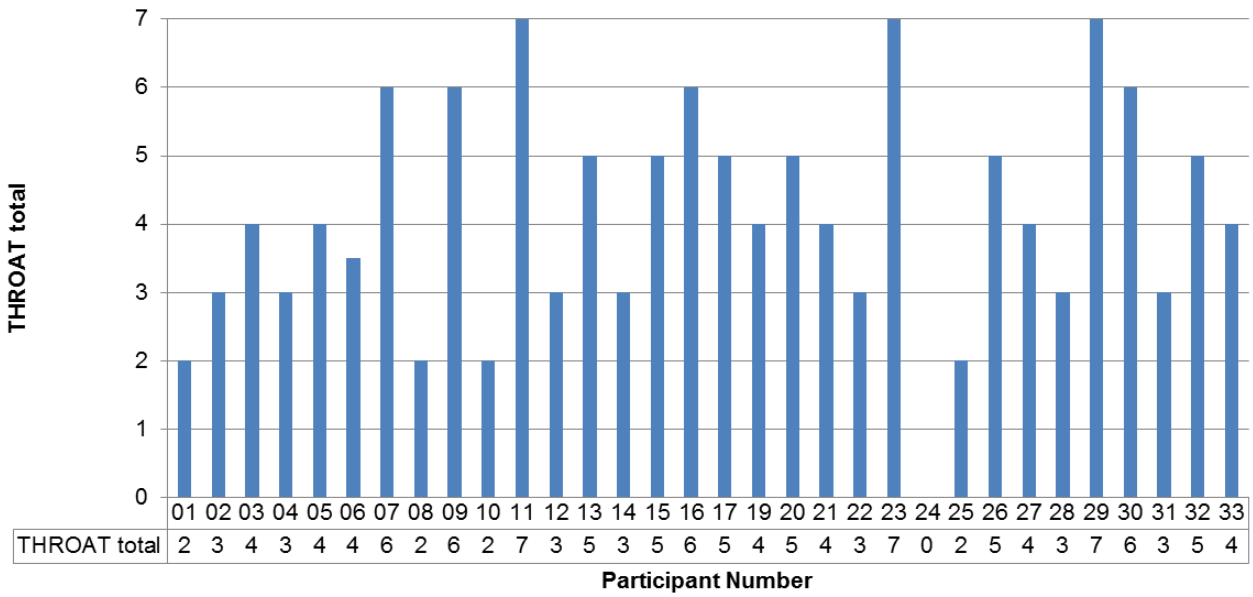
Table 11 Frequency distribution of THROAT component scores among the study participants

		Abnormal		
THROAT component	Normal: **score 0 Number of subjects (n)**	Mild: **score 1 Number of subjects (n)**	Moderate: **score 2 Number of subjects (n)**	Severe: **score 3 Number of subjects (n)**
Lips	9	22	1	0
Teeth/Denture	4	19	4	5
Gums/gingiva	28	4	0	0
Mucous membranes	32	0	0	0
Palate	32	0	0	0
Tongue	4	18	9	1
Saliva	19	9	1	3

The highest (worse) score of 3 was seen only in ‘teeth/dentures’, ‘tongue’ and ‘saliva’. The highest scoring component of THROAT was ‘teeth/dentures’ where 9 (28.1%) patients scored a 2 or 3. The next highest scoring component was ‘tongue’ with an average score of 1.22. The average scores for components ‘gums’, ‘lips’ and ‘saliva’ were relatively low, 0.125, 0.75 and 0.625 respectively. All participants scored zero for both ‘mucous membranes’ and ‘palate’. Therefore, the sum of ‘teeth/dentures’ and ‘tongue’ scores had a moderate positive correlation with the THROAT total ($r=0.6956$, $p<0.01$). This may be useful for further modification of THROAT.

Figure 5 displays the THROAT total score for each study participant. The total possible score was 21 however, in this population the highest total THROAT score was 7 and observed in 3 (9.4%) patients.

Figure 5 THROAT total score for each participant

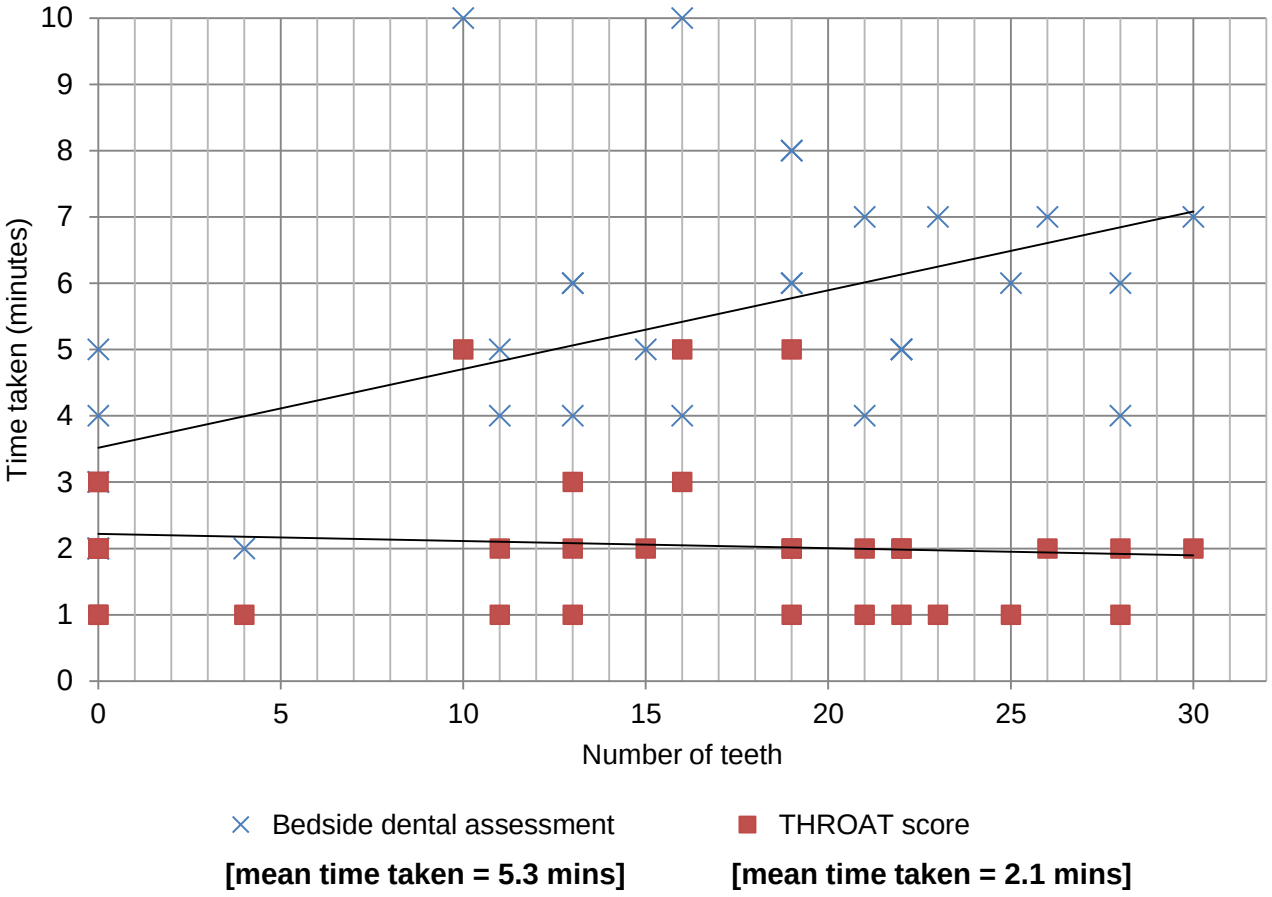


For any analysis of the THROAT totals they were split into a 'low' [1-3] and a 'high' [4-7] score. This is because a total THROAT score of 4 or higher indicates that there are 2 or more components/areas of the mouth that are of concern. The time at which the THROAT score was recorded was also dichotomised into either 0-12 or 12-24 hours post-stroke, and held no significance on the THROAT total score at $p<0.05$ ($\chi^2_{(1)}=0.2576$, $p=0.612$). Where possible the THROAT and the bedside dental examination were carried out consecutively; in 27 out of 32 patients the two oral assessments were completed within 0-3 hours of each other. The time intervals between the oral assessments in the five other patients ranged from 5-11 hours.

4.3.3 Bedside Dental Examination Results

The bedside dental examination was also carried out and completed in all 32 patients. The time taken for completing the examination ranged from 2 to 10 minutes, and the mean time taken was 5.3 minutes. Unlike the THROAT score, there was a moderate positive correlation between the number of teeth and the time taken for the bedside dental examination ($r=0.692$, $p<0.01$) (Figure 6).

Figure 6 The correlation between the number of teeth and the time taken for both oral assessments



The average number of teeth was 15; 30 teeth was the maximum and there were 7 edentulous subjects. There is a moderate negative correlation (r=-0.603, *p*<0.01) with increasing age and the number of teeth in the participants. Since 21.9% of patients had no teeth, this contributed to a shorter time taken for the bedside detailed dental assessment as all measurements were expressed as a percentage of teeth. For these patients the DCP noted down the presence or absence of saliva in all 7 oral cavities and any adverse findings, for which there were none found. In the remaining 25 dentate patients, 21 (84%) had at least one periodontal pocket exhibiting moderate periodontitis (≥4mm and <6mm) and 10 (40%) had at least one periodontal pocket greater than 6mm (severe periodontitis). Table 12 gives a summary of the bedside dental examination components in the **dentate** patients.

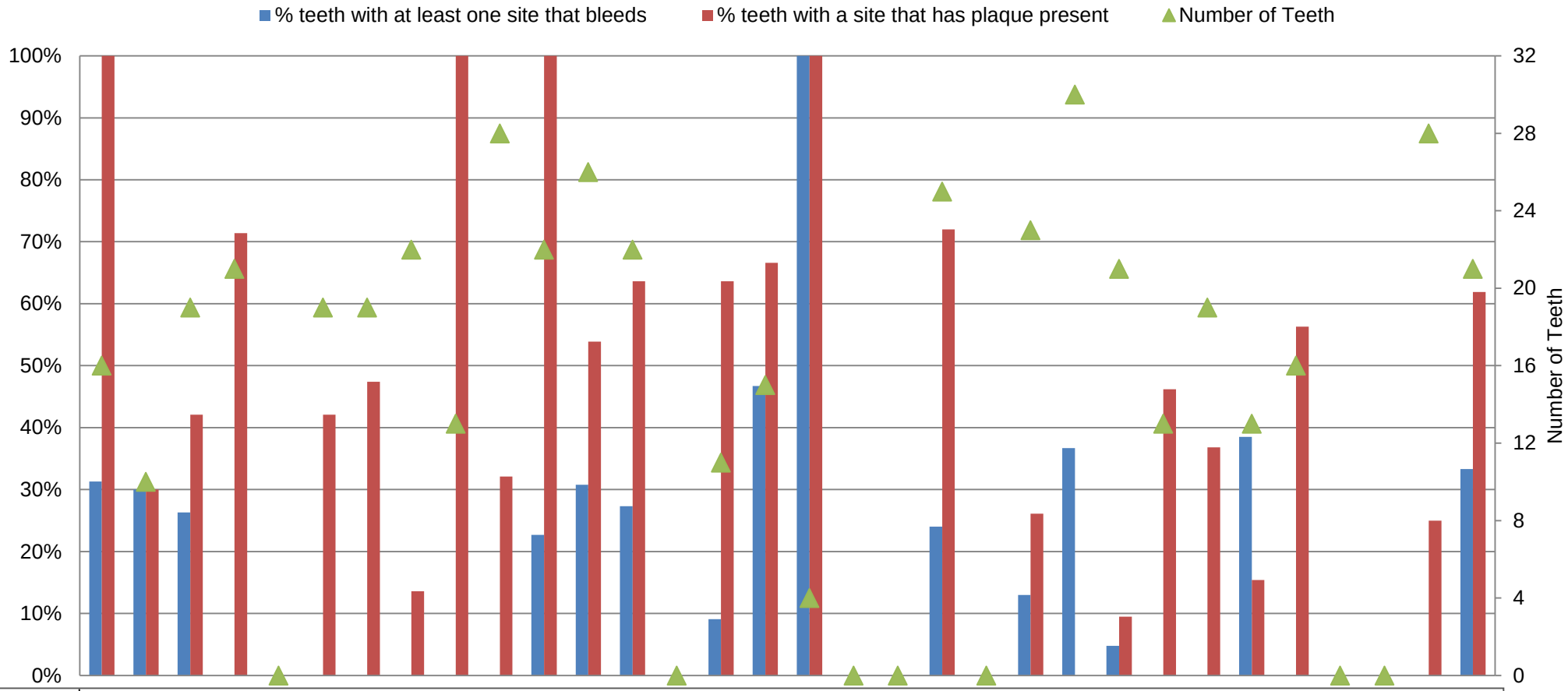
Table 12 Overview of the different components of the bedside dental examination in the 25 dentate patients

Bedside Dental Examination Components	Minimum % of teeth	Maximum % of teeth	Average % of teeth per dentition *(SD)*
≥1 frankly cavitated lesion	0.0	81.3	13.8 *(24.1)*
≥1 site with bleeding on probing	0.0	100.0	19.0 *(22.6)*
≥1 site with plaque present	0.0	100.0	51.0 *(28.7)*
≥1 site with BPE of 3 (PD 3.5-5.5mm)	0.0	100.0	31.7 *(29.4)*
≥1 site with BPE of 4 (PD > 5.5mm)	0.0	100.0	10.1 *(22.2)*

There was no bleeding on probing evident in 10 (40%) of the dentate patients. Comparably, there was no plaque present on teeth surfaces in only 1 (4%) of the patients. The relationship between the bleeding site percentage and percentage of teeth with plaque is shown in Figure 7 for each patient (including those that were edentulous, subjects 05, 14, 19, 20, 22, 30 and 31, and therefore have scores of 0%). 7of the 25 dentate patients had generalised bleeding (>30% of teeth bleed on probing), of which 5 (71.4%) of the patients also had high levels of plaque (>50%). Although there was a modest relationship between the bleeding and plaque percentages (r=0.4552, p<0.01*)*, it is noteworthy that 10 out of the 25 (40%) dentate patients had an absence of bleeding on probing but exhibited relatively high levels of plaque. The DCP noted that, for some of these patients, there were signs of xerostomia in their oral cavities. Only 3 of these 10 patients fell into abnormal range for the 'saliva' component in the THROAT (a score of 1, 2 or 3); the saliva had slight thickening, had a thick and ropey consistency or there was no saliva present. The lips could also indicate xerostomia; 6 out of the 10 patients scored either a '1 – dry/not cracked, or 2 – dry/cracked'. There were no means in which the DCP could accurately record levels of dry mouth, apart from a brief description. From Figure 7 it is evident that the number of teeth does not correspond with the bleeding or plaque percentages. Statistically, there is a weak positive correlation between the number of teeth and the percentage of teeth with plaque present (r= 0.345, p=0.0529) and a negligible relationship between the number of teeth and the percentage of teeth that bleed (r= 0.0989*,* p=0.590). Both the current smokers in the study population had 22 teeth and

exhibited bleeding on probing in less than 30% of their teeth. Being an ex-smoker was not significantly associated with the percentage of teeth with sites that bled.

Figure 7 The number of teeth present and the percentage of bleeding sites vs the percentage of sites that had plaque present for each study participant[3]



Participant Number	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33
Number of teeth ▲	16	10	19	21	0	19	19	22	13	28	22	26	22	0	11	15	4	0	0	25	0	23	30	21	13	19	13	16	0	0	28	21

[3] Patient 18 was consented into the trial but had to be withdrawn due being treated for pneumonia on admission (as aforementioned in the Study Recruitment section of Results) so not listed along the x-axis.

In the bedside dental examination, pocket depth (PD) was used as an indicator for periodontal disease. Table 13 compares the differences between the participants that exhibited signs of periodontitis, BPE 3 or 4, and those that did not. The table uses the same comparative indices as Table 9. It is to be noted that those with no signs of periodontal disease included the subjects that had no teeth (n=7), this was because the measurements were related to the proportion of teeth, these participants scored 0%. Being edentulous was significantly associated with increasing age, not being registered with a GDP and wearing dentures. Therefore, the patients with no teeth have been omitted from these three comparisons in Table 13. From this table, the subjects with periodontal disease were significantly associated with alcohol intake ($p<0.05$).

Table 13 Differences between the study participants with and without signs of periodontal disease

Comparative Indices	**Subjects with signs of periodontal disease (n=21)**	**Subjects with no signs of periodontal disease (n=11†)**	***P*[a]**
Age, median *(IQR)*	74 *(18.0)*	79 *(9.0)*	NA[b]
Female, %	52.4	63.6	0.542
NIHSS, median *(IQR)*	12 *(13.0)*	9.0 *(14.0)*	0.787[b]
Smoking (including ex-smokers), %	38.1	45.5	0.687
Alcohol use, %	61.9	18.2	0.019*
Not registered with GDP, %	9.5	25.0	0.383
Denture wearer, %	38.1	0.0	0.134

IQ, interquartile range; NIHSS, National Institutes of Health Stroke Scale; GDP, General dental practitioner

†n=4 for 'Age', 'Not registered with GDP' and 'Denture wearer'

[a]Chi-square test, unless otherwise indicated. [b]Mann-Whitney U test [NA; sample size too small for this statistical test]

*Result is significant at $p<0.05$

4.3.4 Oral Assessment Validity

Correlation between the individual components of THROAT and the detailed dental examination was poor (Table 13). Since the 'mucous membranes' and 'palate' scored 0 in all patients, they were omitted from the correlation calculations. Table 14 shows there was a fair correlation (r=0.48, *p*=0.00519) between the score for 'teeth/dentures' component of THROAT and 'percentage of teeth with at least one site with plaque present' from the bedside dental examination.

Table 14 Correlation coefficient between the individual components of the THROAT and the detailed dental assessment

THROAT Component	**Bedside Dental Examination Components**				
	% teeth with ≥1 cavitated lesion	% teeth with ≥1 site with bleeding on probing	% teeth with ≥1 site with plaque present	% teeth with ≥1 site BPE of 3 (PD 3.5-5.5mm)	% teeth with ≥1 site BPE of 4 (PD >5.5mm)
THROAT total	0.1174	-0.0038	0.4144	0.2294	-0.0191
Lips	-0.0569	-0.0677	0.1704	0.0457	-0.1115
Teeth/ Dentures	0.3346	0.1512	0.4822	0.2708	0.2086
Gums	0.2236	0.1788	0.0386	0.149	-0.0124
Tongue	-0.2214	-0.1066	0.1006	0.0704	-0.1623
Saliva	0.0123	-0.0862	0.0842	0.0248	-0.0389

The stroke severity (NIHSS) of the patients did not correlate significantly with the corresponding total THROAT score (r=-0.0668, *p*=0.720), number of teeth (r=0.0862, *p*=0.639), percentage of teeth with at least one site with plaque present (r=0.0041, *p*=0.982) and the percentage of teeth with a site that has a probing depth 3.5-5.5mm (r=-0.025, *p*=0.892). There was a weak positive correlation between the NIHSS and the percentage of teeth with cavitated lesions (r=0.3165, *p*=0.0776), percentage of sites with one or more bleeding sites (r=0.1852, *p*=0.310), and the percentage of teeth with a site that has a probing depth of >5.5mm (r=0.1901, *p*=0.297).

There was a statistically significant relationship between patients that had higher THROAT total score [4-7] and those that had not visited a general dental practitioner (GDP) in the preceding 6 months, $\chi^2_{(1)}$=6.10, *p*=0.014. Those that had seen a GDP in the

last 6 months were also significantly associated with fewer periodontal pockets showing signs of moderate periodontitis (BPE 3) and severe periodontitis (BPE 4); $\chi^2_{(1)}$=7.80, p=0.00521 and χ^2(1,N=32)= 9.93, p=0.00163, respectively. However, this was not the case for percentage of teeth with plaque present, percentage of teeth that bled on probing or percentage of teeth with cavitated lesions, at p<0.05.

Nearly half of the subjects that were denture wearers (43%) were not registered with a GDP, compared to the 17% who did not wear dentures. Denture wearing was associated to poorer oral health in relation to the two oral assessments. Those that wore dentures had a higher mean percentage of teeth with plaque; 70.2% compared to 43.6%, higher mean percentage of bleeding sites; 28.0% compared to 15.5%; higher percentage of periodontal pockets (BPE of 3, 51.5% versus 24.1%, and BPE 4, 18.6% versus 6.8%) and a higher mean THROAT total score; 5.5 compared to 3.8.

4.4 Stroke Associated Pneumonia Analysis

As inferred throughout the previous results tables, stroke-associated pneumonia (SAP) was identified in 6 participants (18.8%). Table 15 displays the antibiotic usage recorded and the chest diagnostic assessments for each patient using the CDC Criteria (Appendix 12); those with probable and definite SAP were included. 5 of the SAP patients were treated with antibiotics and 3 SAP patients were kept in hospital beyond 10 days.

Table 15 Antibiotic usage and chest diagnostic assessments of the 6 patients that developed stroke-associated pneumonia

Participant ID	Antibiotic Usage	Chest X-Ray report	Documented respiratory changes	Length of stay (days)
05	Amoxicillin, Gentamycin	Patchy inflammatory changes both lower zones	Bilateral crackles and wheeze	>10
06	Meropenem	No obvious consolidation	Bilateral crackles	6
08	None	Right basal changes	None	3
19	Amoxicillin,	1) Right lower lobe airspace	1) Bilateral	>10

	Tazocin	shadowing suggestive of infection 2) congested patchy opacity RM2	basal crackles 2) coarse creps on right side	
20	Tazocin, Co-amoxiclov	Shadowing - inflammatory, possible lower respiratory tract infection	1) Bilateral crackles (fine & coarse) 2) Reduced air entry bi-basally	>10
31	Clarithmyocin, Benzylpenicillin, Tazocin	For review of NGT placement	Right crackles	7

Three patients were diagnosed with a confirmed urinary tract infection, and one other patient developed acute bronchitis. Before exploration of the implication on oral health assessments on stroke-associated pneumonia (SAP) outcome it is of interest to summarise the variables that have been shown to have statistical significance on development of SAP from the previous tables ($p<0.05$). In univariate logistic regression analysis (Table 5) patients with SAP were older; median age, 89 (IQR 12.0) vs 76 (IQR 18.3) years (OR=1.1, 95%CI: 1.0-1.3). No other significant differences were observed regarding demographic data, stroke type and medical history. Subjects with SAP had fewer teeth or were edentulous (OR=0.9, 95%CI: 0.8-1.0 and OD=15.3, 95%CI: 1.9-122.8 respectively) and were not registered with a general dental practitioner (OR=8.4, 95%CI: 1.2-59.5) (Table 9).

Table 16 shows the different components of the bedside dental examination and the THROAT total score in all study participants; comparing those with and without SAP.

Table 16 Comparison of the different oral health components of the bedside dental examination and THROAT total in all patients (n=32)

Dental Indices	Number of subjects n=32	Without pneumonia n=26	With pneumonia n=6	*P*[a]	Univariate OR (95%, CI)
THROAT Total 4-7, %	62.5	61.5	66.7	0.815	1.3 (0.2-8.1)
% teeth with ≥1 frankly cavitated lesion, Mean *(SD)*	10.7 *(22.1)*	12.9 *(23.9)*	1.5 *(3.4)*	0.268[c]	0.0 (0.0-3.3)
% teeth with ≥1 site with bleeding on probing, Mean *(SD)*	14.8 *(21.4)*	18.3 *(22.4)*	0.0 *(0.0)*	0.0632[c]	0.0
% teeth with ≥1 site with plaque present, Mean *(SD)*	38.4 *(33.0)*	45.2 *(32.3)*	9.3 *(15.5)*	0.0156[c]*	0.0 (0.0-0.7)
% teeth with ≥1 site with BPE of 3, Mean *(SD)*	24.8 *(29.1)*	30.1 *(29.8)*	1.6 *(2.3)*	0.0309[c]*	0.0 (0.0-193.5)
% teeth with ≥1 site with BPE of 4, Mean *(SD)*	7.9 *(20.1)*	9.7 *(21.8)*	0.0 *(0.0)*	0.299[c]	0.0

BPE, Basic Periodontal Exam; PD, pocket depth

[a]Chi-square test, unless otherwise indicated. [b]Mann-Whitney U test. [c]Student *t*-test

*Result is significant at p<0.05; OR, Odds Ratio; CI, Confidence Interval

Those with SAP had lower mean percentage of teeth with lesions, sites that bled on probing and with at least one site with probing depth of >5.5mm.There was a statistical difference, at p<0.05, between those with and without SAP for the percentage of teeth

with plaque and sites with probing depth of 3.5-5.5mm; those without SAP indicated higher percentages. A higher THROAT score did not show an association with SAP. Being edentulous and having SAP were significantly associated, since 4 out of 6 patients with SAP had no teeth, and this may have therefore affected the results of the percentage scores for the bedside dental examination. However, when comparisons in the oral assessments (as in Table 16) were carried out to include just dentate patients, n=25, they did not show any statistical difference between those with and without SAP. It is also disputable to omit the edentulous subjects due to the small study sample size.

The A^2DS^2 scoring tool was applied to each participant with pneumonia (Table 17), and the total scores ranged from 4 to 9 out of a possible 10.

Table 17 Application of A^2DS^2 scoring tool for the subjects with SAP

Participant ID	Age	AF	Dysphagia	Sex	NIHSS	TOTAL
05	1	0	2	0	5	8
06	0	1	2	0	3	6
08	1	1	2	0	5	9
019	1	0	2	0	1	4
020	1	1	2	0	1	5
031	1	1	2	1	1	6
A^2DS^2 scoring tool: Age≥75 years=1, atrial fibrillation (AF)=1, dysphagia=2, male sex=1, stroke severity: NIHSS score 0–4=0, 5–15=3, and ≥16=5						

In the literature the total A^2DS^2 score was dichotomised into lower (0-4) and higher (5-10). Although 83.3% of SAP patients scored the higher total, having SAP was not significantly associated with an A^2DS^2 score of 5-10 when compared to those without SAP, $\chi^2_{(1)}=0.021$ and $p=0.885$. This indicates there are other influential predictive factors.

Patients with SAP were significantly associated with being older, having fewer teeth and not being registered with a GDP compared to the non-SAP cohort. Adding an extra point

for edentulousness to the A^2DS^2 model did not significantly affect the total A^2DS^2 score between SAP and non-SAP patients, $\chi^2_{(1)}$=1.368 and *p*=0.242 .

To evaluate the predictors of SAP in acute stroke a multiple logistic regression model was performed using age and number of teeth as the independent variables; the factors that held significance with SAP outcome (the dependent variable) at p<0.05. Registration with a GDP was not included since being registered and the number of teeth were significantly associated, p<0.00001 (mean number of teeth for those not registered with a GDP was 3.8 versus 19.2 for those who were registered). Additionally, restricting the model to two independent variables was necessary due to the small number of subjects with pneumonia (n=6) because the model was found to be unsuccessful due to over fitting the data.

Since SAP outcome is a binary variable, 0 or 1, modelling using a binomial distribution with probability can be used. Logistic regression models this probability as a function of the two possible explanatory variables (Age and Number of teeth). Full methodology using R programming can be found in Appendix 14.

Conforming to the output, model is: $\text{logit}(\pi_i)$=-5.42 + 0.061*Age + -0.075*Number of teeth

After fitting the model, the overall model fit and hypothesis was then tested regarding a subset of regression parameters using a likelihood ratio test (comparison between the full model with a restricted model where the other variable of interest is omitted) using ANOVA with Chi-squared test. The *p*-values of the tests were calculated using the χ^2 distribution.

The likelihood ratio test statistic is χ^2 = 6.271 with *p*-value of 0.0435, and there is relatively strong confirmation to reject the null hypothesis H_0: $\beta_1=\beta_2=0$. There is no influence of either predictor, Age and Number of teeth, on the incidence of SAP.

To test H_0: $\beta_1=0$ (for Age), z= 0.910 and *p*-value=0.363; the patient's age does not have significant impact of probability of developing SAP, while controlling for the number of teeth. To test H_0: $\beta_2=0$ (for Number of teeth), z = -1.179 and *p*-value=0.239; the number of teeth the patient has does not have significant impact of probability of developing SAP, once age was included in the model.

The results of the logistic regression support that of the applied A^2DS^2 model; there are no significant predictors of SAP. However, due to the small study population there are insufficient results to draw a reliable conclusion. The high incidence of SAP among this

cohort suggests that there are influencing factors but a larger study is required to investigate this further.

5. Discussion

5.1 Main Findings

5.1.1 Feasibility of the oral assessments in acute stroke

This study has confirmed the feasibility of oral assessments in acute stroke patients since both examinations were completed in all recruited patients with no adverse events or complaints. It may be necessary in the future to adhere to the feedback forms to get a more detailed account of the patient's perspective to the oral assessments. 100% feasibility is promising and noteworthy since the oral assessments, particularly the bedside DCP examination, were fairly invasive procedures considering the 24-hour post-stroke time frame.

There was the same DCP carrying out the bedside dental examination at a single time point. This meant there was no intra-rater reliability and this particular bedside dental examination was referred to as gold standard. The average time taken for this was 5.3 minutes which was a much shorter time than had been anticipated; the patient/relative information sheet advised that the examination may take up to 20 minutes. The time taken was significantly associated with the number of teeth ($r=0.692$, $p<0.01$). The longer time taken was also attributed to the difficulties the DCP faced carrying out the examination, the four instances were that a patient was drowsy; lights were off in room due to a headache; tongue obstruction; and a patient was disorientated so they were trying to get up. Although the time taken for the bedside dental examination was double that of the THROAT, 2.1 minutes, it is still a short amount of time in an acute hospital setting. The safety of the oral assessments proved not be of concern, since no adverse events were reported. Bleeding on probing (BOP) could be argued as a degree of trauma, however it was used as a diagnostic measurement, explained in the information sheets and no patients in this study raised concerns over this.

The literature had shown that although dental assessments had been carried out in acute stroke patients, it was uncertain in those that are at greater risk of SAP; older, nil-by-mouth and worse stroke severity. This study confirms the feasibility of oral assessments in such patients since all patients were placed nil-by-mouth as per their dysphagia status. The patients in this study were also older, with a mean age of 75 years, compared to the previous study populations (Grau, Becher et al. 2004); (Pradeep, Hadge et al. 2010); (Ghizoni, Taveira et al. 2012), with mean ages of 60, 52 and 59 years respectively. The aforementioned studies did not give an insight into the severity of the strokes. However, the median NIHSS score of the patients in this study was 10.5 (14.0 IQR) and

comparatively higher than that of the Sentinel Stroke National Audit Programme (SSNAP) registry core-dataset. The median NIHSS score from the database was 4 (7.0 IQR). SSNAP is a UK resource collecting data from participating hospitals In England, Wales and Northern Ireland since January 2013 (Royal College of Physicians 2014). Since oral assessments have been completed successfully in those with a higher stroke severity, then feasibility can be accepted for the general stroke population.

5.1.2 Concurrent Validity of THROAT

One of the main outcomes of this study was to evaluate the concurrent validity of THROAT using the bedside dental examination as criterion standard. From Table 14, it is apparent that the total THROAT score does not correlate with the individual elements of the DCP dental examination. However, some of the correlation comparisons in the table are irrelevant for example the 'lips' and 'saliva' components of THROAT cannot be expected to correspond to any of the dental intra-oral measures. There was a fair correlation (r=0.48, *p*=0.005) between the score for 'teeth/dentures' component of THROAT and the percentage plaque score from the bedside dental examination. The description of the scores for the plaque component of THROAT is quite subjective; 'clean', 'film localised plaque over teeth', 'film of plaque over teeth most areas', 'heavy visible deposits of plaque on and between teeth'. Quantifying the terms 'localised' and 'most' may be necessary and could be explored. Additionally, there were occasions the CRN nurses queried the scoring system with the DCP, as they needed clarification between plaque and calculus. THROAT needs to be simple to use for non-experts and perhaps some prompts (visual and/or descriptive) should accompany the tool.

Another modification to THROAT could be to exclude the 'mucous membrane' and 'palate' from the assessment since all patients in this study scored zero for these components. They are not relevant in the comparison of THROAT and the bedside dental examination. The scoring for these two features in THROAT categorise any inflammation, redness, swelling and ulceration into 'mild, moderate and severe'. From a dental perspective, the condition of the mucous membranes and palate helps identify any abnormalities that may need Oral Medicine referral rather than monitoring or identification of oral health (periodontal disease and dental caries). Removal of these two assessments from THROAT would improve reproducibility and reduce the time spend in the patients mouth; improving patient comfort and minimising aspiration risk.

5.1.3 Occurrence of SAP

Based on the recent Sentinel Stroke National Audit Programme (SSNAP) data, incidence of newly acquired pneumonia between Jan-Jun 2014 was 8.7% (Intercollegiate Stroke

Working Party 2010). The percentage of SAP in this study population was 18.1%. Despite the patients in this study having dysphagia, a risk factor for SAP, the incidence is still considerably higher. The participants who developed SAP (n=6) were significantly older and had significantly less teeth than those who did not have SAP. Although being edentulous was not associated with stroke severity (higher NIHSS) as the previous literature suggests (Slowik, Wnuk et al. 2010), it was significantly associated with SAP. Since edentulousness is a common consequence of periodontitis, there is some suggestion of an association between poor oral health and development of SAP.

However, Table 16 compares the oral assessment results between those with and without SAP. It shows that a lower percentage of teeth with plaque and a lower percentage of teeth exhibiting signs of moderate periodontitis (BPE of 3) were both associated with development of SAP at $p<0.05$. Nevertheless, it is incorrect to make any connections between the oral assessments and SAP because the majority of patients with SAP (66.7%) were edentulous and therefore their 0% scores in the bedside examination would affect the results to indicate a lower, better percentage overall.

5.2.Challenges

5.2.1 Study set up

The study start date was impeded because the study was not eligible for the National Institute for Health Research (NIHR) Clinical Research Network (CRN) Portfolio because of the nature of the study funding. This had implications for participation of additional sites around the Greater Manchester region, and meant that the research team at Salford Royal Foundation Trust (SRFT) needed separate signed agreement from the possible repatriation sites in Greater Manchester to undertake the 48 hourly follow ups. As aforementioned, the participating sites were: Stockport, Wythenshawe, Pennine, and Wigan; with a fee of £100 per repatriation patient. This had a substantial implication on the sample size since 169 patients could not be included because their base hospitals were either outside of Greater Manchester or, more frequently, were not participating sites; Trafford General Hospital, Manchester Royal Infirmary, Tameside General Hospital and Royal Bolton Hospital. Approval from the participating sites was intermittent and took 3 months, during which the number of suitable patients was hindered.

5.2.2 Recruitment Rate

The opening of a hyper-acute stroke ward in April 2015 meant that the number of stroke patients admitted to SRFT increased but, in turn, so did the turnover rate. The time spent

on the ward was brief for the patients that were repatriated on the same day as admission, which occurred more since the opening of the new ward. This made it challenging to approach these patients in time as they were often engaged with other medical professionals before discharge or were waiting for relatives or friends to arrive if they needed a personal consultee to consent on their behalf. Although reassured, 3 patients declined study participation for fear it would affect their relocation time to their base hospital. The increased turnover rate also affected the follow up data; 5 of the recruited patients, coinciding with the ward opening (participants 25, 27, 29, 32, 33), were repatriated within 24 hours of their stroke symptom onset. This affected data collection and as it meant that a repeated NIHSS could not be taken for the 24-hour assessment and an insight into stroke improvement or deterioration was not known for these patients. This was unavoidable, as the repatriation time could never be anticipated as it was dependent on the receiving site having a spare bed.

The eligibility criteria stated that a patient was to be excluded should they have 'discharge home planned from SRFT stroke services within 72 hours'. This was often difficult to predict as there was confliction in doctors' notes from the ward rounds, which occurred twice daily, and the fluctuating condition of the patient. 'Planned discharge' was a common finding in the electronic patient records (EPR) so it was necessary to attend the ward to clarify the discharge status of the patient with the charge nurse.

The 24-hour window after stroke symptom onset proved the main difficulty for recruiting patients. Many patients woke up with stroke symptoms or were alone when they suffered a stroke; in these cases the time of onset was documented as when the patient was 'last seen well'. It was in these instances that if there was delay in attending SRFT then they would be outside of the 24-hour window since their stroke onset and could not be approached for the study. This was also the case for patients that had experienced some stroke symptoms several days before hospital admission.

5.2.3 Oral Assessment Procedure

There was a difficulty in deciding how to record oral health for the patients that did not have any teeth and did not own dentures. The THROAT score does not account for such circumstances and therefore the score for the 'teeth/denture' component was zero. Similarly for the bedside dental examination, patients without any teeth scored 0% in each element because the measurements were related to the proportion of teeth; indicative of good oral health. However, this cannot be assumed since oral health includes being free from tooth loss. Other diagnostics measurements such as microbiological analysis or

reasons for being edentulous (e.g. periodontal disease or trauma) may have had value when evaluating their oral health status. However,

For the patients with no natural teeth, the THROAT covered more aspects of the mouth and in order for the bedside dental examination to be more comparable, the DCP could only record a simple description of the oral cavity; the presence of saliva and state of dentures, if present. The challenge with this is that there are no formal measurements for these two factors thus the descriptions were subjective and a closed 'yes/no' description added little value to the clinical picture of the mouth.

The bedside detailed dental examination revealed that in this population the percentage of bleeding sites and the percentage of sites with plaque had fair correlation (r=0.4552), however, a higher correlation was expected. Figure 7 shows the relationship between the two percentage scores for each patient. Absence of bleeding on probing is an indicator of periodontal stability. Considering the two smokers in the study population (which would reduce the bleeding site percentage), there was no bleeding on probing in the whole dentition for 40% of the patients with teeth. However, these patients also had high levels of plaque, suggesting poor oral health. Because of these results, it was postulated during the study that since stroke can affect the body's metabolic and inflammatory mechanisms then it may halt the progression of active gum disease. It would have been of interest to see if the bleeding on probing was apparent after the patients had recovered from their stroke.

It was noteworthy that since the beginning of the study, the presence of a DCP on the acute stroke ward may have increased the hospital staff's awareness of the ward's oral hygiene regime. Should there have been an improvement in the oral care on the wards, then this may have affected the results for the oral health status for the patients recruited later on in the study and potentially reduce the aspiration risk factor for stroke-associated pneumonia. However, recruitment of patients was within 24 hours of stroke onset and probably too early for any positive effects of oral hygiene by non-experts. Nevertheless, since this was an observational study any confounding factors needed to be kept at a minimum where possible. However, during one bedside dental examination the DCP noted that there was a large amount of excess phlegm at the back of the patient's throat. Nursing assistance was required to perform suctioning in this instance as the DCP held a duty of care to protect the patient. This patient did not go onto to develop pneumonia within this first 10 days after stroke.

5.2.4 Sample Size and Analysis

35% of eligible patients refused study participation and although it is a conservative proportion, it is higher than similar previous studies. In Yoshisha et al., 19.1% declined dental examination however not all the subjects had suffered a stroke and the extent of stroke severity (NIHSS) was not reported.

Regarding the descriptive analyses, the student *t*-test was carried only for the variables that were assumed as evenly distributed. In this particular group of patients, acute stroke, variables such as NIHSS score and age are positively skewed and thus the median values were used for comparisons. Using the univariate analysis for predicting SAP, there were four statistically significant explanatory variables; age, number of teeth, being edentulous and not registered with a GDP. Due to the number of participants, the odds ratio and associated 95% CI for being edentulous and not registered with a GDP had a wide variation, meaning that the true prevalence of SAP in these subjects (with and without teeth or registered and not registered), could be anywhere in the CI range. Therefore, it was necessary to be cautious in exploring these results.

Although 32 patients was a sufficient sample size for a feasibility study, the cases of SAP (n=6) meant that the sample size was too limited to run the full multivariable logistic regression for the predictive component using more than two independent variables as the model tried to over fit the data. The small sample size also meant that any *p*-values not indicating statistical significance could not be ignored, as there still may be some suggestion of an effect on the SAP outcome.

5.3 Future Research Potential

The study has confirmed that oral assessments, basic and invasive, are feasible in acute dysphagic stroke patients. In order to further investigate the concurrent validity of THROAT and gold standard dental assessments, the study should be continued on a larger scale. This would now be relatively straight forward to extend given the difficulties overcome in study set up, the modest participation rate and the higher stroke severity in this population compared to the average (SSNAP).

In this small study population, GDP registration and number of teeth have already shown significant association with SAP. Modification of the nursing tool, THROAT, may be necessary to incorporate a brief dental history and a tooth count. This is an important finding as it emphasizes the importance of a non-experts role in carrying out oral health assessments to highlight any patients that may be of risk of SAP. Identification of such

patients could then allow for informed decisions regarding oral hygiene interventions to reduce SAP risk.

Appendices

Appendix 1 Definition of Stroke adapted from Sacco, Kasner et al. (2013)

Definition of CNS infarction: CNS infarction is brain, spinal cord, or retinal cell death attributable to ischemia, based on
1. pathological, imaging, or other objective evidence of cerebral, spinal cord, or retinal focal ischemic injury in a defined vascular distribution; or
2. clinical evidence of cerebral, spinal cord, or retinal focal ischemic injury based on symptoms persisting ≥24 hours or until death, and other aetiologies excluded.
(Note: CNS infarction includes haemorrhagic infarctions, types I and II; see "Haemorrhagic Infarction.")
Definition of ischemic stroke: An episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction. (Note: Evidence of CNS infarction is defined above.)
Definition of intracerebral haemorrhage: A focal collection of blood within the brain parenchyma or ventricular system that is not caused by trauma.
(Note: Intracerebral haemorrhage includes parenchymal haemorrhages after CNS infarction, types I and II—see "Haemorrhagic Infarction.")
Definition of stroke caused by intracerebral haemorrhage: Rapidly developing clinical signs of neurological dysfunction attributable to a focal collection of blood within the brain parenchyma or ventricular system that is not caused by trauma.

Appendix 2 National Institutes of Health Stroke Scale (NIHSS)

N I H
STROKE
SCALE

Patient Identification. ___ ___-___ ___ ___-___ ___ ___

Pt. Date of Birth ___ ___/___ ___/___ ___

Hospital _____(___ ___-___ ___)

Date of Exam ___ ___/___ ___/___ ___

Interval: [ ] Baseline [ ] 2 hours post treatment [ ] 24 hours post onset of symptoms ±20 minutes [ ] 7-10 days
[ ] 3 months [ ] Other _____(_____)

Time: ___ ___:___ ___ [ ]am [ ]pm

Person Administering Scale _____

Administer stroke scale items in the order listed. Record performance in each category after each subscale exam. Do not go back and change scores. Follow directions provided for each exam technique. Scores should reflect what the patient does, not what the clinician thinks the patient can do. The clinician should record answers while administering the exam and work quickly. Except where indicated, the patient should not be coached (i.e., repeated requests to patient to make a special effort).

Instructions	Scale Definition	Score
1a. Level of Consciousness: The investigator must choose a response if a full evaluation is prevented by such obstacles as an endotracheal tube, language barrier, orotracheal trauma/bandages. A 3 is scored only if the patient makes no movement (other than reflexive posturing) in response to noxious stimulation.	0 = **Alert;** keenly responsive. 1 = **Not alert**; but arousable by minor stimulation to obey, answer, or respond. 2 = **Not alert**; requires repeated stimulation to attend, or is obtunded and requires strong or painful stimulation to make movements (not stereotyped). 3 = Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, and areflexic.	_____
1b. LOC Questions: The patient is asked the month and his/her age. The answer must be correct - there is no partial credit for being close. Aphasic and stuporous patients who do not comprehend the questions will score 2. Patients unable to speak because of endotracheal intubation, orotracheal trauma, severe dysarthria from any cause, language barrier, or any other problem not secondary to aphasia are given a 1. It is important that only the initial answer be graded and that the examiner not "help" the patient with verbal or non-verbal cues.	0 = **Answers** both questions correctly. 1 = **Answers** one question correctly. 2 = **Answers** neither question correctly.	_____
1c. LOC Commands: The patient is asked to open and close the eyes and then to grip and release the non-paretic hand. Substitute another one step command if the hands cannot be used. Credit is given if an unequivocal attempt is made but not completed due to weakness. If the patient does not respond to command, the task should be demonstrated to him or her (pantomime), and the result scored (i.e., follows none, one or two commands). Patients with trauma, amputation, or other physical impediments should be given suitable one-step commands. Only the first attempt is scored.	0 = **Performs** both tasks correctly. 1 = **Performs** one task correctly. 2 = **Performs** neither task correctly.	_____
2. Best Gaze: Only horizontal eye movements will be tested. Voluntary or reflexive (oculocephalic) eye movements will be scored, but caloric testing is not done. If the patient has a conjugate deviation of the eyes that can be overcome by voluntary or reflexive activity, the score will be 1. If a patient has an isolated peripheral nerve paresis (CN III, IV or VI), score a 1. Gaze is testable in all aphasic patients. Patients with ocular trauma, bandages, pre-existing blindness, or other disorder of visual acuity or fields should be tested with reflexive movements, and a choice made by the investigator. Establishing eye contact and then moving about the patient from side to side will occasionally clarify the presence of a partial gaze palsy.	0 = **Normal.** 1 = **Partial gaze palsy;** gaze is abnormal in one or both eyes, but forced deviation or total gaze paresis is not present. 2 = **Forced deviation,** or total gaze paresis not overcome by the oculocephalic maneuver.	_____

Rev 10/1/2003

NIH STROKE SCALE

Patient Identification. ___ ___-___ ___ ___-___ ___ ___

Pt. Date of Birth ___ ___/___ ___/___ ___

Hospital _____(___ ___-___ ___)

Date of Exam ___ ___/___ ___/___ ___

Interval: [ ] Baseline [ ] 2 hours post treatment [ ] 24 hours post onset of symptoms ±20 minutes [ ] 7-10 days
[ ] 3 months [ ] Other _____(___ ___)

3. Visual: Visual fields (upper and lower quadrants) are tested by confrontation, using finger counting or visual threat, as appropriate. Patients may be encouraged, but if they look at the side of the moving fingers appropriately, this can be scored as normal. If there is unilateral blindness or enucleation, visual fields in the remaining eye are scored. Score 1 only if a clear-cut asymmetry, including quadrantanopia, is found. If patient is blind from any cause, score 3. Double simultaneous stimulation is performed at this point. If there is extinction, patient receives a 1, and the results are used to respond to item 11.	0 = **No visual loss.** 1 = **Partial hemianopia.** 2 = **Complete hemianopia.** 3 = **Bilateral hemianopia** (blind including cortical blindness).	_____
4. Facial Palsy: Ask – or use pantomime to encourage – the patient to showteeth or raise eyebrows and close eyes. Score symmetry of grimace in response to noxious stimuli in the poorly responsive or non-comprehending patient. If facial trauma/bandages, orotracheal tube, tape or other physical barriers obscure the face, these should be removed to the extent possible.	0 = **Normal** symmetrical movements. 1 = **Minor paralysis** (flattened nasolabial fold, asymmetry on smiling). 2 = **Partial paralysis** (total or near-total paralysis of lower face). 3 = **Complete paralysis** of one or both sides (absence of facial movement in the upper and lower face).	_____
5. Motor Arm: The limb is placed in the appropriate position: extend the arms (palms down) 90 degrees (if sitting) or 45 degrees (if supine). Drift is scored if the arm falls before 10 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime, but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic arm. Only in the case of amputation or joint fusion at the shoulder, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice.	0 = **No drift;** limb holds 90 (or 45) degrees for full 10 seconds. 1 = **Drift;** limb holds 90 (or 45) degrees, but drifts down before full 10 seconds; does not hit bed or other support. 2 = **Some effort against gravity;** limb cannot get to or maintain (if cued) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity. 3 = **No effort against gravity;** limb falls. 4 = **No movement.** UN = **Amputation** or joint fusion, explain: _____ **5a. Left Arm** **5b. Right Arm**	_____ _____
6. Motor Leg: The limb is placed in the appropriate position: hold the leg at 30 degrees (always tested supine). Drift is scored if the leg falls before 5 seconds. The aphasic patient is encouraged using urgency in the voice and pantomime, but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic leg. Only in the case of amputation or joint fusion at the hip, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice.	0 = **No drift;** leg holds 30-degree position for full 5 seconds. 1 = **Drift;** leg falls by the end of the 5-second period but does not hit bed. 2 = **Some effort against gravity;** leg falls to bed by 5 seconds, but has some effort against gravity. 3 = **No effort against gravity;** leg falls to bed immediately. 4 = **No movement.** UN = **Amputation** or joint fusion, explain: _____ **6a. Left Leg** **6b. Right Leg**	_____

Rev 10/1/2003

NIH STROKE SCALE

Patient Identification. ___ ___-___ ___ ___-___ ___ ___

Pt. Date of Birth ___ ___/___ ___/___ ___

Hospital _____(___ ___-___ ___)

Date of Exam ___ ___/___ ___/___ ___

Interval: [ ] Baseline [ ] 2 hours post treatment [ ] 24 hours post onset of symptoms ±20 minutes [ ] 7-10 days [ ] 3 months [ ] Other _____(___ ___)

7. Limb Ataxia: This item is aimed at finding evidence of a unilateral cerebellar lesion. Test with eyes open. In case of visual defect, ensure testing is done in intact visual field. The finger-nose-finger and heel-shin tests are performed on both sides, and ataxia is scored only if present out of proportion to weakness. Ataxia is absent in the patient who cannot understand or is paralyzed. Only in the case of amputation or joint fusion, the examiner should record the score as untestable (UN), and clearly write the explanation for this choice. In case of blindness, test by having the patient touch nose from extended arm position.	0 = **Absent.** 1 = **Present in one limb.** 2 = **Present in two limbs.** UN = **Amputation** or joint fusion, explain: _____	____
8. Sensory: Sensation or grimace to pinprick when tested, or withdrawal from noxious stimulus in the obtunded or aphasic patient. Only sensory loss attributed to stroke is scored as abnormal and the examiner should test as many body areas (arms [not hands], legs, trunk, face) as needed to accurately check for hemisensory loss. A score of 2, "severe or total sensory loss," should only be given when a severe or total loss of sensation can be clearly demonstrated. Stuporous and aphasic patients will, therefore, probably score 1 or 0. The patient with brainstem stroke who has bilateral loss of sensation is scored 2. If the patient does not respond and is quadriplegic, score 2. Patients in a coma (item 1a=3) are automatically given a 2 on this item.	0 = **Normal;** no sensory loss. 1 = **Mild-to-moderate sensory loss;** patient feels pinprick is less sharp or is dull on the affected side; or there is a loss of superficial pain with pinprick, but patient is aware of being touched. 2 = **Severe to total sensory loss;** patient is not aware of being touched in the face, arm, and leg.	____
9. Best Language: A great deal of information about comprehension will be obtained during the preceding sections of the examination. For this scale item, the patient is asked to describe what is happening in the attached picture, to name the items on the attached naming sheet and to read from the attached list of sentences. Comprehension is judged from responses here, as well as to all of the commands in the preceding general neurological exam. If visual loss interferes with the tests, ask the patient to identify objects placed in the hand, repeat, and produce speech. The intubated patient should be asked to write. The patient in a coma (item 1a=3) will automatically score 3 on this item. The examiner must choose a score for the patient with stupor or limited cooperation, but a score of 3 should be used only if the patient is mute and follows no one-step commands.	0 = **No aphasia;** normal. 1 = **Mild-to-moderate aphasia;** some obvious loss of fluency or facility of comprehension, without significant limitation on ideas expressed or form of expression. Reduction of speech and/or comprehension, however, makes conversation about provided materials difficult or impossible. For example, in conversation about provided materials, examiner can identify picture or naming card content from patient's response. 2 = **Severe aphasia;** all communication is through fragmentary expression; great need for inference, questioning, and guessing by the listener. Range of information that can be exchanged is limited; listener carries burden of communication. Examiner cannot identify materials provided from patient response. 3 = **Mute, global aphasia;** no usable speech or auditory comprehension.	____
10. Dysarthria: If patient is thought to be normal, an adequate sample of speech must be obtained by asking patient to read or repeat words from the attached list. If the patient has severe aphasia, the clarity of articulation of spontaneous speech can be rated. Only if the patient is intubated or has other physical barriers to producing speech, the examiner should record the score as untestable (UN), and clearly write an explanation for this choice. Do not tell the patient why he or she is being tested.	0 = **Normal.** 1 = **Mild-to-moderate dysarthria;** patient slurs at least some words and, at worst, can be understood with some difficulty. 2 = **Severe dysarthria;** patient's speech is so slurred as to be unintelligible in the absence of or out of proportion to any dysphasia, or is mute/anarthric. UN = **Intubated** or other physical barrier, explain: _____	____

Rev 10/1/2003

NIH STROKE SCALE

Patient Identification. ___ ___-___ ___ ___-___ ___ ___

Pt. Date of Birth ___ ___/___ ___/___ ___

Hospital _____(___ ___-___ ___)

Date of Exam ___ ___/___ ___/___ ___

Interval: [ ] Baseline [ ] 2 hours post treatment [ ] 24 hours post onset of symptoms ±20 minutes [ ] 7-10 days
[ ] 3 months [ ] Other _____(___ ___)

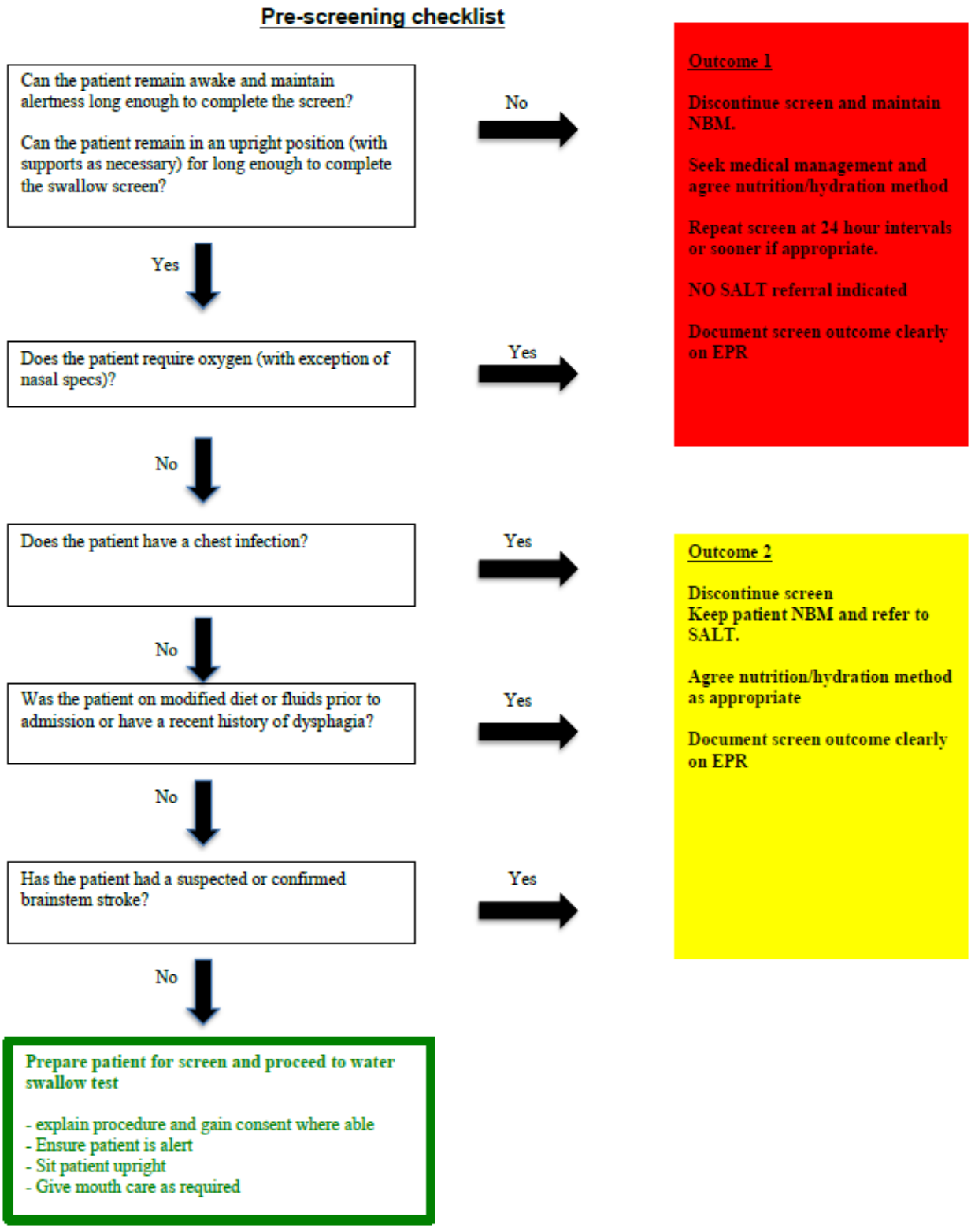
11. Extinction and Inattention (formerly Neglect): Sufficient information to identify neglect may be obtained during the prior testing. If the patient has a severe visual loss preventing visual double simultaneous stimulation, and the cutaneous stimuli are normal, the score is normal. If the patient has aphasia but does appear to attend to both sides, the score is normal. The presence of visual spatial neglect or anosagnosia may also be taken as evidence of abnormality. Since the abnormality is scored only if present, the item is never untestable.	0 = **No abnormality.** 1 = **Visual, tactile, auditory, spatial, or personal inattention** or extinction to bilateral simultaneous stimulation in one of the sensory modalities. 2 = **Profound hemi-inattention or extinction to more than one modality;** does not recognize own hand or orients to only one side of space.	____

____

____

Rev 10/1/2003

Appendix 3 Bedside water swallow screening protocol in stroke at SRFT



The above screen has been adapted from the Greater Manchester Stroke Water Swallow Screening Tool. Greater Manchester & Cheshire Cardiac & Stroke Network. 2011.

Appendix 4 The Holistic and Reliable Oral Assessment Tool (THROAT); modified from Dickinson, Watkins et al. (2001)

		Abnormal				
	Normal: score 0	Mild: score 1	Moderate: score 2	Severe: score 3	Total score	Comments
Lips	Smooth/pink/moist	Dry/ not cracked	Dry/ cracked	Ulcerated/ sores/ bleeding		
Teeth Dentures	Clean Clean	Film localised plaque over teeth Film localised plaque over teeth	Film of plaque over teeth most areas Film of plaque over teeth most areas	Heavy visible deposits of plaque on and between teeth Heavy visible deposits of plaque on and between teeth		
Gums/ gingiva	Coral pink/ moist	Mild inflammation/ slight redness/ slight swelling	Moderate inflammation/ redness/ swelling/ glazing	Severe inflammation/ marked redness/ swelling/ ulceration/ bleeding		
Mucous membranes	Coral pink/ moist	Mild inflammation/ slight redness/ slight swelling	Moderate inflammation/ redness/ swelling/ glazing	Severe inflammation/ marked redness/ swelling/ ulceration/ bleeding		
Palate	Coral pink/ moist	Mild inflammation/ slight redness/ slight swelling	Moderate inflammation/ redness/ swelling/ glazing	Severe inflammation/ marked redness/ swelling/ ulceration/ bleeding		
Tongue	Pink/moist/no coating	Slight coating	Coating/ cracks/ small ulcers	Thick coating/ discoloured/ blistered/ ulcerations/cracks/ bleeding		
Saliva	Watery consistency	Slight thickening	Thick and ropy	No saliva		

Appendix 5 Approval Letter from Wales Research Ethics Committee 5

Part of the research infrastructure for Wales funded by the National Institute for Social Care and Health Research, Welsh Government.
Yn rhan o seilwaith ymchwil Cymru a ariannir gan y Sefydliad Cenedlaethol ar gyfer Ymchwil Gofal Cymdeithasol ac Iechyd, Llywodraeth Cymru

NISCHR RES Gwasanaeth Moeseg Ymchwil | Research Ethics Service

Pwyllgor Moeseg Ymchwil Cymru 5
Wales Research Ethics Committee 5
Bangor

Clinical Academic Office
Ysbyty Gwynedd Hospital
Betsi Cadwaladr University Health Board
Bangor, Gwynedd
LL57 2PW

Telephone/ Facsimile: 01248 - 384.877
Email: Rossela.Roberts@wales.nhs.uk
Website : www.nres.nhs.uk

Miss Kate McKenzie
Hill Top
Willeymoor Lane,
Tushington, Whitchurch
Cheshire
SY13 4QN kate.w.mckenzie@hotmail.com

06 October 2014

Dear Miss McKenzie,

Study title:	**Feasibility and criterion validity of The Holistic and Reliable Oral Assessment Tool (THROAT) in acute dysphagic stroke patients.**
REC reference:	**14/WA/1153**
IRAS project ID:	**161543**

Thank you for your letter of 26 September 2014, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact the REC Manager, Dr Rossela Roberts, rossela.roberts@wales.nhs.uk

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Mental Capacity Act 2005

I confirm that the committee has approved this research project for the purposes of the Mental Capacity Act 2005.
The Committee is satisfied that the requirements of section 31 of the Act will be met in relation to research carried out as part of this project on, or in relation to, a person who lacks capacity to consent to taking part in the project.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering letter		10 September 2014
REC Application Form [REC_Form_10092014]		10 September 2014
Research protocol or project proposal [C SMITH Oral health assessment in acute dysphagic stroke]	2	29 September 2014
Referee's report or other scientific critique report [Peer review Prof Richard Watt]	-	-
Referee's report or other scientific critique report [Peer review Prof Peter Langhorne]	-	08 September 2014
Participant information sheet [Participant information sheet and Consent Form]	2	29 September 2014
Participant information sheet [Easy Access Participant information sheet and Consent Form]	1	01 September 2014
Participant information sheet [Information for Personal Consultee and Consultee Declaration Form]	2	29 September 2014
Participant information sheet [Information for Independent Consultee and Consultee Declaration Form]	1	01 September 2014
Participant information sheet [Retrospective Participant Information Sheet and Consent to Ongoing Participation]	2	29 September 2014
Summary CV for Chief Investigator [Dr Craig Smith]	-	11 July 2013
Summary CV for student [Miss Kate Mckenzie]	-	26 August 2014
Summary CV for Academic Supervisor [Dr Paul Brocklehurst]	-	28 July 2014
Letter from sponsor	-	31 August 2014
Evidence of Sponsor insurance or indemnity	-	31 August 2014
Response to Request for Further Information	-	26 September 2014
Response to Request for Further Information	-	29 September 2014

(end of list)

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

14/WA/1153	**Please quote this number on all correspondence**

Yours sincerely

Rossela Roberts

Mr Derek James Crawford, MBChB, FRCS
Chair
E-mail: rossela.roberts@wales.nhs.uk

Enclosure: "After ethical review – guidance for researchers"

Copy: Sponsor's Contact: Ms Lynne Macrae
Faculty Research Practice Coordinator
FMHS Research Office, 3.53 Simon Building
University of Manchester
M13 9PL lynne.macrae@manchester.ac.uk

Chief Investigator: Dr Craig Smith
Consultant in Stroke Medicine and Honorary Lecturer
Salford Royal NHS Foundation Trust
Brain Injury Research Group, CSB
Stott Lane, Salford
M6 8HD craig.smith2@manchester.ac.uk

Academic Supervisor: Dr Paul Brocklehurst
The School of Dentistry, University of Manchester
Higher Cambridge Street
Manchester
M15 6FH Paul.Brocklehurst@manchester.ac.uk

R&D Office: Rachel Georgiou
Salford Royal NHS Foundation Trust
Research & Development Directorate
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Stott Lane, Salford,
M6 8HD rachel.georgiou@manchester.ac.uk

Appendix 6 Study Schedule

Patient Study Number: Date: 4

STUDY SCHEDULE									
	Evaluation	**Screening**	**Study Entry/ Baseline**	**Within 24hours of stroke onset**	**At 24hours**	**+48 hours (~day 2-4)**	**+48 hours (~day 4-6)**	**+48 hours (~day 6-8)**	**+48 hours (~day 8-10)**
Screening	Demographic details		✓						
	Eligibility screen	✓							
	Informed consent		✓						
Enrolment	NIHSS		✓		✓				
	Baseline assessment		✓						
During study participation	THROAT (Research team)			✓					
	Dental assessment (DCP blinded to THROAT)			✓					
	Swallow/ nutritional status	✓	✓		✓	✓	✓	✓	✓
	SAP screening (Pneumonia/health check)	✓	✓		✓	✓	✓	✓	✓
	Antibiotic usage	✓	✓		✓	✓	✓	✓	✓

Appendix 7 The Oxfordshire Community Stroke Project (OSCP) Classification of Stroke (Bamford, Sandercock et al. 1991)

OP subgroup	Clinical syndrome(s)
TACS	*All of the triad:* · Contralateral hemiparesis (±hemisensory loss) · Contralateral homonymous hemianopia · New disturbance of higher cerebral function
PACS	*Any of the following:* · Contralateral hemiparesis/ hemisensory loss and homonymous hemianopia · Contralateral hemiparesis/ hemisensory loss and new higher cerebral dysfunction · New higher cerebral dysfunction and contralateral homonymous hemianopia · New higher cerebral dysfunction alone · Restricted contralateral hemiparesis/ hemisensory loss (e.g. monoparesis)
POCS	*Any of the following:* · Ipsilateral cranial nerve palsy (ies) and conralateral hemiparesis/ hemisensory loss · Bilateral hemiparesis/ hemisensory loss · Disorder of conjugate eye movement · Cerebellar dysfunction (without long tract signs) · Isolated contralateral homonymous hemianopia or cortical blindness
LACS	Maximum deficit from a single vascular event*, in the absence of*: visual field deficit, new higher cerebral dysfunction or impaired conscious level · PMS: unilateral motor weakness involving at least two out of three entire areas of face, arm and leg · PSS: unilateral sensory disturbance involving at least two out of three entire areas of face, arm and leg · SMS: unilateral motor weakness and sensory disturbance involving at least two out of three areas of face, arm and leg · AH: ipsilateral cerebellar and motor weakness, with or without dysarthria

TACS: total anterior circulation syndrome, PACS: partial anterior circulation syndrome, POCS: posterior circulation syndrome, LACS: lacunar syndrome, PMS: pure motor stroke, PSS: pure sensory stroke, SMS: sensorimotor stroke, AH: ataxic hemiparesis

Appendix 8 Patient Information Sheet and Consent Form

PARTICIPANT INFORMATION SHEET

Oral health assessment in acute dysphagic stroke

V2; 29/9/14

MANCHESTER 1824 The University of Manchester

MAHSC

NHS

Salford Royal NHS

Manchester Vascular & Stroke Centre

Institute of Cardiovascular Sciences, University of Manchester, CSB, Salford Royal Foundation Trust, Salford in collaboration with Manchester Dental School

Dr Craig Smith	Dr Paul Brocklehurst	Sharon Hulme	Victoria O'Loughlin	Kate McKenzie
Consultant Stroke Physician	Senior Clinical Lecturer (Dentistry)	Research Manager	HSRC Lead	Dental Care Practitioner
Tel: 0161 206 0623	Tel: 0161 275 6609	Tel: 0161 206 5755	Tel: 0161 206 0626	Tel: 0161 206 2188

Feasibility and criterion validity of The Holistic and Reliable Oral Assessment Tool (THROAT) in acute dysphagic stroke patients

Short title: Oral health and development of stroke-associated pneumonia

REC Ref: 14/WA/1153

You are invited to take part in a research study. We understand this is a stressful time for you and we appreciate you taking time to read this information. The study will focus on patients who are unable to swallow following a stroke. It will assess whether assessment of the mouth is useful in patients who have swallowing problems caused by their stroke and if there is any relationship between mouth health and development of pneumonia after stroke. The knowledge we gain from this study will inform future studies aimed at improving the health and cleanliness of the mouth and preventing pneumonia after stroke.

Before you agree to participate in the study, you need to understand why the study is being done and what it will involve. Please take time to read this information. Talk to others about the study if you wish. The information sheet is divided into two parts:

- **Part 1** why the study is being done and how will it affect you.
- **Part 2** information in more detail.

Please ask if you need more information. Take time to decide whether or not you wish to take part.

PARTICIPANT INFORMATION SHEET
Oral health assessment in acute dysphagic stroke
V2; 29/9/14
PART 1

What is the purpose of the study?

The study aims to establish if assessing of the mouths of stroke patients is useful in identifying a link between the condition of a patient's mouth after stroke and risk of pneumonia. This study will focus on patients who also have difficulties with swallowing caused by their stroke, known as dysphagia.

All patients with suspected stroke undergo an assessment of their swallowing in the Emergency Department or on the stroke unit. If a patient is assessed as having swallowing problems (dysphagia), they will be prevented from eating or drinking for a period of time, referred to as *'nil by mouth'*. Such patients may be at increased risk of chest infection (pneumonia) when food, drink and even saliva can enter the lungs instead of the stomach. A healthy mouth already contains millions of germs (bacteria) so when a person has problems with their gums or teeth and the number of bacteria in the mouth and saliva is greatly increased; the risk of pneumonia becomes even higher. Dysphagia can resolve in the hours and days after stroke; so the swallow assessment is repeated; however the risk of pneumonia remains high even when the ability to swallow is restored.

This study will assess the condition of the mouth at admission in patients with dysphagia after stroke. The research team will record what happens to patients during their hospital stay and will monitor the patient's general condition for up to 10 days. These assessments will help establish if the condition of the mouth at the time of stroke is associated with development of pneumonia. The study will increase what is known about dysphagia and stroke-associated pneumonia, which we hope will lead to the development of interventions to reduce the chances of pneumonia occurring. This study is also been carried out as part of an educational project (Master of Philosophy) for Miss Kate McKenzie.

Why have I been asked to take part?

You have suffered a stroke and have been assessed as having problems with your swallowing. You will be a patient on the stroke unit at Salford Royal NHS Foundation Trust until you are discharged home or returned to your local hospital.

Do I have to take part?

No, you do not have to take part in this study. If you decide that you want to take part, you will be given this information to keep and asked to sign a consent form. If your condition should change during participation, the consent you give will remain valid and you will remain in the study. You are free to withdraw from the study at any time. You do not have to give a reason for doing so and this will not affect the care you receive. If you are unable to sign the consent form yourself, you can nominate someone to sign it on your behalf.

What will happen if I decide to take part?

Research practitioners will check that you are eligible to participate in the study and will ask for your consent to participation. They will record details of your past medical history, current medications, details of your stroke, whether you are able to swallow and presence of any infections.

In the first 24 hours after your stroke, a research practitioner will assess the health of your mouth using a scoring system that is designed to be used by nurses (THROAT score). Your lips, gums, tongue, and teeth will be assessed for soreness or dryness.

Also within the first 24 hours after stroke, you will undergo a more detailed assessment of your mouth by a dental hygienist. This assessment is similar to a check-up by the dentist. She will record if you have any existing problems with your teeth or mouth before conducting a full mouth examination. She will record any missing or damaged teeth and the condition of your gums and tongue. This will involve gently probing between your teeth and gums to see if they are healthy. This will take up to 20 minutes. **The dental hygienist will not administer any treatment, but may advise if further dental assessment is required.**

The research practitioners will continue to check your progress during your hospital stay. This will continue on alternate days for up to 10 days after your stroke. If you leave Salford Royal and return to your local hospital, this will continue to be performed by research practitioners at the local site. **No blood tests or samples will be collected.** The assessment on day 10 will complete your study participation. Your discharge from hospital will not be delayed by participation in the study.

What are the possible benefits of taking part?

There are no direct benefits to you taking part in the study. You will be helping to inform what is known about mouth hygiene and pneumonia, which may help in the development of new interventions to reduce pneumonia and ultimately improve outcome for patients after stroke.

What are the possible risks/side effects of taking part?

You may find the assessment of your mouth a little uncomfortable, as you will need to keep your mouth open wide, intermittently, for up to 20 minutes. The hygienist will take regular short breaks or can stop completely if you show any signs of distress.

Withdrawal from the study

You are free to withdraw from the study at any time without giving a reason. Withdrawal from the study will not affect your clinical care. We would like to include the information we gather about you up to the point of withdrawal in our final analysis. If you prefer this information to be destroyed, please tell the researcher.

Will I be paid for taking part?

You will not receive payment for taking part in the study. The research staff will not receive any payment for your involvement in this study.

PART 2

What if new information becomes available?

Sometimes during the course of a research project, new information becomes available relating to what is being studied. If this happens, a researcher will tell you about it and discuss if you want to continue in the study. You may be asked to confirm your willingness to continue by signing a new consent form.

What if there is a problem?

Complaints: If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. If they are unable to resolve your concerns or you wish to make a complaint regarding the study, please contact a University

Research Practice and Governance Coordinator on 0161 276 7583 or 0161 275 8093 or by email to researchgovernance@manchester.ac.uk

Harm: In the event that something does go wrong and you are harmed during the research you may have grounds for legal action for compensation against The University of Manchester but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you. If a crown or filling becomes dislodged during the examination, there are no special arrangements in place for these to be replaced and you will be advised to seek standard dental care on discharge from hospital.

Confidentiality

If you decide to take part your hospital notes and other health records may be seen by authorised people (other researchers and people checking the study conduct). Your name will not appear in any publications arising from the study. All study documentation taken as part of the assessments and examinations will be identified using a unique code assigned to you after consent.

What happens when the research study stops?

The results of the study will be submitted for publication to medical journals and at conferences. The results will also be submitted to authorities within the United Kingdom who are responsible for overseeing the conduct of research studies. If you wish, we can send you a summary of the study findings but this may not be for some time. The results of the study will be submitted for publication to medical journals and at conferences. Miss Kate McKenzie (Dental Care Professional) will be using the information from this study as part of her Masters of Philosophy (MPhil) degree. Your name will not be identified by name in any publication.

Data storage and usage

In order to ensure we have an accurate record of your history and clinical presentation, we will also need to access your clinical records. Anonymised data will also be shared by members of the research team based within Salford Royal NHS Foundation Trust and the University of Manchester. All study data and clinical information will be anonymised before it is stored. Anonymised research data may also be used in future projects however these may not be undertaken by the original research team.

The study is funded by The University of Manchester Dental School and the Salford Royal Foundation Trust Hyperacute Stroke Research centre. We will be following the recognised guidelines regarding the sharing of study data. This means that the anonymised data from the study will be available to others. The data and information from the study will be stored for up to 5 years.

Organisation of the study

The study is organised by the Manchester Stroke & Vascular Centre at Salford Royal Foundation Trust and The Dental School within the University of Manchester.

Who has reviewed the study?

The study has been reviewed by NRES Committee Wales Research Ethics committee 5 and has received a favourable opinion

If you have any queries or questions relating to the study please contact: The Stroke Research Network nurses on telephone: 0161 206 2188

Thank you for your time.

PARTICIPANT INFORMATION SHEET

Oral health assessment in acute dysphagic stroke

V2; 29/9/14

PARTICIPANT CONSENT

REC Ref No: **14/WA/1153**

Title of Project: Feasibility and criterion validity of The Holistic and Reliable Oral Assessment Tool (THROAT) in acute dysphagic stroke patients?

Name of Lead Investigator: Dr Craig Smith

		Please initial box
1.	I confirm that I have read the information sheet dated 29th September, 2014 (version 2) and have had the opportunity to ask questions	☐
2.	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	☐
3.	I understand that my consent to participation in the study will remain valid regardless of changes in my condition during the period of participation, unless I choose to withdraw.	☐
4.	I understand that sections of any of my medical notes may be looked at by responsible individuals from Salford Royal Foundation Trust and the University of Manchester or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.	☐
5.	I agree to take part in the above study	☐

Name of research subject *Please print*	Date	Signature of patient or nominated signatory (* if the patient is unable to sign for themselves)
Name of Witness to Signature *Please print*	Date	Signature
Member of research team member *Please print*	Date	Signature

3 copies required: top copy for researcher; one copy for patient; one copy to be kept with research participants notes

Do you wish to receive information about the results of this study? Yes/No *please circle*

Appendix 9 Easy Access Participant Information Sheet and Consent Form

EASY-ACCESS PARTICIPANT INFORMATION SHEET

Oral health assessment in acute dysphagic stroke

V1; 1/9/14 **REC Ref: 14/WA/1153**

MANCHESTER 1824 The University of Manchester

MAHSC

Salford Royal NHS NHS Foundation Trust

University Teaching Trust

safe • clean • personal

Manchester Vascular & Stroke Centre

Institute of Cardiovascular Sciences, University of Manchester, CSB, Salford Royal Foundation Trust, Salford in collaboration with Manchester Dental School

Dr Craig Smith
Consultant Stroke Physician
Telephone: 0161 206 0623

Dr Paul Brocklehurst
Senior Clinical Lecturer (Dentistry)
Telephone: 0161 275 6609

Sharon Hulme
Research Manager
0161 206 5755

Victoria O'Loughlin
HSRC Lead
Tel: 0161 206 0626

1. Study title: Oral health and development of stroke-associated pneumonia

2. The invitation. You are invited to take part in a **research study**

To have **checks of** your mouth

By a **nurse** and a **Dental Hygienist**

Before you decide, it is **important** for you to **understand** why the research is being done and **what it will involve.**

Please take the time to read the following information.

Ask if anything is **not clear** or if you would like **more information.** ++

3. What is the purpose of the study?

We want to see if an **assessment of** the mouth after stroke is useful,

so we can check for a **link** between the **condition** of the mouth is after stroke and the development of **pneumonia.**



If we can **identify** pneumonia **earlier**, it can be **treated** sooner


leading to **improved recovery** from stroke and shorter hospital stay.



4. Why have I been chosen?

You have had a **stroke**

You are unable to **swallow**

You will be in **hospital** for at least 3 days


5. Do I have to take part?

No. It is **up to you** to decide whether or not  to take part.

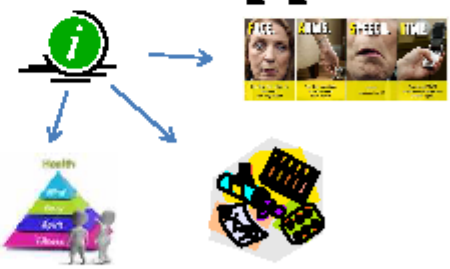
The **standard of care** you receive will not be affected in any way 

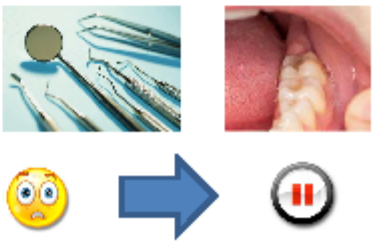
6. What will be involved if I agree to take part?

Whilst you are in **hospital** Salford Royal NHS

We would like to carry out **two examinations** of your mouth. Each will last about half an hour.  **X2** 

These will be done by a **research nurse** and a **dental hygienist** on the **first day** after your stroke.  **&**  **on** 

The research nurse will record **information** about your **health,** including **medication** you currently take and **details of your stroke** 

The dental hygienist will perform a full examination of your mouth; including your **teeth** or **dentures.**
She will also **inspect** the gaps between your teeth. This may be slightly **uncomfortable.**
The hygienist will **pause** as often as necessary. 

The research nurse will visit on **alternate days** to see **how you are.**

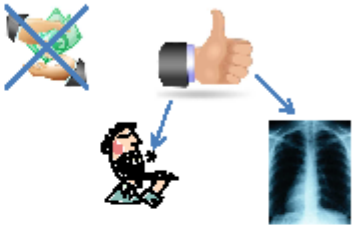
She will record **changes** to your **medication**, check if you can **eat and drink** and check your **general health.**

This will **continue** to do this even if you **leave Salford Royal** and **return to your local hospital**

Assessments will continue for **up to 10 days** after your stroke. After this time your participation in the study will end.

7. What are the benefits of taking part?

Taking part in the study will **not benefit you** but you will help **increase our understanding** of **mouth hygiene** and **stroke-associated pneumonia**



8. What are the risks of taking part?

We do not anticipate there to be any **risks** to participation.

You may pause or stop the assessments at any time.

You are free to withdraw from the study at any time.

9. Will my taking part in the study be kept confidential?

All your **personal information** (name, address and telephone number) will be kept confidential

and **securely stored** at Salford Royal Hospital

Salford Royal NHS

Your name will not be shown ~~John Smith~~ You will be identified by a number **C131**

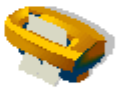
Only **authorised** people will be **allowed** to see your information.

10. What will happen if I do not want to carry on with the study?

You are **free to withdraw** from the **study** at **any time**

If you withdraw, we will use the information already collected in the final analysis.

If you do not want us to use your information, please tell us and it will be confidentially destroyed.



11. Who is organising and funding the research?

This study is **organised** by the Stroke and Vascular Centre and the Dental School within the **University of Manchester**

The study is **funded** by **The University of Manchester Dental School**

This study has been **approved** by a **NHS Research Ethics Committee**

12. What will happen to the results of the research study?
We will **publish** the **study results** in an academic journal.

The results may be **presented** at **conferences**.

The results will be part of an **educational project** for Kate McKenzie, Dental Care Professional. **You will not be identified.**

13. What if I need more information or there is a problem?

If you need further **information**

or have any concerns about the study please contact the research team on:
0161 206 2188

If you decide you would like to take part, please read and sign the consent form.

You will be given a copy of this information and signed consent form to keep.

Please take time to decide whether you want to take part.

Thank you for reading about this study.

EASY-ACCESS PARTICIPANT INFORMATION SHEET

Oral health assessment in acute dysphagic stroke

V1; 1/9/14 REC Ref: 14/WA/1153

Oral health and development of stroke-associated pneumonia

Consent Form for Patients

V1; 28/7/14

Please initial the boxes

	**1.** I confirm that I have **read** and **understood** the **information** sheet dated 28/7/14 (version 1) for the above study. I have had the opportunity to ask **questions.**	
	**2.** I understand that my participation is **voluntary** and that I am free to **withdraw** at any time without giving a reason and without medical care or legal rights being affected.	
	**3.** I understand that my data will be collected for this study and may be used as part as part of an educational project. Data protection regulations will be observed. **Confidentiality** will be maintained.	
	**4.** I understand that even if I withdraw from the study, the data already collected from me will contribute to the study unless I specifically withdraw consent for this.	
	**5.** I agree to my **data** being stored by the Stroke and Vascular Centre and the Dental School at The University of Manchester. This will be **anonymised** as soon as possible.	
	**6.** I understand that authorised individuals may require access to my personal detail in order to monitor study conduct.	
	**7.** I agree to take part in the above study.	

EASY-ACCESS PARTICIPANT INFORMATION SHEET
Oral health assessment in acute dysphagic stroke
V1; 1/9/14 **REC Ref: 14/WA/1153**

Participant:

Name (capitals)	Date	Signature

Witness:

Name (capitals)	Date	Signature

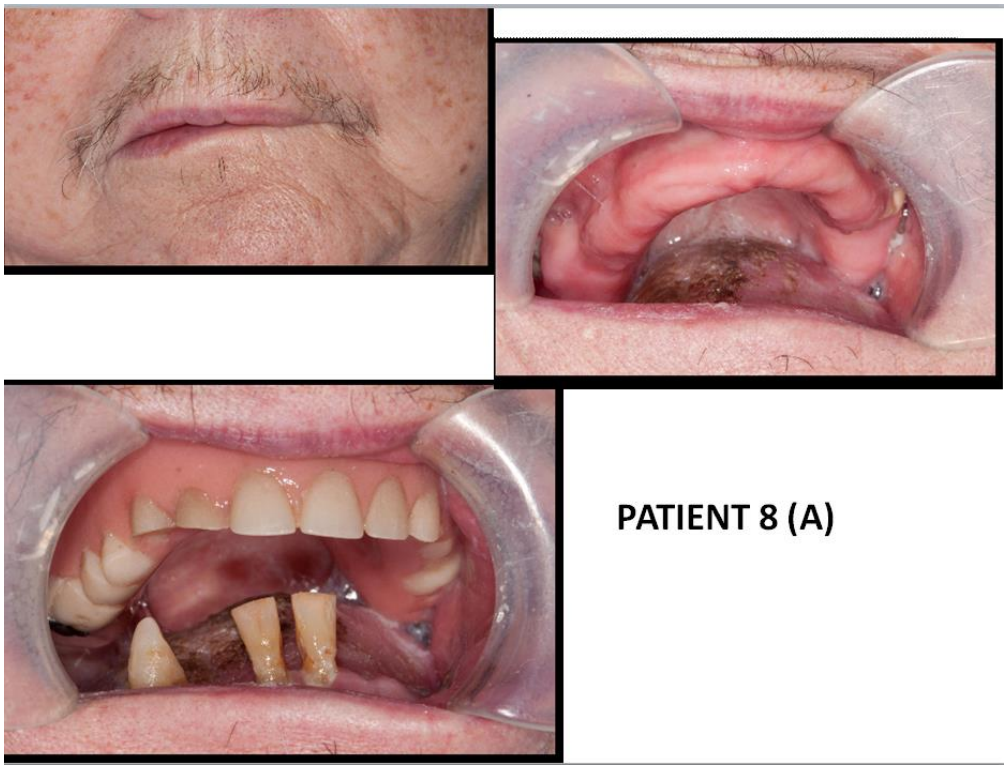
Researcher:

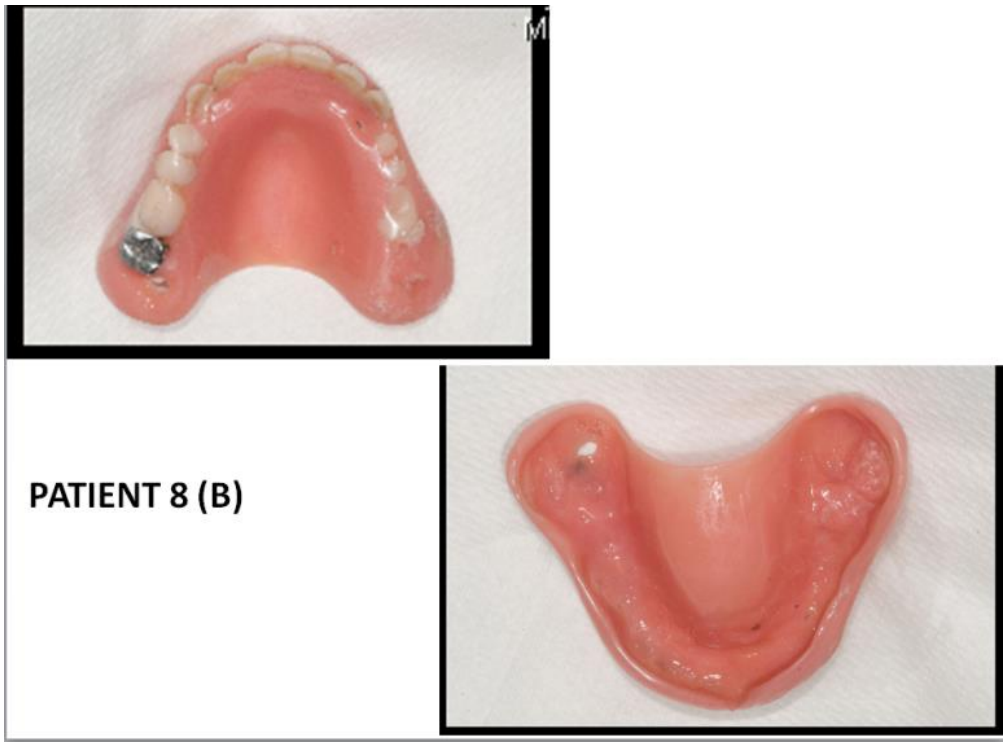
Name (capitals)	Date	Signature

(1 copy for the participant, 1 copy for CRF, 1 copy for notes)

Do you wish to receive information about the results of this study? Yes/No *please circle*

Appendix 10 THROAT Training Resource: Oral Digital Photos[4]





[4] Images of 10 different patient mouths were used in the training resource. These slides are an example of 1 of the cases. Photographs were taken from an oral hygiene intervention study that took place on the stroke ward at SRFT in 2013.

Appendix 11 Bedside Dental Assessment Sheet

Patient Study Number: Date: 11

Bedside Dental Assessment

To be completed within 24 hour of stroke onset by a research DCP blinded to the results of the THROAT scale.

Date ☐☐☐ Completed by: _____ (name)

Time start ☐☐ **24:00 hr clock**

Time finish ☐☐ **24:00 hr clock**

Using the data from the full-mouth measurements overleaf page to calculate:

Number of teeth present =

Proportion of teeth with frankly cavitated lesions

.....

.....=

Proportion of teeth with at least one periodontal sits that bleeds

.....

.....=

Proportion of teeth with a site that has plaque present

.....

.....=

Proportion of teeth with a site that has a periodontal pocket depth between 3.5-5.5mm (BPE code 3) - see appendix

.....

.....=

Proportion of teeth with a site that has a periodontal pocket depth greater than 5.5mm (BPE code 4) - see appendix

.....

.....=

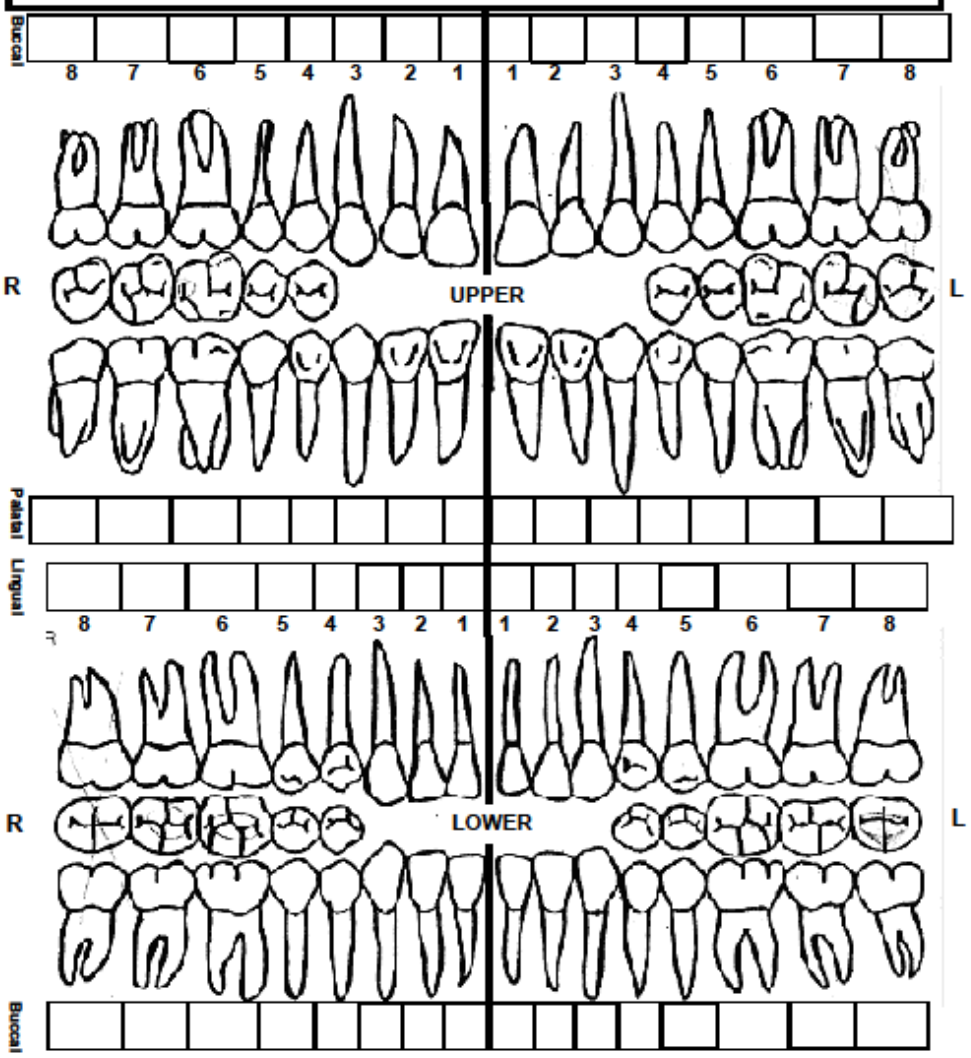
Adverse Findings Yes ☐ No ☐ **If yes, record this and follow up in Appendix 3**

Case Report Form Version 1 20th October, 2014

Patient Study Number: Date: 12

Full Mouth Measurements

⇒ Chart full dentition: use —— for teeth not present
⇒ To annotate frankly cavitated lesions: use **O**
⇒ Record BPE code of mesial and distal aspect of each tooth surface e.g. 3 1
(see Appendix 3)
⇒ If bleeding present on probing, circle measurement in red e.g. (3) 1
⇒ If plaque present on tooth surface underline the measurement e.g. (3) 1



Appendix 12 Diagnosis of Stroke-associate Pneumonia (SAP) Based on the Centers for Disease Control and Prevention (CDC) Criteria (Horan, Andrus et al. 2008)

Proposed CDC modified criteria for definite and probable SAP in non-ventilated adults (Smith, Kishore et al. 2015)

Signs and symptoms:

AT LEAST ONE of the following:

- Fever (>38°C) with no other recognised cause
- Leukocytosis (WBC ≥12x10^9/l) or leukopenia (<4x12x10^9/l)
- For adults ≥70years old, altered mental status with no other recognised cause

AND AT LEAST TWO of the following:

- New onset of purulent sputum or change in character of sputum over a 24 hours period or increased respiratory secretions, or increased suctioning requirements
- New onset or worsening cough, or dyspnoea or tachypnoea (respiratory rate >25/min)
- Rales, crackles, or bronchial breath sounds
- Worsening gas exchange (e.g. O_2 desaturations [eg PaO_2/FiO_2 ≤240], or increased oxygen requirements *[category of increased ventilator demand removed]*

Radiology:

Two* or more serial chest radiographs with **AT LEAST ONE** of the following:

- New or progressive and persistent infiltrate
- Consolidation
- Cavitation

* In patients without underlying pulmonary or cardiac disease, 1 definitive chest radiograph is acceptable

CDC, Centers for Disease Control and Prevention; CXR, chest x-ray; FiO_2, fraction of inspired oxygen; PaO_2, partial pressure oxygen; SAP, stroke-associated pneumonia; and WBC, white blood cell.

Probable SAP: all CDC criteria met, **BUT** initial CXR and serial/repeat CXR non-confirmatory (or not undertaken), and no alternative diagnosis or explanation.

Definite SAP: **ALL** CDC criteria met, including diagnostic CXR changes (on at least one)

Appendix 13 Sponsor's Liability Insurance Letter

The University of Manchester

Faculty of Medical & Human Sciences
The University of Manchester
Oxford Road
Manchester M13 9PT

www.manchester.ac.uk

Sunday, 31 August 2014

To whom it may concern

This is to confirm that, where appropriate, insurance policies held by the University of Manchester will cover the research project entitled **'Feasibility and criterion validity of The Holistic and Reliable Oral Assessment Tool (THROAT) in acute dysphagic stroke patients'** which we have been informed is being conducted by **Kate McKenzie** under the supervision of **Dr Craig Smith** and **Dr Paul Brocklehurst.**

The University has insurance available in respect of research involving human subjects that provides cover for legal liabilities arising from its actions or those of its staff or supervised students. The University also has insurance available that provides compensation for non-negligent harm to research subjects occasioned in circumstances that are under the control of the University.

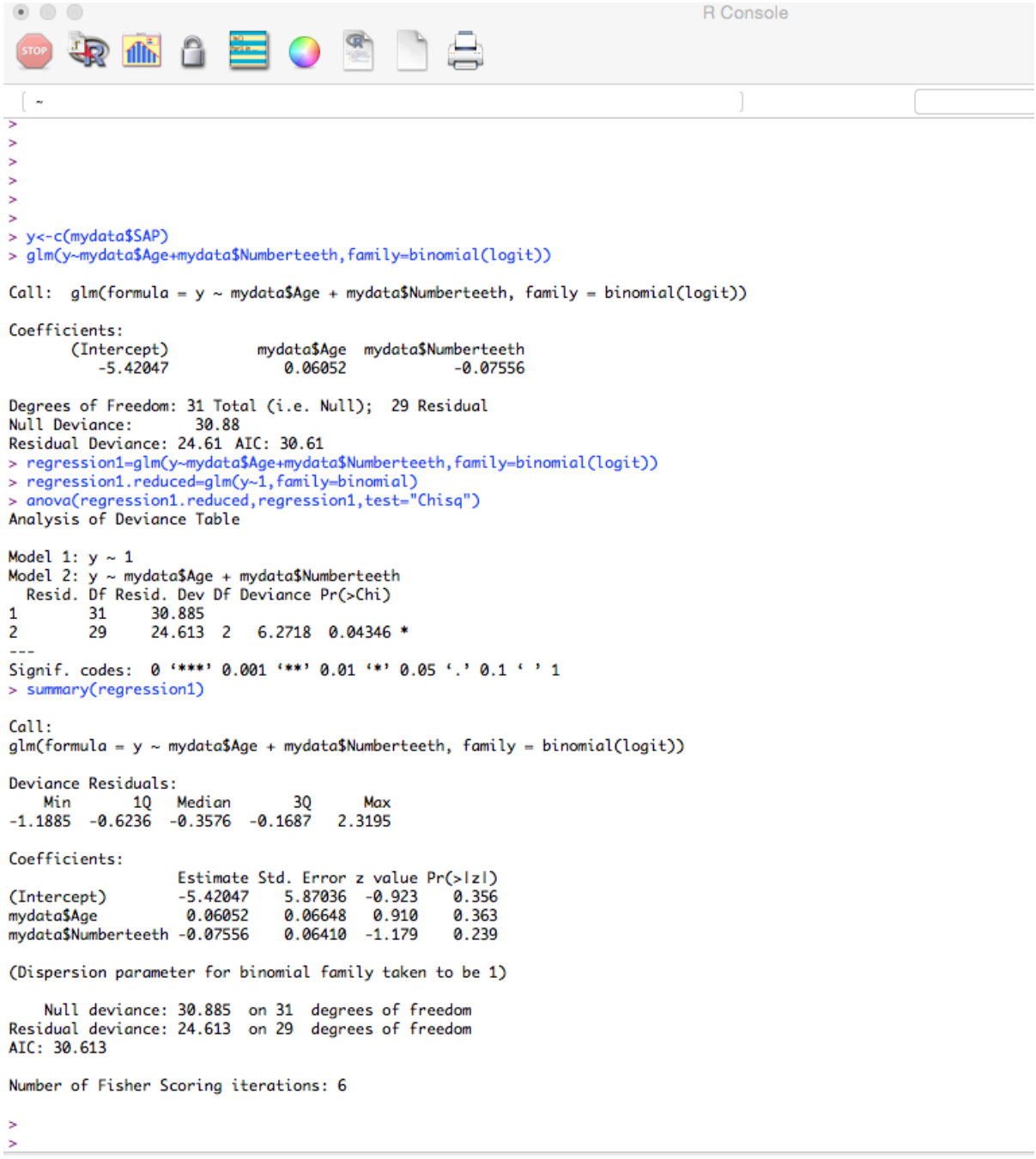
Provision of this insurance cover in respect of a specific project may be subject to the acceptance of the project by the University's insurers and is conditional upon the project receiving approval from an appropriate ethics committee.

Signed on behalf of the University of Manchester,

Lynne MacRae

Lynne MacRae Dated: **31.08.2014**
Research Practice Coordinator
Faculty of Medical & Human Sciences

Appendix 14 Calculation screenshots for multiple regression using R programming



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