INCIDENCE RATES AND MULTIDISCIPLINARY RESPONSE TO DELIRIUM IN ACUTE STROKE: A MIXED METHODS INVESTIGATION

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Abstract

Delirium is a serious medical condition affecting up to 30% of hospital in-patients and associated with significant negative consequences such as increased mortality, morbidity as well as an increased long term risk of cognitive impairment. Delirium is difficult to identify due to its fluctuating course and the various subtypes, which are not well recognised by hospital staff. Stroke patients display a number of the precipitating and predisposing factors for delirium, yet the incidence of delirium in this population is not well documented. It is not known how best to identify delirium in this population and the ways in which multidisciplinary healthcare staff understand the condition.

This thesis outlines the mixed methods of investigation which set out to answer these questions, utilising a systematic review and meta-analysis, an online survey, and online focus groups. The thesis makes a novel contribution to the field of stroke research in identifying the incidence of delirium as 28.1% (95% CI: 22.9 to 33.2), as well as synthesising research on the specific risk factors and outcomes associated with delirium in this population. The thesis also highlights the inconsistent practice of delirium identification in acute stroke, in both research and clinical practice. A further contribution is in the response of various healthcare professionals when it comes to identifying delirium in stroke patients: more doctors than nurses identify delirium, nurses have a recognised role in highlighting physiological changes associated with the condition and allied health professionals may lack confidence in their knowledge of the condition, as seen in their use of tentative language to discuss delirium. Despite this, the data suggest that the appropriate management of the condition takes place. The thesis argues that more education and organisational recognition of delirium as a diagnostic priority needs to take place in order to potentially improve outcomes for this population.

Keywords: Delirium; acute stroke; cognitive assessment; multidisciplinary; mixed methods research.

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Glossary and Abbreviations

4AT	The 4 As Test
ACE-III	Addenbrook Cognitive Examination
ACS	Acute Confusional State
ADL / ADLs	Activity / Activities of Daily Living
AMT	Adult Mental Test
AHP/AHPs	Allied Health Professional/s
BASP	British Association of Stroke Physicians
CAM	Confusion Assessment Method
CAM-ICU	Confusion Assessment Method for the Intensive Care Unit
CI	Confidence Intervals
CRP	C-Reactive Protein: non-specific measure of infection or inflammation
DRS	Delirium Rating Scale
DSM III-DSM V	Diagnostic and Statistical Manual, American Psychiatric Association (versions III to V)
GT	Grounded Theory
ICC	Interclass Correlation Coefficient
ICD-10	International Classification of Diseases 10th Edition, World Health Organization
ICU	Intensive Care Unit
IQCODE	Informant Questionnaire of Cognitive Decline in the Elderly
LACI	Lacunar Infarct
MA	Meta-Analysis
MCA	Middle Cerebral Artery
MDT	Multidisciplinary Team
MMSE	Mini Mental State Examination
MOCA	Montreal Cognitive Assessment
NHS	National Health Service

NICE	National Institute of Health and Clinical Excellence
NIHSS	National Institute of Health Stroke Scale
NOK	Next of Kin
NPV	Negative Predictive Value
OBS Scale	Organic Brain Syndrome Scale
OT/OTs	Occupational Therapy / Occupational Therapist/s
PACI	Partial Anterior Circulation Infarct
PCA	Posterior Cerebral Artery
POCI	Posterior Circulation Infarct
PPV	Positive Predictive Value
PT	Physiotherapist
QUADAS	Quality Assessment of Diagnostic Accuracy in Studies tool
RASS	Rankin Agitation and Sedation Scale
RCP	Royal College of Physicians
RCT	Randomised Controlled Trial
SAH	Subarachnoid Haemorrhage
SIGN	Scottish Intercollegiate Guidelines Network
SLT	Speech and Language Therapist
SR	Systematic Review
SSAHPF	Scottish Stroke Allied Health Professionals Forum
SSNF	Scottish Stroke Nurses Forum
SSRN	Scottish Stroke Research Network
TACI	Total Anterior Circulation Infarct
TIA	Transient Ischaemic Attack
UTI	Urinary Tract Infection
VLE	Virtual Learning Environment
WTU	Ward Test Urine

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Chapter I

Introduction

This chapter sets the scene for the thesis through definitions of stroke and delirium, as well as a brief exploration of the usual care environment in the acute stages of stroke in Scottish stroke services. The process of diagnosing delirium is also discussed, with specific reference to key publications which provide guidance on best practice. An initial exploration of the phenomenon of delirium in acute stroke is provided, with the intention of covering this specific topic in greater depth in the literature review. Some of the gaps in the literature are highlighted in this introductory chapter, culminating in the aims of the programme of research. Throughout this thesis, the term 'older adults' is used in reference to adults over the age of 65, as consistent with national guidelines on delirium (National Institute for Health and Care Excellence 2010).

1.1 Stroke and its burden in Scotland

Stroke is a disease of cerebral blood vessels, defined by Hatano (1976) as "signs of focal (at times global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin" (p3350). The term stroke includes subarachnoid haemorrhage (SAH) despite the fact that SAH has different clinical manifestations (Hatano 1976, Allen et al. 2006). According to Allen et al. (2006), transient episodes of ischaemia, also referred to as Transient Ischaemic Attack

(TIA) are strokes which last less than 24 hours, with the signs and symptoms resolving completely within the 24 hour period. In epidemiological studies, TIA and stroke are treated separately, thus, the term ‘Stroke’ is used when symptoms last more than 24 hours (Allen et al. 2006).

Worldwide, stroke is the second leading cause of death and third leading cause of disability (World Health Organization 2017). According to Johnson et al. (2016), 70% of strokes occur in low- and middle-income countries, rates which have more than doubled in the last 40 years, whereas in the same time frame, stroke incidence has declined by 42% in high-income countries. Kuklina et al. (2012) conducted a comprehensive review of published studies to highlight the global risk factors for stroke, identifying these as hypertension, elevated blood lipids, diabetes, atrial fibrillation and lifestyle (obesity, diet, smoking, alcohol intake and physical inactivity). In Scotland, stroke is one of the commonest causes of death and severe adult disability: an estimated 15,000 people per annum experience a stroke (ISD Scotland 2014) with around 20% of people dying within one month of onset (Scottish Intercollegiate Guidelines Network 2010). According to Lewsey et al. (2010) who conducted a 15 year longitudinal investigation, 45% of strokes occur in men and the median age at the time of hospital admission is 74 years (ranging from 65 to 81). Stroke is estimated to cost the Scottish health service around £100 million per annum, with significant additional costs to the Scottish economy associated with lost employment and loss of functional independence (ISD Scotland 2014). Reducing the number of deaths associated with stroke has been a clinical priority for health services in Scotland (NHS Scotland) since the 1990s (The Scottish Government 2014).

1.2 Acute stroke care

The benefits of organised stroke care in dedicated treatment units (acute stroke units) are clearly established with an early collaborative systematic review demonstrating that patients treated in acute stroke units have higher chances of survival and are likely to regain functional independence and return home than those treated in conventional hospital wards (Stroke Unit Trialists' Collaboration 1997). Therefore, setting up dedicated stroke units in all hospitals in Scotland was a key priority of the 2009 Stroke Care Improvement Action Plan (The Scottish Government 2014). The components of effective stroke unit care have also been outlined in the literature (Langhorne and Pollock 2002) and used in government guidelines (Scottish Intercollegiate Guidelines Network 2010). These clearly specify the need for a multidisciplinary approach to care, setting out not only the ideal staff-patient ratio, but also the make-up of teams of professionals and their requirements for specialist training (Langhorne and Pollock 2002). Specialist training of staff working in acute stroke units continues to be a key priority of policy makers as it is seen as crucial in improving stroke care in NHS Scotland (The Scottish Government 2014).

1.3 Delirium

Delirium (referred to in the past as ‘acute confusional state’) is a condition common among elderly patients in most hospital settings with a typical prevalence of 20-30% (Siddiqi et al. 2006). Delirium is characterised by its transient nature, acute onset, and fluctuating levels of confusion, inattention and arousal, in addition to changes in cognition and perception, all of which are attributable to an underlying physical cause (Young and Inouye 2007, Carson et al. 2010). Delirium may be hyperactive (hyperalert,

accompanied by overt psychotic symptoms and agitation); hypoactive (hypoalert, characterised by sedation); or mixed, i.e. both hypoactive and hyperactive (Carson et al. 2010). The clinical impact of delirium is significant: it is associated with increased mortality, increased morbidity and length of hospital stay as well as an increased risk of developing dementia in the long term (McCusker et al. 2003, Jackson et al. 2004, Young and Inouye 2007, European Delirium Association and American Delirium Society 2014).

1.4 The challenge of delirium diagnosis

Delirium has been recognised by the American Psychiatric Association in their 1980 publication of the third version of the Diagnostic and Statistical Manual (DSM-III) (Cole et al. 2003), and the diagnostic criteria have been revised several times since (Schuurmans et al. 2003, Tussey et al. 2010). Delirium diagnosis poses a variety of challenges, well documented in the literature: from the challenges arising from differences in the terms used to describe delirium (Schuurmans et al. 2003) to low detection rates for all subtypes (Inouye et al. 2001). Levkoff et al. (1991) proposed that the reasons for low detection of delirium arise from the fluctuating nature of the condition, which poses challenges to those trying to identify it as well as the considerable variation in presentation of delirium symptoms, depending on the subtype. Indeed, Carson et al. (2010) warned that the hypoactive - hypoalert type is often misdiagnosed as depression. Furthermore, Levkoff et al. (1991) discussed the challenges of distinguishing between dementia and delirium as the symptoms bear resemblance. The final challenge raised by Levkoff et al. (1991) relates to the evolution of diagnostic criteria over the years, a matter which continues to affect delirium research to this day: the fifth version of the DSM (American Psychiatric Association 2013) saw an important change in diagnostic criteria

in the removal of reference to ‘consciousness’ and its replacement with ‘arousal’, a change which has led to some concern regarding the misdiagnosis of delirium in those whose arousal is impaired so that they are unable to undergo cognitive testing (European Delirium Association and American Delirium Society 2014).

Delirium diagnosis relies on a full clinical examination that allows clinicians to recognise the symptoms and arrive at an accurate diagnosis (Carson et al. 2010). In addition to this clinical diagnostic method, a variety of standardised measures are available (Carson et al. 2010), some of which are designed to be used by clinicians with no psychiatric training, such as the Confusion Assessment Method (CAM) (Inouye et al. 1990). Such standardised measures were developed in order to improve detection rates (Inouye et al. 1990) and to date several tools have emerged and subsequently critically reviewed (Schuurmans et al. 2003, Wong et al. 2010). Many of the tools that have been developed are not suitable for routine clinical use, either because they require specialist training or they take too long to administer, and are thus impractical in the clinical setting (Schofield 2008). Whilst the CAM requires specialist training, it is relatively brief as it reportedly takes five minutes to administer (Tussey et al. 2010). Based on its psychometric properties and clinical utility, it has been adopted in parts of the UK as the diagnostic tool of choice (National Institute for Health and Care Excellence 2010, National Institute for Health and Care Excellence 2014). Conversely, Healthcare Improvement Scotland (2014) advocate the use of ’The 4 As Test’ or 4AT (Bellelli et al. 2014a) as the tool of choice for rapid screening of patients by any clinician, without specific delirium detection training. It is noteworthy that this tool does not provide a definitive diagnosis, it is rather a prompt for a comprehensive diagnostic process (Healthcare Improvement Scotland 2014). It is not yet known whether the tool is used in this way or whether there is an over-reliance on this screen in clinical practice as the author has been unable to

identify any published research on the ways in which clinical teams use this tool in practice.

In terms of the roles of various professionals within clinical teams when it comes to diagnosing delirium, it is important to note that whilst the application of DSM criteria to reach a conclusive diagnosis may seem like the domain of psychiatrists alone (Regal 2012), NICE guidelines (2010) do not specify the professional identity of the persons responsible for delirium diagnosis - merely that it should be carried out by clinicians who are trained and competent in delirium diagnosis. There is a strong argument for involving nurses in the diagnostic process since they come into daily contact with patients and are best able to monitor the fluctuating nature of the condition (Inouye et al. 2001, Lemiengre et al. 2006). Allied health professionals (AHPs) also spend a considerable amount of time with patients in the clinical setting and could also play a role in delirium diagnosis. Indeed, Occupational Therapists (OTs) are recognised as specialists in cognitive screening (Scottish Intercollegiate Guidelines Network 2010) yet only a few papers report to have included AHPs in their investigations of knowledge and recognition of delirium symptoms (Foster et al. 2010, Bellelli et al. 2014b, Li et al. 2010).

Effective and timely recognition of delirium seems to be a challenge across a variety of hospital settings as well as various healthcare professionals: Flagg et al. (2010) found that nurses across intensive care and medical / surgical units had only modest confidence levels in identifying delirium in clinical practice. Ryan et al. (2013) found that medical and nursing staff detect different delirium features: nurses tend to notice delusions, inattentiveness and emotional lability, whereas doctors tend to detect the presence of short-term memory impairment and inattention. Davis and MacLullich (2009) and Jenkin et al. (2014) reported that junior doctors lack accurate knowledge about prevalence, diagnostic means and confidence in diagnosing delirium in the general

medical setting. Infrequent use of standardised tools for the screening and/or diagnosis of delirium were also identified in the literature: routine screening and utilisation of standardised observation tools were still the exception when diagnosing delirium despite a recognition of the importance of delirium as an underdiagnosed condition of potentially serious consequences (Flagg et al. 2010, Forsgren and Eriksson 2010, Patel et al. 2009).

Foster et al. (2010) investigated multidisciplinary staff perceptions (including medical, nursing and allied health staff) and knowledge of delirium in a general medical setting. They identified a need for more staff education to enable early recognition and intervention to prevent delirium in groups particularly at risk of developing it while in hospital. Hare et al. (2008) identified nurses' lack of knowledge of delirium as a barrier to correct diagnosis, as they reported that nursing staff often label a delirious patient as 'confused', attributing this to normal aging process rather than an acute delirium. This reinforces the call for improvement in clinician education on delirium identification (Foster et al. 2010, Davis and MacLullich 2009, Hare et al. 2008) as well as taking a more standardised approach to the diagnostic process (Inouye et al. 2001, Lemiengre et al. 2006).

1.5 Diagnosing delirium in acute stroke

Stroke is considered to be one of the risk factors for developing delirium (Hshieh et al. 2008, Carson et al. 2010) yet at the time of commencing this doctoral programme in 2008, the body of literature on this specialist topic was relatively small, consisting of studies examining precipitating factors such as lesion site or type of stroke (Caeiro et al. 2005, Ferro et al. 2002, Shih et al. 2007) or the incidence of this complication and its relationship to outcome (Caeiro et al. 2004b, Hénon et al. 1999, Sheng et al. 2006).

Within the acute stroke setting, reports of delirium incidence ranged from 13% to 48% (Caeiro et al. 2004a, Gustafson et al. 1993, Gustafson et al. 1991). The wide range of incidence rates reported is noteworthy: Oldenbeuving et al. (2007) proposed that this wide range stems from differences in diagnostic procedures in addition to the differences in case mixes and operational definitions of the condition, reinforcing the argument above regarding the variety of challenges in delirium diagnosis. A further difficulty in identifying delirium in stroke patients is discussed by Lees et al. (2013) who highlighted that cognitive screening of stroke patients can be particularly difficult if they are acutely unwell or experience communication and cognitive difficulties arising from the stroke.

There is currently no clear guidance on whether stroke patients should be routinely screened for delirium, and if so, what is the best way to screen for or diagnose the condition. The National Institute for Health and Care Excellence (NICE) have published two best practice guidelines on delirium (National Institute for Health and Care Excellence 2010, National Institute for Health and Care Excellence 2014) but there is no specific mention of the diagnosis of delirium in a stroke unit. The NICE guidelines on the management of stroke mention the need for screening patients for both cognitive and attention difficulties, but delirium *per se* is not explicitly mentioned (National Institute for Health and Care Excellence 2013). The Scottish Intercollegiate Guidelines Network (SIGN) is, at the time of writing this thesis, at the consultation stage of developing a policy document on delirium (Scottish Intercollegiate Guidelines Network 2017), and in its guidelines on stroke treatment, there is no specific mention of delirium as a complication of stroke, rather, generic advice on screening to identify cognitive strengths and weaknesses (Scottish Intercollegiate Guidelines Network 2010).

1.6 Overall aims of this doctoral programme

In summary, at the time of the inception of this doctoral programme in 2008 there was a clear gap in the literature on delirium in acute stroke, despite stroke being an important precipitating factor for the development of delirium (Pitt 1998, Hshieh et al. 2008, Inouye et al. 2014) and delirium being a serious complication of stroke, which is associated with significantly poorer outcomes (Oldenbeuving et al. 2011, van Rijsbergen et al. 2011). Particularly striking was the lack of specific guidance on the screening and diagnosis of this complication, including identification of the key players responsible for screening procedures. Correct identification of delirium has the potential to lead to a swifter resolution and more favourable outcomes for patients (National Institute for Health and Care Excellence 2014), a matter which would be congruent with the Scottish Government's pledge to work to improve stroke services (The Scottish Government 2014). Accurate and timely identification of delirium relies on clinical team members being able to not only recognise the manifestations of the condition (Carson et al. 2010) but also be confident in the ways in which delirium is diagnosed, including the use of appropriate diagnostic or screening tools (Schuurmans et al. 2001, Davis and MacLullich 2009, Flagg et al. 2010). In order to begin to address the gap in the literature around delirium in acute stroke, it was important to shed light on the scale of the problem within this setting. Additionally, as a means of identifying any potential barriers to achieving early identification of the condition, it was important to explore the response of clinicians in the stroke unit to patients who may be experiencing a delirium, therefore, the overall aims of this doctoral programme were:

1. To identify, from the literature, the incidence of delirium in acute stroke, methods used to identify the condition and the clinical factors associated with developing delirium in acute stroke.
2. To identify the ways in which Scottish doctors and nurses screen for and diagnose delirium in acute stroke.
3. To explore the perspectives of stroke unit staff working with a patient who may exhibit the symptoms of delirium.

This doctoral programme was made up of three separate studies, combining a variety of methods, which allowed the researcher to address each aim listed above. Each study had its own distinct aims and objectives, which are set out in the chapters corresponding with each strand, as summarised in figure 1 (p.24). The programme took place over nine years, from the initial conception of ideas in October 2008 until the final thesis being prepared for submission in August 2017 (appendix 1.1 details the timeline of this programme).

The three strands of this doctoral programme are linked in that the first strand scoped the available literature on the topic, highlighting not only how frequently is delirium found in stroke patients but also, the reported means of delirium identification in this population. The first strand investigated research practice and it served to inform the second strand as the tools identified in the systematic review of the literature were used to explore the reality of clinical practice in finding out how delirium is identified by doctors and nurses working in acute stroke settings in Scotland. The third strand explored some of the issues identified in the literature around the ways in which multidisciplinary healthcare staff make sense of patients who may be experiencing delirium. As a whole, this thesis explores

both research and clinical practice of delirium identification in the acute stroke setting, utilising a mixed methods pragmatic approach to data collection and analysis.

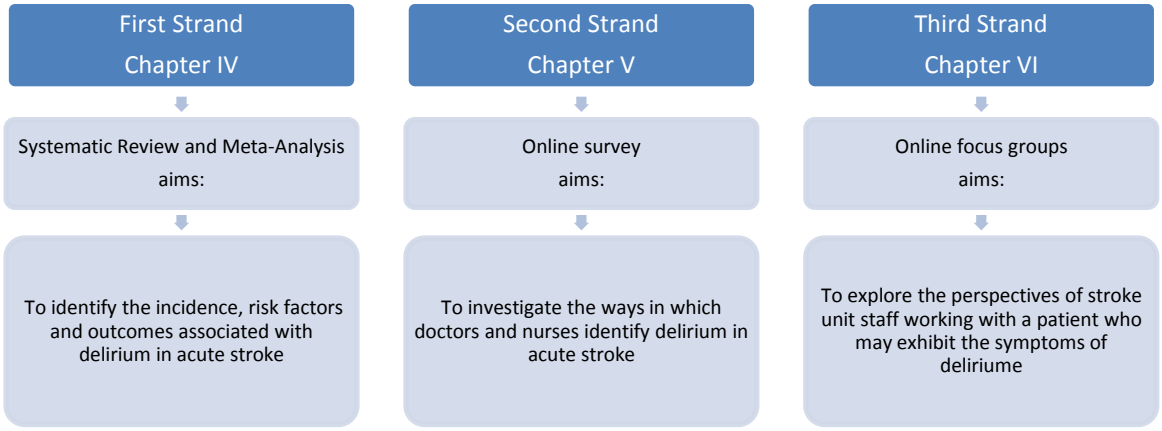

Figure 1: Programme of investigation and aims

Chapter II

Literature Review

2.1 Introduction

This literature review examines the phenomenon of delirium in depth, giving a brief history of the concept as well as discussing the diagnostic criteria for delirium. The evolution of the diagnostic criteria for delirium is also mentioned, in the context of the challenges of delirium identification, particularly in the move between the fourth and fifth versions of the DSM (American Psychiatric Association 2002, American Psychiatric Association 2013). The incidence of delirium is discussed, including a critical examination of the means by which delirium is identified in research practice. The consequences of delirium, in terms of the impact upon the person, their significant others and the health service as a whole are discussed as well as the optimal management of the condition. Where possible in the literature review, the specific issues of delirium in acute stroke are explored. Since this is a relatively specialist topic of exploration, literature on specific issues covered in this review may not stem from the field of stroke-delirium research. In these cases, literature from other areas of the acute hospital setting has been drawn upon.

2.2 The phenomenon of delirium

Delirium as a concept can be traced back to Hippocrates, who described the term several times in his medical writings (Lipowski 1991, Burns et al. 2004). Pitt (1998)

proposed that Shakespeare's *King Lear* presents an observation of delirium. In the play some of the most important features of delirium are portrayed: a condition that affects older people as a result of infection, having an impact on behaviour, being reversible but ultimately leading to death (Pitt 1998).

Since then, delirium has been described in a number of works over the years, as reviewed in seminal publications by Engel and Romano (1959, reprinted 2004) and later by Lipowski (1987). Pitt (1998) referred to a number of definitions that have been suggested over the years. A definition which most corresponds to today's classification of the condition comes from Lipowski (1987):

> *"Delirium (acute confusional state) is a transient disorder of cognition and attention, one accompanied by disturbances of the sleep-wake cycle and psychomotor behaviour…acute onset of a fluctuating state of awareness, accompanied by sleep–wake disruption, lethargy or agitation and nocturnal worsening of symptoms are diagnostic".* (p.1789)

The aetiology of the condition is regarded as "non-specific" and often there are multiple underlying causes of delirium (Carson et al. 2010, Inouye et al. 2014). The most common causes of delirium are: intoxication and withdrawal (e.g. from prescription drugs, illicit drugs or alcohol), metabolic causes (e.g. hypoglycaemia, fluid and electrolyte imbalance), infection, head trauma, epilepsy and vascular disorders (cardiovascular and cerebrovascular) (Lipowski 1991, Blass et al. 1991, Carson et al. 2010). The two most prominent working hypotheses regarding the pathophysiology of delirium relate to neurotransmitter function and inflammatory processes (Khan et al. 2011). Marcantonio et al. (2006) presented a complex pathophysiological picture which demonstrated that it is the interactions of a variety of neurotransmitter systems which are responsible for delirium symptoms rather than any single neurotransmitter. Hshieh et al. (2008) reviewed the evidence, supporting the hypothesis that acetylcholine (or 'cholinergic') deficiency

plays an important role in the development of delirium. They supported this by highlighting that medication known to induce delirium often antagonises acetylcholine and links were drawn between dementia and delirium based on this disruption of acetylcholine (Hshieh et al. 2008). Mukadam et al. (2008) also explored the role of acetylcholine in the emergence of delirium suggesting that the cognitive deficits associated with delirium (such as disorder of attention) are the neuropsychological functions associated with cholinergic neuronal transmission.

Khan et al. (2011) reviewed the evidence around the various inflammatory biomarkers which may be indicative of a delirium. They suggested that it is the overlap between the role of inflammatory mediators and cholinergic systems which are implicated in the development of delirium symptoms (Khan et al. 2011). One of the biomarkers Khan et al. (2011) found to be associated with development of delirium is cortisol, albeit only two of the studies included in their review examined cortisol as a biomarker for delirium (Khan et al. 2011). Kazmierski and Kloszewska (2011) explained that elevated cortisol levels are associated with a stress response in certain groups of patients (e.g. acutely ill), they stated that despite cortisol being important in coping with stress, in prolonged and excessive release it may contribute to delirium. Hall et al. (2011) conducted a systematic review of cerebrospinal fluid biomarkers and reported that among other biomarkers, cortisol may have a role in the development of delirium in elderly patients. However, they concluded that not enough evidence could be identified and more research was required (Hall et al. 2011). Despite this inconclusive evidence, Khan et al. (2011) called for biomarkers for delirium to be used more widely in clinical practice in order to aid identification of the condition. Chu et al. (2011) were more cautious, highlighting some of the limitations of biomarker identification in delirium research and suggesting that more rigorous research in the field is needed.

2.2.1 Characteristics and subtypes of delirium

The hallmark characteristics of delirium are the acute onset and fluctuating disturbance of function (White and Bayer 2007) which, according to established knowledge, typically last around two weeks (Pitt 1998). This timescale is now revisited, as Cole et al. (2009) suggested that delirium can be more persistent, particularly in older people. Delirium is described as a complex cluster of symptoms affecting a number of domains: cognitive, perceptual, motor behaviour, sleep-wake pattern, arousal and speech and language (Gupta et al. 2008). The details of these disruptions in function are presented in Table 1 (p.29).

Schofield (2008) reviewed the experience of delirium, which enables one to put the described characteristics of the condition into the context of a person's presenting symptoms:

> *"In the hyperactive subtype, the person is visibly restless, excitable and on their guard. They can be continuously on the move, searching, shouting, combative, leaving their bed or ward and resisting when staff try to calm them..."* (p.171)

The fluctuating nature of delirium, coupled with the hypoactive-hypoalert manifestations, increase the challenges of identifying delirium in medical in-patient settings, challenges which are frequently described in the literature (Lipowski 1990, Levkoff et al. 1991, Siddiqi et al. 2006, Young and Inouye 2007, Ryan et al. 2013). These challenges link with delirium research when it comes to the establishment of an incidence rate for the condition, as will be discussed later in this review.

Table 1: Characteristics of Delirium (adapted from Pitt 1998)

Domain	Characteristics
Impaired consciousness	Failure to maintain attention, distractibility, drowsiness, unconsciousness. All of these fluctuate.
Perceptual disturbances	Visual hallucinations, impaired ability to judge distance, disturbance of body image, distortion of time.
Impaired cognitive function	Impaired abstract thinking and comprehension, logic, reason and judgement, impaired memory.
Psychomotor disturbance	Here a distinction is made between the two subtypes of delirium: (a) Hyperalert–hyperactive: agitation, distractibility, tremor, sweating, rapid pulse and breathing, dry mouth, raised blood pressure and dilated pupils. (b) Hypoalert–hypoactive: lethargy, withdrawal, delayed responses (c) Mixed: unpredictable fluctuations between (a) and (b).
Disruption of sleep-wake cycle	Reversal of sleep-wake patterns: sleeping during the day and insomnia at night. Daytime sleep may be accompanied by vivid dreams which could lead to a distorted sense of reality.
Emotional disturbance	Apathy, anger, irritation, terror, apprehension, bewilderment and emotional lability.

2.2.2 Precipitating and predisposing factors

Young and Inouye (2007) claimed that because the pathophysiology of delirium is poorly understood and multiple factors contribute to the development of delirium, it is more helpful to examine the precipitating and predisposing factors for the development of the condition. Davis et al. (2013) considered the need to identify clearly both the precipitating and predisposing factors as well as the relationship between these factors in observational studies of delirium. Young and Inouye (2007) explained the relationship between these two factors, claiming that precipitating factors do not cause a delirium on their own, rather these interact with any underlying risk or predisposing factors. Young

and Inouye (2007) explained further that a relatively minor change (e.g. change of medication) can result in delirium in a person with many risk factors, which is why older people with multiple morbidities tend to be more prone to developing delirium. Lorenzo et al. (2013), in their comprehensive review of delirium in critically ill patients, provided a clear account of the factors contributing to the development of delirium, among the many precipitating factors listed are: use of urinary catheters, pain, certain medications (e.g. anticholinergics, benzodiazepines), fever, disruption of sleep, malnutrition and dehydration, orthopaedic trauma and surgery, heart surgery, admission to the intensive care unit (ICU) and stroke. As for the predisposing factors, Lorenzo et al. (2013) listed older age (over 65 years), smoking, cognitive impairment, previous delirium, vision or hearing impairment, hypertension and male sex.

2.3 Diagnostic criteria for delirium

A uniform terminology for delirium was only achieved in 1980 as the third edition of the Diagnostic and Statistical Manual of Mental Disorders was published and the clinical features of the condition were categorised (Lipowski 1991). Some of the early terms that were used to describe delirium were: ‘frenzy’ or ‘febrile insanity’, later, ‘encephalopathy’, ‘acute confusional state’, and ‘acute organic brain syndrome’ (Tussey et al. 2010). Thus, the classification of delirium was significant in encouraging a more universal use of terminology to describe the condition (European Delirium Association and American Delirium Society 2014).

Two psychiatric diagnostic systems exist: The Diagnostic and Statistical Manual of Mental Disorders (DSM) published by the American Psychiatric Association and the International Classification of Diseases (ICD) published by the World Health

Organization. The diagnostic criteria of both classification systems have been revised several times between the editions (Schuurmans et al. 2003, Tussey et al. 2010, Levkoff et al. 1991, Burns et al. 2004, Schuurmans et al. 2001). The DSM is currently on its fifth version (DSM-V) (American Psychiatric Association 2013) whereas the eleventh version of the ICD is due to be published in 2018 (World Health Organization 2016). Table 2 (p.32) compares the diagnostic criteria for delirium listed in the latest versions of the DSM and the ICD (American Psychiatric Association 2013, World Health Organization 1992).

It is noteworthy that the DSM criteria tend to be favoured by delirium experts across Europe (Morandi et al. 2013). According to Meagher et al. (2008) this is due to the fact that the ICD-10 criteria were not as sensitive to delirium as the DSM, predominantly because of the inclusion of emotional disturbance in the ICD-10 which introduces a variability that contributes to this lack of sensitivity (Meagher et al. 2008). Perhaps as a result of this favouring of the DSM criteria, the bedside tools used to detect delirium reported in the literature all seem to be based upon the DSM (Schuurmans et al. 2003, Wong et al. 2010, Adamis et al. 2010).

Table 2: DSM-V and ICD-10 Diagnostic Criteria for Delirium.

DSM-V	ICD-10
A. Disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment).	Impairment of consciousness and attention (on a continuum from clouding to coma; reduced ability to direct, focus, sustain and shift attention).
B. The disturbance develops over a short period of time (usually hours to a few days), represents an acute change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day.	Global disturbance of cognition (perceptual distortions, illusions and hallucinations, most often visual; impairment of abstract thinking and comprehension, with or without transient delusions, but typically with some degree of incoherence; impairment of immediate recall and of recent memory but with relatively intact remote memory; distortion of time as well as, in more severe cases, of place and person).
C. An additional disturbance in cognition (e.g. memory deficit, disorientation, language, visuospatial ability, or perception)	Psychomotor disturbances (hypo- or hyperactivity and unpredictable shifts from one to the other; increased reaction time; increased or decreased flow of speech; enhanced startle reaction).
D. The disturbances in Criteria A and C are not better explained by a pre-existing, established or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal such as coma.	Disturbance of the sleep-wake cycle (insomnia or, in severe cases, total sleep loss or reversal of the sleep–wake cycle; daytime drowsiness; nocturnal worsening of symptoms; disturbing dreams or nightmares which may continue as hallucinations after awakening).
E. There is evidence from the history, physical examination or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e. due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple aetiologies.	Emotional disturbances, (e.g. depression, anxiety or fear, irritability, euphoria, apathy or wondering perplexity).

The fifth version of the DSM delirium diagnostic criteria has come under criticism by several authors: The European Delirium Association (2014) expressed concern regarding the erroneous diagnosis of delirium in those whose arousal is impaired and they are unable to undergo cognitive testing. Adamis et al. (2015) compared prospectively the fourth and fifth version of the DSM in a cohort of 200 elderly inpatients and found the DSM-V to be more restrictive, thus, patients who met the diagnostic criteria for delirium under the DSM-IV, did not meet the same criteria under the DSM-V. Meagher et al. (2014) conducted a retrospective comparison of the two classification systems in a larger cohort of 768 patients and found similarly that when the DSM-V criteria were applied strictly, fewer cases of delirium were identified as compared with the more inclusive DSM-IV. Neufeld (2015) warned that the application of DSM-V criteria may result in misidentification of delirium in nearly half of cases and called for either reverting back to the DSM-IV criteria, or the application of the two versions together to avoid cases of missed diagnosis. The national clinical guidelines for delirium published by the National Institute for Health and Care Excellence (NICE CG103, 2010) precede the publication of the fifth version of the DSM (American Psychiatric Association 2013), it would therefore be interesting to note whether any future updates of these guidelines will recommend the use of DSM-V diagnostic criteria.

2.4 The incidence of delirium in acute hospital settings

Morandi et al. (2012) distinguished between prevalent and incident delirium: within the hospital setting, prevalent delirium is detected on admission whereas incident delirium occurs during the course of hospital stay. The challenges of case identification of delirium which result in variations in the estimates of incidence rate are discussed

widely in the literature (Siddiqi et al. 2006, Inouye et al. 2001, Inouye et al. 1990, Burns et al. 2004, Trzepacz 1999). Despite these challenges, a comprehensive systematic review placed the incidence rates for delirium between 20-30% in elderly medical inpatients across most general medical settings (Siddiqi et al. 2006). These incidence rates for delirium are cited in the most recently published government guidelines on treatment of delirium (National Institute for Health and Care Excellence 2014). It is noteworthy that Siddiqi et al. (2006) cited Inouye's early work (1994, in: Siddiqi et al. 2006) regarding delirium non-detection rates of up to 66% of patients in medical settings, they thus warned that their incidence rates are likely to be underestimated. More recently, Inouye et al. (2014) were critical of the incidence rates reported in single studies, stating that they were affected by selection bias since many of the studies reported the exclusion of patients with dementia or other cognitive impairment, thus they supported the view that the true incidence rates for delirium are underestimated.

2.4.1 Incidence of delirium in acute stroke

In the early stages of this doctoral programme, the incidence rates reported in the stroke literature ranged from 10% (Dahl et al. 2010) to 48% (Gustafson et al. 1991). This wide range observed has been attributed mainly to the varied diagnostic tools and protocols employed across studies (Oldenbeuving et al. 2007). McManus et al. (2007) added that due to the fluctuating nature of the condition, it is likely that incidence rates would be higher the more frequently patients are monitored, as is the case in Gustafson et al.'s (1991) methodology. This wide range of incident delirium in acute stroke suggested a need to perform a synthesis of the data available at the time, in order to be able to pinpoint the incidence rates more confidently. The first strand of this programme

addresses this need as can be seen in chapter IV of this thesis, which reports the results of a systematic review and meta-analysis of the incidence of delirium in the acute stroke setting.

2.5 Bedside tools used to detect delirium

Systematic determination of the incidence of delirium across hospital settings is enabled by the use of standardised tools (Tussey et al. 2010). A wide variety of standardised tools for the detection and measurement of delirium severity exist (Schuurmans et al. 2003, Schofield 2008, Wong et al. 2010). This section examines the tools used to identify incident delirium in older patients, first in the general hospital settings and then with specific interest in the acute stroke setting. Delirium diagnosis is complex, as like many other psychiatric diagnoses, there are no laboratory or radiologic tests that can definitively confirm the diagnosis (Neufeld et al. 2014). Accurate diagnosis therefore relies on a full clinical assessment of the symptoms presented (Carson et al. 2010, Inouye et al. 2014). UK national clinical guidelines (National Institute for Health and Care Excellence 2010) stipulate that the diagnosis of delirium should be achieved either by clinical assessment or by use of a diagnostic tool, specifically, the Confusion Assessment Method (CAM)(Inouye et al. 1990). However, more than 28 delirium instruments are cited and reviewed in published studies (Schuurmans et al. 2003, Wong et al. 2010, Adamis et al. 2010, van Velthuijsen et al. 2016). The tools selected for this review are those which have been reported in the stroke literature. It is however important to draw attention to the use of language around these tools as the terms “screening” and “diagnosis” differ from each other, yet they seem to be used synonymously in the literature. Rapp et al. (2000) attached a variety of verbs to these tools: screen, assess,

detect, diagnose and rate. Holly et al. (2013) referred to these tools as “screening tools” whereas Wong et al. (2010) used the term “bedside instruments”. van Velthuijsen et al. (2016) pointed out that while many of the instruments are designed and used either as screening or as diagnostic tools, the distinction between them is not always clear. Clinical guidelines refer to the CAM as an option for the diagnosis of delirium (National Institute for Health and Care Excellence 2010, National Institute for Health and Care Excellence 2014). However, Hall et al. (2012) suggested that delirium assessment should consist of two stages: a brief, simple and sensitive instrument followed by a formal diagnosis according to the diagnostic criteria (as outlined in section 2.3). Thus, bedside instruments should be only part of the diagnostic process of delirium. Indeed, in a survey of delirium experts across Europe (n=200), 63% of respondents reported that the final diagnosis of delirium is made based on DSM criteria, after initial screening using a variety of bedside delirium detection tools (Morandi et al. 2013). All bedside tools mentioned in this review have undergone testing of some or all of their psychometric properties, Table 3 (p.38) provides a summary of these data.

Various terms are used to indicate the performance of diagnostic tests, these terms denote the metric data relating to the testing of their performance in a target population (Quinn and Takwoingi 2016): ‘Sensitivity’ is the proportion of true positives correctly identified by the measure and ‘specificity’ is the proportion of the true negatives that are correctly identified, or in other words, the tool’s ability to correctly exclude people who do not have the condition (Altman 2000, Greenhalgh 2015, Quinn and Takwoingi 2016). According to Altman (2000), because sensitivity and specificity are proportions, confidence intervals (CI) need to be calculated and presented alongside the calculated proportions. Where available these are presented in table 3 (p.38). The positive and

negative predictive values (PPV and NPV) are means of identifying the proportion of patients with abnormal test results (e.g. positive delirium screen) who truly have the condition, thus, the PPV is the proportion of patients with positive test results who are correctly diagnosed (Altman 2000, Quinn and Takwoingi 2016). The NPV is the proportion of patients with negative test results who truly do not have the condition (Quinn and Takwoingi 2016), thus, similar to sensitivity and specificity scores, these proportions should also have the CI presented alongside them (Altman 2000). The Kappa statistic is used to compare between assessors carrying out the same test thus a percent of agreement beyond the level of agreement expected by chance is calculated: A maximum value of 1 indicates perfect agreement and 0 indicates that the agreement is no better than chance (Altman 2000). Similarly, the Intraclass Correlation Coefficient (ICC) is a measurement which can be used to determine observer variation (Bland 2015). The final property mentioned in some of the psychometric performance studies is internal consistency: using Cronbach's Alpha it is possible to measure how closely the items within the scale relate to each other (Bland 2015). Due to the multiple validation studies conducted for some of the tools, wherever possible, the original validation study is used and when a systematic review of diagnostic accuracy is available, it is reported as pooled data alongside the original publication of the tool's psychometric properties. Useful syntheses of psychometric data for a variety of tools can be found in other studies (Wong et al. 2010, Adamis et al. 2010, van Velthuijsen et al. 2016).

Table 3: Psychometric properties of bedside tools cited in this review

Scale / Authors	Test Accuracy Metrics					
	Sensitivity (95% CI)	**Specificity (95% CI)**	**Inter-rater**	**Internal consistency**	**PPV% (95% CI)**	**NPV% (95% CI)**
General geriatric or medical population						
Confusion Assessment Measure (Inouye et al. 1990)	Site 1: 100 (66 to 100) Site 2: 94 (68 to 100) Pooled (Shi et al. 2013): 82 (69 to 91)	Site 1: 95 (73 to 100) Site 2: 90 (54 to 100) Pooled (Shi et al. 2013): 99 (87 to 100)	Kappa=1.0 -	-	Site 1: 91 (no CI) Site 2: 94 (no CI) Pooled (Shi et al. 2013): Between 75 and 100 in various studies	Site 1: 100 (no CI) Site 2: 90 (CI) Pooled (Shi et al. 2013): Between 80 and 98.7 in various studies
Confusion Assessment Measure for the Intensive Care Unit CAM-ICU (Ely et al. 2001a)	Nurse 1: 95 (77 to 100) Nurse 2: 96 (78 to 100) Pooled (Shi et al. 2013): 81 (57 to 93)	Nurse 1: 93 (68 to 100) Nurse 2: 93 (68 to 100) Pooled (Shi et al. 2013): 98 (86 to 100)	Nurse 1: Kappa 0.84 (0.63 to 0.99) Nurse 2: Kappa 0.79 (0.64 to 0.95) -	-	- Pooled (Shi et al. 2013): Between 88	- Pooled (Shi et al. 2013): Between 20 and 96 in

					and 100 in various studies	various studies
Scale / Authors	**Test Accuracy Metrics**					
	Sensitivity (95% CI)	**Specificity (95% CI)**	**Inter-rater**	**Internal consistency**	**PPV% (95% CI)**	**NPV% (95% CI)**
Delirium Rating Scale (Trzepacz et al. 1998) (Rockwood et al. 1996)	- 82 Pooled Wong et al. (2010): 95 (90 to 98)	- 94 Pooled Wong et al. (2010): 79 (58 to 91)	ICC= 0.97	-	-	-
Delirium Rating Scale Revised -98 (Trzepacz et al. 2001)	92	95	ICC= 0.98	-	-	-
Organic Brain Syndrome Scale (Björkelund et al. 2006)*	-	-	r^2: 0.93-0.98 or 0.71-1.0 in two different studies	α= 0.88 one study only.	-	-
The 4As Test (4AT)(Bellelli et al. 2014a)	89.7	84.1	-	α= 0.80	-	-

The Mini Mental State Examination (Mitchell et al. 2014)	84.1 (75.8 to 90.9)	73 (59.6 to 84.5)	-	-	25.7 (17.3 to 39.5)	97.6 (95.7 to 98.8)
Stroke population						
CAM-ICU (Mitasova et al. 2012)	76 (54.9 to 90.6)	98 (93.2 to 99.8)	Kappa=0.94	-	90.5 (69.6 to 98.8)	94.4 (88.3 to 97.9)
CAM compared with 4AT (Lees et al. 2013)	100 (0.74 to 1.00)	82 (0.72 to 0.89)	-	-	43	100
The 4AT (Kutlubaev et al. 2016)	86	93	-	α= 0.80	86	85.6
The 4AT (Infante et al. 2017)	90.2	64.5	-	-	-	-

α: Cronbach's alpha.
r^2: Spearman Rank Correlation.
-: an empty rubric denotes the data were not reported in the study

* Björkelund et al. (2006) did not provide summary statistics for the seven studies they report, nor did they conform to the standard reporting of psychometric properties of scales, thus it is difficult to compare with the data for other scales.

2.5.1 The Confusion Assessment Method (CAM)

This is reportedly the most widely used tool in clinical and research practice (Morandi et al. 2013, Shi et al. 2013). Translated into 12 different languages (Inouye et al. 2014) and adapted for use in the ICU (Ely et al. 2001a, Ely et al. 2001b), it is the tool of choice in UK best practice guidelines (National Institute for Health and Care Excellence 2010, National Institute for Health and Care Excellence 2014). The tool was designed to be brief – it takes five minutes to administer (Tussey et al. 2010) and to enable clinicians with no psychiatric training to be able to identify delirium quickly and accurately (Inouye et al. 1990). However, optimum use of the tool does require training on the tool's utility (Inouye et al. 2014). The CAM assesses the presence, severity and fluctuation of nine delirium features: acute onset, inattention, disorganised thinking, altered level of consciousness, disorientation, memory impairment, perceptual disturbance, psychomotor agitation or retardation and an altered sleep-wake cycle (Wong et al. 2010). The original paper describing the tool and its psychometric properties detailed the work undertaken by Inouye et al. (1990). 56 participants were included in the study which was conducted across two hospital sites in the USA. The particulars of the psychometric properties established in this study are detailed in Table 3 (p.38). The CAM has been studied widely since its first publication, both in single studies and in systematic reviews confirming the tool's high sensitivity and specificity and moderate to high reliability (Wong et al. 2010, Shi et al. 2013, van Velthuijsen et al. 2016) (Table 3). Whilst it is regarded as a diagnostic tool (National Institute for Health and Care Excellence 2010, National Institute for Health and Care Excellence 2014), Wong et al. (2010) stated that in cases where not all categories are assessed as impaired, the tool should be supported by expert clinical judgement in order to reach an accurate diagnosis. An additional point to note is

that both Wong et al. (2010) and van Velthuijsen et al. (2016) claimed that the CAM performed better when used by physicians as opposed to nurses, possibly related to the requirement for specialist training in the use of the tool

The CAM-ICU, originally validated on a sample of n=38 patients in the intensive care unit, was designed to be used with mechanically ventilated patients (unable to speak) (Ely et al. 2001a). Thus it incorporates an objective assessment which does not require a verbal response from the patient (Ely et al. 2001a). In this original development and validation study Ely et al. (2001a) conducted paired assessments between a physician and two intensive care nurses. They found the CAM-ICU to demonstrate excellent reliability and validity, however, Shi et al. (2013), in their meta-analysis found the pooled (n=11 studies) sensitivity of the CAM-ICU to be lower (see Table 3, p.38). It is worth considering that due to the consequences of delirium and the need to adapt treatment in patients found to have delirium, for a tool to be clinically useful, higher sensitivity would be preferable to higher specificity (Lees et al. 2013).

2.5.2 Delirium Rating Scale (DRS)

Reported to be the first valid and reliable published diagnostic instrument for delirium (Trzepacz et al. 1988), the DRS was designed to be used by clinicians with psychiatric training. It is widely used in research and clinical practice and has been translated into at least seven languages (Trzepacz 1999). The DRS comprises 10 items, including: temporal onset, perceptual disturbances, hallucinations, delusions, psychomotor behaviour, cognitive status, physical disorder, sleep-wake cycle, emotional lability and variability of symptoms (Wong et al. 2010). The tool provides the assessor with a score ranging from 0-32, a score of twelve or more indicating the presence of

delirium, thus the DRS may be used to rate the severity of delirium (Trzepacz et al. 1988). The primary paper describing the tool's components and characteristics did not report the sensitivity and specificity but did evaluate the inter-rater reliability (Trzepacz et al. 1998). The validation study published earlier by Rockwood et al. (1996) found the tool to have high sensitivity (82%, no CI stated) and excellent specificity (94%, no CI stated). Conversely, Wong et al. (2012), in their pooled analysis (n=4 studies, n=943 patients) found excellent sensitivity (95%, 95% CI 90 to 98) but only moderate specificity 79%; 95% CI 58 to 91) (Table 3). This tool was later revised to produce the DRS-R98 (Trzepacz et al. 2001), which is a more comprehensive version and separates into two components: a diagnostic item comprising three categories for initial rating, and a 13 item scale for repeated measurement. Trzepacz reported the sensitivity and specificity of this tool to be substantial (1999), however, Adamis et al. (2010) stated that this depends on the cut-off point used for delirium diagnosis: in their review they found that if the cut-off score was lowered, the sensitivity and specificity of the tool rose. Other studies have compared the DRS and the CAM and found a high level of agreement between the two (Adamis et al. 2005, McManus et al. 2009b). Additionally, in a study of diagnostic accuracy on a sample of n=200 with and without dementia, the DRS-R98 was compared to the last three versions of DSM criteria as well as ICD-10 criteria for delirium (Sepulveda et al. 2016). Overall, the DRS-R98 performed better as compared with DSM-III-R criteria (American Psychiatric Association 1987) with a sensitivity of 81.6% (95% CI 67.5 to 90.8) and specificity of 89.4% (95% CI 83.1 to 93.6) (Sepulveda et al. 2016). This raises questions regarding the performance of this tool against the most recent diagnostic criteria: as discussed in point 2.3, diagnostic criteria undergo revision with every new version, in the case of the DSM, the criterion of "disorganised thinking" was dropped from versions newer than DSM-III-R (Sepulveda et al. 2016). Sepulveda et al. (2016)

suggested that as “disorganised thinking” is a core domain of delirium, it should be included in DSM diagnostic criteria once again.

2.5.3 The Organic Brain Syndrome (OBS) Scale

The OBS Scale was developed for the evaluation of disturbance of awareness and orientation and other signs of confusion in elderly patients (Björkelund et al. 2006). Reportedly taking up to one hour to complete (Sandberg et al. 1999, Adamis et al. 2010), the OBS Scale consists of two subscales: OBS1 for disorientation and OBS2 for confusion. They comprise 16 and 39 items respectively. For both subscales, the severity of symptoms are ranked in four ordinal scale steps from zero to three, where zero denotes a correct response and three denotes an incorrect response. According to Björkelund et al. (2006) various studies have demonstrated the scale’s sensitivity to detecting a range of organic brain syndromes and high inter-rater reliability and has been reported to show good responsiveness to cognitive symptoms in an elderly population. Despite the aforementioned, there is no published reference to any psychometric properties of this tool (White and Bayer 2007, Adamis et al. 2010). A comparison between the OBS Scale and the Mini Mental State Examination (MMSE) was carried out by Jensen et al. (1993). The two tools were found to have good agreement, however, perhaps due to the length of time taken to administer, this OBS scale is not reported to be widely used in research. Since the publication of the systematic review of its utility (Björkelund et al. 2006) only two studies which reported utilising the tool could be identified (Eriksson et al. 2011, Mathillas et al. 2013). Indeed, two of the three reviews of delirium rating scales published do not mention the OBS Scale (Schuurmans et al. 2003, Wong et al. 2010).

2.5.4 The 4-As Test (4AT)

This tool was developed to address the need to have a tool which would enable rapid assessment, could be used by non-specialists, and could be used on patients whose cognitive function would previously be “untestable” (due to communication difficulties or severe drowsiness) (Bellelli et al. 2014a). The 4AT was being used fairly widely in the UK prior to formal publication of its psychometric evaluation and indeed, it is now the screening tool recommended by NHS Scotland as the tool of choice for delirium detection (Healthcare Improvement Scotland 2014). The 4AT is a four component assessment requiring both direct observation and information regarding the onset as well as fluctuation of ability from other reliable informants (Healthcare Improvement Scotland 2014). The first component observes levels of alertness; the second component uses the Four Item Abbreviated Mental Test (AMT-4) as a brief cognitive screen (Schofield et al. 2010); the third component assesses attention using the ‘Months Backwards’ test (Katzman et al. 1983) and the final component requires an observation of the onset (acute or insidious) and whether the changes are fluctuating (Bellelli et al. 2014a). Scores range from 0-12 with anything over 4 being indicative of a requirement to formally asses for delirium (Healthcare Improvement Scotland 2014). The performance of the 4AT was evaluated in a cohort of 234 patients over the age of 70, across two difference sites in Italy and was found to be a reliable screening tool for delirium, with high sensitivity and specificity, see Table 3 (Bellelli et al. 2014a). Hendry et al. (2016) also evaluated the 4AT on comparatively larger cohort of n=434. They found the 4AT to have high sensitivity (86.7, 95% CI 77.5 to 93.2), the specificity was reasonable (69.5, 95% CI 64.4 to 74.3) and the PPV was low (40.2, 95% CI 33.0 to 47.8) whereas the NPV was high (95.7, 95% CI 92.4 to 97.8). Hendry et al. (2016) reflected on the lack of agreement on specificity and PPV, suggesting that it could stem from the

difference in sample size as well as the difference in populations. Whilst these results are promising, neither group assessed the inter-rater and test-re-test reliability of the 4AT (Bellelli et al. 2014a, Hendry et al. 2016) and more research into the utility of this screening tool is required. It is also worth considering that although the 4AT has demonstrated its ability to correctly identify persons with delirium (high sensitivity), its specificity is less conclusive. Albeit, as mentioned above, from a clinical perspective, higher sensitivity is preferable to higher specificity (Lees et al. 2013). A further point to note, while the tool is designed to be used by non-specialists, Bellelli et al. (2014a) reported that those clinicians using the tool in their study were experienced clinicians. This raises questions regarding the psychometric performance of the tool when used by less experienced clinicians, of different training and professional backgrounds.

It is important to remember that the 4AT is not a definitive diagnosis of delirium, but is a trigger for a more comprehensive assessment (Health Improvement Scotland 2014). Indeed, Infante et al. (2017) warned of the dangers of over estimation of delirium incidence if the 4AT is used on its own. Nevertheless, as a rapid tool it is very promising, given Hendry et al.'s (2016) finding that of the five screening tools evaluated, the 4AT was found to be the most feasible in terms of the high number of patients who completed the assessment.

2.5.5 The Mini Mental State Examination (MMSE)

There is some evidence that the Mini Mental State Examination (MMSE) (Folstein et al. 1975) is used in practice to detect delirium (Morandi et al. 2013). Despite not being designed specifically to detect delirium (O'Keeffe et al. 2005), the data obtained from this assessment can be helpful in establishing the presence of cognitive impairment (Rapp et

al. 2000) and it is reasonable to assume that it may have some utility in delirium identification (Ringdal et al. 2011). The MMSE is a brief measure, widely used in clinical practice and research due to its success in identifying cognitive impairment in elderly patients (O'Keeffe et al. 2005). The MMSE consists of 20 items examining 11 cognitive and perceptual domains: orientation, registration, attention or calculation (serial sevens or spelling), recall, naming, repetition, comprehension (verbal and written), writing, and construction (Mitchell 2009). The scoring is between 0-30, with any score below 24 indicating a degree of cognitive impairment (Ringdal et al. 2011). Mitchell et al. (2014) conducted a systematic review and meta-analysis (n=34 studies) to establish the diagnostic validity of the tool in detecting dementia and mild cognitive impairment. They found that the MMSE was only modestly effective (Table 3) in detecting dementia in hospital settings and suggest that the tool has greater value if used in the community or primary care settings (Mitchell et al. 2014). In terms of utility of the MMSE in recognising delirium, several studies examined its performance against the CAM or DRS: Ringdal et al. (2011) found that with a cut-off score of 24, the MMSE yielded a sensitivity of 88% (no 95% CI provided) to delirium, though the specificity was only 54% (no 95% CI provided). They concluded that it was not an acceptable diagnostic tool but could be used as a screen for the presence of delirium. O'Keeffe et al. (2005) examined the use of the MMSE in repeat testing to establish its responsiveness to the acute changes in cognitive function associated with delirium. They found that a decline in two or more scores on repeat MMSE testing yielded 93% sensitivity and 90% specificity, a positive likelihood ratio of 58.9 (95% CI 5.2 to 15.1) and negative likelihood ratio of 50.08 (95% CI 0.01 to 0.53). However, they found the tool more useful in detecting deterioration rather than improvement in cognitive function, thus they concluded it was not a useful tool in assessing the resolution of delirium (O'Keeffe et al. 2005). Mitchell et al. (2014)

conducted a systematic review of 13 studies which confirmed the findings of O'Keeffe et al. (2005) in that the MMSE is not recommended as a diagnostic test of delirium, but as an initial screen for delirium it performs with 93% accuracy. More specifically to subtypes of delirium, Franco et al. (2014) studied MMSE utility in detecting incident hypoactive delirium: they studied each item of the MMSE for sensitivity and specificity as compared with the DRS-R-98 and found that temporal orientation and visuoconstructional ability were 82% (95% CI 64.8 to 92.6) and 76% (95% CI 54.8 to 88.6) sensitive to hypoactive delirium respectively. It therefore seems that while the MMSE has some degree of utility in screening for delirium, the bedside tools specifically designed to detect delirium are preferred when there are restrictions on time in a busy hospital environment. However, it is recognised that clinicians may be more familiar with the MMSE and more comfortable in using it (Rapp et al. 2000).

2.5.6 The use of delirium bedside tools in acute stroke

At the start of this doctoral programme, none of the existing bedside delirium detection tools had been evaluated as to their performance in a cohort of stroke patients. Based on the research available at the time, the MMSE was found to be unsuitable for use in a stroke population due to its score being influenced by language, mood and sensory and motor function (McManus et al. 2007, Nys et al. 2005). Hall et al. (2012) called for the approach to delirium detection to be tailored to the practice setting, and indeed, in an early review of delirium in acute stroke, McManus et al. (2007) called for a tool to be developed to enable detection of delirium in stroke patients, taking into account the different manifestations of stroke and differentiating cognitive deficit and aphasia from delirium. Other authors commented on the difficulties associated with using delirium

bedside tools in a stroke cohort discussing the challenges of assessing study participants with “language barriers” (Hénon et al. 1999, Oldenbeuving et al. 2011, Melkas et al. 2012, Kara et al. 2013, Oldenbeuving et al. 2014). To date, several studies explored the utility of bedside tools in an acute stroke setting (McManus et al. 2009b, Mitasova et al. 2012, Lees et al. 2013, Kutlubaev et al. 2016, Infante et al. 2017), these are explored below as well as in Table 3.

McManus et al. (2009b) compared the CAM and the DRS in a cohort of acute stroke patients (n=82). They found that in the first four weeks, the incidence of delirium as identified using the CAM (Inouye et al. 1990) was 28% (n=23 with delirium) as compared with the DRS (Trzepacz et al. 1998) which was 27% (n=22 with delirium). These rates returned a good statistical agreement between the two tools with Kappa=0.97 in the first week (McManus et al. 2009b). McManus et al. (2009b) also found strong correlation between a low MMSE score and delirium in this setting (Kappa=1 in the first and fourth weeks). They concluded that the CAM is favourable due to its ease of use but cautioned that appropriate training is essential for use of either tool.

Mitasova et al. (2012) validated the CAM-ICU, (Ely et al. 2001a) in a cohort of 129 patients in the acute phase of stroke. The study found a reasonable sensitivity of 76% (95% CI 54.9 to 90.6) and high specificity of 98% (95% CI 93.2 to 99.8) and overall accuracy of 94% (95% CI 88.2 to 97.3) as compared with the DSM-IV diagnostic criteria. Based on the overall performance of the tool within this cohort, Mitasova et al. (2012) recommended routine screening of stroke patients, using the CAM-ICU and repeated over a minimum of five days, in order to detect the fluctuating course. There are a few words of caution regarding Mitasova et al.’s conclusions (2012): the authors point out that a significant number of stroke patients could not be assessed using the CAM-ICU due to

a variety of stroke-related difficulties. Additionally, Mitasova et al. (2012) warned that those with severe aphasia scored false-positively on the CAM-ICU.

Lees et al. (2013) examined the utility of a variety of brief cognitive screening tools in a cohort of 111 stroke patients, amongst them, the 4AT. They demonstrated the complexity of cognitive screening in stroke patients, stating that using traditional cut off points resulted in the majority of patients being labelled as cognitively impaired. They did however find that as a delirium screen, the 4AT had excellent sensitivity (100%, 95% CI 0.74 to 1.00) and good specificity (82%, 95% CI 0.72 to 0.89) (Lees et al. 2013).

Kutlubaev et al. (2016) translated the 4AT into Russian and used this version to assess a cohort of 73 patients with stroke. The evaluation of the psychometric properties of this tool was among several study objectives (this study is described in greater detail in chapter IV of the thesis). Kutlubaev et al. (2016) found the tool performed well in their cohort with a high sensitivity of 93% and good specificity of 86% although no confidence intervals for these rates are quoted in the paper (Greenhalgh 2015) and Kutlubaev et al. (2016) did not discuss the feasibility of using the 4AT in a cohort of stroke patients.

Infante et al. (2017) published a brief communication of a most recent study comparing methods of detection of delirium in a cohort of stroke patients, both retrospectively and prospectively. In the retrospective phase, Infante et al. (2017) recruited 102 patients, and used case notes to apply the DSM-V criteria before and after specialist training on the application of these criteria. In the prospective phase, Infante et al. (2017) recruited 100 stroke patients and screened for delirium using the 4AT and followed the screening with application of the DSM-V criteria as per good practice guideline (Healthcare Improvement Scotland 2014). They found a significant difference between the incidence of delirium using DSM-V criteria (32%) versus the 4AT (52%, p=0.009). They also reported that the incidence of delirium observed using clinical

examinations was significantly higher than that observed on the basis of non-expert evaluation with DSM-V criteria as applied retrospectively to case notes (p=0.020) (Infante et al. 2017). Lastly, Infante et al. (2017) reported the psychometric properties of the 4AT in their cohort: they found that on admission, the 4AT had a sensitivity of 90.2% and specificity of 64.5% and concluded that these findings are comparable with the rates identified by Bellelli et al. (2014a) (section 2.5.4). It is difficult to assess the detail of this publication since is it so brief and therefore lacking in several important details, such as the reporting of confidence intervals for the validity of the tool (Greenhalgh 2015) or whether any other aspects of the performance of the 4AT were explored (PPV, NPV, feasibility).

To summarise, this subsection discussed key publications examining the performance and psychometric properties of a number of delirium bedside tools originally validated for use in acute hospital settings (Inouye et al. 1990, Trzepacz et al. 1998, Ely et al. 2001a, Ely et al. 2001b Bellelli et al. 2014a). Whilst all of the studies mentioned in this section have modest sized cohorts, this section illuminates important information on the use and performance of delirium bedside tools in a stroke cohort. Important potential limitations were the ability to correctly assess stroke patients with aphasia (e.g. Mitasova et al. 2012) in addition to the requirement for specialist training in order to use the tool (Inouye et al. 1990, Trzepacz et al. 1998, Ely et al. 2001a).

2.6 Consequences of delirium

There are a number of serious consequences associated with developing delirium, particularly for older adults in the acute hospital setting (Cole et al. 2009). Witlox (2010) conducted a comprehensive meta-analysis of the adverse outcomes associated

with delirium in elderly patients: 51 studies were reviewed and synthesised to produce the following important information regarding the outcomes for older people experiencing delirium: compared with controls, they found a higher risk of two year mortality (using seven studies, moderate heterogeneity and hazard ratio 1.95; 95% CI: 1.51 to 2.52) in patients with delirium. A more recent systematic review by Salluh et al. (2015) confirmed this as they identified higher rates of mortality during admission (95% CI: 1.78 to 2.70; p<0.001) across 42 included studies (n= 5280 with delirium).

Delirium is also associated with an increased risk of institutionalisation: Witlox et al. (2010) confirmed this in a meta-analysis of seven studies, around a year post discharge from the acute hospital setting patients experiencing delirium were more likely to be institutionalised (homogeneity found, odds ratio 2.41; 95% CI: 1.77 to 3.29) (Witlox et al. 2010). An additional outcome is the impact of delirium on length of hospital stay: McCusker et al. (2003) found a significant increase in length of hospital stay in patients with incident delirium. Their overall sample size was n=359 with only n=36 with incident delirium, yet the difference in average length of hospital stay was around eight days (95% CI 3.07 to 12.48). More recently, Fortini et al. (2014) confirmed these findings in a cohort of elderly patients (n=560) with an 11% incident delirium in internal medicine wards. Fortini et al. (2014) found that those who experienced delirium were less likely to be discharged home and that delirium was associated with a significant increase of length of stay in hospital (p=0.002). Salluh et al. (2015) also confirmed these findings in their systematic review of 42 studies which identified that delirium was associated with an increased length of hospital stay (95% CI: 0.61 to 1.33; p<0.001).

Delirium is also associated with an increased risk of developing dementia: Witlox et al. (2010) confirmed this in two of the studies included in their review they found an increased risk of developing dementia at follow-up in older people who developed

delirium during their hospital admission. However, this finding is compromised by the significant heterogeneity (54%) with very wide confidence intervals (1.86 to 84.21) and an odds ratio of 12.52 within this small sample. The impact of delirium on long term cognitive impairment was explored by Davis et al. (2012), who studied a cohort of 553 adults over the age of 85 years, 13% of whom had an episode of delirium. They found that delirium was associated not only with an increased risk of incident dementia, but also with worsening of cognitive function in those with pre-existing dementia. Salluh et al. (2015) also reported that despite the fact that fewer studies included in their review assessed outcomes in the long term, the data suggested an association between long-term mortality and cognitive impairment in patients who develop delirium across a variety of hospital settings.

2.6.1 Consequences of developing delirium after a stroke

Several studies examining the consequences of developing delirium in the acute stage of stroke have found that delirium was associated with increased length of hospital stay (Gustafson et al. 1991, Gustafson et al. 1993, McManus et al. 2009a); increased mortality (Hénon et al. 1991, Dostovic et al. 2009, McManus et al. 2009a) and increased dependence (Gustafson et al. 1991, Sheng et al. 2006, McManus et al. 2009a). Studies published more recently produced similar findings: van Rijsbergen et al. (2011) conducted a two-year follow up of 50 patients (n=22 diagnosed with delirium during the acute phase of stroke). They found that delirium in the acute stage of stroke was an independent predictor of developing dementia in the long term (odds ratio: 4.7; 95% CI 1.08 to 20.42). They also found that patients experiencing delirium in the acute phase of stroke had up to a seven fold risk of developing dementia two years later

(odds ratio: 7.2; 95% CI 1.88 to 27.89) (van Rijsbergen et al. 2011). Turco et al. (2013) studied a cohort of 176 stroke patients in the rehabilitation setting, of whom 33% had delirium on admission. They found that the presence of delirium was an independent predictor of institutionalisation (odds ratio: 7.23; 95% CI 4.79 to 10.91; p≤0.001) and mortality (odds ratio: 4.26; 95% CI 1.15 to 15.81; p=0.03) although Turco et al. (2013) found that in their cohort, delirium did not impact upon functional recovery. A recent systematic review by Ojagbemi and Ffytche (2016) found that while there was an association between delirium in the acute phase of stroke and developing dementia in the long term, they concluded that there was not enough evidence to be able to draw firm conclusions regarding the risk of dementia as a long term consequence of delirium in the acute phase of stroke. Chapter IV of this thesis explores further the outcomes associated with developing delirium in acute stroke (section 4.3.7).

2.6.2 The impact of delirium on the individual and society

The implications of the above consequences of delirium were reviewed in terms of societal and economic costs (in American society) by Leslie and Inouye (2011). They hypothesised that each year, delirium complicates hospital stays for 20% of the 11.8 million inpatients over the age of 65, and suggested that the annual healthcare costs attributable to delirium may range from $143 billion to $152 billion (Leslie and Inouye 2011). Within UK literature, government guidelines on delirium state that if delirium were to be prevented in patients, cost savings would be generated for the National Health Service (NHS) (National Institute for Health and Care Excellence 2010). O'Mahony et al. (2011) estimated that preventing delirium could be associated with savings of up to £8180

per inpatient. Furthermore, they suggested that strategies to prevent delirium are associated with an increase in quality-adjusted life-years (O'Mahony et al. 2011).

Beyond the economic burden of delirium, it is important to recognise the impact this experience has on individuals and the people around them. Partridge et al. (2013) examined the experience of delirium using a synthesis of both qualitative and quantitative methods. They reported that while people often do not recall their delirium experience, when they do, it is remembered as an unpleasant experience. Additionally, distress, anxiety and depression and post-traumatic stress disorder have all been associated with the experience of delirium (Partridge et al. 2013). Perhaps not surprisingly, there is a significant emotional impact on the carers and relatives as well as clinical staff caring for patients experiencing delirium: Partridge et al. (2013) reported that families experience distress, feeling helpless, scared and insecure due to the behaviours they observed in their relative. Belanger and Ducharme (2011) conducted a comprehensive review of qualitative literature on the experience of nurses looking after patients with delirium. They found that nurses experience discomfort at treating individuals, they report finding the unpredictability of delirium stressful in addition to expressing the feeling that the clinical environment does not meet the needs of older people in their charge (Belanger and Ducharme 2011). Recognition of these significant consequences of delirium has led to several calls for action in recent years, concentrating both on prevention and better identification of delirium as well as management strategies and increased research funding in this area (Young et al. 2010, Siddiqi et al. 2011, Teodorczuk et al. 2012, Inouye et al. 2014, Young et al. 2015).

2.7 Optimal management of delirium

Delirium management *per se* is not a key concern of this doctoral programme, however, it is impossible to ignore the link between delirium identification and management of the condition. Interest in delirium research and management has grown substantially in recent years (Inouye et al. 2014), due to the emerging evidence that delirium is preventable and that correct management of delirium can shorten the course of the condition (Teodorczuk et al. 2012). Additionally, there is a shift towards placing an emphasis on prevention of the condition by identifying patient populations at risk as well as monitoring the use of medications with anticholinergic effects which are known to increase the risk of developing delirium (Teodorczuk et al. 2012, Huber 2012, Godfrey et al. 2013, O'Hanlon et al. 2013). The most recent guidelines produced by NHS Scotland urge multidisciplinary team members to "Think Delirium" (Healthcare Improvement Scotland 2014). However, several authors argue that publishing guidelines is not enough to implement change: change is required at organisational level as well as at staff level, through interdisciplinary educational programmes in order to achieve tangible improvements in delirium prevention (Young et al. 2010, Godfrey et al. 2013, O'Hanlon et al. 2013). Indeed, a report commissioned by Health Improvement Scotland, highlighted that delirium was not high enough on the agenda of hospital managers and that staff found it difficult to receive the support needed to gain more knowledge on aspects of delirium (Dewar et al. 2013). The following sections explore the clinical guidelines on delirium identification followed by the evidence base of a variety of approaches to delirium management, from pharmacological treatment and prevention options to multicomponent intervention programmes.

2.7.1 Clinical guidelines on delirium identification in acute stroke

Clinical practice guidelines are systematically developed, expert consensus statements that assist clinicians in making the appropriate decisions in a variety of clinical settings (Field and Lohr, 1990). A variety of practice guidelines relevant to the topics explored in this thesis were consulted in order to establish the best practice in delirium identification in the acute stroke setting. UK clinical guidelines on stroke care were examined first, revealing that neither NICE (National Institute for Health and Care Excellence 2008, National Institute for Health and Care Excellence 2013) nor SIGN guidelines (Scottish Intercollegiate Guidelines Network 2010) referred to delirium as a known or common complication following a stroke. Both sets of guidelines discussed cognitive rehabilitation and cognitive assessment, but not delirium *per se*. It is noteworthy that the word "confusion" is included in the Scottish Intercollegiate Guidelines Network document "Management of Patients with Stroke" (SIGN 118, Scottish Intercollegiate Guidelines Network 2010), however there is no specific guidance about how to screen for or manage it. The fifth edition of the stroke clinical guidelines from the Royal College of Physicians (Intercollegiate Stroke Working Party 2016) introduced the term delirium in the context of memory impairment and clinicians are guided to assess patients for "treatable factors (e.g. delirium)" (Intercollegiate Stroke Working Party 2016, p62). Otherwise, there is no mention of delirium as a serious complication of stroke, and there is no recommendation as to how one should identify the condition in stroke patients. The fourth edition of these guidelines from the Royal College of Physicians which did not mention delirium at all (Intercollegiate Stroke Working Party 2012) were the guidelines available at the time of planning the data collection for the second strand of this doctoral programme.

Stroke related clinical practice guidelines from other English speaking countries were examined by way of comparison: Australian guidelines (National Stroke Foundation 2010) did not mention delirium in stroke patients; American Heart Association (AHA) guidelines included delirium in the context of screening for psychiatric sequelae to stroke in end of life care (Miller et al. 2010); Canadian guidelines were the most detailed, and contained a clear message about the importance of delirium as a complication in acute stroke. This was discussed in relation to screening for cognitive impairment or a change in cognitive function, and there was a clear indication to screen patients at risk, using a validated screening tool (Lindsay et al. 2010).

Routine screening for delirium is considered important in a number of hospital settings and areas such as intensive care, palliative care and orthopaedics have good awareness of the condition and established screening practices (National Institute for Health and Care Excellence 2010, National Institute for Health and Care Excellence 2014, Devlin et al. 2012, Spiller and Keen 2006). UK practice guidelines clearly set out the indicators for delirium, interventions likely to prevent delirium and best way to diagnose delirium in hospital inpatients (National Institute for Health and Care Excellence 2010, National Institute for Health and Care Excellence 2014). Within NHS Scotland, there have been widespread initiatives to improve the care of older patients in acute hospital settings with particular interest in delirium identification (Healthcare Improvement Scotland 2014). Clinicians are urged to “Think Delirium” and use a clear identification pathway utilising the 4AT in conjunction with what is locally known as ‘TIME Bundle’ (Healthcare Improvement Scotland 2014). This bundle asks clinicians to think and exclude possible causes for delirium, investigate potential causes and, take a multidisciplinary approach to the management of the condition (Healthcare Improvement Scotland 2014). It is important to note there is no specific mention of stroke patients in

any of these clinical guidelines. This is problematic given that patients with stroke are recognised as having a number of the risk factors associated with developing delirium (Carson et al. 2010, Makin and Wardlaw 2014, McManus et al. 2009c) and delirium is regarded as a common complication of stroke (Mitasova et al. 2012, Kostalova et al. 2012). It is also compounded by the known difficulties associated with identifying delirium in stroke patients, namely, patients who are acutely unwell or experience communication and / or cognitive difficulties arising from the stroke (Lees et al. 2013).

2.7.2 Early identification of delirium

Early identification of delirium is regarded as a means of reducing the potentially serious consequences of delirium as discussed above, within the context of the general or geriatric acute hospital setting (Holly et al. 2013, Huber 2012, O'Hanlon et al. 2013). In a systematic review of the evidence around delirium identification, prevention and care, Holly et al. (2013) determined that early recognition of the symptoms of delirium was among the most effective means of minimising the deterioration and further complications associated with delirium. Early and accurate identification of delirium can be achieved if staff awareness is increased using education programmes (Young et al. 2010). A fairly substantial body of literature explores the efficacy of staff educational programmes in improving delirium recognition: Yanamadala et al. (2013) conducted a systematic review of educational interventions to improve the recognition of delirium. They included 26 studies describing a variety of educational interventions. They concluded that isolated, didactic teaching sessions on delirium were not effective in improving recognition of the condition, whereas interactive teaching programmes which include enabling strategies (e.g. flow sheets, pocket cards) as well as reinforcing strategies (e.g. feedback in action,

creation of treatment protocols) resulted in improved staff recognition of delirium as well as adherence to treatment protocols (Yanamadala et al. 2013). Subsequently published single studies confirm these findings to an extent: McCrow et al. (2014) report on the short term success of a web-based education programme, though, in the long term the findings suggest that knowledge of delirium was not retained. Wand et al. (2014) reported that despite intensive education of both doctors and nurses there was no change in recognition rates of delirium, however the ward-based interventions that were designed to reduce incidence of delirium (reorientation, delirium risk factor management etc.) were found to yield a significant reduction in the incidence of delirium (n=129 in both groups, pre: 19%, post: 10.1%, p=0.042). van de Steeg et al. (2015) reported on the success of an e-learning programme across 17 hospitals in The Netherlands. They reported an increased knowledge of delirium symptoms, course and consequences, however, they did not explore the impact of this programme on day-to-day nursing practices or whether these results impact upon recognition rates (van de Steeg et al. 2015).

Overall, the studies presented in this section support the widespread recognition that the most effective way to prevent and manage delirium goes beyond isolated approaches: raising awareness through multidisciplinary staff education programmes (Yevchak et al. 2012), including family and caregivers in management approaches (Abraha et al. 2015, Young 2010) and implementing multi-component interventions are considered the most effective means of delirium management (National Institute for Health and Care Excellence 2010, National Institute for Health and Care Excellence 2014). However, Hendry et al. (2016) stated that there is still uncertainty around the diagnosis of delirium, even by geriatric clinicians who have an interest in cognitive impairment. This is confirmed by Jenkin et al. (2014) who reported that speciality experience in geriatric medicine resulted in only a small increase in knowledge about

delirium. This suggests that raising awareness of delirium may not, on its own, improve accurate and timely diagnosis rates. It is therefore important to examine the reported barriers to delirium detection across hospital settings as explored in section 2.8.

2.7.3 Pharmacological management of delirium

Friedman et al. (2014) discussed the importance of distinguishing between pharmacological approaches to prevent delirium (prophylactic approaches), and pharmacological approaches to treat an existing delirium in order to reduce the severity and duration of the episode. This section will discuss both approaches, wherever possible drawing on stroke-specific literature. Current practice guidelines mention the option of treating a delirium in acute hospital settings using antipsychotic medication as a short term measure for those who are distressed, and when other management options have failed (National Institute for Health and Care Excellence 2010, National Institute for Health and Care Excellence 2014). There is no specific mention of pharmacological treatment options for patients in the acute stroke setting, indeed, the body of literature on the pharmacological management of delirium in acute stroke is currently limited. Comprehensive literature searches conducted as part of the systematic review presented in chapter IV identified three studies presenting data on pharmacological treatment of delirium in stroke patients: Oldenbeuving et al. (2008) conducted a pilot study of Rivastigmine, nested in a large (n=527) observational study of delirium in acute stroke (Oldenbeuving et al. 2011). They aimed to assess the feasibility and safety of Rivastigmine, a cholinesterase inhibitor, in the treatment of stroke patients (n=26) with delirium. The final sample size reduced to n=17 due to severe dysphagia or discharge from the acute setting (Oldenbeuving et al. 2008). In this small cohort of patients,

Oldenbeuving et al. (2008) found Rivastigmine to be safe to use and it improved the symptoms of delirium, as measured using the DRS (Trzepacz et al. 1988). Ohta et al. (2013) retrospectively examined stroke patients with delirium (n=7) who were treated with a melatonin receptor agonist (Ramelteon) as compared with patients (n=21) treated with "other drugs" (they listed two sedatives and one antipsychotic as examples). In a simple pre-post intervention design, Ohta et al. (2013) found that the patients treated with Ramelteon had demonstrated improvement on the Richmond Agitation and Sedation Scale (RASS) (Sessler et al. 2002). The authors also compared the Ramelteon treatment arm with the patients receiving other medication and found that in the Ramelteon arm, the reduction in RASS scores was statistically significant (p=0.013). This study is rather limited by its non-randomised design, its small scale and it lacks exploration of dosage, timing of drug administration and safety of drug use in these patients (Ohta et al. 2013). Duan et al. (2016) reported the use of Naloxone, an opioid antagonist that reverses the consequences of opioid medication (Jones and Karalliedde 2006). Naloxone is not mentioned in any reviews of treatment options for delirium (Ford and Almeida 2015, Flaherty et al. 2011, Siddiqi et al. 2016). Duan et al. (2016) stated that the drug can temporarily reduce auditory and visual hallucinations, however they support this claim citing two small scale studies conducted more than 30 years ago (Gunne et al. 1977 and Pickar et al. 1982, in: Duan et al. 2016). Duan et al. (2016) reported "dramatic improvement" in agitated delirium in their sample of n=15 as measured using the DRS-R98 (Trzepacz et al. 2001). It was difficult to assess the quality of this study as it was published as a letter to the editor, thus the reporting is limited (e.g. there was no mention of ethical approval). However, one must question the suitability of this drug as it is not mentioned in any systematic reviews or meta-analyses currently available, nor does it appear in the current evidence-based guidelines for delirium treatment (National Institute

for Health and Care Excellence 2010, National Institute for Health and Care Excellence 2014).

In other medical settings, Friedman et al. (2014), conducted a systematic review of pharmacological approaches to the treatment of delirium and found limited evidence to support the use of antipsychotic or cholinesterase inhibitors as a means of resolving a delirium. Flaherty et al. (2011) examined antipsychotics in the treatment of delirium and also found insufficient quality evidence to support the use of antipsychotics to treat delirium. Flaherty et al. (2011) pointed out that out of 13 studies included in their review, only one was a randomised controlled trial (RCT) thus they called for large, well designs trials to be conducted.

The prophylactic pharmacological approach seems to have a similarly weak evidence base across a variety of medical settings. The efficacy of pharmacological approaches to the prevention of delirium was explored in a comprehensive Cochrane review by Siddiqi et al. (2016) which synthesised the data from 13 studies. No clear evidence was found in support of the prophylactic use of cholinesterase inhibitors, antipsychotic medication or melatonin overall. However, it is worth noting that there was some indication that the use of the antipsychotic Olanzapine may reduce the incidence of delirium (Siddiqi et al. 2016).

The weakness of evidence on the success of the pharmacological approach in the treatment and prevention of delirium may be explained by the understanding that delirium is rarely caused by a single factor (Inouye et al. 1999) and therefore, approaches to prevention and treatment of delirium are most successful when they are comprised of multiple components (Siddiqi et al. 2016).

2.7.4 Non-pharmacological management strategies

A recent publication by Rice et al. (2017) described a pilot RCT of a multi-component delirium prevention intervention in the acute stroke setting. At the time of writing, this was the only publication of an RCT of delirium treatment identified within the stroke literature (confirmed by findings of the first strand of the doctoral programme). Rice et al. (2017) compared usual stroke care with a complex delirium intervention which was based on Inouye et al.'s (1999) Elder Life Program which incorporated cognitive, mobilisation, sensory and sleep related interventions as well as the monitoring of anticholinergic medication. The groups were evenly balanced with the intervention n=59 and control (usual care) of n=66. Rice et al. (2017) found incident delirium in both participant groups, but this was lower in the delirium care group (n=3 versus n=7 for usual care). Rice et al. (2017) found the incidence of delirium in their sample to be 8%, which is lower than other rates reported in the stroke literature (section 2.4.1). This meant that Rice et al. (2017) were unable to test the trial hypothesis that a multicomponent intervention would reduce incident delirium in stroke patients due to the insufficient sample size.

In other medical settings, Siddiqi et al.'s Cochrane review examined multi component intervention programmes for the prevention of delirium in hospitalised patients alongside the pharmacological interventions mentioned above (Siddiqi et al. 2016). These multi-component programmes include uni- or multidisciplinary staff education as well as a variety of approaches such as creation of checklists and protocols, reorientation and attention to sensory deprivation, cognitive stimulation, nutrition and hydration, sleep hygiene and identification of infection (Siddiqi et al. 2016). The authors evaluated these interventions across seven studies (n=2018) and found moderate quality evidence that multi-component, non-pharmacological interventions reduce delirium

incidence in hospitalised patients as well as reducing the risk of delirium by about 30% as compared with usual care (Siddiqi et al. 2016). A meta-analysis of 11 multicomponent, non-pharmacological intervention studies (n=4267 patients) by Hshieh et al. (2015) found that the odds of delirium were 53% lower (odds ratio: 0.47; 95% CI: 0.38 to 0.58) as compared with controls. Hshieh et al. (2015) reported low heterogeneity in their included studies, which stands in contrast to Abraha et al.'s (2015) findings. Abraha et al. (2015) synthesised the data from a variety of trials reporting non-pharmacological management strategies for delirium, all of which included an educational component as well as the variety of interventions mentioned above. They reported wide differences in methodological quality and substantial heterogeneity across the studies (Abraha et al. 2015). Despite some of the inconsistencies raised above, overall, these three meta-analyses indicate that overall, multicomponent interventions were effective in preventing delirium across a variety of hospital settings (Hshieh et al. 2015, Abraha et al. 2015, Siddiqi et al. 2016).

2.8 Barriers to delirium identification

Throughout the period of registration for doctoral studies, literature searches have failed to identify empirical evidence regarding the identification of delirium in the acute stroke setting (appendix 2.1 details the search strategy). Yet, it is well-recognised that stroke poses a number of unique and significant challenges to timely and accurate delirium identification: patients with reduced consciousness (Dahl et al. 2010, McManus et al. 2009b); aphasia (Mitasova et al. 2012, Dostovic et al. 2009, Sheng et al. 2006) and cognitive impairment resulting from the stroke itself (Lees et al. 2013, Mitasova et al. 2012, Kostalova et al. 2012, Hénon and Leys 2007) all pose challenges to accurate

delirium identification in stroke patients. In the absence of stroke-specific literature exploring barriers to delirium identification, literature from acute medical settings is explored below.

In their review of the literature on early recognition of delirium, Schuurmans et al. (2001) found that lack of knowledge of the condition and its symptoms compromise early identification and may have negative implications in terms of outcomes for delirious patients. Flagg et al. (2010) conducted a survey of 61 nurses (response rate not disclosed) across an intensive care and a medical / surgical unit in the Midwest of the USA. They found that nurses did not believe delirium to be a common condition and they had only modest confidence in identifying the condition in clinical practice. These findings were confirmed by both Ettema et al. (2014) and Baker et al. (2015): Ettema et al. (2014) surveyed nurses (n=368, response rate 67.9%) working in a variety of adult hospital settings (none of which were stroke units) across three centres in The Netherlands and found that nurses underestimated the prevalence of delirium, although they recognised the condition to be of serious consequences, requiring immediate attention. More than half the nurses (63%) responding to this survey screened patients routinely, although a majority of the nurses responding (75%) knew that delirium was under diagnosed (Ettema et al. 2014). Baker et al. (2015) surveyed nurses in the South-East of the USA (n=150, response rate 40%). They found that nurses across a variety of medical and surgical settings had inadequate knowledge about delirium and its risk factors. They also found that levels of knowledge were similar across the different grades and years of experience of the nurses in their sample (Baker et al. 2015). Inadequate knowledge of delirium applies to doctors as well as nurses: Davis and MacLullich (2009) reported upon a UK wide survey of junior doctors (n=784, the majority of participating hospitals reported that all potential participants completed the survey). They found that junior doctors lack

accurate knowledge about prevalence, diagnostic means and confidence in diagnosing delirium in the general medical setting. In a survey of European delirium experts, Morandi et al. (2013) found that a lack of knowledge about the condition, lack of staff education and lack of time to carry out the necessary assessment were the main barriers to timely identification of delirium. These findings are confirmed in a variety of clinical settings, both in the UK and the USA as delirium may be missed or mislabelled by physicians in up to two thirds of cases (Collins et al. 2009, Clegg et al. 2010, Suffoletto et al. 2013).

Other potential barriers are mentioned in the literature: Both Hare et al. (2008) and Yevchak et al. (2012) found that nursing staff often label a delirious patient as 'confused', attributing this to the normal aging process rather than an acute delirium. This matter is also discussed critically by Teodorczuk et al. (2012), who claimed that the widespread use of the lay term 'confusion' is a barrier to accurate delirium identification, since the term in itself is used both as a symptom and a diagnosis. Teodorczuk et al. (2012) also discussed the use of bedside tools to identify delirium and suggested that there is competition around the amount of tools used to screen for a variety of conditions and that in a busy in-patient unit, delirium screening was not regarded as a priority. This idea is supported by research findings: routine screening and utilisation of the CAM or the DRS were the exception when diagnosing delirium despite recognition of the importance of delirium as a condition of potentially serious consequences (Flagg et al. 2010, Forsgren and Eriksson 2010, Patel et al. 2009).

2.8.1 The role of Allied Health Professionals

An area receiving less attention in the literature is the ability of allied health professionals (AHPs) to identify delirium in patients with whom they are working. It is

recognised that nursing staff are best placed to assume a role in delirium identification due to their consistent contact with patients over 24-hour cycles (Hall et al. 2012). This role could be extended to AHPs who also come in to contact with patients in the acute stroke setting on a daily basis, particularly occupational therapists (OTs) who have been found to routinely assess cognition in stroke units across Scotland (Lees et al. 2014). OTs have also been recognised as possessing a role in the non-pharmacological treatment of delirium (Aguirre 2010, Brooks et al. 2014). It is therefore surprising that so little attention has been given to the role of AHPs in the delirium literature: repeated searches of the allied health literature revealed very few articles discussing the role of AHPs in the identification or management of delirium (appendix 2.1, search table 2). Schweickert et al. (2009) studied the role of physical and occupational therapy in mechanically ventilated, critically ill patients in the ICU. In an RCT design (n=104) they compared normal care, which meant no occupational or physical therapy during the sedation period with the intervention, which was passive range of movement for sedated patients, followed by exercise and mobilisation once patient interaction was possible. While the study was not examining the effects of this intervention exclusively on delirium, the resolution of delirium was a secondary outcome (Schweickert et al. 2009). The patients in the intervention group had fewer delirium days as measured by the CAM-ICU: 2 delirium days versus the control group which had 4 delirium days (p=0.03). The percentage of time spent in ICU while delirious was also lower: for the intervention group it was 33% of the time, versus 57% of the time in ICU with delirium for the control group (p=0.02). These data suggest that early occupational and physical therapy can contribute to the swifter resolution of delirium in mechanically ventilated ICU patients. Álvarez et al. (2017) reported the results of a pilot RCT of OT interventions in the management of non-ventilated elderly ICU patients (n=140). The comparison was between non-

pharmacological delirium prevention strategies and early, intensive OT interventions, including polysensory and cognitive stimulation, upper limb exercises, activities of daily living and engagement with family (Álvarez et al. 2017). The most striking finding of this study was that the incidence of delirium in the control group was 20% (n=14), as compared with an incidence of 3% in the intervention group (n=2, *p*=0.001) (Álvarez et al. 2017). The process of delirium identification was described, but any difficulties related specifically to the profession of OT were not described in the publication, nor was there a description of any specialist training undertaken in order to be proficient in the administration of the bedside tool used (the CAM, Inouye et al. (1990)). While both these studies are set in the ICU, they both highlight a potential role for involving occupational therapists in the treatment and prevention of delirium in acutely ill patients. Both studies make an important contribution to a field with very little discipline specific research.

A few of the studies examining the efficacy of delirium education interventions have included physiotherapists in their sample: Yanamadala et al. (2013) conducted a systematic review of the evidence around efficacy of educational programmes to improve delirium recognition. Within a sample of 26 studies, only two studies mentioned the inclusion of AHPs (physiotherapists) - both of these studies are set in rehabilitation facilities in the community as opposed to the acute hospital setting (Speciale et al. 2005, Ramaswamy et al. 2011). Other studies reportedly included AHPs within their educational intervention sample: Foster et al. (2010) investigated the perceptions and knowledge of delirium among multidisciplinary staff in a general medical setting. Teodorczuk et al. (2013) explored the learning needs of staff across the healthcare spectrum and reported the inclusion of an OT. It is noteworthy that none of these studies report data specifically relevant to AHP practice (Foster et al. 2010, Ramaswamy et al. 2011, Speciale et al. 2005, Teodorczuk et al. 2013) so it is difficult to draw meaningful

conclusions regarding AHP practices around identification, prevention or management of the condition. Other studies contribute to this topic of discussion: Godfrey et al. (2013) explored knowledge and practices around delirium prevention, within their sample they included AHPs (physiotherapists and OTs). They did not provide specific data on the distinction between the different professions, however, they found that AHPs were not introduced to the concept of delirium during their professional training, neither were they included in post-qualification education programmes on delirium (Godfrey et al. 2013). Furthermore, Godfrey et al. (2013) found that AHPs did not refer to the term 'delirium', rather, they used 'confusion', and seemed to understand the manifestations of hyperactive delirium as a problem for the ward as a whole as patients may behave in a disruptive way. Bellelli et al. (2014b) conducted a large survey (overall n=648, 43% response rate) of recognition and management of delirium and included physiotherapists (n=51) in their sample. Only half of the physiotherapists in the sample were able to correctly define delirium, and only half of the physiotherapists reported to using a bedside tool to screen for delirium.

The studies reviewed above suggest a variety of barriers to early identification, mainly within general medical settings. The roles of AHPs in relation to treatment and identification of delirium are also explored within this context. The barriers to delirium identification seem to stem from lack of knowledge, inability to correctly identify delirium, inconsistent use of bedside tools and a lack of clarity around the use of language to describe delirium, which are all described in the literature in the general medical or geriatric hospital settings. It therefore stands to reason that the same barriers may affect patient care in the acute stroke setting as well, given that the identification of delirium in this setting is further complicated by any language and cognitive deficits arising from the

stroke itself (McManus et al. 2007, Oldenbeuving et al. 2007, Lees et al. 2013). However, this requires to be empirically researched, a key concern of this thesis.

2.8.2 Staff response to a patient with delirium

The lack of knowledge and understanding of delirium, as identified above, may also shape the ways in which various healthcare staff respond towards patients with delirium in their care. As in previous sections, no stroke-specific literature on the matter was found, therefore literature from general medical settings was reviewed. Neville (2008) conducted a discourse analysis on 20 datasets in order to investigate the perceptions of people who have been affected by delirium in a hospital setting. Neville (2008) reported on the apparent ageist practices that affected the healthcare system which he studied. He reported not only a lack of knowledge and understanding of delirium but also the marginalisation of persons affected by delirium. According to Neville (2008) people affected by delirium were treated by less-skilled nurses, moved around the hospital to meet institutional needs and infantilised by some of the staff. The notion of infantilising older adults affected by delirium is echoed in Dahlke and Phinney's work (2008), who interviewed nurses working with older adults affected by delirium. They found that nurses referred to adults with delirium as childlike, and that caring for older people was seen as less important than caring for younger adults within the context of a busy acute hospital. Kjorven et al. (2011) explored the discourse that shapes nursing care of adults with postoperative delirium. They identified a discourse around a perceived legitimacy of the manifestations of conditions they encountered, e.g. the behaviour of a patient with chest pain were accepted, whereas those of a patient with postoperative delirium were not. Within this study, delirium was not considered high priority, nor was it

regarded as a serious complication (Kjorven et al. 2011). Schofield et al. (2012) conducted a critical discourse analysis to reveal how nurses care for older people with delirium. They found that patients with delirium were perceived as disruptive and potentially threatening to others. Additionally, nurses' preoccupation with risk led to a lack of normal interaction between them and the patients with delirium in their care (Schofield et al. 2012). Teodorczuk et al. (2013) added to this that a confused patient may be labelled as a "nuisance" by the staff team. This in turn would lead to staff failing to take ownership of the patient's care, which may feed back into the patient's sense of alienation in the ward environment (Teodorczuk et al. 2013). Clissett et al. (2014) observed the response of healthcare staff to patients with cognitive impairment (including delirium) in a general hospital in the UK. They found that staff viewed patients with cognitive impairment as disruptive, and thus responded in various ways in order to maintain their control of the interactions with patients. Some of the staff responses described by Clissett et al. (2014) were person centred and nurturing, other responses were more negative, putting the needs of staff first or acting in ways which were less helpful to the patient, such as lack of engagement with patients and their families, restricting activities or prioritising the needs of other patients. While this study clusters together various conditions resulting in cognitive impairment in older adults, it does shed some light on the staff response to older patients who may be experiencing delirium in their care within the acute hospital setting (Clissett et al. 2014).

2.9 Summary and conclusion

Several issues have been highlighted by the literature reviewed in this chapter. The phenomenon of delirium was outlined, with a clear distinction between the different

subtypes of the condition. The predisposing and precipitating factors were also described as well as the various diagnostic criteria for delirium. Several standardised delirium bedside tools were discussed, alongside their psychometric properties in the acute hospital setting. It was suggested in earlier publications that some of the tools are not entirely suitable for use in a busy ward environment, and some are particularly unsuitable for use with a cohort of stroke patients (McManus et al. 2007, Nys et al. 2005). The question regarding the suitability of bedside tools for use in a stroke cohort is addressed in four studies which explored the psychometric properties of these tools in detecting delirium in acute stroke (Lees et al. 2013, Mitasova et al. 2012, Kutlubaev et al. 2016, Infante et al. 2017). Whilst each of these studies was medium in scale (see section 2.5.6) and clearly more work is required in this area, this is a promising advance in improving the detection monitoring of delirium after stroke (Mitasova et al. 2012).

It is clear from the literature that the determination of incident delirium in older patients in the acute medical setting is affected by the wide variety of means of identifying delirium and that these incidence rates are regarded as an under-estimate (Inouye et al. 2014). A gap in the literature around the incidence rates of delirium in acute stroke clearly existed at the start of this programme of research: single studies published prior to the commencement of this programme presented a range of incidence of between 10% (Dahl et al. 2010) to 48% (Gustafson et al. 1991). This gap could be filled with a synthesis of the data available from single studies, as presented in chapter IV of this thesis.

Routine monitoring of delirium is important in a variety of settings, as recognition of delirium is key both in the ability to pinpoint incidence rates and in the improvement of day to day care in clinical practice (Hall et al. 2012). Practice guidelines for delirium recommend routine screening in older adults, however the difficulties associated with recognising a delirium in a stroke cohort are not mentioned in either delirium or stroke

practice guidelines (Scottish Intercollegiate Guidelines Network 2010, National Institute for Health and Care Excellence 2010). It is unclear how often and by whom delirium is identified in routine clinical practice within the acute stroke care setting. Chapter V of this thesis aims to address this question, as well as exploring clinicians' views on the suitability of generic bedside tools when used with stroke patients.

The literature review synthesised material from the general medical and geriatric settings to illustrate the serious consequences associated with developing delirium: increased mortality and morbidity, increased length of hospital stay and an increased risk of developing dementia in the long term (Witlox et al. 2010). Single studies suggested that these consequences are similar in stroke patients (McManus et al. 2009a, van Rijsbergen et al. 2011). Furthermore, delirium is associated with significant economic costs (Leslie and Inouye 2011, O'Mahony et al. 2011) as well as having an emotional impact on the individual, their significant-others and the professionals caring for them in hospital (Belanger and Ducharme 2011, Partridge et al. 2013). A recognition of these important consequences of delirium have led to a call upon clinicians and healthcare managers to work to prevent delirium in at-risk populations and improve the management of this condition (Young and Inouye 2007, Young et al. 2010, Teodorczuk et al. 2012, Inouye et al. 2014).

Early recognition of delirium is a key step in effective management (Holly et al. 2013), yet several barriers to early, accurate identification of delirium are identified in the literature. These range from lack of knowledge and understanding of the condition (Morandi et al. 2013) to lack of clarity around the use of language to describe a delirium (Yevchak et al. 2012) in addition to some evidence of negative attitudes towards people experiencing delirium (Neville 2008, Dahlke and Phinney 2008, Kjorven et al. 2011). These barriers further compound an already established difficulty in identifying the

condition and the distinction between the subtypes of delirium (Siddiqi et al. 2006, Young 2010, Inouye et al. 2014). The symptoms of stroke often heighten the challenge of delirium identification: patients are often seriously ill and have communication difficulties as well as cognitive impairment resultant from the stroke itself (Lees et al. 2013, Mitasova et al. 2012). This leaves a problem unique to a stroke patient population, yet at present, the specific challenges to delirium identification as experienced by stroke care teams are not reported in the literature. A further gap in the literature relates to the involvement of AHPs in the recognition of delirium: It is recognised that multidisciplinary team work is crucial in the identification and management of delirium (Yevchak et al. 2012, Schwartz et al. 2016) yet most of the literature describes the barriers experienced by doctors and nurses alone (Flagg et al. 2010, Davis and MacLullich 2009, Baker et al. 2015).

Therefore, the aims of this doctoral programme, as outlined in section 1.6 are designed to address these identified gaps: chapter IV details the work undertaken in the systematic review which scoped the field of delirium in acute stroke, pinpointing the incidence rates by means of a meta-analysis and shedding light on the means by which delirium is identified in stroke research, as well as the risk factors and outcomes associated with the condition. Chapter V details the Scotland-wide survey of doctors and nurses in an attempt to reveal their screening and diagnostic practices within an acute stroke population. Chapter VI details the qualitative work undertaken to explore how multidisciplinary staff within the acute stroke unit reportedly respond to a suspected delirium (Figure 2 on p.80 captures the three strands of the programme). This research highlights an important area, previously unexplored in the literature, the response of occupational therapists to a patient with delirium in their care.

Chapter III

Methodology

3.1 Introduction

This chapter outlines the overarching methodology of the thesis, provides justification for the choice of mixed methods research and identifies the guiding philosophical standpoint as pragmatism. This chapter summarises the design considerations and demonstrates how each strand of the programme of research is linked in a sequential manner to gain a broad understanding of delirium in acute stroke. This chapter does not outline the details of each methodology employed in the separate strands, these particulars are presented within the chapters corresponding to each strand (Figure 1). A uniting element of the separate studies within this programme of research is the utilisation of online methods as a means of collecting data: from using powerful online search engines and databases to utilising an online survey tool and finally, an online platform upon which focus groups were hosted. This is discussed within this chapter, alongside a mention of some of the overarching ethical considerations that are relevant to this unique research environment.

3.2 Philosophical standpoint

Creswell and Plano Clark (2011) regarded the articulation of philosophical standpoints and assumptions as crucially important stages in the designing of mixed methods studies. These assumptions, described as the worldview or paradigm are the beliefs and assumptions about the knowledge that informs a study (Creswell and Plano Clark 2011). Both Feilzer (2009), and later Bishop (2014), discussed the philosophical challenge of conducting mixed methods research as such programmes do not sit comfortably within either the positivist or the constructivist paradigms. Greene (2007) as well as Creswell and Plano Clark (2011) suggested that as a response to this, mixed methodologists sought to create an alternative framework, within which they could comfortably operate. It is proposed that pragmatism is this alternative research paradigm: it avoids issues of contention such as 'truth' and 'reality' (positivism) and accepts that there are both singular and multiple realities open to empirical study (Feilzer 2009, Creswell and Plano Clark 2011, Bishop 2014, Florczak 2014). Pragmatism is a paradigm in which the focus is more on the consequences of the research rather than the methods employed, since the methods are pluralistic, producing practice-relevant answers (Creswell and Plano Clark 2011). According to Greene (2007), pragmatism is most suited to mixed methods research as it translates into research practice as the paradigm that allows researchers to choose the combination of methods and approaches which best answer the research questions. Furthermore, Greene (2007) proposed that the advantage of pragmatism as a suitable paradigm for mixed methods enquiry is in the acceptance of both a realist and constructivist standpoints. The paradigm fits best with the personal standpoint of the author, as well as the aims of this programme of research. From a personal perspective, the researcher's own career encompassed experience of

conducting a variety of studies, utilising a variety of methods, so perhaps it is no surprise to find oneself rather comfortable with the notion of pragmatism: the experience of asking different types of questions, utilising different types of methods convinces one that all types of knowledge are valid in the exploration of complex phenomena (Florczak 2014).

3.3 Choosing a mixed methods approach

Johnson et al. (2007) defined mixed methods research as an intellectual and practical synthesis of both qualitative and quantitative types of enquiry within the same programme of research. Johnson and Onwuegbuzie (2004) stressed that the goal of mixed methods is to employ the best of both approaches in the one piece of research. Johnstone and Onwuegbuzie (2004) and Ivankova et al. (2006) suggested that mixed methods designs allow for a greater depth and breadth of exploration of the phenomenon under investigation. Greene (2007) outlined the various purposes of mixed methods research, suggesting that most common is the purpose of complementarity: a study which seeks to broaden, deepen and enhance knowledge around one complex phenomenon. Glogowska (2010) suggested this approach to be particularly suited to healthcare research. This fits well with the conceptualisation stage of this programme of research: at the time of writing the research proposal there was a fairly substantial literature base on delirium in the acute hospital setting yet relatively few peer-reviewed publications specifically on delirium in acute stroke. Thus, the study as a whole set out to explore the phenomenon of delirium in acute stroke and its effect on the patient journey through acute stroke services. The main emphasis of the programme of research was on the identification of delirium by various healthcare professionals. A key concern was to

construct a practice-relevant programme of research that would generate answers to questions not yet asked in the field of acute stroke care.

3.4 Design considerations

Glogowska (2010) outlined the debate in the literature about the nature of the various mixed methods designs, pointing out that methods could be mixed, combined or integrated. Greene (2007) defined the integrated design as one in which the methods interact with one another during the course of the study, stating that this design is most suitable for mixed methods research conducted for the purpose of complementarity as the integrated designs examine the same phenomenon. This serves to justify the choice of an integrated design, as the three strands of this programme of research (Figure 2, p.80) are interlinked. According to Glogowska (2010) the interlinking can occur at any stage throughout the programme of investigation, from conceptualisation to writing up.

3.4.1 Description of overall design

The conceptualisation of this programme of research took place in the weeks leading up to October 2008 (appendix 1.1 details the timeline). The data collection and analysis consisted of three strands, each of which can stand as a study in its own right. As consistent with integrated mixed methods designs the different strands have an 'interactive' relationship (Greene 2007), as the design of each strand relies to some extent on the data generated from the strand preceding it. The first strand is a systematic review and meta-analysis, hence, quantitative. The second strand is a survey which relies mainly on quantitative data generated via multiple-choice questions, but it also has an element of qualitative data generated via open-ended questions. The construction of

the survey relied on the data generated in the first strand. The third and final strand is a focus group study, whose qualitative methodology drew inspiration from the Grounded Theory approach to data generation and analysis. Figure 2 represents the three strands as a sequential process, outlining the overarching methodology for each strand. Conventions of diagrammatic representations of mixed methods research were followed (Creswell and Plano Clark 2011).

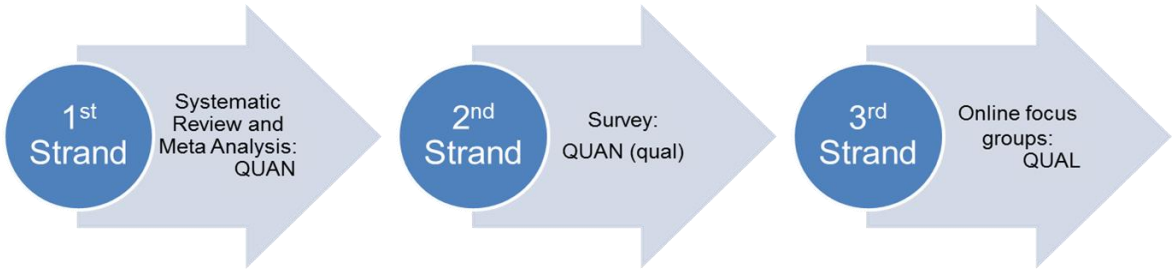

Figure 2: Programme of research in three strands

3.4.2 Utilising online research

The internet has a major impact on research methods and the popularity of utilising the online environment for the purpose of research has increased (Warrell and Jacobsen 2014). As researchers recognise the potential of online methods of data capture, methods such as internet surveys, virtual ethnographies or harvesting large amounts of data archived online are just a few of the methods available to researchers (Lee et al. 2008). Hesse-Biber and Griffin (2012) argued that online methods hold the prospect of enhancing the overall understanding of the phenomenon under investigation. Advocates for the use of online methods of data collections discussed the numerous benefits and potential pitfalls of this approach (Mann and Stewart 2000, Hesse-Biber and

Griffin 2012, Walker 2013a, Walker 2013b, Ryan 2013), these are synthesised in Table 4.

Table 4: Advantages and disadvantages of online research.

Advantages	Disadvantages
Extending access to participants: wider geographical locations, harder-to-reach populations (including shift workers) and closed-access sites such as some hospitals.	The effort in building rapport with participants is more considerable in the absence of face to face contact.
Resource savings, primarily in time and cost: a more expedient process of data collection and savings associated with lack of need to travel, hire a venue, pay for transcription or stationery.	Specialist software used in online research does have a resource implication which may be considerable.
Convenience for participants who are able to make contributions to the research process in their own time and the environment of their choice.	In focus group research utilising asynchronous methods, there is potential for staggered communication due to time lapses between each posting.
Potential for higher participation rates due to matters of convenience as mentioned above.	It is unknown to what extent this may transcend the various methods available to online researchers and debate around the potential increase in participation rates is ongoing.
Eliminating the power dynamic which may exist at times in face to face interviews or focus groups may facilitate a more open and honest response from participants.	The lack of face to face contact can make communication more difficult due to the absence of non-verbal communication.

(Mann and Stewart 2000, Hesse-Biber and Griffin 2012, Walker 2013a, Walker 2013b, Ryan 2013).

These advantages and disadvantages were carefully considered when conceptualising the research design and the advantages were perceived to outweigh the disadvantages in light of the fact that the research was carried out part time, whilst negotiating over the period of registration various personal and professional transitions, the research therefore had to be practical and feasible. Another major consideration was

access to participants: as it was important to try to scope a wide variety of stroke units across Scotland, the obvious choice was to utilise online methods.

Once the decision to utilise online methodology was taken, it was important to consider the ethical implications of research in the online environment as there are ethical issues which are unique to this particular virtual environment (Roberts 2015). Ethical issues around data collection in the online environment can be split into the two different types of online research – passive and active (Rooke 2013). In passive online research the individuals involved are not aware that they are being researched, e.g. mining data from social media platforms; whereas in active online research, individuals are participating in the research having given their consent to participate (Rooke 2013). The ethical issues relevant to this programme of research are around the latter type of online research therefore the two main ethical issues relevant are confidentiality and anonymity (Markham and Buchanan 2012). According to Eynon et al. (2008) the researcher has a responsibility not only to ensure that the confidentiality of the data is maintained in online modes of data collection, but also to reassure participants that their contributions will be dealt with responsibly. In this programme of research, despite the fact that the data collected were not considered sensitive, all data collection took place via password-protected platforms, and stored in password-protected University servers, and the participants were indeed reassured of this. As for anonymity, Saunders et al. (2015) discussed the importance of maintaining anonymity of participants in online research and proposed a variety of strategies researchers can employ to safeguard their participants' anonymity in online environments. One of these strategies is to encode or disguise participants' personal data so that their identity is not exposed to other online users. A further aspect of maintaining anonymity is discussed by Eynon et al. (2008), who highlighted the potential pitfalls of communicating with participant via email, since email

addresses can often identify the person's personal details. Both these issues were considered carefully and the necessary steps to maintain confidentiality and anonymity are outlined in relation to each study in the relevant chapter sections (5.2.7 for the survey; 6.2.3 for the focus group study).

3.4.3 The use of a research journal

The final design consideration was the importance of using a research journal in the process of undertaking the doctoral studies. Due the length of time anticipated for this the programme of research to take, it was considered vital to keep a journal to record decisions taken and the rationale for these, to ensure that the process of writing up the thesis would be as accurate and true to actual events that had occurred in the process of conducting the research. Walker et al. (2013) highlighted specific benefits of keeping a research journal across various phases of a mixed methods doctoral programme. They suggested that the use of diaries complements the research process and enhances the researcher's understanding of themselves through the process of reflection (Walker et al. 2013). Consistent with Finlay's ideas around reflexivity (2002), Walker et al. (2013) described the process of diary-keeping as a means of evaluating the researcher's role in the processes and interactions encompassed in the research as a whole. Clarke (2009) discussed the use of research diaries as audit trailing in qualitative research. This particular aspect is discussed further in section 6.3.4 in relation to the focus group study. The journal kept for the entire programme of research went beyond reflexivity: it was a means by which to ensure that decisions taken are transparent (Clarke 2009) and as a tool to record thoughts, experiences, and the insights which evolve during the research process (Hiemstra 2001). The benefits of using a journal became most obvious when

the writing up of this thesis commenced: it was referred to time and again to ensure that the methods section of each chapter was accurately recorded. It also depicted very clearly the careful decision making process that took place over matters such as the choice of review tool to utilise in the systematic review. Appendix 3.1 provides an example of this as it is a journal extract from the systematic review strand.

3.5 Conclusion

This chapter outlined the philosophical standpoint as well as the design considerations which were key in the construction of this doctoral programme. Pragmatism was discussed as the overarching paradigm most suited to a mixed methods programme of research, as it enabled the researcher to conduct the research from both a realist and a constructivist standpoint (Greene 2007). The choice of conducting a mixed methods programme of research was justified within the context of practice-relevant research, which would explore the identification of delirium in acute stroke, the impact on patients and the response from stroke unit staff. Combining quantitative and qualitative methods was seen as an appropriate way of generating the answers to the questions which at the time of embarking on the programme, had not yet been asked in the field of acute stroke care. The overall design of the programme was discussed within the context of an interactive mixed methods programme, utilising online methods as a means of data generation, whereas the specific methods employed in each strand of the programme are discussed in detail within the corresponding chapters.

Chapter IV

First Strand: Systematic Review and Meta-analysis

4.1. Introduction

This chapter details the process of the systematic review and meta-analysis carried out to address the first aim of the programme of research: to identify from the literature, the incidence of delirium in acute stroke, methods used to identify the condition and the clinical factors associated with developing delirium in acute stroke. The data collection and analysis were first conducted in 2010, however, due to the time elapsed between conducting the review and writing up the doctoral thesis, an update was conducted in 2016. The data presented in this chapter are a synthesis of the findings of both the original and the update review, key published guidelines for the structure, process and reporting of systematic review have been consulted and adopted as a guide to the setting of this chapter (Stroup et al. 2000, Moher et al. 2009).

4.1.1 Rationale for conducting a systematic review and meta-analysis

A decision was taken to conduct a systematic review early on in the programme of research as the initial literature searches conducted during the formulation of the research proposal established that there were a limited number of published studies on delirium in acute stroke. It was decided that a systematic review and if possible, a meta-analysis would be the most appropriate means of identifying reported incidence rates of

delirium in acute stroke, as well as identifying diagnostic practice and suitability of existing tools for identifying delirium after stroke.

It is widely accepted that systematic reviews (SR) are important in forming the evidence base of healthcare research (Moher et al. 2009, Khan et al. 2003). An SR is considered an essential tool for healthcare workers and consumers of research as it is the least biased way of collating and examining evidence from the literature (Downs and Black 1998; Pellicrew and Roberts 2006). Green et al. (2011) described the goals of SRs as attempting to "collate all empirical evidence that fits pre-specified eligibility criteria in order to answer a specific research question." (section 1). They added that the characteristics of an SR are:

- *"a clearly stated set of objectives with pre-defined eligibility criteria for studies;*
- *an explicit, reproducible methodology;*
- *a systematic search that attempts to identify all studies that would meet the eligibility criteria;*
- *an assessment of the validity of the findings of the included studies, for example through the assessment of risk of bias; and*
- *a systematic presentation, and synthesis, of the characteristics and findings of the included studies."* (section 1.2.2).

According to Sanderson et al. (2007) a meta-analysis is a tool often contained within a systematic review, which offers a means of synthesising quantitative data in a way that allows a summary of evidence to be produced. Bland (2015) defined a meta-analysis as a set of statistical techniques that enable one to summarise results of several studies into one single estimate of effect, e.g. treatment or risk factor. Stroup et al. (2000) referred to meta-analyses as the most robust means of systematically searching, appraising and synthesising research data, enabling the researcher to draw relevant conclusions regarding the topic under investigation. Stroup et al. (2000) also highlighted the importance of synthesising research evidence gleaned from observational studies,

which, according to Egger et al. (2001a) enhances the precision of estimates of the incidence rates of the condition explored.

4.1.2 Aim and objectives of the systematic review

The process of developing the aims and objectives for a systematic review requires first to develop and then frame a research question so as to be able to determine from an early stage, which research evidence will be included in the SR (Cooper 2009). Khan et al. (2011) outlined the structured approach to formulating questions for systematic reviews which is to use four components: population, interventions or exposure, outcomes and design of the studies which would address the question. These matters are discussed further in section 4.2.1 in the description of the protocol development process.

The overall aim of this review was to identify from the literature, the incidence of delirium in acute stroke, methods used to identify the condition and the clinical factors associated with developing delirium in acute stroke. The specific objectives were to systematically answer the following questions:

1. What is the incidence of delirium in acute stroke?

2. How is delirium screened for and diagnosed in acute stroke?

3. What are the psychometric properties (sensitivity and specificity, positive and negative predictive values) of the screening / diagnostic tools when applied to a cohort of stroke patients?

4. What is the feasibility of using the tools identified above in a cohort of stroke patients, specifically considering language difficulties typical in this population?

5. What are the predictors of developing delirium in acute stroke and what is the impact of delirium on outcome post stroke?

4.2 Methods

The structure of the protocol for this SR was guided by a combination of key publications on systematic review process and reporting: Stroup et al.'s (2000) Meta-Analysis of Observational Studies In Epidemiology (MOOSE) statement on reporting systematic reviews; The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al. 2009) and guidelines published by the Cochrane Collaboration (Reitsma et al. 2009). The aims and objectives, once defined, were used to construct a study protocol with the aim of eliminating bias and providing a rigorous structure to follow throughout the various stages of the SR.

4.2.1 Protocol development

Cook et al. (1995) detailed the essentials of protocol development for SRs, some of these already addressed in section 4.1.2 above:

- Pose the question
- Specify the population
- Specify interventions and outcomes of interest
- Specify the methods used to search and identify all potentially relevant data

- Specify the selection criteria
- Specify means of establishing methodological quality

These guidelines were followed when developing the protocol, with particular care and attention taken over the selection of quality assessment checklists, discussed in 4.2.4. The protocol underwent several rounds of writing and re-writing until the final version was approved by the supervisory team in October 2010 and revised in 2016 prior to the update taking place. Booth (2013) discussed the importance of publishing protocols of systematic reviews as a means of ensuring transparency as well as helping to identify potential bias by allowing readers to compare the protocol with the published findings. Allers et al. (2018) expanded on this by stating the reasons for publishing SR protocols go beyond avoidance of duplication of reviews. They claimed the most important reasons for publishing SR protocols are in minimising bias by ensuring the a priori determination of important aspects of a review such as study selection criteria, analytical methods etc. Allers et al. (2018) warned that if review authors do not publish the protocol in advance, there is a risk that their judgement may be influenced by the review findings. Finally, Allers et al. (2018) found that despite the fact that SRs with published protocols took longer to reach the stage of publication as comparted with SRs without published protocols, those with published protocols tended to be SRs of higher quality. The protocol of the update systematic review can therefore be found in appendix 4.1.

4.2.2 Search Strategy

The search strategy was devised based on The Cochrane Collaboration guidelines (Lefebvre et al. 2011) and included the following databases: The Cochrane

Stroke Group Trials Register, the Cochrane Dementia and Cognitive Improvement Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (1950 to present), EMBASE (1980 to present), CINAHL (1981 to present), PsycINFO (1840 to present), Web of Science, British Nursing Index (1985 to present), Physiotherapy Evidence Database (PEDro), The Australian Occupational Therapy literature database (OTseeker) and the Canadian Occupational Therapy Data Base (OTDBASE). In an effort to identify further published, unpublished, and on-going studies, the following additional searches were carried out: ISI proceedings for conference abstracts were searched in order to allow the researcher to contact authors to establish whether a publication of their results is forthcoming; reference lists of studies and reviews potentially fulfilling the inclusion criteria were examined and any new material retrieved. The first search period commenced from 31.10.2010 and was completed by 30.11.2010.

In the time that has elapsed between conducting the reported systematic review and the writing up of the thesis it became clear that an update of the systematic review and meta-analysis was necessary. Garner et al. (2016), reporting on an interdisciplinary panel of experts defined an update as “a new edition of a published systematic review with changes that can include new data, new methods, or new analyses to the previous edition” (p2). The author therefore set out to update the literature searches in order to capture and include any new data published between January 2010 and September 2016. The same databases were searched other than two specialist databases, for which access could not be established during the update: British Nursing Index (1985 to present) and OTDBASE.

Table 5: Keywords, subject headings and combinations employed in search

Stroke	Delirium	Combinations
1. Stroke, stroke (SH), post stroke, acute stroke [not heat stroke] [not cardiac]	6. delirium, delirium (SH), deliri* [not delirium tremens] [not orthopaedics]	1 [and] 6; 1 [and] 7 1 [and] 8; 1 [and] 9 1 [and] 10; 1 [and] 11 2 [and] 6; 2 [and] 7 2 [and] 8; 2 [and] 9 2 [and] 10; 2 [and] 11 3 [and] 6; 3 [and] 7 3 [and] 8; 3 [and] 9 3 [and] 10; 3 [and] 11 4 [and] 6; 4 [and] 7 4 [and] 8; 4 [and] 9 4 [and] 10; 4 [and] 11 5 [and] 6; 5 [and] 7 5 [and] 8; 5 [and] 9 5 [and] 10; 5 [and] 11
2. cerebrovascular accident, cerebrovascular accident (SH), CVA, cerebrovascular [and] disorder [or] insult	7. Acute confusion [or] acute confusional state [not mania] [not depression]	
3. Cerebral [or] cerebellar [or] brain [and] infarct [or] ischemia [or] thrombo* [or] emboli*	8. Acute [and] organic [or] psychoorganic [or] psychosyndrome [not schizophrenia]	
4. Subarachnoid haemorrhage (SH), cerebral [or] brain [or] subarachnoid [and] haemorrhage [or] hemorrhage	9. Acute brain syndrome	
5. Brain attack	10. Metabolic encephalopathy	
	11. Clouded [or] clouding of [and] state [or] consciousness	

4.2.2.1. Key words used / combinations

The Liaison Librarian at Queen Margaret University was consulted regarding the search strategy to ensure that no databases were overlooked and that methods of searching were correct. Based on search strategies published in the Cochrane Library for topics on both stroke and delirium, the key words, subject headings (SH) and combinations that were used are outlined in Table 5 above. “Not” searches were utilised to eliminate obviously irrelevant topics such as delirium tremens or delirium after hip

fracture. Each database was searched using the same keyword combinations which were entered systematically and the number of hits and duplicates were recorded. A 'search record sheet' was used to document the outcomes of the search strategy, including any immediate decisions to exclude studies which can be seen in appendix 4.2.

4.2.3 Study eligibility and minimisation of sampling bias

Cooper (2009) discussed the issue of priori versus posteriori exclusion of studies, based on their methodological quality. The debate centres around the idea of excluding poorly designed or poorly executed studies from research syntheses because they may reduce the overall quality of the synthesis. According to Cooper (2009), the disadvantage of this approach is that the study selection process in itself will be biased as researchers vary in their opinion and judgements of methodological quality. Therefore, in order to avoid sampling bias (Leandro 2005) no studies were excluded based on their methodological quality. Leandro (2005) outlined the various sources of sampling bias in SRs, including, publication bias which arises as a consequence of editorial boards or authors' reluctance to publish negative results or results lacking statistical significance (Egger et al. 2001b, Leandro 2005, Song et al. 2013). The assessment of publication bias in systematic reviews of interventions is an important step in ensuring the validity of the findings of the meta-analysis since there is the possibility of unpublished studies changing the results of the systematic review (Egger 1997, Song et al. 2013, Bland 2015). One of the ways of avoiding such bias when conducting SRs of interventions is searching trial registers (Egger et al. 2001b). A further approach is to conduct literature searches without setting limits that are based on outcome, that is, using MeSH headings and collecting all of the literature available, irrespective of findings (Song et al. 2013). Song

et al. (2013) recognised the difficulties in locating unpublished studies, particularly observational studies, since no equivalent of the trial register exists. According to Bland (2015) the detection of publication bias using statistical methods is an important step which is closely linked with the meta-analysis process, discussed further in point 4.2.6.4.

Other sources of bias mentioned by Leandro (2005) are indexing bias: arising due to poor indexing in the searchable databases; and search bias: arising due to difficulties with the search strategy. Every effort to minimise these potential sources of bias was made by putting together a detailed search strategy, using multiple databases to ensure all potential sources were examined, searching databases from their inception and sourcing all citations via all means available – interlibrary loans and membership of external databases such as The Knowledge Network. Additionally, Song et al. (2013) proposed that minimising the effect of publication bias in systematic reviews is achieved by regularly updating reviews, a matter addressed within this chapter.

The inclusion criteria for the 2010 SR were as broad as possible, in an attempt to scope all of the available literature on the topic. However, during the process of the update literature searches, new evidence emerged around treatment options for delirium in acute stroke, a matter not explored in this review. It therefore became necessary to adjust the inclusion and exclusion criteria, as supported by the guidance published by Garner et al. (2016). Thus, all publications reporting on treatment of delirium post stroke were excluded from the review. This decision also resulted in the updated literature searches not including the Cochrane trial registers as reported in 4.2.2, since these report on trials of interventions to prevent or treat delirium.

The final inclusion and exclusion criteria for the 2016 update are summarised in Table 6, and discussed in sections 4.2.3.1 to 4.2.3.4.

Table 6: Inclusion and exclusion criteria

Category	Include	Exclude
Study design and n=?	Non-experimental: all observational studies: prospective, retrospective, cross sectional, cohort studies Case series n>2	Experimental: Studies investigating treatment of delirium Case studies n<2 Systematic reviews and Meta-analyses
Participants	Humans Adults ≥ 18 years	Animals Children / Minors < 18 years
Reason for admission: diagnosis of stroke	Stroke or subarachnoid haemorrhage (Hatano, 1976)	Transient ischaemic attack Confusion or unobvious stroke which is discovered in the days following hospital admission.
Diagnosis of delirium	Clinical assessment based on ICD10, DSM III, DSM III-R, DSM IV, DSM V or bedside tools based on these criteria.	Unclear process of diagnosing delirium
Publication type	Full publications, letters reporting data.	Conference proceedings, presentations, posters, abstracts, opinion pieces, letters containing no data
Language	English, Dutch, French, German, Hebrew, Spanish.	Any other language

Titles and abstracts identified from database searches were reviewed by the author and obviously irrelevant work was eliminated. The author categorised all citations as either ‘Include’, ‘Exclude’ or ‘Possible’ using a form agreed by the supervisory team. The reasons for exclusion were also logged on this form (appendix 4.3). All abstracts of

included, possible and excluded studies were reviewed by the author, and a second opinion was sought from within the supervisory team as two persons acted as independent reviewers who screened for relevance and fulfilment of inclusion criteria. Disagreements were resolved by discussion among the supervisory team.

4.2.3.1 Design

All non-experimental, observational designs were eligible for inclusion: prospective, retrospective, cross sectional, cohort studies, case control studies and case series (Petticrew and Roberts 2006). According to Devillé et al. (2002) the minimal sample size to be included in systematic reviews assessing diagnostic accuracy varies. However, case studies or case series with fewer than two participants were excluded due to the fact that the incidence of delirium would not be addressed in a sample of n=1.

4.2.3.2 Participants

Human only, adult (≥18 years) participants with stroke or subarachnoid haemorrhage (SAH) who present to the hospital with a clear diagnosis of stroke or SAH. Due to the paucity of literature in the field at the time of the original review, the decision was taken to include SAH so as to ensure that the scope of the review was as wide as possible. Hatano's (1976) definition of stroke is provided in section 1.1 of this thesis.

4.2.3.3 Diagnosis of delirium

Only studies where the diagnosis of delirium in acute stroke was made by established diagnostic criteria (e.g. DSM IV or bedside tools based on published criteria as reviewed in chapter II) were included. Studies where the diagnostic process for

delirium was not described were excluded, as it would not have been possible to critique the method of diagnosis if this was not described in the paper.

4.2.3.4 Types of publication

Only full publications were considered for the review, therefore conference proceedings and letters to the editor which contained no research data were excluded. Review articles as well as systematic reviews identified in the 2016 searches were excluded, albeit, reference lists were consulted to ensure that no studies were missed in the process of literature searching. Excluded publications were read, and if appropriate, the authors were contacted for further information or clarification regarding the prospects of a full publication. Publications in the following non-English languages were eligible for inclusion: Dutch, French, German, Hebrew, and Spanish.

4.2.3.5 Dealing with duplicate studies

Villar (2015) described the practice of duplicate publications, stating that this happens when the same material is published more than once by the same author or group, at times appearing as publications in different languages. In instances such as these, where exact duplicates were identified, these were excluded from the review. There is however, a further type of duplicate, sometimes referred to as 'salami-slicing' (Haworth et al. 2014), where larger studies are divided into several publications, essentially presenting data on the same cohort of participants. Tramér et al. (1997) discussed the dangers of including duplicate data in meta-analyses, stating that analysing data from the same patient cohorts more than once is likely to lead to bias, giving the examples of increased estimates of treatment efficacy, or a false impression of drug safety. Wood (2008) also warned against the practice stating that it will result in certain cohorts of patients being given additional weighting by including them more than once.

Suspected duplicate publications were therefore scrutinised carefully and decisions taken regarding exclusion are described in the results section 4.3.1.

4.2.4 Methodological quality assessment

Sanderson et al. (2007) conducted an SR to review tools suitable for quality assessment in observational studies. This work helped to focus on the most relevant, validated tools available. Several tools came under consideration following the examination of Sanderson et al.'s (2007) work, after a lengthy process of investigation and attempting to pilot the tools with two observational papers, the choice was narrowed down to three tools: Downs and Black (1998); Effective Public Health Practice Project (Effective Public Health Practice Project 2009), and the 14 item tool for the Quality Assessment of studies of Diagnostic Accuracy included in Systematic reviews known as the QUADAS Tool (Whiting et al. 2003). Both Downs and Black (1998) and the Effective Publish Health Practice Project are useful checklists for quality assessment of both randomised and non-randomised studies. However, these were both rejected because they were not specific enough to allow the appraisal of different types of observational studies, since these are predominantly designed to assess studies of healthcare interventions. The tool eventually selected for the quality assessment of the methodology of the papers selected for the SR is the QUADAS (Whiting et al. 2003), despite the fact that this SR did not set out to evaluate test accuracy. This tool was of use because the wide range of delirium incidence rates reported in the acute stroke literature seemed to stem from varying diagnostic procedures, therefore, it was appropriate to choose a tool specifically designed to critique the quality of diagnostic studies. Reitsma et al. (2009) recommended the use of the QUADAS checklist and indeed the Cochrane Collaboration

endorsed it (Reitsma et al. 2009). At the time of conducting the SR this was the most suitable tool to use to assess diagnostic accuracy, however, since then a revised version named QUADAS-2 was published (Whiting et al. 2011). The use of the QUADAS-2 was considered for the update conducted in 2016, however, in order to maintain consistency of methods employed in the 2010 review, the decision was taken to continue to use the 14 item QUADAS (Whiting et al. 2003) which is reproduced with permission in Table 7 (p.99). In addition to applying the QUADAS, other items were added to the overall quality assessment of each paper (Cook et al. 1995, Downs and Black 1998, Greenhalgh 2015), these were:

- Reporting and reproducibility of methods
- Bias minimisation or internal validity
- Generalisability or external validity
- Use of outcome measures and blinding
- Appropriateness of statistical methods employed

4.2.4.1 Utilising the QUADAS tool

Each item in the QUADAS tool had been designed to assess the reliability of specific aspects of a study's methodology (Whiting et al. 2003). Individual items are scored as 'yes', 'no' or 'unclear'. 'Yes' scores indicate that the methodology has minimised bias and increased reliability of the study outcomes, while a high number of 'no' or 'unclear' scores question the reliability of the diagnostic procedure (Whiting et al. 2003). When completing the QUADAS checklist, the Reference Standard (QUADAS items 5-7, see Table 7, p.99) was regarded as a clinical assessment of delirium using established diagnostic criteria (Deeks 2001, Quinn and Takwoingi 2016) that is, any

version of the DSM (American Psychiatric Association 1980, 1987, 1994, 2002, 2013). The Index Test (QUADAS items 8 and 10, Table 7) was regarded as any bedside tool (Quinn and Takwoingi 2016) such as the CAM (Inouye et al. 1990), the DRS (Trzepacz 1999), and others outlined in section 2.5 in the literature review.

Table 7: QUADAS tool (Whiting et al. 2003)

Reproduced with first author's kind permission.

	Question	Yes	No	UC*
1.	Was the spectrum of patients representative of the patients who will receive the test in practice?	()	()	()
2.	Were selection criteria clearly described?	()	()	()
3.	Is the reference standard likely to correctly classify delirium?	()	()	()
4.	Is the time period between reference standard and index test short enough to be reasonably sure that the delirium did not change between the two tests?	()	()	()
5.	Did the whole sample receive verification of delirium using a reference standard of diagnosis?	()	()	()
6.	Did patients receive the same reference standard regardless of the index test results?	()	()	()
7.	Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard?)	()	()	()
8.	Was the execution of the index test described in sufficient detail to permit replication of the test?	()	()	()
9.	Was the execution of the reference standard described in sufficient detail to permit its replication?	()	()	()
10.	Were the index test results interpreted without knowledge of the results of the reference standard?	()	()	()
11.	Were the reference standard results interpreted without knowledge of the results of the index test?	()	()	()
12.	Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?	()	()	()
13.	Were uninterpretable / intermediate test results reported?	()	()	()
14.	Were withdrawals from the study explained?	()	()	()

*UC=Unclear

In cases where only one method of diagnosis was utilised, that method was regarded as the reference standard and items 4, 6-8, 10-11 were scored as non-applicable (N/A). Item 7 of the QUADAS was given some consideration as some of the bedside tools ("index tests") utilised in practice (Trzepacz 1999, Inouye et al. 1990) are developed based on DSM diagnostic criteria ("reference standard") and therefore one may argue that they are not entirely independent. Nevertheless, the guidance from Whiting et al. (2003) is that the index test should not form part of the reference standard assessment, therefore these were regarded as independent from each other.

4.2.5. Data extraction

The data extraction process was carried out by means of a four-page data extraction form (appendix 4.4), which consisted of both descriptive and critical elements. The form was designed to be able to gather the information required to answer the research question, and included a critical view of the methodology, as detailed in point 4.2.4. The form was piloted by 3 members of the research team in order to ensure that the data being extracted were relevant to the research question. Following the pilot, minor adjustments were made and the final draft circulated among the team for approval (Cooper 2009) prior to the data extraction process commencing. The following data were extracted:

1. Year of publication, study design, and characteristics of study participants.
2. Sample size, inclusion and exclusion criteria.
3. Tools used to diagnose and or screen for delirium including any data provided regarding psychometric properties of tool as used in a cohort of stroke patients.

4. Number of patients who experienced delirium, predictors of developing delirium and outcomes associated with delirium in acute stroke.

4.2.6. Statistical methods

Combining studies into a meta-analysis may produce spurious results due to heterogeneity of the data at hand (Stroup et al. 2000, Egger et al. 2001a, Bland 2015). For this reason, the meta-analysis component was originally conceived as an option, depending on the data extracted in the review process. The Queen Margaret University statistician was consulted in order to explore whether a meta-analysis of the incidence rates of delirium in acute stroke would be feasible. The process of exploring the degrees of heterogeneity of the data was undertaken by the statistician, this was done in order to guide the author not only as to whether to attempt to combine the studies into a meta-analysis but also, which model to use in combining them (Bland 2015). The following sections describe the statistical methods as well as the decision making involved in the performance of the meta-analysis of incidents rates of delirium in acute stroke. The various sections below (4.2.6.1 to 4.2.6.4) describe the step-by-step approach of each statistical method performed by the university statistician using the '*metan*' command in STATA version 14.0. The '*metan*' command allows one to explore the statistical significance and level of heterogeneity, as described in section 4.2.6.2. This command is also used when performing the random-effects analysis, as described in section 4.2.6.3 (Higgins et al. 2008, Chaimani et al. 2014).

4.2.6.1 Derivation of 95% confidence intervals

The first step in exploring the possibility of a meta-analysis was to derive a single, summary statistic for each study (Deeks 2001, Harris et al. 2008). This was achieved by

extracting data on incidence from each study and calculating a 95% confidence interval (CI) for each study's reported incidence rates. CI calculations were performed using an online calculator (Sergeant, 2016) utilising the Wilson score. This method is used for estimating a proportion of a sample and is recommended due to its accuracy in use with any sample size (Newcombe 1988, Newcombe and Altman 2002), a matter which was relevant to the dataset given the wide variation in sample sizes and proportion of patients identified as experiencing delirium. Only one study (Oldenbeuving et al. 2011) provided a 95% CI for the proportion of delirium positive patient in their cohort. Oldenbeuving et al. (2011) did not state which method was used to calculate the CI, and when attempting to replicate this based on the Wilson score, there was a difference in both the upper and lower limits of the confidence intervals: Oldenbeuving et al. (2011) quoted an incidence of 11.8%; CI 9.0 to 15.1 as compared with the Wilson score which returned the CI as 9.2 to 14.8. Following consultation with the University statistician, it was decided that although the differences are not substantial, it would be more accurate to use the same method of calculating the confidence intervals for the entire dataset, thus the Wilson score was calculated for Oldenbeuving et al. (2011).

4.2.6.2 Measuring heterogeneity

Heterogeneity is the term used to describe the variability between studies, both clinically and statistically (Bland 2015). Clinical heterogeneity is the result of different study designs, difference in participant demographics and settings as well as differences in outcome measures used (Israel and Richter 2011). Statistical heterogeneity occurs when the variation between the true effect size of the studies is beyond that which would be expected by chance, therefore statistical heterogeneity can be detected on statistical grounds using specialised tests (Israel and Richter 2011, Bland 2015). Cochran's Q

statistic is a test for heterogeneity which examines the null hypothesis that all studies are evaluating the same effect, producing a P value, based upon which one would establish whether the heterogeneity detected is statistically significant (Higgins et al. 2003, Israel and Richter 2011). Cochran's Q statistic does not state the level of heterogeneity, merely whether the heterogeneity is significant, therefore a further test is required (Sedgwick 2012). Quantifying the level of heterogeneity is possible using the Higgins I^2 statistic, a test which represents the percentage of variation between the sample estimates, producing a percentage range from 0% to 100% (Israel and Richter 2011, Sedgwick 2012, Bland 2015). According to Higgins and Green (2006) a value greater than 50% may represent substantial heterogeneity, they thus suggested two ways of addressing heterogeneity: the first is performing the meta-analysis using a random effects model, the second, performing a subgroup analysis. Both of these approaches were utilised and are presented in the results section (4.3.4.4).

4.2.6.3 Using a random effects model

The broad classification of the different meta-analytic methods is either fixed effect or random effect models (Deeks et al. 2001). In fixed effects models, studies are weighted according to the amount of information they contain, based on the assumption that there is one true effect size across all studies and that any deviations from this are due to sampling error. Conversely, random-effects models incorporate an estimate of between-study variation in the weighting, thus allowing the true effect to vary from study to study, as is applicable when heterogeneity is detected (Deeks et al. 2001, Schultze 2004, Leandro 2005). As described in the results section (4.3.4.4), substantial heterogeneity was found in the dataset, therefore, the DerSimonian and Laird approach, the random-effects approach recommended by the Cochrane Handbook for Systematic

Reviews (Deeks et al. 2011), was utilised. First published in 1986, this random effects model distributes some of the observed effect (in this case, incidence of delirium post stroke) into two components: the true effect observed and the sampling error (DerSimonian and Kacker 2007). The model is based on the idea that the effect noted in each study is influenced by a number of factors, namely patient characteristics, design and execution of the study. The model takes into account the true effect noted in the studies, the mean effect for a population (i.e. of stroke patients) and the deviation each study has from this population mean. This model regards the studies considered as a sample from the population and uses the observed effects to estimate the mean effect as well as the population variance (DerSimonian and Laird 1986).

A statistical measure used in random effects models primarily associated with the DerSimonian and Laird approach (1986) is the Tau statistic (Kontopantelis et al. 2013). According to Deeks et al. (2011) the Tau statistic is a way of estimating the between-study variance in a meta-analysis which uses a random-effects approach. The figure presented is the square of Tau (i.e. Tau^2), which is the estimated standard deviation of any underlying effects across different studies (Deeks et al. 2011). According to Kontopantelis et al. (2013) a higher Tau^2 results in wider confidence intervals around the effect estimate taking into account the variability of this effect across the different studies. Conversely, a Tau^2 of zero effectively assumes there is study homogeneity, therefore precluding the use of a random effects model (Kontopantelis et al. 2013).

4.2.6.4 Assessment of publication bias

The assessment of publication bias includes both a graphical method knowns as the funnel plot as well as analytical methods to test hypotheses regarding the presence or absence of “small study effect”, that is, the association between treatment effect and

sample size (Sterne et al. 2001, Song et al. 2013, Bland 2015). Much of the discussion around publication bias centres around RCTs of treatment effects and the impact of the unpublished studies resulting in negative findings on a meta-analysis of treatment effects (Egger 1997, Leandro 2005, Sterne et al. 2001). This does not apply to the synthesis of incidence rates observed in a population, as explored in this meta-analysis. Consultation with the University statistician regarding the possibility of exploring publication bias statistically took place following the update of the systematic review in 2016. It was decided that since the meta-analysis was dealing solely with incidence rates rather than risks or associations, that the statistical exploration of publication bias would not be required at this stage. This may be a step to be considered in future work undertaken.

4.3. Results

This section presents the outcomes of the latest version of the systematic review and meta-analysis, it therefore combines the findings of the 2010 and 2016 studies. Where appropriate, reference is made to decisions taken in the 2010 review if these differ from the 2016 version. Two checklists guided the presentation of the results: The PRISMA statement (Moher et al. 2009) (appendix 4.5) and the MOOSE statement (Stroup et al. 2000) both of which were developed to encourage high quality of reporting for SRs and MAs (Greenhalgh 2015), with the MOOSE statement being more specific to the reporting of SR and MAs of observational studies in particular (Sanderson et al. 2007).

4.3.1 Study selection

28 studies met the inclusion criteria for this review. Figure 3 (p.109) uses the PRISMA flow chart (Moher et al. 2009) to summarise the study selection process that was followed as the selection criteria outlined above were applied. This flow chart consolidates the process of study selection from 2010 as well as 2016. Keyword combinations returned a total of 6623 citations, hand searching resulted in eight citations, once duplicates were removed, 6250 titles were screened for eligibility, 6023 rejected due to irrelevance. Following the application of the inclusion / exclusion criteria, 172 studies were rejected leaving, 55 full texts which were retrieved for scrutiny. All of these studies were read carefully, 27 were excluded due to various reasons: eight publications contained no new data: McManus et al. (2009b), McManus et al. (2011), van Rijsbergen et al. (2011), Oldenbeuving et al. (2013). See below for a description of decisions on duplicate publications; three systematic reviews: Carin-Levy et al. (2012), Shi et al. (2012), Ojagbemi and Ffytche (2016); one study protocol by Klimiec et al. (2015). Four publications dealt with treatment approaches to delirium in acute stroke: Oldenbeuving et al. (2008), Ohta et al. (2013), Duan et al. (2016) and Rice et al. (2016). Other reasons for exclusion were language, single case studies, one paper studied delirium in the post-acute phase (Turco et al. 2013), one survey of practice (Carin-Levy et al. 2013) and one paper which did not distinguish between stroke and TIA and dealt with cognitive impairment generally rather than delirium *per se* (Pendlebury et al. 2011).

Several instances of duplicate publications (discussed in section 4.2.3.5) had emerged, these were dealt with carefully, case-by-case, details as follows:

In the original 2010 review, two publications by the same group emerged (McManus et al. 2009a and 2009b). Both papers described the identification of delirium in the same cohort of stroke patients, without cross-referencing the other study within the

methods section, a matter which is considered crucial when publishing multiple studies presenting data from the same cohort (Haworth et al. 2014). One paper, published in *Age and Ageing* (McManus et al. 2009a) described identification of delirium in a cohort of 82 stroke patients using the CAM. The second paper, published in the *International Journal of Geriatric Psychiatry* (McManus et al. 2009b) compared the CAM and the DRS on the same cohort of patients. At the time of the 2010 review, this matter was discussed within the supervisory team and a decision to include both papers was taken, based on the fact that there was a small amount of studies found and the incidence rates found for delirium using either tool were not identical. It was therefore decided that for the purpose of the meta-analysis, the incidence rates of delirium found using the CAM (28%) could be used as one set of data (McManus et al. 2009a), and the DRS rates (27%) could be used as a separate set of data (McManus et al. 2009b). This decision was later reversed when conducting the 2016 update, following careful consideration and realisation that including one cohort twice is likely to give added weight to the cohort (Wood 2008). The decision was therefore taken to include only McManus et al. (2009a) and exclude McManus et al. (2009b).

The 2010 review included a pilot study of a drug treatment which was nested in a large observational study (n=527) (Oldenbeuving et al. 2008). In the 2016 update, four other publications by the same group of authors, describing the same cohort of participants were identified (Oldenbeuving et al. 2011, van Rijsbergen et al. 2011, Oldenveuving at al. 2013, Oldenbeuving et al. 2014). Following careful scrutiny of these papers the following decisions were taken:

- Oldenbeuving et al. (2011) to replace Oldenbeuving et al. (2008) due to the data presented in the 2011 publication being more relevant to the SR question, and the

2008 publication being a pilot study of a drug to treat delirium in a cohort of stroke patients.

- Oldenbeuving et al. (2013) to be excluded as it presents data on the same cohort of n=527 already included in the SR (Oldenbeuving et al. 2011).
- van Rijsbergen et al. (2011) was to be excluded as it was a case-control nested within the data presented by the publication by Oldenbeuving et al. (2011), which was already included in the review.
- Oldenbeuving et al. (2014) presented a model of predicting delirium in two cohorts, the first of which was the cohort presented in the 2011 study, the second, a new cohort of 273 participants. The diagnostic procedures in this new cohort were clearly described and it was therefore possible to include this publication in the SR and MA.

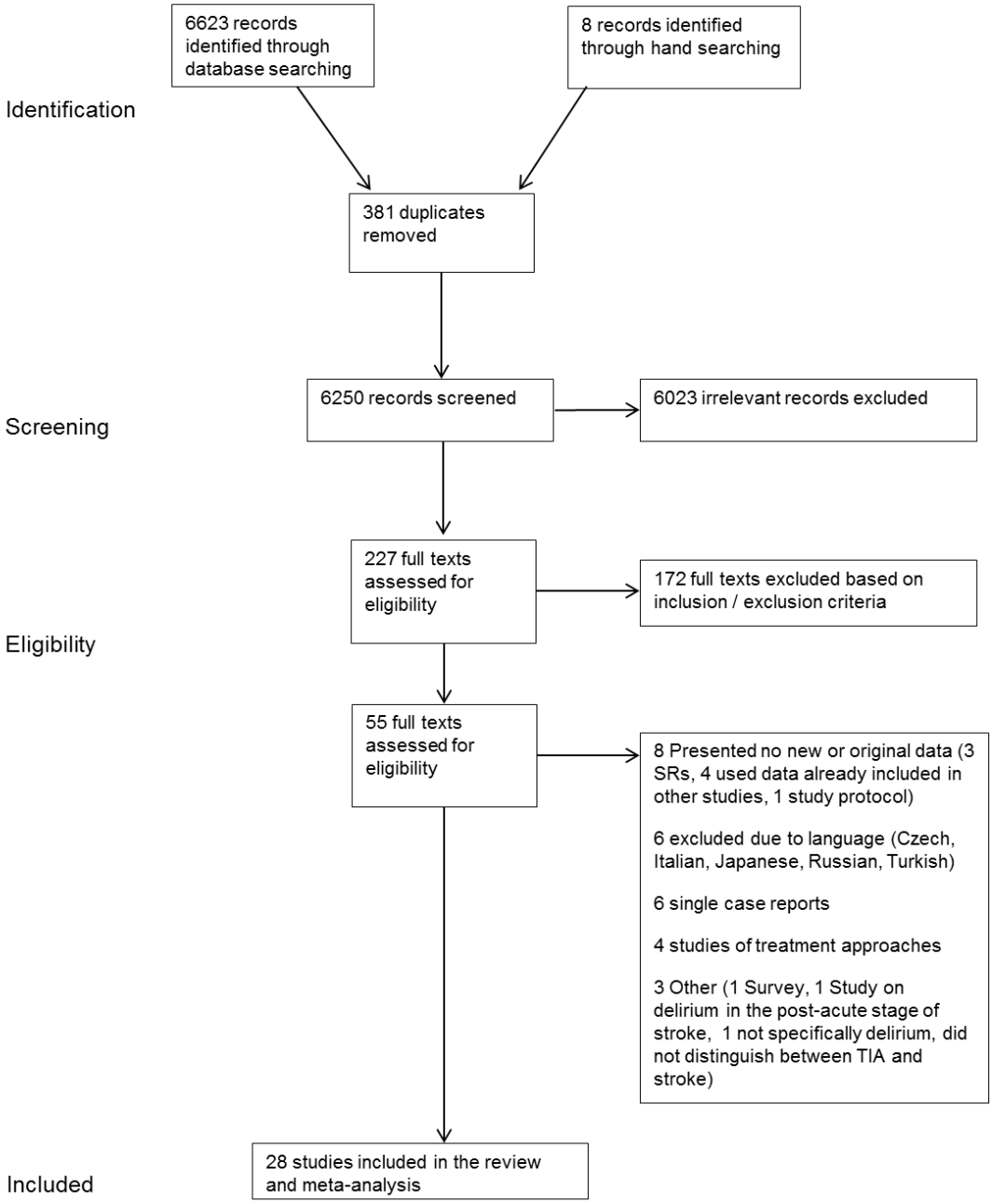

Figure 3: Study Selection: PRISMA flow chart (Moher et al. 2009)

4.3.2 Description of studies included in the review

All included studies originated from hospital based cohorts, most of which stated that delirium assessments were conducted within one week of hospital admission. Wherever available, the description of study design was gleaned from the paper itself. However, where not explicitly stated, the study design was categorised using the NICE algorithm for classifying quantitative study designs (National Institute for Health and Care Excellence 2012) as well as Bland's (2015) definitions of the different methods of sampling in observational studies, where a cohort study is one that includes a follow-up period. All studies were observational, the specific designs employed were: prospective designs (n=12), retrospective designs (n=3), cohort studies (n=7), case controls (n=3), cross sectional (n=2) and one case note review. In terms of geographical spread, the majority of studies were conducted in European countries (n=19), of which, two were from the UK. Four studies were conducted in Asia, two studies in Australia two in North America and one in Turkey. Table 8 (p.115) provides these details in full.

4.3.3 Sample size and characteristics

The sample sizes of studies included in this review were between n=23 and n=527, data on mean age, standard deviation and range are presented in Table 8. Most studies include detailed reports of recruitment, inclusion and exclusion criteria. Three studies were unclear about their sample (Fassbender et al. 1994, Sandberg et al. 2001, Dahl et al. 2010): in these studies the quality of the reporting of sampling was not detailed enough to determine the potential for sampling bias (Greenhalgh 2015).

4.3.4 Identification of delirium and reports of incidence in acute stroke

This section describes the processes undertaken to identify delirium by the studies included in the review. Where bedside tools were used, these will be highlighted including any reported psychometric properties (a full description of these tools is provided in section 2.5 of chapter II). The section will then discuss the rates of incident delirium as reported by the various studies included in this review. These data will be synthesised using meta-analytic methods to establish the overall incidence estimate of delirium in a stroke cohort.

4.3.4.1 Diagnostic criteria

17 studies reported applying DSM diagnostic criteria when assessing patients for delirium, either in conjunction with a tool (see below) or as the sole method of diagnosis: 10 (35%) studies applied DSM IV (Hénon 1999, Sandberg 2001, Caeiro 2004, Sheng 2006, Dostovic 2009, Dahl 2010, Kostalova 2012, Melkas 2012, Kara 2013, Kutlubaev 2016). Two studies (10%) applied DSM IV-R (Caeiro et al. 2005, Caeiro et al. 2004a). Three (10%) studies applied DSM III-R (Gustafson et al. 1991, Fassbender et al. 1994, Gustafson et al. 1993). Dunne et al. (1986) were the only group to have reported application of DSM III criteria. Six studies (21%) reported using bedside tools as the only diagnostic method, without making use of DSM criteria as the reference standard (McManus et al. 2009a, Oldenbeuving et al. 2011, Miu and Yeung 2013, Lees et al. 2013, Naidech et al. 2013, Oldenbeuving et al. 2014). Three studies (15%) referred to “clinical assessment” but did not detail any diagnostic guidelines (Shih et al. 2007, Nicolai and Lazzarino 1994, Mori and Yamadori 1987), and one study referred to the diagnosis of “disorientation” using a simple 3 point scale (Marklund et al. 2004).

4.3.4.2 Utilisation of delirium bedside tools

Of the 21 studies reported to have utilised a delirium bedside tool, six used the DRS or DRS R-98 (Hénon et al. 1999, Caeiro et al. 2004a, Caeiro et al. 2004b, Caeiro et al. 2005, Dostovic et al. 2009, Kara et al. 2013). Three studies used the CAM on its own (McManus et al. 2009a, Miu and Yeung 2013, Oldenbeuving et al. 2014), whereas studies by Dahl et al. (2010) and Oldenbeuving et al. (2011) used both the CAM (to screen for presence or absence of delirium) and the DRS (to assess for severity of symptoms). Two studies reported using the 4AT in conjunction with the CAM or application of DSM criteria (Lees et al. 2013, Kutlubaev et al. 2016) and three studies used the CAM-ICU (Kostalova et al. 2012, Mitasova et al. 2012, Naidech et al. 2013). Three studies reported using the OBS Scale (Gustafson et al. 1991, Gustafson et al. 1993, Sandberg et al. 2001). Lastly, two studies reported using the MMSE to diagnose delirium (Nicolai and Lazzarino 1994, Mori and Yamadori 1987).

The frequency of use of delirium screening tools varied considerably between the studies: 19 studies reported the application of diagnostic procedures within the first week of admission. Seven of these studies assessed for delirium more than once within the first week of admission (Caeiro et al. 2005, Oldenbeuving et al. 2011, Kostalova et al. 2012, Miu and Yeung 2013, Kutlubaev et al. 2016, Oldenbeuving et al. 2014). Five studies assessed more than once daily (Gustafson et al. 1991, Gustafson et al. 1993, Dahl et al. 2010, Mitasova et al. 2012, Naidech et al. 2013). Kara et al. (2013) reported "close monitoring" and Kutlubaev et al. (2016) reported assessing twice within the first 24 hours of admission. The remaining six studies did not report on the time-points of delirium assessment (Schmidley and Messing 1984, Dunne et al. 1986, Nicolai and Lazzarino 1994, Hénon et al. 1999, Sandberg et al. 2001, Shih et al. 2007). Table 8 outlines further relevant details.

4.3.4.3 Psychometric properties of bedside tools used in stroke settings

Among the studies included in the review, those which reported using either the DRS or the CAM referred to the original papers where psychometric properties of the tool were available, albeit, these were not studied in a cohort of stroke patients (see Table 8). Three studies reported on the performance of bedside tools as applied to a stroke cohort: Mitasova et al. (2012) studied the CAM-ICU, Lees et al. (2013) studied both the 4AT and the CAM and Kutlubaev et al. (2016) studied the 4AT. These data are presented in Table 3 within the literature review, however it is important to examine the data related to stroke cohorts here, in order to address objective 3 of this review.

Mitasova et al. (2012) validated a Czech version of the CAM-ICU in a cohort of 129 patients in the acute phase of stroke. The study found a sensitivity of 76% (95% CI 54.9 to 90.6) and specificity of 98% (95% CI 93.2 to 99.8) and overall accuracy of 94% (95% CI 88.2 to 97.3) as compared with the DSM-IV diagnostic criteria as the reference standard. Mitasova et al. (2012) were the only publication to report on the inter-rater reliability of the CAM-ICU in stroke patients, they found a kappa score of 0.94. Naidech et al. (2013) quoted these figures in their own publication. Lees et al. (2013) examined the utility of a variety of brief cognitive screening tools in a cohort of 111 stroke patients, amongst them, the 4AT. They compared the 4AT against the CAM, and found it performed well, a sensitivity of 100% (95% CI 0.74 to 1.00), specificity of 82% (95% CI 0.72 to 0.89), Positive Predictive Value (PPV) of 43% and the Negative Predictive Value (NPV) of 100% (Lees et al. 2013). Kutlubaev et al. (2016) used a Russian version of the 4AT on a cohort of 73 patients with stroke. They found the tool performed with a sensitivity of 93% and specificity of 86%, for internal consistency the tool achieved an alpha score of 0.80, the PPV was 86 and NPV was 85.6 (No CI given for these findings, Kutlubaev et al. 2016).

A number of studies considered the challenge of using bedside tools in acute stroke: 11 studies reported excluding patients with reduced consciousness (Dunne et al. 1986, Mori and Yamadori 1987, Gustafson et al. 1991, Gustafson et al. 1993, Caeiro et al. 2004b, Marklund et al. 2004, Caeiro et al. 2005, Dahl et al. 2010, McManus et al. 2009a, Naidech et al. 2013, Kutlubaev et al. 2016). Eight studies excluded patients with aphasia (Dostovic et al. 2009, Sheng et al. 2006, Gustafson et al. 1993, Mori and Yamadori 1987) or "severe aphasia / language barrier" (Oldenbeuving et al. 2011, Melkas et al. 2012, Kara et al. 2013, Oldenbeuving et al. 2014). Caeiro et al., in the three publications (Caeiro et al. 2004a, Caeiro et al. 2004b, Caeiro et al. 2005) reported scoring zero in certain items of the DRS if patients had "language difficulties", however, no specific details of these difficulties were provided. Hénon et al. (1999) considered the possibility of erroneously diagnosing patients with dementia or aphasia with delirium and reported that patients had to score over 10 on the DRS. Gustafson et al. (1991) referred to the use of clinical observation of rapid behavioural changes and disorientation on the ward as indicative of delirium in aphasic patients.

Table 8: Studies included in the review

Authors and study design	Population / Country	Mean Age (SD)	N	Method of Diagnosis	Timing of test	n=Delirium (%)	95% CI
Caeiro et al. (2004a) Case control	Stroke Portugal	57.3 (13)	218	DSM IV TR; DRS	within 4 days	22 (11.5%)	7.6 to 16.7
Caeiro et al. (2004b) Case control	Stroke Portugal	63.6 (12.8)	190	DSM IV criteria ; DRS	within 4 days	29 (13.3%)	9.4 to 18.5
Caeiro et al. (2005) Prospective observational	SAH Portugal	55.5 (14.5)	68	DSM IV R; DRS	daily for first 4 days	11(16%)	9.3 to 26.7
Dahl et al. (2010) Prospective observational	Stroke Norway	73	178	DSM criteria; CAM	twice daily for 1 week	18 (10%)	6.5 to 15.4
Dostovic et al. (2009) Prospective observational	Both Bosnia & Herzegovina	70.0 (11.3)	223	DSM IV criteria ; DRS R-98	within 4 days	59 (25.3%)	20.7 to 32.2
Dunne et al. (1986) Retrospective observational	Both Australia	68	387	DSM III, lack of adequate description		9 (2.3%)	1.2 to 4.4
Fassbender et al. (1994) Prospective observational	Stroke Germany	72	23	DSM III R	in first days of admission	9 (39%)	22.2 to 59.2

Authors and study design	Population / Country	Mean Age (SD)	N	Method of Diagnosis	Timing of test	n=Delirium (%)	95% CI
Gustafson et al. (1991) Prospective observational	Stroke Sweden	73	145	DSM III R; OBS Scale	twice daily	69 (47.5%)	39.5-55.7
Gustafson et al. (1993) Case control	Stroke Sweden	74.37 (8.1)	83	DSM III R; OBS Scale	several times daily	35 (42%)	32.1 to 52.9
Hénon et al. (1999) Prospective cohort	Stroke France	75	202	DSM IV; DRS		49 (24.3%)	18.9 to 30.6
Kara et al. (2013) Prospective cohort	Stroke Turkey	delirium: 68 (1.87) Non delirium: 61.2 (1.29)	150	DSM IV; DRS	"monitored closely" in first 5 days	42 (28%)	21.4 to 35.7
Kostalova et al. (2012) Prospective observational	Stroke Czech Republic	73.5 (11.5)	100	DSM IV; CAM-ICU	daily for first 7 days	43 (43%)	33.7 to 52.8
Kutlubaev et al. (2016) Prospective observational	Stroke Russia	74	73	DSM IV; 4AT	twice within first 24 hours	33 (45%)	34.3 to 56.6
Lees et al. (2013) Cross-sectional	Stroke UK	74 median	111	CAM	within 4 days	11 (11%)	6.1 to 18.3
Marklund et al. (2004) Prospective observational	Stroke Sweden	71 (11)	88	Diagnosis of "disorientation" on a 3 point scale	days 1 and 4	23 (26%)	18.1 to 36.2

Authors and study design	Population / Country	Mean Age (SD)	N	Method of Diagnosis	Timing of test	n=Delirium (%)	95% CI
McManus et al. (2009a) Prospective observational	Stroke UK	66.4 (15.9)	82	CAM	within 4 days	23 (28%)	19.5 to 38.6
Melkas et al. (2012) Prospective cohort	Stroke Finland	70.8 (7.4)	263	Application of DSM-IV criteria to case notes	within 7 days	50 (19%)	14.7 to 24.2
Mitasova et al. (2012) Prospective observational	Stroke Czech Republic	71.2 (11.5)	129	DSM-IV; CAM-ICU	twice daily	55 (42.6%)	34.4 to 51.3
Miu and Yeung (2013) Prospective cohort	Stroke China	72.9 (10.3)	314	CAM	once daily for first 5 days	86 (27.4%)	22.7 to 32.6
Mori and Yamadori (1987) Prospective observational	Stroke Japan	68.2 (10.9)	41	Clinical Examination, MMSE	within first 2 weeks	25 (61%)	45.7 to 74.3
Naidech et al. (2013) Prospective cohort	Haemorrhagic stroke USA	63 (13.8)	114	CAM-ICU	twice daily	31 (27%)	19.8 to 36.0
Nicolai and Lazzarino (1994) Case note review	Stroke Italy	71.7 (6)	78	Clinical Examination, MMSE		13 (16%)	10 to 26.5
Oldenbeuving et al. (2011) Prospective observational	Stroke The Netherlands	72	527	CAM to screen; DRS for severity if CAM positive	once in days 2-4	62 (11.8%)	9.2 to 14.8

					repeat in days 5-7		
Oldenbeuving et al. (2014) Prospective cohort	Stroke The Netherlands	72	273	CAM	once in days 2-4 repeat in days 5-7	41 (15%)	11.3 to 19.7
Sandberg et al. (2001) Cross sectional	Stroke Sweden	77.1 (7.7)	133	DSM IV; OBS Scale		88 (66%)	57.8 to 73.7
Schmidley and Messing (1984) Retrospective observational	Stroke USA	71 and 68 (for n=2)	46	Review of case notes, criteria unclear		2 (4.3%)	1.2 to 14.5
Sheng et al. (2006) Prospective cohort	Stroke Australia	79.2 (6.7)	156	DSM IV criteria	within 3 days	39 (25%)	18.9 to 32.3
Shih et al. (2007) Retrospective observational	Stroke Taiwan	65.55	29	Review of case notes		14 (48%)	31.4 to 59.2

CI: Confidence intervals; SAH: Subarachnoid haemorrhage; SD: Standard deviation

4.3.4.4 Meta-analysis of incidence rates

The incidence rates of delirium in the acute phase of stroke reported in single studies varied widely between 2.3% (Dunne et al. 1986) and 66% (Sandberg et al. 2001). When attempting the meta-analysis of incidence rates it was observed that Dunne et al.'s study (1986), which utilised a retrospective examination of case notes to diagnose delirium was given the most weight in the analysis on the basis that the upper and lower limits of the 95% confidence intervals were very close to each other, generally due to the overall sample being larger (Gardner and Altman 2002). Egger et al. (2001a) discussed the danger of large studies which are poorly conducted having an increased weight within a meta-analysis, resulting in spurious findings. This raised the question of accuracy of the diagnostic procedures, since Dunne et al. (1986) conducted a retrospective analysis of clinical data available to them (including autopsy results) but did not conduct clinical assessments face-to-face with patients in order to reach a diagnosis of delirium. In response to this, the question of excluding studies which relied upon retrospective reviews of case notes had arisen due to the reduced accuracy of this diagnostic method reported in the literature: Inouye et al. (2005) and Saczynski et al. (2014) warned that using case-note review methods to diagnose delirium without a face-to-face clinical assessment may result in under-estimation of delirium cases. It was therefore decided that retrospective examinations of case-notes would be included in the narrative synthesis but not the quantitative meta-analysis component of this review. The following three studies were therefore removed from the meta-analysis: Schmidley and Messing (1984), Dunne et al. (1986) and Shih et al. (2007).

The overall incidence estimate that was observed for delirium occurring in acute stroke was difficult to pinpoint precisely and the overall estimate should be interpreted

with caution (Israel and Richter 2011) due to the substantial heterogeneity observed when analysing the entire sample. Therefore, a subgroup analysis was performed using the various methods of delirium identification as means of grouping studies together. Table 9 outlines the heterogeneity statistics for the subgroup analysis as well as the various group estimates, which ranged from an incidence of 16.6% (95% CI 11.0 to 22.3) to 52.1% (95% CI 37.7 to 66.5). Deeks et al. (2011) suggested that when conducting a sub-group analysis, the different effect estimates should be observed but that these should not be considered separately, rather, one should informally compare effect sizes while observing the overall summary effect size alongside the subgroup results. The synthesised incidence of delirium in acute stroke using the DerSimonian and Laird random effects approach (DerSimonian and Laird 1986) was 28.1% (95% CI of 22.9 to 33.2).

Table 9: Subgroup analysis tests of heterogeneity

Tool	Estimated delirium incidence	Heterogeneity statistic: X^2	degrees of freedom	P=	Higgins I^2	Tau^2
DRS	19.6%	30.3	5	0	83.50%	43.3
CAM	16.6%	42.6	5	0	88.30%	41.6
CAM-ICU	37.4%	9.1	2	0.011	78.00%	69.5
MMSE	38.1%	28.5	1	0	96.50%	977.02
OBS	52.1%	16.3	2	0	87.80%	141. 7
Other*	24.1%	6.2	3	0.1	52.00%	17.01
4AT	45%	Not relevant, only one study utilised this tool				
Overall	28.1%	411.6	24	0	94.20%	157.4

*Other: method of identification was based on DSM criteria alone or a 3 point scale (Marklund et al. 2004).

A forest plot was produced to illustrate the results, a method widely accepted as standard in the presentation of meta-analysis findings (Borman and Grigg 2009). This

method combines text and graphics to display the results from each study as a square and a horizontal line, representing the effect estimate as well as the CI (Harris et al. 2008). According to Borman and Grigg (2009) the forest plot represents simultaneously the uncertainty around effect size, the summary effect and the extent to which each study contributes to the overall result. The forest plot presented in Figure 4 (p.122) has the point estimate of each study represented alongside the 95% CI for each study (horizontal lines on either side of the point). The size of the box around the point estimate (shaded square around each point) represents the proportional weight of each study within the analysis (Borman and Grigg 2009). Finally, the pooled estimate (28.1% incidence rate) is represented as a diamond. These incidence rates are slightly higher than the rates identified in the 2010 review, which can be seen in the publication (Carin-Levy et al. 2012) presented in appendix 7.1.

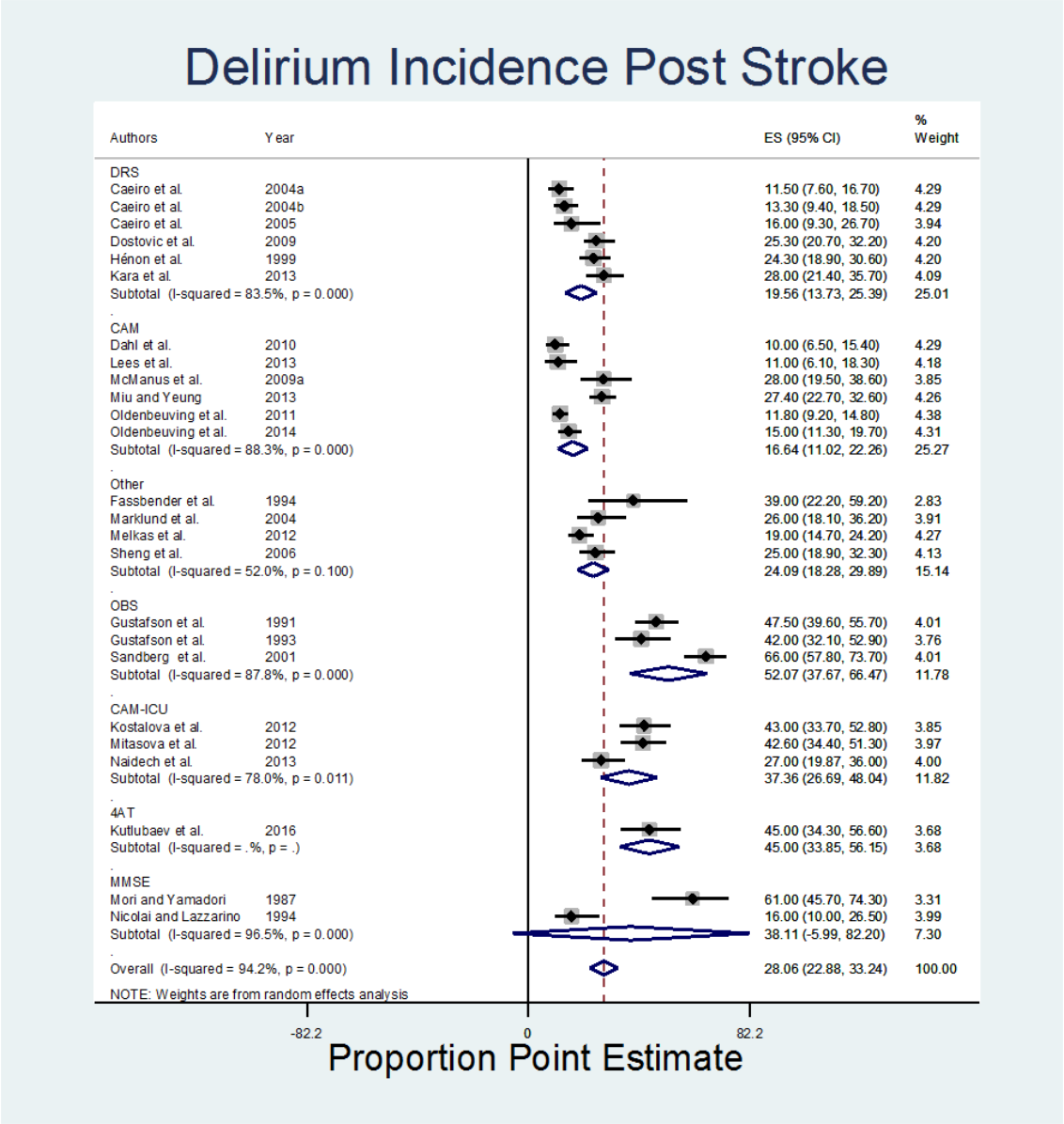

Figure 4: Forest Plot: Meta-analysis of incidence rates

4.3.5 Application of QUADAS checklist

Since the QUADAS checklist does not include an overall quality score (Whiting et al. 2003), a simple view of the studies which scored the highest number of 'yes' items on the QUADAS may highlight those studies with high quality of reporting. This was

discussed by Whiting et al. (2003) as a potential disadvantage of the tool as at times negative QUADAS ratings may be related to poor reporting rather than poor study design. There are a number of studies which do not utilise more than one method of identifying delirium in their cohort, these studies tended to have fewer positive scores. Table 10 (p.124) gives the details of QUADAS scores, these are colour coded for ease of interpretation: items scored ‘yes’ appear in green, items scored ‘no’ appear in red.

Table 10: QUADAS items per paper

ITEM / STUDY	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Caeiro et al. 2004a	v	x	v	?	v	v	v	v	v	x	x	v	?	?
Caeiro et al. 2004b	v	v	v	v	v	v	v	v	v	?	?	v	?	v
Caeiro et al. 2005	v	v	v	v	v	v	v	v	v	?	?	v	?	v
Dahl et al. 2010	v	v	v	v	?	x	v	v	v	v	x	v	?	x
Dostovic et al. 2008	x	v	v	?	?	?	v	x	x	?	?	?	?	?
Dunne et al. 1986	v	v	?	?	?	?	?	?	?	?	?	v	x	x
Fassbender et al. 1994	v	v	v	?	?	NA	NA	NA	x	NA	NA	?	x	?
Gustafson et al. 1991	v	v	v	v	v	v	v	v	v	x	x	v	?	?
Gustafson et al. 1993	v	v	v	?	v	v	v	x	v	x	x	v	x	?
Hénon et al. 1999	v	v	v	?	v	v	v	v	x	?	?	v	?	v
Kara et al. 2013	v	v	v	?	v	v	v	x	x	?	?	v	x	x
Kostalova et al. 2012	v	v	v	v	v	v	v	v	v	v	?	?	?	v
Kutlubaev et al. 2016	?	v	v	v	v	v	v	v	v	?	?	?	?	?
Lees et al. 2013	v	v	v	v	v	v	v	v	v	v	v	v	v	x
Marklund et al. 2004	v	v	?	?	v	NA	NA	NA	x	NA	NA	v	?	v
McManus et al. 2009a	v	v	v	NA	v	NA	NA	NA	v	NA	NA	v	x	?
Melkas et al. 2012	x	v	v	NA	v	NA	NA	NA	v	NA	NA	v	x	v
Mitasova et al. 2012	v	v	v	v	v	v	v	v	v	v	v	v	?	v
Miu and Yeung 2013	v	v	v	NA	v	NA	NA	NA	v	NA	NA	v	x	x
Mori & Yamadori 1987	v	v	?	x	?	v	v	v	v	?	?	v	?	?
Naidech et al. 2013	v	v	v	NA	v	NA	NA	NA	x	NA	NA	v	v	v

Nicolai & Lazzarino 1994	v	x	?	?	?	?	v	v	x	?	?	v	x	x
Oldenbeuving et al. 2011	v	v	v	v	v	v	v	v	v	x	x	v	?	v
Oldenbeuving et al. 2014	v	v	v	NA	v	NA	NA	NA	v	NA	NA	v	?	v
Sandberg et al 2001	v	x	v	?	v	?	v	v	x	?	?	v	?	x
ITEM / STUDY	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
Schmidley & Messing 1984	v	v	?	NA	?	NA	NA	NA	x	NA	NA	v	?	?
Sheng et al. 2006	v	v	v	?	v	v	NA	NA	v	NA	NA	v	NA	v
Shih et al. 2007	x	x	x	NA	v	NA	NA	NA	x	NA	NA	v	?	NA

Items are scored: Yes (v); No (x); Unclear (?); or Non Applicable (NA). It is useful to view this table in conjunction with Table 7: QUADAS tool (Whiting et al. 2003), p.99.

4.3.6 Risk factors for developing delirium in acute stroke

The factors associated with developing delirium after stroke were examined in 25 of the 28 studies (n=866 with delirium). Different variables were examined, utilising a variety of statistical methods. Not all studies examining risk factors used logistic regression analyses to explore independent predictors of developing delirium after stroke. The quality of reporting of the results varied, it was therefore not always clear which of the risk factors identified were independent predictors of developing delirium in acute stroke. Table 11 (p.129) synthesises the data from these studies to indicate the most frequently mentioned independent risk factors for developing delirium in the acute phase of stroke.

4.3.6.1 Stroke severity / stroke symptoms

Stroke severity or individual symptoms resultant from stroke were statistically significantly associated with developing delirium in acute stroke in 11 studies. The rigour or assessment and quality of reporting varied markedly across these studies, with four studies (n=224 with delirium) assessing stroke severity using the National Institute of Health Stroke Scale (NIHSS) (Brott et al. 1989) (Oldenbeuving et al. 2011, Kostalova et al. 2012, Miu and Yeung 2013, Kutlubaev et al. 2016). The remaining seven studies (n=184 with delirium) did not apply the standardised NIHSS scale but they examined the specific symptoms resultant from the stroke such as aphasia, neglect or dysphagia, all of which were identified as risk factors for delirium (Caeiro et al. 2004a, Caeiro et al. 2004b, Caeiro et al. 2005, Sheng et al. 2006, McManus et al. 2009a, Dahl et al. 2010, Kara et al. 2013).

4.3.6.2 Presence of premorbid cognitive impairment or dementia

Four studies (n=176 with delirium) used the Informant Questionnaire on Cognitive Decline in the Elderly IQCODE (Jorm and Jacomb 1989) to rate whether patients in their cohort had pre-existing cognitive decline (Hénon et al. 1999, McManus et al. 2009a, Oldenbeuving et al. 2011, Kara et al. 2013). A further five studies (n=236 with delirium) recorded the presence or absence of premorbid dementia or cognitive impairment, however this was done by means of recording a past medical history (Sheng et al. 2006, Dahl et al. 2010, Kostalova et al. 2012, Melkas et al. 2012, Miu and Yeung 2013). In all of these studies, premorbid cognitive impairment or a diagnosis of dementia were statistically associated with developing delirium in the acute phase of stroke.

4.3.6.3 Older age

Older age was identified as a risk factor by eleven studies (n=455 with delirium), however, it should be noted that not all studies specify the age, e.g. over 65 years (Gustafson et al. 1991, Hénon 1999, Caeiro et al. 2004a, Caeiro et al. 2005, Sheng et al. 2006, McManus et al. 2009a, Dahl et al. 2010, Oldenbeuving et al. 2011, Kostalova et al. 2012, Miu and Yeung 2013, Kutlubaev et al. 2016).

4.3.6.4 Lesion location and stroke type

The association between lesion location and developing delirium in the acute phase of stroke was studied in 17 publications (n=591 with delirium): four found an association for right sided lesions (Schmidley and Messing 1984, Dunne et al. 1986, Mori and Yamadori 1987, Oldenbeuveing et al. 2011) and four for left sided lesions (Gustafson et al. 1991, Gustafson et al. 1993, Shih et al. 2007, Kutlubaev et al. 2016). One study associated lesions of the posterior cerebral artery (PCA) with the development of delirium (Nicolai and Lazzarino 1994). Three studies (Hénon et al. 1999, Dahl et al. 2010,

Kostalova et al. 2012) found no significant association between lesion type or location with the development of delirium. Three studies associated haemorrhagic stroke with developing delirium in the acute phase (Caeiro et al. 2004b, Sheng et al. 2006, Kostalova et al. 2012). Using the Oxfordshire Community Stroke Project ratings (Bamford et al. 1991), five studies found a statistical association between Total Anterior Circulation Infarcts (TACI) and the development of delirium (McManus et al. 2009a, Oldenbeuving et al. 2011, Kostalova et al. 2012, Miu and Yeung 2013, Kara et al. 2013). Miu and Yeung (2013) found that Posterior Circulation Infarcts (POCI) or TACI strokes to be independent predictors for developing delirium. Oldenbeuving et al. (2011) found a statistical association between Partial Anterior Circulation Infarcts (PACI), but following multivariate analysis, this was not found to be an independent predictor of delirium in the acute phase of stroke.

4.3.6.5 Functional independence

Seven studies (n=303 with delirium) examined the association between activities of daily living (ADL) scores on admission and the development of delirium after stroke (Hénon et al. 1999, Sandberg et al. 2001, McManus et al. 2009a, Dahl et al. 2010, Melkas et al. 2012, Kara et al. 2013, Kutlubaev et al. 2016). The ADL outcome measures used were: the Barthel Index (Mahoney and Barthel 1965) (Hénon et al. 1999. Sandberg et al. 2001, McManus et al. 2009a, Dahl et al. 2010, Melkas 2012, Kara et al. 2013); the Modified Rankin Scale (Rankin 1957) (Kutlubaev et al. 2016); and the Katz ADL (Katz and Akpom 1976) (Gustafson et al. 1993, Melkas et al. 2012). Low ADL scores, irrespective of the scales used were found to be independent predictors of developing delirium in the acute phase of stroke by five of the seven studies examining these

associations (Sandberg et al. 2001, Dahl et al. 2010, Hénon et al. 1999, Kutlubaev et al. 2016, McManus et al. 2009a).

Table 11: Independent risk factors for delirium in acute stroke

Study	Older age	Cognitive Impairment	Stroke symptoms or severity	Infection	Low ADL Scores
Caeiro et al. 2004b	√		√		
Dahl et al. 2010	√	√	√	√	
Gustafson et al. 1991	√		√		
Gustafson et al. 1993	√		√		
Hénon et al. 1999		√		√	
Kutlubaev et al. 2016			√		√
McManus et al. 2009a			√		√
Melkas et al. 2012		√			√
Miu and Yeung 2013	√	√	√		
Oldenbeuving et al. 2011	√		√	√	
Sandberg et al. 2001					√
Sheng et al. 2006	√	√			

Shaded areas denote that the domains were not explored in the study.

4.3.6.6 Role of medication

The association between medications taken on admission and the development of delirium in acute stroke was studied in six publications (n=300 with delirium). Four studies found that taking anticholinergic medications was an independent predictor of developing delirium (Gustafson et al. 1991, Caeiro et al. 2004b, Kara et al. 2013, Miu and

Yeung 2013). Kostalova et al. (2012) and Miu and Yeung (2013) both found that polypharmacy was associated with a risk of developing delirium, however, using regression analyses, neither found polypharmacy to be an independent predictor of developing delirium. Naidech et al. (2013) examined whether the use of benzodiazepines given intravenously for sedation of ICU patients were associated with developing delirium in their sample. They found no statistical association between low dose benzodiazepines and developing delirium in patients with haemorrhagic stroke.

4.3.6.7 Other factors

Several other factors were examined in association with developing delirium in acute stroke: impaired vision, infection rates and elevated cortisol levels. Impaired vision, either as a result of the stroke or pre-morbid visual disturbance were identified by four studies (n=168 with delirium) (McManus et al. 2009a, Sandberg et al. 2001, Sheng et al. 2006, Dahl et al. 2010), however, of these, only McManus et al. (2009a) and Sandberg et al. (2001) found that impaired vision was an independent predictor of developing delirium. Elevated cortisol was studied by three groups (n=67 with delirium): Fassbender et al. (1994) did not find a statistically significant association between cortisol release and developing delirium; Marklund et al. (2004) found a statistical association between elevated cortisol and delirium ($p<0.05$, no other data provided); Gustafson et al. (1993) were the only group to establish that elevated cortisol was an independent predictor for developing delirium after stroke. Biomarkers of infection were studied by seven groups, all found a statistically significant association with infection rates and developing delirium (n=310 with delirium) (Hénon et al. 1999, Sheng et al. 2006, McManus et al. 2009a, Dahl et al. 2010, Oldenbeuving et al. 2011, Miu and Yeung 2013, Kutlubaev et al. 2016) four of which, established the presence of infection as an

independent predictor of delirium in stroke patients (Hénon et al. 1999, McManus et al. 2009a, Oldenbeuving et al. 2011, Miu and Yeung 2013).

4.3.6.8 Predictive models for delirium

Two studies developed predictive models for delirium in acute stroke (Kostalova et al. 2012, Oldenbeuving 2014). Oldenbeuving et al. (2014) reported that the patients at highest risk of delirium were those who had a combination of infection with older age, more severe effects of the stroke and a partial anterior circulation infarct (PACI) or total anterior circulation infarct (TACI). Kostalova et al. (2012) reported that older age, haemorrhagic stroke, large ischaemic strokes and metabolic disturbances were predictive of developing delirium in their cohort.

4.3.7 Outcomes associated with delirium in acute stroke

15 publications examined the direct impact of delirium on outcomes (n=661 with delirium). One study examined the relationship between elevated cortisol levels and outcomes after stroke (Marklund et al. 2004). All studies demonstrated that those who experienced delirium were found to have the following unfavourable outcomes: increased length of hospital stay, increased morbidity and mortality as well as increased rates of long term cognitive impairment.

4.3.7.1 Increased length of hospital stay

Data on length of hospital stay were examined by nine studies (n=418 with delirium) (Gustafson et al. 1991, Gustafson et al. 1993, Sheng et al. 2006, McManus et al. 2009a, Dahl et al. 2010, Oldenbeuving et al. 2011, Mitasova et al. 2012, Naidech et al. 2013, Miu ad Yeung 2013). All of the studies stated that stroke patients who developed delirium had higher mean number of hospital days in the stroke unit as

compared with patients without delirium. Seven of the studies stated these rates were statistically significant with p values lesser than 0.05 (to various extents), Dahl et al. (2010) were the only group to state the length of hospital stay was “significantly longer” without providing the p value to support this. Conversely, Mitasova et al. (2012) and Naidech et al. (2013) used a time-dependent covariate analysis to establish that a longer stay in hospital was independently associated with developing delirium in the acute phase of stroke.

4.3.7.2 Mortality rates

Nine studies (n=445 with delirium) found statistically significant associations between increased rates of mortality in patients who developed delirium in acute stroke: Sheng et al. (2006), Melkas et al. (2012) and Mitasova et al. (2012) examined long term mortality rates. Dostovic et al. (2009), McManus et al. (2009a) and Kara et al. (2013) examined in-hospital mortality only. Hénon et al. (1999), Miu and Yeung (2013) and Oldenbeuving et al. (2011) studied both in-hospital and long term (one year and six months respectively) mortality. Hénon et al. (1999) did not find a difference in mortality between the delirium and non-delirium groups in their cohort. Caeiro et al. (2004b) clustered “dependence” and mortality together, making it difficult to determine exact mortality rates to compare between those with delirium and those without delirium in their cohort. Marklund et al. (2004) are not included in the above list since they studied the relationship between cortisol levels and mortality, thus the link between acute cognitive dysfunction and increased mortality after stroke is indirect.

4.3.7.3 Increased morbidity

Morbidity was examined by a number of groups, utilising a number of measures. Four studies (n=217 with delirium) recorded discharge destination (whether patients were

discharged to their own home or a care institution) and used this to establish that patients with delirium were more dependent than those not experiencing delirium in the acute stage of stroke (Gustafson et al. 1991, Sheng et al. 2006, McManus et al. 2009a, Miu and Yeung, 2013). Nine studies (n=411 with delirium) carried out standardised ADL assessments to explore functional ability in their cohorts (Hénon et al. 1999, Caeiro et al. 2004b, Sheng et al. 2006, Dahl et al. 2010, Oldenbeuving et al. 2011, Mitasova et al. 2012, Kara et al. 2013, Miu and Yeung 2013, Naidech et al. 2013). All studies found a statistically significant association between experiencing delirium in the acute stage of stroke with a reduction in ADL scores, irrespective of which standardised measure was used. Dahl et al. (2010) were the only group who did not report a p value to support their findings. Mitasova et al. (2012) and Naidech et al. (2013) were the only groups to report that delirium in acute stroke was independently associated with poor ADL scores: Mitasova et al. (2012) reported reduced ADL scores at the end of the first week of admission (p=0.031), however, this was not sustained at six month follow up (p=0.07). Naidech et al. (2013) reported worse outcomes on the NIHSS (p=0.002) as well as the Modified Rankin Scale (p=0.003) at 14 days following admission as well as reduced quality of life specifically in the domains of fatigue (p=0.01) and executive function (p=0.045) at 28 days following admission. Naidech et al. (2013) were the only group to explore quality of life using the NeuroQoL, a standardised measure designed and validated to be used specifically in neurological research, examining psychiatric domains as well as upper and lower limb function, emotional adjustment, sleep and higher cognitive function (Cella et al. 2012).

4.3.7.4 Long term cognitive impairment

Three studies (n=138 with delirium) included in this review examined long term cognitive impairment following delirium in acute stroke (Hénon et al. 1999, Sheng et al. 2006, Melkas et al. 2012) all found a statistically significant association (with $p<0.05$) between patients with delirium and cognitive impairment in up to 12 months following the stroke.

4.4. Discussion

This section will discuss the outcomes of the systematic review and meta-analysis, aspects related to quality are discussed where appropriate throughout the entire section. The discussion will address the original aims of the systematic review as set out in section 4.1.3 as well as sources of bias in individual studies included in this review.

4.4.1 Incidence of delirium in acute stroke

The meta-analysis placed the incidence rate of delirium in acute stroke at 28.1% (95% CI 22.9 to 33.2), a rate consistent with the rates of delirium found in other medical settings (Siddiqi et al. 2006). At the time of the 2010 version of this systematic review and meta-analysis going to publication (Carin-Levy et al. 2012) it was the first study to attempt to provide an estimate of the rates of delirium in acute stroke. Shortly after this work was published, another systematic review and meta-analysis was published in the field of delirium in acute stroke (Shi et al. 2012). That systematic review aimed to establish the incidence risk, associated factors and clinical outcomes for people experiencing delirium in acute stroke (Shi et al. 2012). Shi et al. (2012) reported the incidence of delirium in acute stroke as ranging from 10% to 48% but when they excluded

Gustafson et al. (1991) from the analysis, they reported that the upper limit of the range reduced to 28%. Shi et al. (2012) did not provide a meta-analysis of the incidence rates, rather they performed a meta-analysis of mortality rates and institutionalisation. The incidence of 28.1% found in the current meta-analysis fits within the range discussed by Shi et al. (2012).

4.4.2 Method of delirium identification

It is important to regard the rigour of the diagnostic procedures of the studies presented in this review in light of the decades in which these studies were carried out. Three of the studies included in this review were conducted in an era that predates the development of a validated bedside delirium detection tool (Dunne et al. 1986, Mori and Yamadori 1987, Schmidley and Messing 1984). Dunne et al. (1986) published a retrospective case note review and shall be discussed separately below. Mori and Yamadori (1987) investigated the presence of acute agitated delirium and acute confusional state (ACS) following right MCA infarcts. Although the authors stated that mental state examinations were carried out, there was no mention of diagnostic criteria used. Also, the MMSE was applied within two weeks of admission, arguably, this time period is too long, as it is possible that cases of ACS were missed within that time period. This matter is reflected in the more recent studies included in this review, all of which recruited patients and screened for delirium within the first few days. Schmidley and Messing (1984) did not explicitly refer to diagnostic criteria used, however, they did detail the definition of ACS which follows DSM III criteria. Three of the studies included in this review relied on case-note reviews in order to diagnose delirium retrospectively in their sample (Shih et al. 2007, Dunne et al. 1986, Schmidley and Messing 1984) in order to

establish the incidence of delirium after stroke. As discussed in section 4.3.4.4, these were removed from the meta-analysis due to the lack of confidence in this approach to the diagnosis of delirium. One other study used case-note reviews as their method of diagnosis, but this was done prospectively (Melkas et al. 2012). Case note reviews were found to be a valid method of delirium diagnosis as long as the reviews were used in conjunction with a clinical assessment: Inouye et al. (2005) created and tested the psychometric properties of a chart based method to identify delirium as compared with clinical assessment using the CAM. They found that the chart based method performed reasonably well (overall agreement 82% (95% CI 80 to 85); sensitivity 74% (95% CI 65 to 81): specificity 83% (95% CI 80 to 86), however, they clearly stated that the high proportion of false negatives (26%) were attributed to poor chart documentation. They therefore recommended that chart reviews are not utilised for diagnostic purposes in clinical practice (Inouye et al. 2005). Saczynski et al. (2014) conducted a similar study and found similarly, that the overall agreement was 80%, however, the rate of diagnosis using the chart-based method consistently missed cases of delirium where the psychomotor and agitation features were not present. Overall, they concluded that case-note reviews should only be used together with a clinical assessment to avoid missing cases of delirium in hospital patients (Saczynski et al. 2014).

In other instances it was difficult to comment on the rigour of diagnostic procedures because of a lack of sufficient detail in the report: Sandberg et al. (2001) and Kara et al. (2013) described the scales used to diagnosed delirium, however, the frequency and timing of assessment are not detailed thus it is difficult to critique the methods beyond the choice of tools. Dostovic et al. (2009) and Fassbender et al. (1994) also provided insufficient details regarding the execution of the delirium assessments, thus it is difficult to judge the methods employed to diagnose delirium in their cohort.

Marklund et al. (2004) provided sufficient detail of their diagnostic protocol as they aimed to investigate the relationship of serum cortisol levels post stroke and relate these to the presence of disorientation. It is interesting that they chose to investigate the presence of 'disorientation', which is a manifestation of delirium, but in itself does not constitute a medical or psychiatric condition and therefore, it is not enough to determine a delirium diagnosis as per DSM criteria (American Psychiatric Association 2002, American Psychiatric Association 2013). It is also noteworthy that Marklund et al. (2004) assessed 'disorientation' by means of a non-standardised three point scale, the psychometric properties of which are unknown.

The application of bedside tools to assess for delirium varied considerably between the studies. Five studies assessed patients for delirium more than once daily (Gustafson et al. 1991, Gustafson et al. 1993, Dahl et al. 2010, Mitasova et al. 2012, Naidech et al. 2013), in three of which the incidence of delirium was found to be over 40% (Gustafson et al. 1991, Gustafson et al. 1993, Mitasova et al. 2012). McManus et al. (2007) had attributed high incidence rates to the frequency of assessment, suggesting that due to the fluctuating nature of the condition, the more often delirium is screened for, the more frequently it will be found. This review cannot confirm or refute this suggestion: Dahl et al. (2010) conducted twice daily delirium assessments and placed the incidence as low as 10% in their sample, whereas Naidech et al. (2013) conducted delirium assessments twice daily and found the incidence to be 27%. Conversely, Kostalova et al. (2012) who assessed stroke patients once daily for the first seven days, found an incidence rate of 43%. There are other publications which placed the incidence of delirium above 40% (Shih et al. 2007, Mori and Yamadori 1987, Sandberg et al. 2001) however, these studies did not report the timing of assessment with enough clarity to be able to establish whether McManus et al.'s (2007) postulated link between frequency of

assessment and higher incidence of delirium to be true. Kostalova et al. (2012) argued that due to the difficulties in assessing patients for delirium in the acute stage of stroke, serial, frequent testing is recommended and La Mantia et al. (2014) proposed that there is not enough evidence to be able to pinpoint the ideal delirium assessment schedule in terms of repeated testing and called for more research to be conducted in order to gain clarity on this matter.

4.4.3 The use of a bedside tool in a stroke population

An important aspect arising from this review is the application of bedside tools developed for use in a general medical environment within a stroke cohort. In their narrative review, McManus et al. (2007) reflected upon the drawbacks of using the CAM and the DRS in a stroke population, based mainly on language difficulties and the fluctuating nature of cognitive function within the acute phase of stroke. In a study excluded from this review as a duplicate, McManus et al. (2009b) compared the CAM and the DRS in the acute stroke population and found that there was good agreement between the two screening tools (Kappa=0.97 in the first week). McManus et al. (2009b) also found a strong correlation between a low MMSE score and delirium in this setting (Kappa=1 in the first and fourth weeks). They concluded that the CAM is favourable due to its ease of use but cautioned that appropriate training is essential for use of either tool, although they do not specify whether this training should be tailored to a stroke population (McManus et al. 2009b).

Three studies included in this review explored the psychometric properties and performance of bedside tools in a stroke population (Lees et al. 2013, Mitasova et al. 2012, Kutlubaev et al. 2016). Mitasova et al. (2012) found reasonable sensitivity (76%)

and high specificity of (98%) and reported an overall accuracy of 94% as compared with the DSM-IV diagnostic criteria as the reference standard. Mitasova et al. (2012) also reported good inter-rater reliability of the CAM-ICU in stroke patients and concluded that the CAM-ICU is a valid instrument for the diagnosis of delirium in a stroke cohort. Neto and Slooter (2012), however, were less positive about the use of the CAM-ICU with stroke patients. They surmised that the CAM-ICU has reduced sensitivity when applied at the bedside of patients in the neurological ICU, and questioned whether it is too difficult to determine a change in mental status in a cohort of patients with neurological disorders. Lees et al. (2013) examined the performance of the 4AT as the index test as compared with the CAM as the reference standard. They found excellent sensitivity (100%) and high specificity (82%). The PPV was low (43%), however, the NPV was excellent (100%) (Lees et al. 2013). The paper is very detailed in its reporting and the authors concluded that the 4AT performs well as a delirium screen in a stroke population (Lees et al. 2013). It is, however, worth considering the use of the CAM as the reference standard in this study. Despite the CAM being the most widely used delirium screen (Morandi et al. 2013, Shi et al. 2013) it has not yet been validated for use in a stroke population. It is also problematic to regard it as the reference standard assessment since delirium diagnosis is complex (Neufeld et al. 2014) and accurate diagnosis therefore relies on a full clinical assessment of the symptoms (Carson et al. 2010, Inouye et al. 2014), ideally combining a bedside tool with expert clinical judgement (Wong et al. 2010). Kutlubaev et al. (2016) used the DSM-IV criteria as the reference standard as compared with the Russian version of the 4AT. They found that it performed well, with high sensitivity (93%), specificity (86%) and internal consistency (alpha score of 0.80). The PPV and NPV were also high (86 and 85.6 respectively) (Kutlubaev et al. 2016). It is worth noting that Kutlubaev et al. (2016) did not report the confidence intervals for their validity scores (Greenhalgh 2015)

and they did not report on the inter-rater or test-re-test reliability of the tool. Despite the minor points of critique for each of these studies, it is of immense value to have data on the performance of the CAM-ICU (Mitasova et al. 2012) and the 4AT (Lees et al. 2013, Kutlubaev et al. 2016) as applied to a cohort of stroke patients.

A tool less frequently used by studies in this review is the OBS Scale. According to Bjorklund et al. (2006) various studies have assessed the OBS scale's sensitivity to detecting a range of organic brain syndromes and found high inter-rater reliability. The OBS Scale has also been reported to show good responsiveness to cognitive symptoms in an elderly population (Björkelund et al. 2006) but according to White and Bayer (2007) and Adamis et al. (2010) there is no published reference to the validity and feasibility of using this tool to detect delirium. A comparison between the OBS Scale and the MMSE as applied to patients with dementia was carried out by Jensen et al. (1993) and the two were found to have good agreement, however, the sample comprised of patients with dementia, not delirium. Additionally, the applicability of the OBS Scale in a stroke setting is not described in the literature. The fourth tool reported in this review is the MMSE, a tool which has reported restrictions in the application in stroke due to its score being influenced by language, mood and sensory and motor function (McManus et al. 2007).

4.4.4 Sources of bias

Some of the studies included in this review were limited by selection bias (Olsen et al. 2010). Mori and Yamadori (1987) and Schmidley and Messing (1984) investigated the presence of ACS in MCA infarcts, reportedly due to the fact that the relationship between right hemisphere infarctions and ACS had been previously described. Similarly, Nicolai and Lazarino (1994) restricted their cohort to PCA territory infarcts, however,

unlike the aforementioned studies, the presence of ACS in this type of infarct is not well documented in the literature, and indeed, they report a small number of new cases of PCA infarcts with ACS. Another factor relevant to selection bias is exclusion criteria. Eight studies excluded patients with aphasia (Dostovic et al. 2009, Sheng et al. 2006, Gustafson et al. 1993, Mori and Yamadori 1987) or "severe aphasia / language barrier" (Oldenbeuving et al. 2011, Melkas et al. 2012, Kara et al. 2013, Oldenbeuving et al. 2014). Aphasia has been reported in up to 35% of patients with acute stroke across several studies (Engelter et al. 2006, Dickey et al. 2010, Flowers et al. 2013), therefore it is possible that a substantial proportion of patients have been excluded from the study of incidence rates of delirium.

Eight studies excluded patients with a history of dementia (Schmidley and Messing 1984, Dunne et al. 1986, Mori and Yamadori 1987, Nicolai and Lazzarino 1994, Sheng et al. 2006, Shih et al. 2007, Dostovic et al. 2009, Kutlubaev et al. 2013), presumably to enable more accurate distinction between delirium and dementia. However, other authors have reported a statistical association between pre-existing cognitive impairment and developing delirium in acute stroke (Hénon et al. 1999, Sheng et al. 2006, McManus et al. 2009a, Dahl et al. 2010, Oldenbeuving et al. 2011, Kostalova et al. 2012, Melkas et al. 2012, Miu and Yeung 2013, Kara et al. 2013). Inouye et al. (2014) argued that excluding patients with a history of dementia is likely to result in an under-estimation of incidence of delirium, an issue which is likely to also affect the population of stroke patients.

4.4.5 Risk factors for developing delirium after stroke

Inouye et al. (2014) stated that while a single factor may lead to the development of delirium, in older people, delirium is more likely to be multifactorial. Populations who are vulnerable to developing delirium have been clearly identified as older people, those with pre-existing dementia or cognitive decline, and those with multiple comorbidities (Inouye et al. 2014). Inouye et al. (2014) reviewed 11 studies that had validated predictive models for delirium across hospital settings, highlighting findings which are consistent with the findings of this systematic review. Older age (over 75 years), severe illness, premorbid cognitive impairment have all been consistently identified as risk factors for the development of delirium (Young and Inouye 2007, National Institute for Health and Care Excellence 2010, Vasilevskis et al. 2012, Inouye et al. 2014). Reduced functional capacity as well as visual and hearing impairment have all been found to increase the risk of developing delirium in general medical settings (Inouye et al. 2014, Ahmed et al. 2014) all of which are confirmed by the findings of this review. Inouye et al. (2014) identified stroke as a specific risk factor for developing delirium in cardiac patients, however, stroke is not included in the list of precipitating factors for delirium. This matter is addressed in two of the studies included in this review: based on predictive models, Oldenbeuving et al. (2014) and Kostalova et al. (2012) identified stroke severity and certain sub-types of stroke to predict the development of delirium in their cohorts.

The role of medication in the developing of delirium is also documented across medical settings: polypharmacy was found to be a precipitating factor in the development of delirium (Tune and Egeli 1999, Marcantonio et al. 2006 Young and Inouye 2007, Inouye et al. 2014, Ahmed et al. 2014). However, the evidence around the use of anticholinergic medication is less conclusive: Moorey et al. (2016) reported on various studies with conflicting findings regarding the statistical association between

anticholinergic medication and developing delirium in the general hospital setting. In their own case-control observational study, Moorey et al. (2016) found that only acetylcholinesterase inhibitors were associated with delirium in their cohort. They explained the correlation as these drugs are commonly prescribed in patients with dementia, who are at risk of developing delirium. While Moorey et al.'s (2016) findings conflict with the results of the four studies included in this review (Gustafson et al. 1991, Caeiro et al. 2004b, Kara et al. 2013, Miu and Yeung 2013) it should be noted that Moorey et al. (2016) examined the link between anticholinergic medication and delirium in a cohort of patients in an acute medical ward, not specifically in a stroke setting.

More specifically to stroke, 17 studies included in this review studied the link between lesion type and location and the development of delirium, with mixed findings. Earlier studies seemed to link MCA territory strokes with the development of delirium, a matter reiterated in a review by Caplan (2010). However, in the more recent studies the Oxfordshire Community Stroke Project classifications (Bamford et al. 1991) were used, making it difficult to compare findings. Whilst a statistical association between TACI strokes and developing delirium was found by some of the studies included in this review (McManus et al. 2009a, Oldenbeuving et al. 2011, Kostalova et al. 2012, Miu and Yeung 2013, Kara et al. 2013) only Miu and Yeung (2013) found using multivariate analysis that POCI or TACI strokes are independent predictors for developing delirium.

The link between elevated cortisol and developing delirium in stroke patients was made by a minority of the studies included in this review (Fassbender et al. 1994, Marklund et al. 2003, Gustafson et al. 1993) however, only Gustafson et al. (1993) were able to determine that elevated cortisol was an independent predictor for developing delirium after stroke. In single studies in post-operative hospital settings, the link between elevated cortisol and development of delirium is also made (Pearson et al. 2010,

Kazmierski et al. 2014). However, in a systematic review on the link between biomarkers and delirium, Hall et al. (2010) argued that individual studies do not always adjust for potential confounders such as physiological stress, dementia and multiple comorbidities. Interestingly, Baurgh et al. (2014) conducted a systematic review of cortisol levels after stroke. They found that in the majority of the studies in their sample (26 studies, combined n=1,340) cortisol levels were elevated in the first seven days after stroke and that higher levels of cortisol were associated with higher mortality and morbidity (Barugh et al. 2014). The association between elevated cortisol and delirium in acute stroke clearly requires further investigation (Hall et al. 2010).

4.4.6 Outcomes associated with delirium in acute stroke

Among the studies included in this review, 14 examined the adverse outcomes associated with developing delirium in acute stroke. This is well-established in the general medical literature: patients with delirium are more likely to have longer hospital stays as compared with patients without delirium (McCusker et al. 2003, Fortini et al. 2014, Weinrebe et al. 2016). Increased mortality and morbidity are also consistently reported across a variety of hospital settings (McCusker et al. 2003, National Institute for Health and Care Excellence 2010, Witlox et al. 2010). The findings of this review have also been confirmed by Shi et al.'s systematic review (2012) which reported that stroke patients who experience delirium are more likely to die in hospital within 12 months, more likely to have poorer functional outcomes and more likely to be discharged into a long term care facility.

The link between experiencing delirium in the acute phase of stroke and long term cognitive impairment was explored by three studies included in this review (Hénon et al.

1999, Sheng et al. 2006, Melkas et al. 2012). This has been confirmed in other hospital settings: Davis et al. (2012) and Witlox et al. (2010) found that delirium was associated not only with an increased risk of dementia, but also with worsening of cognitive function in those with pre-existing dementia. In stroke populations, van Rijsbergen et al. (2011) reported on a nested case control within the larger cohort study published by Oldenbeuving et al. (2011) and included in this review. van Rijsbergen et al. (2011) found that developing delirium in the acute phase of stroke independently predicts the development of dementia and is associated with poor cognitive function two years post stroke. Ojagbemi and Ffytche (2016) conducted a systematic review to explore whether stroke survivors are at higher risk of post stroke dementia. They included all of the relevant studies presented in this review in addition to the study by van Rijsbergen et al. (2011) discussed above. Ojagbemi and Ffytche (2016) reaffirmed the findings of this review, stating that the single studies consistently reported an association between delirium in the acute stage of stroke and an increased risk of dementia and cognitive impairment (Hénon et al. 1999, Sheng et al. 2006, van Rijsbergen et al. 2011, Melkas et al. 2012). Ojagbemi and Ffytche (2016) also conducted a meta-analysis of MMSE scores found by Hénon et al. (1999) and Sheng et al. (2006). They used a fixed-effects model to demonstrate that there are lower MMSE scores in patients with delirium as compared with those without it (mean MMSE score reduction of 4.8, 95% CI 3.4 to 6.3). They concluded that given the paucity of the evidence, more research is required to establish a clear link between delirium in the acute stage of stroke and long term cognitive impairment and dementia (Ojagbemi and Ffytche 2016).

4.4.7 Strengths and limitations of this review

A significant strength of this review is that at the time of the publication of the 2010 version of this systematic review (Carin-Levy et al. 2012), it was the first to synthesise the literature on delirium after stroke. There were however several aspects of the review which were reflected upon critically in the process of writing up the thesis. These are explored below.

The review was designed with a comprehensive search strategy which utilised all the recommended data sources in order to identify the available relevant literature, in an attempt to ensure that no citations were missed (Lefebvre et al. 2011, Greenhalgh 2015). However, there was a balance to be struck between the sensitivity of the search strategy versus the precision it achieves (Lefebvre et al. 2011). Lefebvre et al. (2011) warned that increasing the comprehensiveness of the search risks reducing the precision and resulting in more non-relevant citations. The search strategy employed in this review put greater emphasis on comprehensiveness, compromising aspects of precision, as can be seen by the high number of citations returned, many of which were irrelevant. Indeed, Karimi et al. (2010) acknowledged that at times the use of targeted Boolean phrasing is required in order to save time in searching through multiple irrelevant citations, thus the decision to utilise the 'NOT' Boolean phrase in some of the search phrases was taken. It is acknowledged that this is a practice discouraged by Lefebvre et al. (2011), nevertheless it was taken so as to eliminate obviously irrelevant records such as delirium tremens, mania, depression or heat stroke, thus these were used with caution so as not to miss any publications which were of interest.

Approaches to the minimisation of bias were carefully utilised, examining abstracts for publications in a variety of languages, as well as running an update six years after the first review was conducted, in an attempt to identify as many publications as

possible. A rigorous protocol was followed when applying the inclusion and exclusion criteria and during data extraction. At the time of the original review being published, a systematic review by Shi et al. (2012) confirmed the strength of the search strategy as Shi et al. (2012) did not include in their review any new studies published within a similar time frame. The data extraction process was piloted, and the studies were scrutinised blindly by three reviewers. The entire process was re-implemented in 2016, allowing for the search strategy to be revalidated as well as the inclusion and exclusion criteria to be revised, resulting in a greater confidence in the rigour of the process. The time that elapsed between conducting the first SR in 2010 and the update in 2016 resulted in eight more publications being identified in addition to the author learning more about the techniques utilised. This has allowed for certain revisions to be made, resulting in a more robust process (e.g. the exclusion of McManus et al. (2009b) as described in section 4.3.1).

Assessment of methodological quality is a key element of a systematic review (Greenhalgh 2015). For this purpose, the validated and rigorous QUADAS checklist (Whiting et al. 2003) was applied so as to assess the rigour of the delirium diagnostic processes of each study. Studies scoring the most number of 'yes' items (see Table 10, p.124) on the QUADAS checklist utilised more than one method of identifying delirium in their cohort, thus resulting in greater confidence in the incidence rates of delirium found. Whilst the QUADAS checklist seemed the most suitable at the time of conducting the first review (discussed in section 4.2.4), there were limitations identified, namely, for those studies which utilised only one method of identification of delirium items 7, 10 and 11 of the QUADAS had to be scored as "non-applicable". This is not an option available in this version of the checklist which allows only "Yes", "No" or "Unclear" as the options for rating (Whiting et al. 2003). This matter is addressed in the revised edition of the tool (named

QUADAS-2) which is an 11 item checklist (Whiting et al. 2011). It is possible that using the QUADAS-2 would have resulted in a more accurate assessment of the quality of diagnostic procedures in the studies included in this review. However, even if the QUADAS-2 checklist had been used, lower ratings would have been scored for those studies which used one method of delirium identification, as Harrison et al. (2017) proposed, this is a matter affecting studies examining cognitive tests when evaluating their quality using the QUADAS checklist. It is therefore important to acknowledge that the quality assessment offered for each study included in the review could have been more accurate, had a more suitable tool been used. A tool suggested by Harrison et al. (2017), designed specifically for the quality assessment of observational studies (both cohort and case-control) in the meta-analytic process is the Newcastle-Ottawa Quality Assessment Scale (Wells et al. 2014). According to the authors (Wells et al. 2014), the evaluation of this scale is currently in progress, yet other authors have studied the inter-rater reliability of the scale and found it to be low (Ka-Lok Lo et al. 2014; Hartling et al. 2013), an issue that needs to be considered when using the tool. Despite the findings of these two studies, the tool appears to be useful and perhaps more appropriate for the critical evaluation of observational studies than the QUADAS tool (Whiting et al. 2003) had been in this review. Clearly, this tool was not available at the time of conducting the original review, but it could potentially be used in the process of preparing the manuscript of the updated review for publication.

A further restriction of this review stems from the substantial heterogeneity of data across the various studies included in the review. Despite conducting a sub-group analysis based on the methods of delirium identification, there was a wide variation between the different synthesised effects observed. Nevertheless, the combined

summary incidence rate of 28.1% is consistent with the delirium incidence reported in other relevant medical settings (Siddiqi et al. 2006, Inouye et al. 2014).

It is interesting to note the differences in approaches taken between this review and that of Shi et al. (2012). Shi et al.'s systematic review and meta-analysis (2012) included only ten studies. They reported removing the study by Gustafson et al. (1991) for the incidence range and removing Hénon et al.'s (1999) study from the outcome meta-analysis, in order to address the heterogeneity in the data. Deeks et al. (2011) proposed the removal of studies from a meta-analysis as an option for dealing with heterogeneity, assuming any particular study is an outlier, however, they also noted that this approach may introduce bias. Gustafson et al.'s (1991) findings of an incidence of 48% stood out in Shi et al.'s (2012) dataset, however in the dataset analysed for the meta-analysis presented here, Gustafson et al.'s finding was not regarded as an outlier. Despite this difference in the meta-analytical approach, it is reassuring that the summary incidence found by Shi et al. (2012) was fairly close to that presented in this review.

4.5 Conclusions and implications for practice

The systematic review and meta-analysis presented in this chapter bring to light several important factors in a growing area of research: the incidence of delirium in the acute phase of stroke was pinpointed for the first time, placing it at 28.1% of acute stroke patients. This finding, alongside the synthesis of the finding of studies included in the review highlight the impact of this problem upon the person as well as the health service: reduced functional capacity, increased mortality and increased risk of long term cognitive impairment were all discussed. The review also highlighted that those patients who develop delirium in the acute stage of stroke have an increased length of hospital stay

and increased morbidity. All of these require a response from healthcare providers as well as carrying the associated financial toll (Leslie et al. 2011, O'Mahoney et al. 2011, Inouye et al. 2014).

This review also discussed some of the risk factors associated with developing delirium in a stroke population (e.g. stroke type, stroke severity), these can serve to help healthcare staff be alert to the possibility of delirium in the patients in their care, thus potentially intervening to reduce the incidence of delirium as per national clinical guidelines (National Institute of Health and Care Excellence 2010, Health Improvement Scotland 2014).

This review demonstrated that a variety of bedside tools were applied, utilising widely disparate assessment schedules in the process of delirium identification. It is also important to note that not all of the tools utilised in research were validated specifically for use in a stroke setting. Despite the fact that three of the tools identified in the review were psychometrically evaluated in cohorts of stroke patients, (Mitasova et al. 2012, Lees et al. 2013, Kutlubaev et al. 2016), it is interesting that the most recently published paper assessing inter alia, the incidence of delirium in acute stroke, chose a tool not yet validated in a stroke cohort (Kozak et al. 2017). Additionally, it is not clear whether the tools identified in this review are similar to those used in clinical practice, therefore this systematic review and meta-analysis informs the next two strands of the doctoral programme as the inconsistencies observed in delirium identification in research practice will henceforth be explored in the clinical setting: chapter V will explore the means of delirium identification by doctors and nurses and chapter VI will explore the response of multidisciplinary stroke unit team members to a patient with suspected delirium in their care.

Chapter V

Second Strand: Web-Based Survey

5.1 Introduction

This chapter discusses the second strand of the programme of research: a survey of doctors' and nurses' use of bedside tools to identify delirium in the acute stroke setting. The links with the findings detailed in chapter IV are drawn and justification for the chosen methodology and decisions taken are offered. The issue of ethics in survey methodology is explored as well as the steps taken to try to increase participant response rate. The findings of the survey are presented and discussed within the context of literature from the acute hospital setting.

5.1.1 Rationale and links with previous findings

The systematic review conducted for the first strand of the programme demonstrated that over a quarter of stroke patients develop delirium in the acute phase (Carin-Levy et al. 2012, Shi et al. 2012). Chapter IV also draws attention to the important negative consequences of developing delirium in acute stroke: increased mortality, increased morbidity, increased length of hospital stay and a higher risk of developing dementia in the long term (Carin-Levy et al. 2012, Shi et al. 2012, van Rijsbergen et al. 2011, Melkas et al. 2012). The literature reviewed in chapter II highlighted the importance of delirium identification as key in preventing deterioration and shortening the course of delirium in hospitalised older people (Teodorczuk et al. 2012, Holly et al. 2013). Routine

screening for delirium is considered important across a number of hospital settings (National Institute for Health and Care Excellence 2014, Devlin et al. 2012) and UK practice guidelines clearly set out the best way to identify delirium in hospital inpatients. However, there is no specific mention of stroke patients in these guidelines (National Institute for Health and Care Excellence 2010, National Institute for Health and Care Excellence 2014). Similarly, national clinical guideline for care of patients in the acute stroke setting do not set out a specific requirement for delirium screening (Scottish Intercollegiate Guidelines Network 2010, National Institute for Health and Care Excellence 2013), yet this is an area which requires attention: patients in the acute stroke setting have a number of the risk factors associated with developing delirium (Carson et al. 2010, Makin and Wardlaw 2014, McManus et al. 2009a) and existing bedside delirium detection tools may not perform as reliably when used in stroke due to a variety of stroke-related symptoms, such as aphasia or reduced consciousness (McManus et al. 2007, Mitasova et al. 2012, Neto and Slooter 2012). Hall et al. (2012) called for the practice of delirium detection to be tailored to the specific patient group, and indeed, there are a few studies examining the performance of delirium detection tools in a stroke population (Mitasova et al. 2012, Lees et al. 2013, Kutlubaev et al. 2016). However, it is unclear what actually takes place in clinical practice, namely, how is delirium identified and diagnosed, and by whom. Literature from the general medical and geriatric settings give an indication that delirium is under-recognised, and staff do not routinely use screening tools in daily practice (Teodorczuk et al. 2012, Wells 2012). This matter has not been rigorously established in the acute stroke setting, thus it would be important to find out whether delirium recognition in acute stroke follows the same patterns as in other medical settings.

5.1.2 Aims and objectives of this study

The aim of this study was to explore the ways in which doctors and nurses identify delirium in patients in acute stroke services across Scotland. This aim was addressed by answering the following specific questions:

1. Is delirium screened for routinely in patients in the acute stroke setting?
2. Do any of the Scottish hospitals have a policy regarding routine screening of acute stroke patients?
3. How often does screening for delirium in acute stroke take place and what is the method of screening and diagnosis in clinical practice?
4. Who is most likely to identify delirium in acute stroke?
5. Which delirium identification tools (if any) are used?
6. What are clinicians' views about the use of the screening tools within acute stroke care?

Given the nature of these objectives, in order to explore what takes place in clinical practice across Scotland, survey methodology was regarded as the most appropriate means of answering these questions. A survey is a useful tool for learning about people's behaviours and opinions (Dillman et al. 2009) as well as reaching a large number of respondents, across a wide geographical spread, with relatively low expenditure (Depoy and Gitlin 2011). Both points relate well to the study objectives, as the author wished to capture a picture of delirium identification practice in acute stroke services across Scotland: this includes the behaviour reported by clinicians on the ward and their opinion about certain modes of delirium identification. The choice of utilising a survey therefore seemed the obvious one when the questions were relatively straightforward as delineated in the aims of the study above.

5.2 Methods

The following section will outline the various stages of planning the survey, the decisions taken concerning the mode of delivery and steps taken in an effort to maximise the response rate. The survey pilot is described as well as the amendments which followed the piloting stage. Finally, ethical considerations are detailed as well as the approach to sampling.

5.2.1 Planning the survey

Czaja and Blair (2005) outlined the five stages of conducting survey research. These are presented in Figure 5 and have been followed throughout the process of this study.

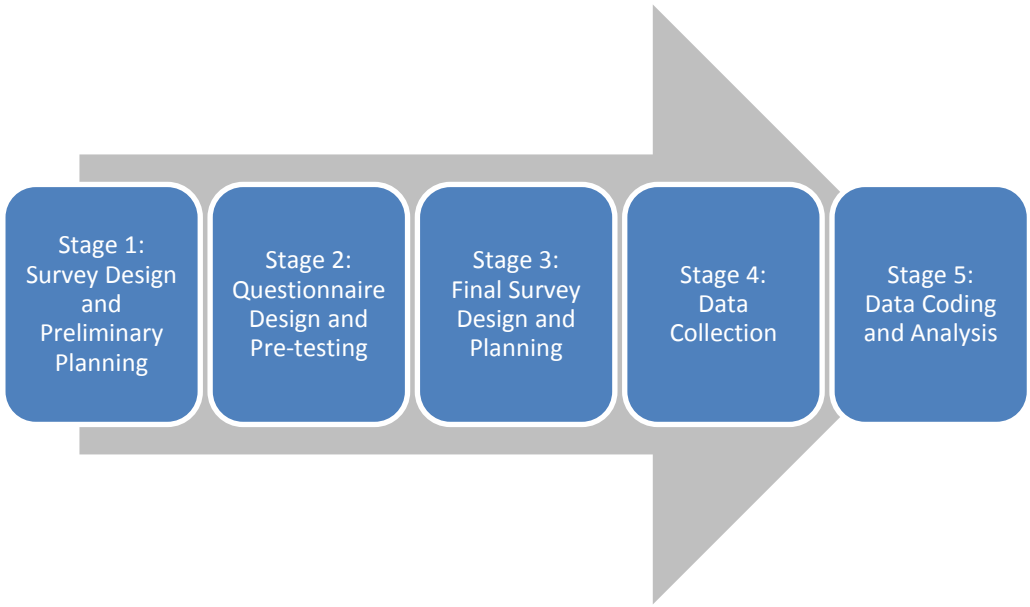

Figure 5: Five stages of a survey (Czaja and Blair 2005)

Calder (1998) suggested that the initial stage of the survey is identifying the problem under investigation and the practical constraints which may affect the survey design. One of the findings of the systematic review and meta-analysis was that there was no standardised way of identifying delirium in patients who have had a stroke. There was also no specific tool recommended for delirium identification and researchers are using a variety of tools, utilised at different time-points and intervals (Carin-Levy et al. 2012). Following the examination of guidelines from different settings as well as other English speaking countries as described in chapter II (section 2.7.1), coupled with the lack of literature on this specific topic, it was clear that a survey would be a good starting point to investigate what actually happens in clinical practice.

5.2.1.1 Choosing the survey design

There were external and internal constraints affecting this particular study. Calder (1998) discussed the constraints of time, finance, and personnel which will be considered the internal constraints affecting the study. Other constraints were access to participants and geographical location which have determined the way this survey was designed. In terms of time, finance and personnel, this study, as part of a part-time, unfunded, doctoral programme had to be pragmatic and achievable. It was not the most important consideration in choosing the survey design, nevertheless, it was a factor to be considered. The external constraints were: surveying clinicians in wide-spread geographical locations across Scotland and contacting a potentially large number of clinicians to invite them to participate in the survey. A further factor which came into play was the consideration of the time available for clinicians to participate in activities within their working hours (Kaner et al. 1998, Curtis and Redmond 2009).

5.2.1.2 Descriptive or analytic survey?

Surveys can either describe or explain a phenomenon, and some surveys may do both: Data collected by means of a survey can serve descriptive or analytical purposes. Descriptive surveys are atheoretical, concerned with finding out about an unknown characteristic of a population or phenomenon, without offering an explanation as to why these characteristics exist. The analytical survey is driven by theoretical questions, where the data are often used to explain a phenomenon, draw links between variables or highlight relationships that may explain the phenomenon under investigation. An analytical survey is often linked with a hypothesis to be tested (Czaja and Blair 2005, Calder 1998, Kent 2001, Buckingham and Saunders 2004). From its inception, this survey was designed with description in mind, there were no hypotheses to be tested, but rather an intention to explore the unknown, namely, the methods and means of identifying delirium in patients post stroke. With these factors in mind, the descriptive survey questionnaire could be constructed.

5.2.1.3 Mode of data collection

Czaja and Blair (2005) outlined four different types of survey designs: mail, telephone, internet and face-to-face questionnaires. Each has its own distinct advantages and disadvantages, but no method is superior to another as it is the research question, coupled with the constraints as highlighted above, which dictate the most appropriate survey tool to be utilised (Czaja and Blair 2005, Calder 1998). It was decided that the survey needed to possess the following characteristics in order to engage participants and answer the research questions effectively: the survey needed to be brief; the questions needed to be straightforward and not arduous or lengthy; and the ease of use and ease of return were also considered to be of great importance to maximise

response rates. Telephone or face-to-face questionnaires were ruled out due to the burden placed on both the researcher and the participants (Czaja et al. 2005), which left a choice between mail and web-based surveys. Dillman et al. (2009) discussed the rise of internet based communication in general and the rise of email communication within the workplace in particular. Dillman et al. (2009) argued that the popularity of email communication in the workplace has meant that it is more difficult to conduct mail surveys, as so many people expect their communication to be via the internet. It is also argued that in the past decade, internet modes of survey have become popular, software dedicated to conducting web surveys has been developed and research interest in methodological rigour has grown, so the researcher conducting web surveys is no longer in the minority (Dillman et al. 2009). Czaja and Blair (2005) stated that web based surveys are suitable for short (under 15 minutes in duration) and moderately complex questionnaires, with the possibility of cheaply, and swiftly distributing a questionnaire across a wide geographical area. These factors have led to the decision to use a web survey, the advantages and disadvantages of which are to be discussed in point 5.2.2.

5.2.2 The web survey

According to Doherty (2006), web surveys are inexpensive, easy to administer and allow the data to be analysed as soon as they are logged on the online survey tool. The advantages and disadvantages of administering the survey online were examined: An important advantage raised by Czaja and Blair (2005) is that web surveys allow data to be collected at a faster rate in comparison to the traditional mail survey, where researchers are waiting for questionnaires to be distributed and returned by post. Another advantage is the ability to incorporate a “skip pattern” within the questionnaire –

so that participants are routed to answer certain questions based on previous answers. The ability to programme skip patterns into a web based survey increases the ease of use, which puts these at an advantage in comparison with paper surveys where the respondent has to make the decisions regarding skipping a question themselves, leaving room for potential errors (Czaja and Blair, 2005). Web-based surveys were found to yield the same findings as paper surveys in terms of content: both Kaplowitz et al. (2004) and Huang (2006) compared print and web surveys among college students and found that the responses recorded for both paper and web surveys were comparable (Huang 2006, Kaplowitz et al. 2004). Kaplowitz et al. (2004) also found that the response rate in their cohort was the same, regardless of the method utilised to collect the data. This point is under debate in the literature, as later studies have found the response rate in web surveys to be lower than traditional methods (Dillman et al. 2009, Fan and Yan 2010). Dillman et al. (2009) attempted to explain response rates to internet based surveys using social exchange theory. They claimed that people are likely to be more motivated to respond to an online survey if there is a reward for participating in the survey; if the cost of participating in the survey is low and finally, if they trust the person from whom the survey is received. Dillman et al. (2009) also claimed that recruiting persons who are interested in the topic of the survey is likely to increase participation. They offered advice on the ways in which participation may be increased, utilising ideas generated by social exchange theory (Dillman et al. 2009). These ideas were taken into consideration: It was felt that it would be inappropriate to offer an incentive for a very short questionnaire, and it was hoped that clinicians with an interest in stroke would have the intrinsic motivation to participate in this short survey. Additionally, it was considered that the 'cost' of participation was low, as the questionnaire was both online (reducing the burden of having to return the completed questionnaire by post) and it was planned to be

considerably short, thus reducing the burden of time taken to complete this questionnaire. In terms of trust, two issues were considered to increase trust, these are discussed below: the first is related to web-survey design and is discussed in point 5.2.3: accessing the survey via a Queen Margaret University server. The second is discussed in point 5.2.8: distribution of email invitations via clinicians' trusted associations and special interest groups.

5.2.3 The Bristol Online Survey (BoS) Tool

The BoS tool was used to design the layout of the questionnaire and subsequently collect and analyse the survey data. This tool is recommended by Queen Margaret University's (QMU) Centre for Academic Practice: it is widely used by Universities and other public bodies in the UK (Bristol Online Surveys 2011) and increasingly by researchers conducting online surveys (Allen and Roberts 2010). There are many software packages offering a wide variety of features (Kaczmirek 2008), however, the two main advantages of using BoS were:

- It can be customised to the researcher's requirements;
- Respondents access the survey through a QMU server (Shaw 2012) thus the web address contains 'QMU' within it, as shown: http://surveys.qmu.ac.uk/.

5.2.4 Increasing response rate: design considerations

Efforts were made to maximise response by following the advice found in several publications on the topic. These strategies were:

- Selecting the BoS tool, as mentioned in point 5.2.3 above: it is customisable, uses the University brand, thus potentially trusted by participants (Allen and Roberts 2010, Perkins 2011).
- Keeping the survey as short as possible and utilising a clear structure (Fan and Yan 2010). Additionally, guidance on effective question writing by Fowler et al. (2008) was followed: using unambiguous language, avoiding technical terms and advice on how to frame the questions so that they will be consistently understood by a variety of people.
- Choosing a scrolling design (rather than the questions set over several webpages) to maximise ease of use and minimise potential technical difficulties (Brace 2008). This design is reputed to reduce the time taken to complete the survey, thus potentially increasing the response rate (Dillman and Smyth 2007).
- Limiting the use of "drop down boxes" as response options as they are considered burdensome to respondents (Manfreda and Vehovar 2008).

5.2.5 Constructing and organising the survey questions

Buckingham and Saunders (2004) suggested there are several stages in the construction of a descriptive survey questionnaire, these are listed in Figure 6 (p.161) and were followed during the process of questionnaire design.

The process of listing the key themes involved examining the research questions (outlined in 5.1.2). These were then translated into concepts and then variables, as demonstrated by the example in Table 12 (p.162). The process of writing the questionnaire involved organising the material into a simple, logical structure and deciding whether questions should be open or closed ended (Buckingham and Saunders

2004). According to Buckingham and Saunders (2004) closed ended questions should be used when there are a pre-determined range of values (such as a choice of delirium screening tools) whereas open-ended questions allow the respondents to answer in any way they want. Buckingham and Saunders (2004) stressed the value of using closed ended questions: they are easier to answer, therefore may increase the engagement with the survey; they make it easier to record and analyse the data, saving time for the researcher and force respondents to answer in a standardised way.

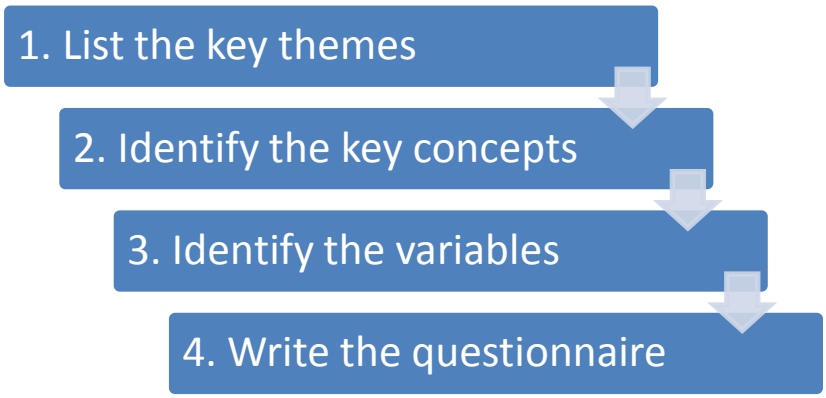

Figure 6: Stages of constructing a descriptive survey

The first section of the questionnaire was designed to obtain information about participant characteristics and place of work. It requested the respondent to give minimal information about themselves: profession, grade, which hospital they worked in and whether they worked on a specialist stroke ward. This information was used to address research objectives 2 and 4. This section contained a combination of closed and short-answer questions, e.g. requesting the participant to enter their grade in a character-restricted answer box (all survey questions can be found in appendix 5.1).

Table 12: Developing a theme into a questionnaire item

Theme	Concept	Variable: questionnaire item
Delirium identification	Routine screening for delirium	• Do clinicians routinely screen new patients admitted to a stroke unit / ward? • Is there a ward policy about routine screening for delirium in stroke patients?
Delirium identification	Regular screening for delirium	• Do clinicians screen for delirium in stroke patient on a regular basis? • Do clinicians screen for delirium in stroke patients at regular time intervals?

The second section of the questionnaire (screening for delirium) requested information regarding the existence of a screening policy on hospital wards and clinicians' specific practice regarding screening for delirium as a matter of routine. These questions addressed research objectives 1-4. This section contained mainly closed ended questions, but in order to ensure that respondents were able to answer as accurately as possible, they had the option of selecting "other" and specifying their response in a character-restricted answer box. Another point to note was that using the BoS tool enabled the researcher to streamline the question, so that if in question 5 (appendix 5.1) a respondent selected "no", the option below to select the frequency of screening disappeared.

The third and final section of the questionnaire (diagnosis of delirium) addressed research objectives 4-6. The section dealt with the actual diagnosis of delirium in a stroke patient, looking specifically at the tools used and whether clinicians felt these

tools were suitable for use in stroke patients. Design of the questions in this section relied on information processed from the findings of the systematic review described in chapter IV: the delirium identification tools mentioned in the literature were listed in the responses to question 7, and the question regarding their suitability for use with stroke patients was a result of the findings of the systematic review (Carin-Levy et al. 2012). This section of the survey contained both open and closed questions, to enable participants to express their opinion regarding tool suitability as freely as possible. Options for questions 6a and 6b and 6c appeared based on the selection made in question 6 (appendix 5.1). Questions 7 and 8 asked respondents to select the standardised tools they used to detect delirium and address their suitability for use with stroke patients. Here the tools listed were mainly based on the findings of the systematic review, one additional tool was added, based on a review of delirium tools available at the time (Schuurmans et al. 2003).

5.2.6 Piloting the survey

The process of pre-testing, or piloting a questionnaire is used to check for language, structure and sequence of the questions presented (Naithani 2012). Campanelli (2008) discussed the importance of testing survey questions to ensure that questions are understood correctly, so as to eliminate potential measurement error associated with participants misunderstanding the questions. Campanelli (2008) recommended making use of experts in the field to pilot a questionnaire. For this reason, a copy of the questionnaire was distributed to three clinicians with relevant clinical and research experience: a consultant stroke physician, a stroke nurse specialist and a consultant in liaison psychiatry. These experts were not asked to answer the questionnaire, merely to

comment on phrasing, clarity and structure of the survey. The piloting process identified the following two issues relating to the wording of items:

- Consistency of use of the term ‘screening’ versus the use of the term ‘diagnosis’ as they relate to utilisation of standardised tools.
- A lack of clarity in the options presented as answers to question 2. “Do you work with stroke patients?”

The issues raised by the piloting process above were rectified and the final version of the questionnaire is presented in appendix 5.1.

5.2.7 Ethical considerations

According to South East Scotland Research Ethics Service regulations, no formal ethical scrutiny was required as this study was an opinion survey seeking the views of staff on service delivery. A letter of confirmation was obtained from the Scientific Officer to confirm this (appendix 5.2). Ethical approval was also gained from Queen Margaret University Ethics Committee (appendix 5.3). This notwithstanding, Buckingham and Saunders (2004) advised that regardless of whether a survey requires formal ethical approval, the basic principles of ethics in biomedical research (Beauchamp and Childress 1994) must apply to survey research as well. Buchanan and Hvizdak (2009) and Allen and Roberts (2010) provided useful guidance on ethical considerations for online survey research, Table 13 (p.165) uses this guidance to maps the ethical principles and the ways in which these were upheld in this study.

Table 13: Ethical principles applied to the survey

Ethical Principle	How it relates to this study?	How this was upheld?
Beneficence	A survey that is not worthwhile or cannot be justified is an unethical study (Buckingham and Saunders 2004, Buchanan and Hvizdak 2009).	The necessity in answering the research questions was justified in the introduction
Non- Maleficence	Asking sensitive questions has the potential of causing psychological distress to the participants (Buckingham and Saunders 2004)	No questions considered sensitive were asked in this survey.
Respect for autonomy	Informed consent and establishing trust: participants need to be able to trust the researcher as genuine (Buchanan and Hvizdak 2009) and be given relevant information about the study before they respond. This includes making participants aware that they have the right to withdraw from the study (Buckingham and Saunders 2004) and allowing participants the chance to discuss the study prior to completing the survey (Buchanan and Hvizdak 2009).	The email invitation and the first page of the survey contained the relevant information, including a statement regarding participants' professional association support for the survey. The information provided in the introductory statement was on a separate web page, the participants had to click a button to commence the survey, thus, moving to the next page and commencing the survey was deemed as consent to participate in the study (see Figure 7, p.167) The email invitation included an offer to discuss this survey prior to completion.
Justice and respect for persons	Maintaining anonymity and confidentiality are crucial in any study. Likewise in survey research, participants must be assured that the responses they give are treated in confidence	Participants were informed that no personal / identifying data were requested in this survey. Also, the BoS tool does not store any personal data or Internet Protocol (IP) addresses (Bristol Online Surveys 2011) as these

	and no identifying data will be kept (Buckingham and Saunders 2004)	are considered a threat to anonymity (Allen and Roberts 2010).

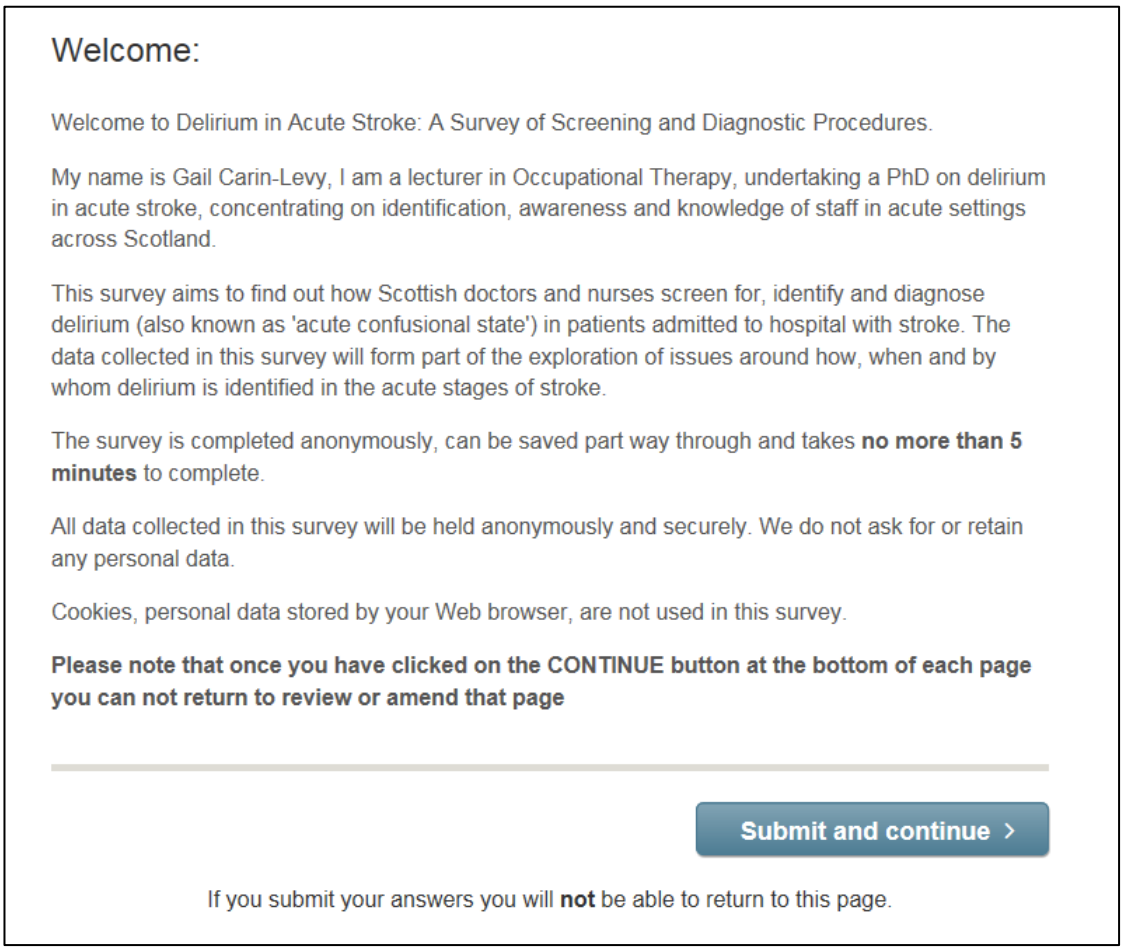

Figure 7: Screenshot of first page of survey

5.2.8 Sample, sample size and recruitment

The approach to recruitment was carefully considered to maximise engagement with this survey, thereby increasing the potential rate of response. Dillman (2009) advocated recruiting persons with an interest in the topic of the survey, it was therefore decided that the professionals to whom this survey would be most relevant were doctors and nurses. This decision was driven by the knowledge that doctors and nurses saw stroke patients on a daily basis, immediately upon their admission to the stroke unit. Consideration was given to the inclusion of other professionals such as AHPs, but based on the literature and clinical standards

available at the time of writing the survey protocol in the Autumn of 2011, the author could find no information to suggest that AHPs were involved in any way in delirium identification (see also search strategy in appendix 2.1). A further consideration (mentioned in point 5.2.3) was the importance of clinicians being able to trust the researcher, therefore it was felt that the survey should originate via professional associations and special interest groups. The national special interest groups were identified by discussion with a leading, local stroke physician and corroborated by a general internet search to identify any other groups that may have been overlooked. In order to be able to determine the anticipated sample size, the administrators of each association were contacted in order to establish the size of membership. The associations approached for recruitment, including size of membership can be found in Table 14. All members of the associations listed in Table 14 were eligible to participate in the survey.

Table 14: Professional associations targeted for recruitment

Name	Professions included	Description	n=
British Association of Stroke Physicians (BASP)	Doctors	Among their objectives, BASP have set out to improve and assure doctors' training in stroke medicine and to promote and disseminate stroke research across the UK. Web: www.basp.ac.uk/	60
Scottish Stroke Research Network (SSRN)	Doctors and Nurses	Among their objectives is to expand and assure high quality research in stroke medicine throughout Scotland. The network supports researchers in setting up and running stroke studies in Scotland. Web: www.ssrn.org.uk/	43
Scottish Stroke Nurses Forum (SSNF)	Nurses	Among their objective, the SSNF has set out to promote the work of stroke nurses, share and develop knowledge and expertise, promote research in the field and incorporate evidence into practice. Web: www.ssnf.scot/	114

Lohr (2008) discussed geographical coverage in surveys, emphasising the importance of ensuring complete coverage of the target population so as to minimise potential bias in the results. It was impossible to capture the views of every clinician working in stroke units in Scotland as email addresses are not in the public domain, and particularly foundation year doctors, who tend to frequently move between training placements (National Health Service 2014). Thus, they may not have chosen to subscribe to a professional association at this point in their career progression. Another factor related to coverage relates to nurses' subscription to the SSNF: it is assumed that a number of nurses working in stroke across Scotland have not registered with the SSNF, since the forum's stated strategy is to increase membership among Scottish stroke nurses (Scottish Stroke Nurses Forum 2011). It is therefore assumed that a number of practicing stroke nurses were not reached. Lohr (2008) stipulated that although it is impossible to accurately assess coverage in a survey, a prerequisite for good coverage in web based surveys is an up-to-date list of email addresses of participants. It was decided that in order to improve the accuracy of calculation of coverage and response rate, respondents would not be asked to disseminate the email invitation among their colleagues, however it is impossible to determine whether this may have happened. Distribution lists were provided by the administrators of both the SSRN and SSNF, however, the researcher was only able to approached SSNF members by group email directly, as the protocol of research dissemination for BASP and the SSRN stipulated that the administrators of the database are the only persons to contact members directly. The process of recruitment took place during the summer of 2012, with an overall sample of 217 clinicians contacted (Table 14, p.168). The author cross-checked the complete distribution lists of SSRN and SSNF and removed duplicate names and email addresses before contacting SSNF members. The BASP database was not shared

with the author therefore it was not possible to check for duplicates with other databases.

Email reminders are considered an important factor in maximising response rates in online surveys, however, there is no mention of a recommended number of reminders to be sent (Nulty 2008). A judgement had to be made regarding this factor, as Buchanan and Hvizdak (2009) warned that multiple reminders may be perceived as harassment. It was therefore decided that no more than two email reminders were to be sent following the initial invitation. This was the case for SSRN and SSNF members, as for members of BASP, only one email invitation was permitted. The initial invitations were sent by email to all three participating associations in July 2012. Reminders were sent to SSRN and SSNF members two weeks apart, in August 2012 (see appendix 5.4).

5.3 Data analysis

This descriptive survey collected two types of data: quantitative, for closed questions and qualitative for open questions inviting free text comments (Brace 2008). Thus, a combination of analytic methods was required: quantitative and content analysis.

5.3.1 Quantitative analysis

Descriptive statistics were used to analyse the frequencies and percentages arising from the data (Buckingham and Saunders 2004). The BoS tool offers a simple method of analysing the data, due to the simplicity of the questions and responses this was deemed to be sufficient for the analysis.

5.3.2 Content analysis

Content analysis methodology was used for the analysis of responses to open ended questions (Cole 1998): the researcher read and re-read the words used in the responses and then classified these into small sets of categories of shared meaning. The codes were counted to determine how frequently they appear within the text responses and patterns relating to the key themes emerged (Elo and Kyngas 2008, Morgan 1993, Krippendorf 2004).

5.3.3 Hospital size and number of stroke beds

Question 2 of the survey requested respondents to select the name of the hospital they work in. This question was used in conjunction with data on size of the stroke unit and number of stroke beds per hospital. These data were obtained from Information Service Division Scotland (ISD Scotland 2010), which at the time of conducting this research, was the most up-to-date version of this document available to the public.

5.4 Results

This section presents the findings of the survey. The data are presented in accordance with the order of appearance of the questions on the survey itself. Due to the decision to conduct a descriptive survey, descriptive statistics are used to summarise the findings.

5.4.1 Questions 1 and 2: Participant characteristics

A total of 65 (30% overall response rate) responses were logged during the period of data collection. A total of 36/90 (40%) of doctors replied, 29/127 (23%) of nurses replied. The profession and grade of respondents are summarised in Table 15. As

for area of practice, most participants stated they worked in a specialised stroke unit, most participants also indicated that they worked in relatively large units (receiving between 250-500 stroke patients each year). Table 16 outlines the details of these data.

Table 15: Profession and grade of participants

Participants	**n=65 (%)**
Profession	
Doctors	36 (53.7)
Nurses	29 (43.3)
Grade	
Consultant	24 (36.9)
Senior Trainees (doctors)	12 (18.4)
Senior nurse (band 7 and above)	14 (21.5)
Main grade nurse (band 6 and below)	15 (23.0)

Table 16: Participants' main area of practice

Area of Practice	**n=65 (%)**
Specialist stroke unit	47 (72.3)
General hospital ward	8 (12.3)
Both of the above	10 (15.4)
N of stroke patients admitted to respondents' workplace each year (ISD Scotland 2010)**:**	
>500	15 (23)
250-500	39 (60)
100-250	7 (10.7)
<100	4 (6.1)

5.4.2 Questions 3 to 5: Screening for delirium

In response to the question: "does your ward have a policy on screening new patients for delirium?" 21/65 (32%) respondents selected 'yes', 35 respondents (53.5%) replied 'no' and 9 respondents (14%) responded 'unsure'. In response to the question "do you routinely screen for delirium on admitting new patients to the ward" 31 (48%) selected "yes" and 34 (52%) selected "no". The following question: "Do you

screen patients for delirium on a regular basis during admission?" yielded the same result, 31 (48%) selected "yes" and 34 (52%) selected "no". Of the 31 respondents who selected "yes", 25 (81%) reported screening "as the need arises" and two (6.5%) selected "once weekly". Table 17 highlights these results as well as the differences between doctors' and nurses' responses, thus percentages refer to the number for each staff group rather than the overall number of respondents (n=65).

Table 17: Doctors' and nurses' practice of screening for delirium

Question	Doctors (n=36)	Nurses (n=29)
3. Does your ward have a policy on screening new patients for delirium?		
Yes	13 (36.1%)	8 (27.5%)
No	15 (41.6%)	17 (58.6%)
Not sure	2 (5.5%)	4 (13.8%)
4. Do you routinely screen for delirium on admitting new patients to the ward?		
Yes	22 (61.1%)	9 (31%)
No	14 (38.8%)	20 (69%)
5. Do you screen patients for delirium on a regular basis during admission?		
Yes	19 (52.7%)	12 (41.3%)
No	17 (47.2%)	17 (58.6%)
5.a. Please state the most common frequency of screening patients on the ward		
As the need arises	15 (41.6%)	10 (34.5%)
Once weekly	1 (2.7%)	1 (3.4%)
Twice weekly	0	0
Fortnightly	0	0
Other	3 (8.3%)	1 (3.4%)

Four (13%) respondents selected the option "other" in reply to question 5a, the text explanations were examined and cross-checked against profession and grade: one consultant physician responded that screening occurred daily, a further consultant physician reported screening "routinely on ward rounds but also if there is

concern by nursing or therapy staff". Another doctor, a senior trainee, stated that screening occurred "briefly at each ward round". Only one nurse (consultant specialist) stated that screening occurred on admission (which answers the original question 4 "do you routinely screen for delirium on admitting new patients to the ward?").

5.4.3 Question 6: Diagnostic methods

In response to the question: "How do you normally diagnose delirium in stroke patients?" 28 respondents (43%) reported applying their clinical judgement, two respondents (3%) reported using a standardised tool and the remaining respondents reported combining clinical judgement with the application of a standardised tool (n=21, 32.3%). Two respondents selected "other", one reported using: "amt (Abbreviated Mental Test) and urine testing, observations" and the other reported using the CAM (Inouye et al. 1990) to diagnose delirium. 12 respondents (18.5%), all of whom were nurses of all grades, stated that they do not diagnose delirium in their practice and for question 6b, all of which selected the option "I have not been trained to use a standardised tool". Table 18 (p.175) summarises these results, percentages refer to the n= for each staff group rather than the overall n=65.

No responses were logged for questions 6a on delirium diagnosis (see appendix 5.1). Once all the responses were logged and the analysis commenced, this matter was investigated. It appeared that the way the questions were routed online meant that none of the respondents were able to see this question as the researcher had set up the routing of questions 6a incorrectly. This matter will be discussed further in section 5.5.4 of the discussion.

5.4.4 Question 7: Choice of bedside tool

Table 18 outlines the structure of the questions relating to the choice of diagnostic tool. Free text comments made in response to the question on clinicians' choice of diagnostic tool revealed that six (9%) respondents used the 4AT (Bellelli et al. 2014a), this tool was not listed as one of the main options as the survey predates the formal publication of this tool (Healthcare Improvement Scotland 2014). Four respondents reported using either the Abbreviated Mental Test (AMT)(Hodkinson 1972) or the MMSE (Folstein et al. 1975).

Table 18: Questions regarding diagnostic practices and tools used

Question	**Doctors n=36**	**Nurses n=29**
6. How do you normally diagnose delirium in stroke patients?		
Standardised tool	1 (2.7%)	1(3.4%)
Clinical judgement	22 (61%)	6 (20.6%)
Both the above	13 (36.1%)	8 (27.5%)
I do not diagnose delirium in my practice	0	12 (41.3%)
Other	0	2 (6.8%)
7. If you use a tool to diagnose or screen for delirium in stroke patients please indicate which tool you use:		
CAM	11 (30%)	7 (24.1%)
CAM-ICU	2 (5.5%)	0
DRS	0	0
Delirium Symptom Interview	1 (2.7%)	0
Organic Brain Syndrome Scale	0	0
Other	8 (22.2%)	4 (13.7%)
No response	14 (38.8%)	18 (62%)

5.4.5 Question 8: Suitability of the bedside tool in stroke patients

Respondents were asked "Do you think the tool you use is suitable for a stroke population?". A total of 52 (80%) of the 65 respondents answered this question.

Seven respondents selected “yes” (13%), 16 respondents selected “no” (31%) and the remaining 29 selected “not sure” (56%).

Figure 8 cross-references those who selected their tool of choice with clinicians’ opinion regarding suitability for stroke patients. 15 (23%) participants gave free text comments: The majority (53%, n=8) of comments related to the difficulty using a generic screening tool with persons who experience communication difficulties such as aphasia. Four respondents questioned the validity of the tool in a stroke population and discussed in particular cognitive or “neurological abnormalities” arising from the stroke. One respondent felt the tool they used had “reasonable face validity” and one further respondent advocated the use of the CAM (Inouye et al. 1990).

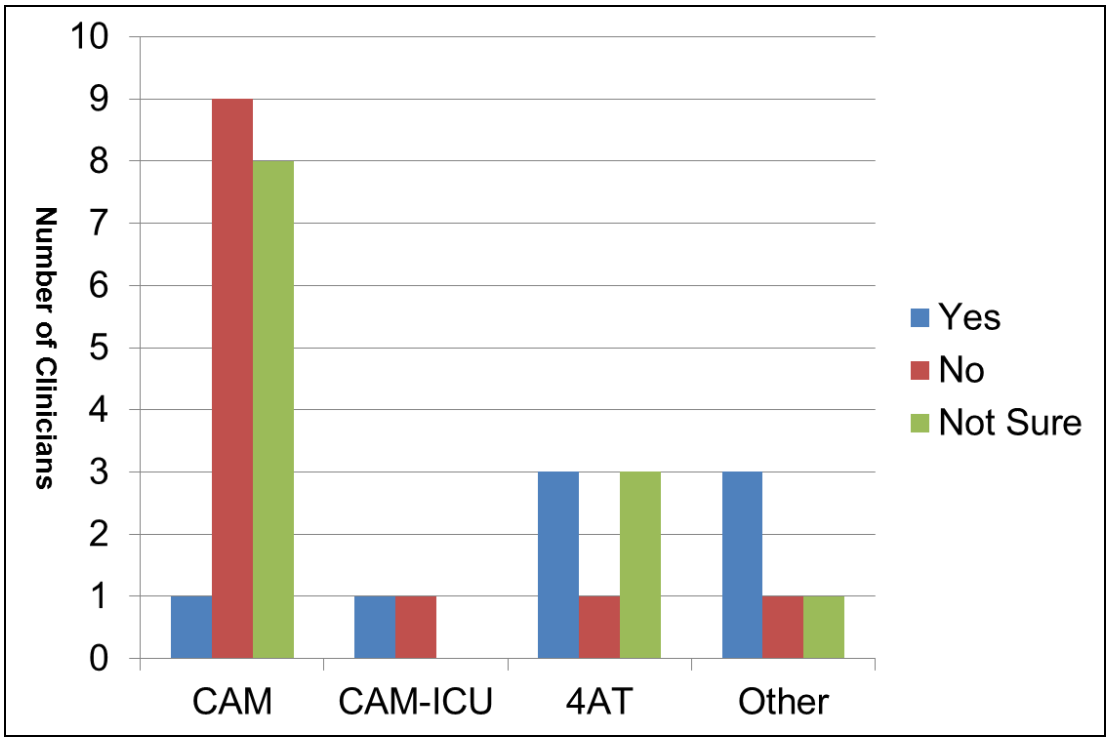

Figure 8: "Is the tool you use suitable for use in stroke patients?"

5.5 Discussion

The survey results highlight a number of key findings that illuminate previously unknown delirium diagnostic and screening practice in Scottish stroke services. This section will discuss the results of the survey, drawing, where possible, on relevant literature from the published surveys of delirium practice across a variety of medical settings.

5.5.1 Routine screening for delirium

Responses indicated that most stroke units either did not have a screening policy for the identification of delirium in acute stroke, or the clinicians were unaware of such policy. Almost half of respondents to this survey stated that they did not routinely screen for delirium in actue stroke. Both these points also revealed interesting differences between doctors and nurses: more doctors reported they were aware of a policy of screening new patients, and that they screened for delirium as a matter of routine (Table 17, p.173). Whilst it was not possible to confirm these findings with similar findings in the stroke literature, some could be related to a variety of studies based in other hospital settings: Ely et al. (2004), in a large multidisciplinary survey of 912 clinicians working in ICU found that the majority of those surveyed did not screen for delirium routinely, despite the belief that the literature supported routine screening for delirium. Patel et al. (2009) surveyed 1384 clinicians (mainly nurses and doctors) across a wide variety of hospital settings and found that only around half of respondents routinely screened for delirium in their patients. Flagg et al. (2010) surveyed nurses in the ICU and medical–surgical settings (n=61) in the USA to establish that only a minority (ten respndents) reported routinely screening for delirium in their practice. Steen et al. (2013) surveyed 110 clinical heads of geriatric and medical services in Belgium to establish that only one quarter or respondents reported

to have a policy on delirium identification and management and less than a quarter of respondents (21%) reported routinely screening for delirium in patients in their care. Selim and Ely (2016) surveyed 215 clinicians working in the ICU setting in Egypt, finding that only 26% of respondents screened routinely for delirium in their patients, none of the respondents reported following delirium practice protocols. It therefore seems that lack of routine screening and lack of awareness or existence of practice protocols around delirium identification is a matter that affects a variety of healthcare settings across a number of countries.

5.5.2 Method of delirium diagnosis

This study highlighted that the diagnosis of delirium was made mainly by doctors, in most cases by means of clinical judgement, and only in around a third of cases was this combined with the use of a standardised tool. This issue of relying on clinical judgement to arrive at a delirium diagnosis is confirmed in a survey across a wide variety of non-critical acute care settings by Neufeld et al. (2014), who reported that nearly all of the respondents used their clinical judgement, on occasion combining this with a bedside tool. Similarly, Forsgren and Eriksson (2010), in a national survey of Swedish ICU head nurses, reported that the majority of ICUs diagnosed delirium by observing the symptoms, and only one unit used a standardised tool. This finding is confirmed to some extent by a survey of acute hospital settings throughout NHS Scotland in which Hendry (2017) identified that around a third of clinicians reported using clinical judgement alone or no diagnostic criteria in the process of delirium diagnosis.

This survey found that in Scottish stroke units there did not seem to be a consistent approach to the diagnosis of delirium regarding frequency and use of standardised tools. The inconsistency in use of standardised tools to identify delirium

is widely reported in the literature: MacSweeney et al. (2010), conducted a UK wide survey of doctors' delirium management in the intensive care setting and found that 75% (n=681) of respondents did not use a screening tool for the identification of delirium in that setting. Salluh et al. (2009) conducted a survey of Brazillian critical care physicians and found that less than 15% of respondents used validated delirium assessment tools. An interesting finding from a survey of European delirium experts, 67% of whom were doctors, revealed that only 26% of those surveyed (n=200) used a validated scale to assess for delirium (Morandi et al. 2013). At the other end of the expertise hierarchy, a finding from a survey of junior doctors working in a variety of medical settings in the UK revealed that the fundamental cause of under-recognition and under treatment of delirium lies in the lack of knowledge of the diagnostic criteria and standardised screening tools (Davis and MacLullich 2009). These finding were later confirmed in a repeated survey, using the same questions distributed across the UK to 1,215 participants (Jenkin et al. 2016). Jenkin et al. (2016) found that while there was an increase in knowledge of delirium prevalence, the familiarity with diagnostic criteria and use of screening tools remained poor.

A further noteworthy point from the survey is that 41% (n=12) of nurses who responded to this survey claimed they do not diagnose delirium in their practice, citing lack of training to use a standardised tool as the main reason. This finding is supported by Flagg et al. (2010), who surveyed nurses across intensive care and general medical and surgical units, finding that nurses have only modest confidence levels in identifying delirium in clinical practice. Devlin et al. (2008) surveyed ICU nurses (n=331) and found 47% of nurses routinely assessed for delirium, and interestingly, only 12% of respondents reported receiving training in delirium assessment. In a review of the literature, Wells (2012) attempted to identify the reasons why Australian ICU nurses do not perform delirium assessments routinely. Lack of adequate knowledge about the condition, its manifestations and impact on

patients were cited as the main barrier to timely, accurate identification of the condition among nurses (Wells 2012). Similarly, Sinvani et al. (2016) also reported upon the differences between doctors and nurses in terms of the knowledge underpinning their practice of delirium identification. They found that lack of knowledge of delirium symptoms as well as the infrequent utilisation of screening tools were barriers to effective recognition of the condition (Sinvani et al. 2016).

5.5.3 Suitability of bedside tools for a stroke population

Cognitive and communication difficulties resultant from stroke are the main barrier for use of standardised delirium bedside tools (McManus et al. 2007, Mitasova et al. 2012, Neto and Slooter 2012). Indeed, some of the survey respondents reported difficulties in using delirium bedside tools with stroke patients because of aphasia. The results of the systematic review described in chapter IV of this thesis confirm this by highlighting that a number of studies have excluded patients with aphasia from their cohorts for the same reason (Carin-Levy et al. 2012). Within this survey, a small number of respondents reported using delirium bedside tools, all of which, at the time of conducting the survey, had not been validated for the use in acute stroke: Four respondents reported using either the MMSE or the AMT to detect delirium: Some studies found a degree of usefulness in detecting cognitive changes, which might be due to delirium, using the AMT (Hodkinson 1972) or the MMSE (Folstein et al. 1975) (McManus et al. 2009b, O'Keeffe et al. 2005, Ni Chonchubhair et al. 1995). However, these are not delirium specific bedside tools (Levkoff et al. 1991, Hall et al. 2012, Ely et al. 2004) and have reported restrictions when used in acute stroke (Nys et al. 2005). Six respondents reported using the 4AT (Bellelli et al. 2014a), a tool which at the time of the survey was relatively new, but has since attracted substantial attention and has now become the preferred method of screening for delirium across hospital settings

in NHS Scotland (Healthcare Improvement Scotland 2014). Since conducting the survey, the 4AT has also been validated for use in stroke patients (Lees et al. 2013, Kutlubaev et al. 2016, Infante et al. 2017). Two respondents reported using the CAM-ICU (Ely et al. 2001a). Similar to the 4AT, at the time of conducting the survey, the psychometric properties of this tool as used with stroke patients had not yet been published (Mitasova et al. 2012). It is not known whether the publication of these validation studies (Mitasova et al. 2012, Lees et al. 2013, Kutlubaev et al. 2016, Infante et al. 2017) would have an impact on the number of clinicians choosing to use either the CAM-ICU or the 4AT in a stroke setting. It likely that following the rolling out of the "Think Delirium" initiative from Healthcare Improvement Scotland (2014), that the 4AT (Bellelli et al. 2014) will be the tool of choice in many clinical settings across NHS Scotland.

5.5.4 Strengths and limitations of this study

Several issues affected the quality of this survey. In the intervening years between the completion of the survey and the writing up of the thesis, deep reflection on the limitations this survey had taken place. These are addressed in the subsections below.

5.5.4.1 Response rate

The response rate for this survey was 30%, a rate lower than a number of surveys (both online and traditional) of delirium identification published within the last few years (Davis and MacLullich 2009, Forsgren and Eriksson 2010, Patel et al. 2009, Salluh et al. 2009, Jenkin et al. 2016). The response rate seems to be influenced by the noteable difference between doctors and nurses responses to the invitation to participate: only 23% of the nurses approached actually completed the survey. Eley et al. (2009) identified that nurses have poor access to computers while in the ward

environment because of the time pressures associated with the demands of their work. This may be a reason why the response rate from the nurses in this survey was comparatively low. Another interesting point to add is that Lawrence et al. (2009) carried out a postal survey of the same population of SSNF nurses and achieved a considerably higher response rate (54.8%). It is possible that a higher response rate would have been achieved if a postal survey had been utilised instead of, or in conjunction with the web-survey. However, it is worth noting that according to Fan and Yan (2010), it is not clear whether delivering mixed-mode surveys increases response rates. This notwithstanding, the response rate was moderate but consistent with the literature on online surveys return rates (Fan and Yan 2010, Cook et al. 2000).

5.5.4.2 Missing data

Sanchez-Fernandez et al. (2012) offered a different perspective on the success of a survey, they argued that perhaps response rate is not the most important indicator of success, but rather the quality of the responses, and the rates of missing data which should be used as an indicator of the success of a survey. Reflecting upon this, while the quality of the data is acceptable, a problem with missing data affected question 6 (the diagnosis of delirium) as no responses were logged for question 6a (appendix 5.1). The author had set up the web based survey in a way that meant that question 6 routed according to the selections respondents made. This was in an attempt to simplify the survey and reduce the burden on participants, a strategy reportedly important in increasing response rates in online surveys (Dillman and Smyth 2007). This factor was not identified in the piloting of the survey since it was not possible to carry out the pilot using the BoS tool itself: the tool is set up in such a way that once a survey is launched, the researcher cannot change the questions within. This meant that in order for the pilot to be possible, the questions had to be transcribed into paper form. This was done, making sure that the paper

copy was as close as possible to the electronic version, however, the pilot participants were not able to comment on any aspect of the software itself, which would have been useful in flagging up unforeseen difficulties and given the researcher the opportunity to test how procedures would work in practice (Dillman et al. 2009). The result was that data were missing from the survey – a matter which would have been avoided had the survey been piloted in the web-based form rather than paper form.

5.5.4.3 Generalisability

Several issues affect the generalisability of the findings of this survey, these are largely due to decisions taken at the time of writing the study protocol in 2011. While these decisions were taken by consensus within the team of supervisors and external advisers working with the researcher, in retrospect, some of these were misguided. The recruitment procedures were affected by sampling error as the coordinators of the 12 stroke managed clinical networks in Scotland were missed off the list of clinicians to be approached at the time of recruitment. These networks could have potentially helped disseminate the invitation to participate in the survey to clinicians who did not belong to a special interest group. A further issue affecting coverage of the survey and therefore generalisability of the findings was the importance placed on calculating response rates accurately. According to Lynn (2008) response rate is an important indicator of the success of the survey in terms of representing the target population and should therefore always be included in the outcome data for the survey. This was key in the decision to choose a convenience approach to sampling as opposed to snowballing. Streeton et al. (2004) outlined the advantages and disadvantages of snowballing recruitment in surveys, one of the disadvantages is the difficulty in verifying respondents' eligibility to participate. An important advantage, according to Streeton et al. (2004), is in reaching populations that are difficult to approach, an issue that is clearly a concern in this survey as

clinicians' email addresses are not in the public domain and particularly for junior doctors who may not be registered with any professional interest groups, snowballing the recruitment may well have enabled the researcher to reach these clinicians.

5.5.4.4 Participants

The decision to exclude AHPs from participating in the survey needs to be viewed in light of the era in which this survey was conducted. The survey was designed and distributed prior to the rolling out of the multidisciplinary 'Think Delirium' programme in Scotland (Healthcare Improvement Scotland 2014). In the time prior to this programme being rolled out, the multidisciplinary rapid assessment tool for the detection of delirium was not yet disseminated widely among clinicians, and the literature had limited reference to AHPs taking a role in delirium identification. In hindsight, it would have been interesting to include AHPs in the mix of professionals targeted to respond to this survey since it is likely to have revealed interesting data on professional roles in delirium recognition, a matter not previously discussed in the allied health literature. A further issue related to participants was the restriction of the survey to Scottish stroke units only rather than disseminating the survey throughout the UK. It is recognised that this decision had impacted on the ability to generalise the findings of the survey to health services in other parts of the UK. However, from the outset, the second and third strands of this programme of research were conceived to be restricted to NHS Scotland. This decision was taken in recognition of the potential to triangulate some of the findings (e.g. methods of delirium identification) for the purpose of complementarity, as consistent with the integrated mixed methods designs discussed in chapter 3 (section 3.4) of the thesis.

In summary, several adaptations of this survey would have allowed for the findings to be more representative of clinical practice, as well as greater potential for

the findings to be generalisable: less of an emphasis on calculating response rate would have freed the researcher to use snowball sampling in order to increase the sample size and potentially disseminate the survey to difficult-to-reach clinicians (Streeton et al. 2004). Including the coordinators of the stroke managed clinical networks as well as adapting the inclusion criteria to allow the inclusion of AHPs would have allowed for a more representative clinical picture to be revealed through the data gleaned from the survey. Finally, the piloting of the survey should have taken place online rather than on paper form. This would have identified the problems with the options to question 6 being routed incorrectly and potentially prevented the problem of missing data as discussed in section 5.4.3. Despite the limitations highlighted above, these data are of interest because this is, to the best of the author's knowledge, the first survey of diagnostic and screening practice in relation to delirium in acute stroke services in Scotland or indeed the rest of the UK.

5.7 Conclusions and implications for practice

This chapter details the second strand of the doctoral programme, an online survey of practice of delirium identification in the acute stroke setting in Scotland. Despite the limitations reflected upon in the sections above, this survey contributes to a growing body of knowledge on delirium identification in acute stroke patients. The findings of this survey suggest that in Scotland, at the time of data collection, no standardised guidelines regarding the identification of delirium in stroke patients existed. The survey also highlighted the inconsistent approach to the screening and diagnosis of delirium, echoing the results of the systematic review presented in chapter IV of this thesis, as the diagnostic processes of delirium described in the literature also seems to be inconsistent. It would therefore be beneficial for future practice guidelines in stroke care to incorporate information on delirium and perhaps

consider establishing a standardised way of identifying the condition in this population, who clearly possess some of the important risk factors for developing the condition. Given the impact of delirium upon the patient as well as the health service (Inouye et al. 2014), it is important to ensure that staff are provided with clear guidance on how to best identify this condition in acute stroke. Practice guidelines on delirium identification are likely to lead to an increase in the amount of correctly identified delirium cases. This in turn is likely to lead to better outcomes for these patients as well as the potential for cost benefits to the health service (National Institute for Clinical Excellence 2010).

The survey highlighted that there are differences in the practice of doctors and nurses when it comes to delirium identification in this setting. Based on the literature consulted in the discussion, this finding may relate to a difference in confidence in delirium identification between doctors and nurses, although confidence in delirium identification was not explicitly explored in this survey. The differences in approach to delirium identification between doctors and nurses working in the acute stroke setting raised a question regarding the response of various members of the multidisciplinary team to delirium in patients in their care. The next chapter of this thesis attempts to address this by exploring the perspectives of a variety of health professionals working in Scottish stroke units.

Chapter VI

Third Strand: Online Focus Groups

6.1 Introduction

This chapter discusses the third and final strand of data collection and analysis for this programme of research: a qualitative exploration of multidisciplinary clinicians' response to delirium in the acute stroke setting. The links with the findings detailed in chapter IV and V are drawn and justification for the chosen methodology and decisions taken is offered. The approach to the principles of Grounded Theory data collection and analysis are detailed as well as the ethical consideration and the approach to participant recruitment. The findings of this qualitative exploration are presented and discussed within the context of related sources of literature both from the acute stroke setting as well as related acute hospital environments.

6.1.1 Rationale and links with previous findings

Chapter IV and V of this thesis identified the frequency of incident delirium in acute stroke patients, the serious consequences of developing delirium after a stroke (Carin-Levy et al. 2012) and the practice of doctors and nurses when it comes to delirium identification. A key finding in chapter V was around the differences between doctors and nurses in the practice of delirium identification (Carin-Levy et al. 2013), a matter which is also reported in the literature from general acute settings: healthcare professionals responding to a suspected delirium differently, depending on their level of training; a reported lack of routine screening as well as the challenges of delirium identification (Rice et al. 2011, Ryan et al. 2013, Panitchote et al. 2015, Sinvani et al.

2016). This raises the question around the experiences of different healthcare professionals when it comes to working with a stroke patient exhibiting symptoms of delirium. A further concern raised by the literature is the reported negative attitudes that may exist towards patients with delirium (Neville 2008, Belanger and Ducharme 2011, Teodorczuk et al. 2013, Clissett et al. 2014), although these reports do not arise from literature in the field of stroke patient care, since no literature on the ways in which staff respond to a delirium in the acute stroke setting could be identified (appendix 2.1). Therefore, it is worth exploring whether these attitudes to patients with delirium exist in the acute stroke setting.

Given that the most effective means of managing a delirium is by adopting a multi-disciplinary approach to employ multi-component interventions (Health Improvement Scotland 2014, Hshieh et al. 2015, Abraha et al. 2015, Siddiqi et al. 2016) and given the serious consequences of developing a delirium in acute stroke (Carin-Levy et al. 2012, Shi et al. 2012, Melkas et al. 2012) it is important to explore how various members of the multidisciplinary stroke unit team respond to a suspected delirium. This would not only build on the knowledge that already exists from other areas of medicine but also establish whether similar approaches to delirium identification are apparent in the acute stroke setting.

6.1.2 Aims and epistemological approach

This study aimed to explore the subjective experience of doctors, nurses and allied health professionals (AHPs) working in an acute stroke unit. Taking a pragmatic epistemological approach to the doctoral programme as a whole (discussed in chapter III) enabled the researcher to choose the methods that work best for answering each research question within the programme (Johnson and Onwuegbuzie 2004). This study sought to identify a picture of what occurs in clinical practice, which

fits within a realist or positivist approach to knowledge production (Willig 2013, Urquhart 2013). Willig (2013) discussed the two approaches that exist within the realist approach: the direct, or naïve approach and the critical approach. The direct approach assumes that the data represent the reality of the phenomenon under investigation. The critical approach assumes that the data tell the researcher something about "the real world" but this cannot be taken at face value, rather, the data need to be interpreted in order to gain a full understanding of the phenomenon under investigation (Willig 2013). The broad aim of this study was to explore how various professionals make sense of a case presentation, which may or may not be a delirium. The 'phenomenon' therefore is complex as it relies on a hypothetical response, not an active observation of the response of staff members. With this in mind, it was felt that a critical realist approach was most suited: the researcher wished to gain an idea of what happens in the real world, but due to the complexity of the phenomenon under investigation, the approach to interpretation of the data generated needed to be critical rather than naïve (Willig 2013).

The overall aim of the present study was to explore the perspectives of stroke unit staff working with patients who may exhibit the symptoms of delirium. To pursue this aim, the study drew upon recognised principles of Grounded Theory (GT), an approach which has the flexibility to work in either a positivist or interpretivist paradigm (Urquhart 2013, Charmaz 2014). Willig (2013) stressed that within GT methodology, it is important that the research questions are framed without making assumptions about the phenomenon under investigation. Sbaraini et al. (2011) suggested that in GT research it is important to set aims which are as open as possible so that the researcher can learn from the participants about the phenomenon. Principles of GT were therefore especially useful in exploring the subjective experiences of stroke unit staff interacting with patients who may or may not be experiencing delirium. The specific objectives were to explore the following two questions:

- How do health professionals make sense of the symptoms of delirium as they may manifest in a stroke patient?
- How do health professionals respond when they come across a patient who may be experiencing delirium following a stroke?

6.2 Methods

This section provides a detailed account of the methods employed in this study. The overarching approach of GT is discussed as the method used to guide the analysis in addition to providing a description of the process of data generation, participant recruitment and the ethical principles that were followed. In the interest of presenting a coherent picture, the process of recruitment as well as the final sample and make-up of the discussion groups are discussed within this section, consistent with the recommendations for writing up the methodology section of qualitative research (White et al. 2014).

6.2.1 A Grounded Theory approach

Grounded Theory emerged in pioneering work by Glaser and Strauss (1967), the premise of the approach was to discover theory from data systematically obtained in social research. Generating theory that is grounded in qualitative data would allow researchers to offer theory about social phenomena which quantitative data cannot explain in full (Glaser and Strauss 1967, Bryant and Charmaz 2007, Urquhart 2013). In their seminal text, Glaser and Strauss (1967) discussed the credibility of grounded theory as a rigorous and structured approach which legitimises qualitative research by holding an equivalent status to quantitative work. The main characteristics of GT are that the theory is discovered from the data by the process of constant comparison,

and theoretical sampling (Glaser and Strauss 1967). Urquhart (2013) interpreted these characteristics as follows: constant comparison involves all parts of the data being compared with all concepts and constructs in order to enrich an existing theory or generate new theory. Theoretical sampling involves examining the data in order to determine how and where to continue sampling, decisions which are taken on theoretical grounds (Urquhart 2013).

Kenny and Fourie (2014) provided an historical account of the emergence of several versions of GT since its conception, stating that Glaser and Strauss deviated in their views of what GT constitutes as a methodology, essentially resulting in a split between the two. There are various approaches to GT methodology described in the literature: 'Glaserian' or classic GT in which the emphasis is on theory emerging from the data and openness to theory emerging should include abstaining from the literature prior to the study taking place (Kenny and Fourie 2014). Straussian GT, published by Strauss and Corbin (1990) incorporates some deductive analysis, acknowledging the role of existing theories and knowledge in sensitising the researcher (Willig 2013). This version challenges the abstinence from literature prior to embarking on the study (Kenny and Fourie 2014), an aspect which was one of the key features of Glaser and Strauss' (1967) original ideas around GT. Charmaz's constructivist GT is more flexible than the Glassarian and Staussian versions of GT and acknowledges the researcher's position in constructing, rather than "discovering" the theory (Kenny and Fourie 2014).

Urquhart (2013) stressed that with the passage of time, GT has evolved to become more of an approach to data analysis as opposed to the generation of theory. This fits well with the way in which this study was conceptualised: forming part of a three strand, mixed methods programme of research, this study was intended as a grounded analysis, drawing inspiration from the principles of GT as opposed to a complete and comprehensive GT investigation. As such, one of the key features of

GT methodology, theoretical sampling, was not carried out in this study. This decision was taken since there was no intention to generate theory, rather to explore the themes emanating from the data by employing methods which are based on the principles of Charmazian, constructivist GT (Charmaz 2014), these are described in detail in section 6.3.

6.2.2 Data collection

Willig (2013) discussed the importance of selecting the most appropriate methods of data collection in order to address the research questions. Willig (2013) reviewed the various qualitative approaches to data collection, highlighting the ways in which the various methods fit within the different qualitative methodologies. Within a GT approach, the options for collecting data are interviews, focus groups and participant observations (Urquhart 2013, Lewis and McNaughton Nicolls 2014). According to Lewis and McNaughton Nicholls (2014) the choice between these approaches should be determined by the nature of the data sought, the subject area and the potential participant group. Willig (2013) stated that the popularity of focus group research has steadily risen over the years as an alternative to semi-structured interviews. This is largely due to the idea that the group process can contribute to the richness of the data generated, when group members respond to issues raised by others (Willig 2013). A further strength of focus groups as a means of data collection, according to Willig (2013), is in the fact that a group process is less artificial than a one-to-one interview, suggesting that the data generated by means of a focus group have a higher ecological validity. In order to explore the realities of practice without engaging in fieldwork and participant observations, it was decided that focus groups would be the most appropriate means of generating data for this study. The next

section outlines the approach to data collection chosen for this study whilst justifying the various decisions and choices made in the process.

6.2.2.1 Online focus groups

Willig (2013) acknowledged the emergence of the internet as a means of collecting data in qualitative research. Peacock et al. (2009) defined online focus groups as "a selected group of individuals who have volunteered to participate in a moderated, structured online discussion in order to explore a particular topic for the purpose of research" (p.119). Kenny (2005) cited a number of advantages for conducting online focus groups as opposed to the traditional face-to-face method. The practical advantages suggested are reduced cost, ability to consult participants from a variety of geographical locations and a longer time frame in which the group takes place, thus richer data may be generated over time, rather than one or two face-to-face sessions. Moloney et al. (2003) discussed the advantages of online focus groups, citing increased convenience, which increases likelihood of recruiting participants to the study. Moloney et al. (2003) also discussed the increased participant comfort in the anonymous interaction enabled online. Willig (2013) reiterated this as she considered the online focus group to allow one to contribute to research from what is likely to be a safe space. This was regarded as extremely relevant to this study, as it was considered likely that some members of staff would not feel comfortable in exposing lack of knowledge or certain attitudes in a face-to-face interaction. Sweet (2001) cited another advantage of online focus groups, which relates to the generation of transcripts, as the data are available to be analysed as soon as participants contribute to the discussion (thus cutting the necessity of transcribing audiotapes). Mann and Stewart (2000) added that online methods reduce transcription bias and facilitate an easier handling of data. Sweet (2001) also discussed the importance of moderating such groups, where the researcher has a

key role in generating fruitful discussions, knowing when to step in with further questions, and being aware when to allow participants to discuss matters among themselves. Rezabek (2000) raised two obvious disadvantages to online focus group research: one related to the lack of facial expressions to aid communication, and the other, the loss of some of the complexity that comes with verbal, face-to-face communication, including the differing dynamics of communication in an online platform. Additionally, Peacock et al. (2009) discussed the potential lack of personal contact between the researcher and participants, where the researcher in online discussion groups would find it more difficult to build a rapport with the participants, in comparison to face-to-face groups. Albeit, Tates et al. (2009) reassured that the quantity and the quality of the data generated by online focus groups is comparable to traditional focus groups.

In summary, it is believed that the many relevant advantages such as the ability to unite geographically separate participants, the anonymity and safety afforded and the practical advantages related to transcription and cost (Sweet 2001, Moloney et al. 2003, Kenny et al. 2005, Willig 2013) outweighed any potential disadvantages, making this choice of approach suitable for this study.

A decision had to be taken regarding synchronous versus asynchronous focus groups: When using asynchronous focus groups, participants can log on at any time, read each other's comments and post their own response, whereas synchronous focus groups happen when all participants are logged on at the same time, participating in 'real-time' discussions (Tates et al. 2009). The synchronous approach to conducting online focus groups came under consideration for the design of this study, however, the requirement to have all participants logged into the online platform at the same time would have made data collection much more complex due to staff working patterns (part time working and shift work). Additionally, synchronous focus groups would have inevitably resulted in less and possibly more superficial discussion

from the participants, simply due to the practicalities of having a set time for the discussions (Rezabek 2000). Indeed, Cartwright (2000) found that participants valued being able to read other people's posts before making their own comments as this meant they were reflecting more deeply upon the content of their own contributions. Williams et al. (2012) added that there is a distinct advantage in allowing participants time to carefully consider their response as a factor which contributes to the quality of the data collected. Finally, Walker (2013b) cited an important advantage of asynchronous groups in allowing the participants to contribute outside of working hours (Walker 2013b). This certainly was an important consideration which came into play since the participants were clinicians working in busy hospital environments (Peacock et al. 2009). The decision was therefore taken to conduct asynchronous online focus groups, which also carried a methodological advantage in enabling the researcher to begin to analyse the data while they were being generated through the discussion boards, a matter which is congruent with principles of GT research (Charmaz 1995).

6.2.2.2 Study platform

Peacock et al. (2009) described the use of a virtual learning environment (VLE) in support of qualitative online research, highlighting the importance of the online environment being user-friendly and conducive to generating meaningful discussion among participants. Based on the recommendation of the University's Technology Enhanced Learning team, a VLE hosted by Blackboard® called CourseSites was utilised. The advantage of this VLE was that participants were able to choose their own pseudonym and the discussion boards utilised a very similar method of operation to the one the researcher was very familiar with from using Blackboard Learn® in teaching activities. Peacock et al. (2009) set out a number of recommendations of ways to potentially enhance participant engagement with online

focus groups. These include welcome messages, provision of sufficient instructions of use and creating discussion threads within the VLE which would elicit responses. Despite Peacock et al. (2009) not couching this advice in evidence of its effectiveness, it stood to reason that this approach constituted good practice, based on Peacock et al.'s (2009) reflections on the experience of facilitating online focus groups for the purpose of research, this advice was therefore followed. The study VLE therefore had its own home-page, within which participants could access the following areas by clicking on tabs: the discussions area, specific help-pages put together for the study, a Blackboard® generic help site, and information about the study, which also contained material on reflection on learning which were considered to be of use for all participants when they have completed the process of the study. Figure 9 shows the participant's view of the home-page.

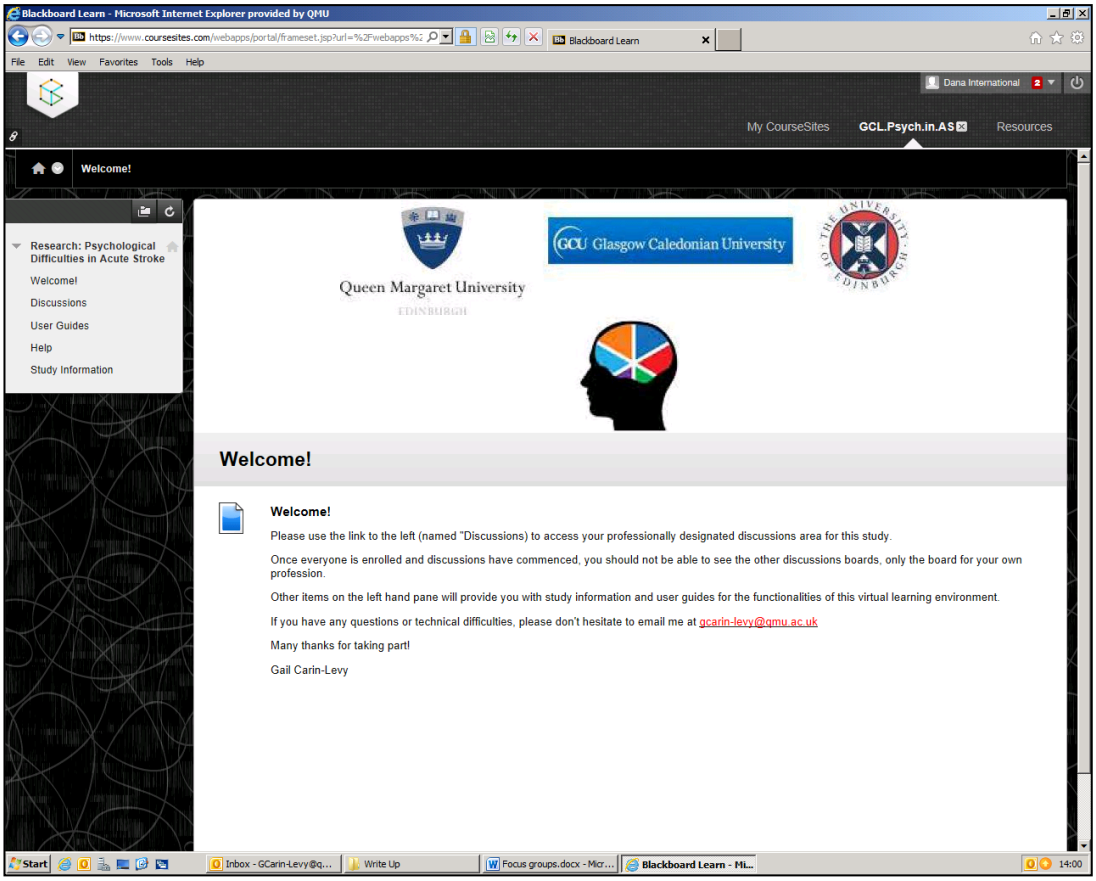

Figure 9: The study home page

6.2.2.3 Use of case vignettes

Scenarios are useful in creating a narrative with which the participants may identify, in addition to bringing the subject matter to life (Pommeranz et al. 2012). Bloor et al. (2001), considered vignettes as "focusing exercises", which are presented to participants in order to develop discussion. Furthermore, Jenkins et al. (2012) described a method of utilising vignettes in qualitative studies where the researcher releases information in stages and poses questions that are based on the information released at each stage. Spalding and Phillips (2007) suggested that the use of vignettes stimulates a deeper reflection on practice, which may eventually lead to an enhancement of one's practice following the process of participating in such a study. Hughes and Huby (2002) regarded vignettes as a useful tool, which enables the researcher to explore participants' understanding and attitudes towards a real-life situation. According to Hughes and Huby (2002), an important advantage of this method is that it reduces the likelihood of participants responding in a "desirable" way (i.e., what they perceived to be the desirable response to a question or trigger) as they will be responding to a hypothetical scenario rather than drawing entirely from their own experiences. A potential pitfall to the use of vignettes to support discussion may be in the language used: Bloor et al. (2001) suggested that in focus group discussions the researcher may choose to have vignettes purposefully unclear or somewhat vague so that they stimulate rich discussion and debate. There is a potential danger that the vignette may be too vague and the details misunderstood, as Hughes and Huby (2002) pointed out, for this type of trigger to be successful, the language may need to be adapted when used with different groups of participants. This point was considered carefully when constructing the scenarios with the view that if necessary, the language could be adapted to meet the requirements of the

different professional groups participating in the study. Spalding and Phillips (2007) warned that because vignettes are constructed by their author, they cannot represent an absolute truth and warned of the danger of compromised authenticity when they are not verified by a person with lived experience of the condition described. Another potential limitation of the use of vignettes was highlighted by Hughes and Huby (2002), who stated that by their nature, vignettes are selective and do not accurately mirror the complex realities of clinical practice. Due to this, Hughes and Huby (2002) argued that the analysis of data generated by use of vignettes needs to be more cautious as it cannot be easily generalised. Despite some of these limitations, vignettes have been used successfully in a variety of methodological designs (Bloor et al. 2001, Hughes and Huby 2002, Lee and Tsai 2011, Jackson et al. 2015). Most relevant to this investigation are Fick et al.'s (2013) and McCrow et al.'s (2014) studies. Both used case vignettes of delirium superimposed on dementia to explore delirium knowledge and recognition in nurses. Fick et al. (2013) reported the process of standardising the case vignettes depicting a delirium superimposed on dementia prior to conducting their study. All of these cases were carefully read and adapted to be suitable for use in a stroke environment. For the present study, two vignettes of hypothetical case scenarios were developed based on the Fick et al. (2013) models drawing on the researcher's clinical experience working as an AHP in a stroke unit to ensure they would be relevant to this setting. Based on Jenkins et al.'s (2012) model of use of vignettes in stages, it was decided to construct the vignettes as a brief scenario which unfolds over a number of weeks, with trigger questions to be asked following each new piece of information released. This model also made sense clinically, in an attempt to emulate what may happen in practice, when patients develop a delirium over the course of a few days. The scenarios were based on real clinical manifestations of patients with a diagnosis of delirium following a stroke: the first depicting a predominantly hypoactive delirium, followed by the second, depicting

a hyperactive delirium. The baseline information for both case scenarios was the same. The vignettes and the schedule of questions were circulated among the supervisory team, following this, some minor changes in the details of the case presentations were made. Once the cases were approved by the team, they were not piloted formally, but rather sent to a consultant stroke physician and a consultant in liaison psychiatry who also suggested some minor changes in language, mainly around accuracy of the description of symptoms of the hypoactive delirium case. The vignettes were then approved for use, the final version can be seen in appendix 6.1.

6.2.2.4 Participant engagement

Tates et al. (2009) described the role of the moderator in establishing an environment to foster positive, open communication to generate rich data. Part of the role of moderator is to frequently monitor the online discussion boards, to ask questions for clarification and to encourage group discussion (Tates et al. 2009). A further approach to encourage participation comes from Moloney et al. (2003), who stressed the importance of setting up email reminders for participants to check into the discussion boards regularly, so that they do not miss the discussion as it develops. Both approaches were utilised throughout the discussion period as the author frequently posted onto the boards to ensure discussion was not halted, as well as sending email reminders when necessary. Despite best efforts to engage all of the participants, a problem emerged in the running of the groups: due to NHS Firewall restrictions, participants were unable to access the VLE during work time. This meant that participants had to engage with the discussions in the evenings, from their homes. At times this proved problematic as some participants did not engage regularly without repeated prompting, particularly the nurse participants, for whom this approach to participation in the discussion simply did not work. The decision had to be taken that

the nurse participants would contribute to the data collection by alternative means, therefore, email interviews were used. The email interviews followed the same schedule of vignette and trigger questions which were sent individually to each nurse participant. This change in data collection approach within this group of participants allowed the researcher to investigate further some of the perspectives of the nurse participants in greater depth thus, once the initial set of data (collected via online focus groups) were examined, emails were sent out to the nurse participants, offering some of the insights from the initial analysis and seeking to confirm or refute these. Figure 10 (p.215) depicts the process of data generation via focus groups and email exchanges as well as the stages of data analysis.

6.2.3 Ethics

Ethical approval was gained from Queen Margaret University Ethics Committee in February 2014. This study protocol was sent to the Research and Development department of NHS Lothian and exempt from full ethical review in October 2013 (appendix 6.2). Under the Department of Health guidelines for research governance this study did not require full NHS ethical review as it did not meet any of the criteria outlined in section 2.3 Policy Requirement for Research Ethics Committee Review of the document (DH Research and Development Directorate (England) et al. 2011) (appendix 6.2). This notwithstanding, principles of good ethical practice were followed throughout this study. Table 19 (p.202) outlines these against Beauchamp and Childress' principles of research ethics (1994).

6.2.3.1 Incentives to participate

In 2014, the author was successful in securing a Chest Heart and Stroke Scotland (CHSS) Minor Research Award. The sum of £500 was awarded in support of recruitment and retention of participants, a sum which enabled the author to

purchase gift vouchers which were given to participants on completion of the data collection phase (appendix 6.3). The decision to apply for this grant money was taken based on the knowledge that this study would require significant commitment from the participants, considering that they would be asked to participate in the study in their spare time. Several authors explore the ethical standpoint around offering financial incentives to research participants: Phillips (2011) acknowledged that offering payment to research participants is a common method to maximise recruitment, yet warned that such payments should be modest, so as to avoid this practice as constituting undue inducement. Russell et al. (2000) explored the conditions under which payment to participants would be acceptable, several of these were highlighted, the most relevant of which is the recognition of participants' time and efforts invested in taking part in the study. Draper et al. (2009) specified that it would be appropriate to offer payment to participants if they are required to contribute to a study which takes place out of office hours. It was therefore deemed appropriate to offer modest incentives to participate, despite the ethical quandaries involved in paying research participants (Russell et al. 2000, Draper et al. 2009, Phillips 2011).

Table 19: Ethical principles related to focus group study

Ethical Principle	How it relates to this study?	How this was upheld?
Beneficence	Maximising the potential benefits of participating in the study (Markham and Buchanan 2012, Smith 1995)	The study was designed not only to provide the researcher with information which would address the research question, but also as a learning opportunity for participants. Participants were encouraged to reflect on their learning using a published reflective log (College of Occupational Therapists 2014). Participants were also encouraged to use their engagement with this study as a self-certified Continuous Professional Development activity (Health and Care Professions Council 2014). As explored in section 6.2.3.1, participants were offered a modest cash equivalent gift voucher in recognition of their commitment to the study.
Non- Maleficence	Protecting participants from harm (Fox et al. 2003); Avoidance of any psychological distress which may come to the participants (Smith 1995).	• It was not expected that participating in this study would cause any manner of psychological harm or distress since participants were asked to reflect on their own routine practice. • Protecting the identity of participants could be related to the issue of protection from harm in case a participant should expose issues related to their practice, which may lead to undesirable consequences if read by a colleague. This matter was overcome by carefully safeguarding the identity of participants (Fox et al. 2003).

Respect for autonomy	Obtaining informed consent in the online environment mirrors the processes of informed consent in the offline environment when traditional data collection methods are employed (Roberts 2015). Participants should be given relevant information about the study before they provide their consent to participate, including making participants aware that they have the right to withdraw from the study (Buckingham and Saunders 2004).	These issues were addressed by the information sheet and consent form (appendix 6.4).
Justice and respect for persons	Maintaining anonymity and confidentiality are paramount and researchers have a responsibility of ensuring that the confidentiality of the data and privacy of participants are maintained throughout (Eynon et al. 2008, Saunders et al. 2015). Participants must be	• Attention and care were taken to ensure that participants remained anonymous. The information sheets sent out to participants instructed them on how to create an alias (appendix 6.5). If participants registered in their own name, thus potentially exposing their identity to others, they were prevented from posting to the discussion boards until this was rectified. And they were prompted to rectify this with a further instruction from the researcher. • When communicating by email with participants, the author ensured that all emails were sent anonymously, using the Blind Carbon Copy (BCC) facility of Microsoft Outlook©. • In the process of analysing and writing up the data, participants aliases were converted into a unique participant code as can be seen in Table 22, p.209.

	reassured that their privacy is upheld and the steps taken to ensure privacy need to be made explicit (Eynon et al. 2008, Saunders et al. 2015).	• Data storage: The handling of data was compliant with statutory requirements under the Data Protection Act (HM Government 1998). Electronic data were stored on a password protected network, owned and maintained by Queen Margaret University. No data were taken outside this electronic server. Paper copies were kept to a minimum. Wherever paper copies containing participant information were required, these were kept together, in a locked cabinet placed in a shared office in the University building, for which swipe card access is required at all times. The author was the only person able to access personal details regarding the participants.

6.2.4 Sampling and recruitment

Purposive sampling is the deliberate selection of participants who would reflect particular features of the phenomenon under exploration (Ritchie et al. 2014). According to Ritchie et al. (2014) the aims of purposive sampling are to ensure that the main populations that are relevant to the study would be recruited, as well as ensuring enough diversity among participants so that the impact of the various characteristics of participants may be explored. Within this approach to sampling, Ritchie et al. (2014) highlighted that when there are different stakeholders with distinctive positions in relation to the research question, multiple groups within one sample would be required. This point was relevant to this study as the approach to sampling was intended to gather the views of multiple professionals within the stroke unit team. Having multiple groups within the one sample has implications on the overall sample size and considering that large qualitative datasets can be difficult to manage, in qualitative studies the sample size is usually under 50 (Ritchie et al. 2014). As this study formed part of a larger programme of research, a manageable sample size of 20 participants was the target for recruitment, a figure supported in face-to-face discussion groups (Kenny 2005) as well as online focus group studies (Williams et al. 2012). In order to achieve this target of 20 participants, the approach to recruitment consisted of targeting participants from the medical, nursing and AHP staff groups working in stroke units across Scotland (the same stroke units from which data were generated for the online survey described in chapter V).

Recruitment commenced in March 2014, recruitment adverts (appendix 6.6) were sent to the research groups and associations outlined in Table 20 (p.206). An initial email was sent to all networks, in cases where a response was not received with confirmation of dissemination of these adverts, a repeat email was sent two weeks later. In cases

where professional networks had a Twitter account, this was used in two posts over the course of three weeks.

Table 20: Recruitment strategy

Clinical group	Network	Email approaches	Twitter posts
AHPs	Scottish Stroke Allied Health Professionals Forum	1	2
OT	College of Occupational Therapy Specialist Section-Neurological Practice	1	No Twitter account found
PT	Association of Chartered Physiotherapists Interested in Neurology	1	2
Nurses	Scottish Stroke Nurses Forum	1	2
Doctors	British Association of Stroke Physicians	1	No Twitter account found
Doctors Nurses	Scottish Stroke Research Network	Initial email and one reminder email	No Twitter account found
Doctors Nurses	Stroke Managed Clinical Networks	1	No Twitter account found
Doctors	British Geriatric Society in Scotland	Initial email and one reminder email	No Twitter account found
Any	Chain	Initial email and one reminder email	2

Professionals interested in the study were invited to email the researcher directly. The researcher returned an email containing the participant information sheet, consent form (appendix 6.4) and demographics questionnaire (appendix 6.7). The inclusion / exclusion criteria were then applied, these are outlined in Table 21.

Table 21: Inclusion and exclusion criteria

Inclusion	Exclusion	Rationale
NHS Staff currently employed in a clinical capacity	Non NHS staff, not employed in a clinical capacity	Participants must be able to reflect on their own current clinical practice
Working at least 1 session or ½ a day per week with acute stroke patients	Working fewer than 1 session or ½ a day per week with acute stroke patients	Participants must be in regular contact with stroke patients in the acute hospital setting as this is when a delirium is most likely to develop, and when the concept of "early identification" would apply
Any member of the multidisciplinary team who is in daily contact with stroke patients: doctors, nurses, occupational therapists, physiotherapists, speech and language therapists	Members of the multidisciplinary team who see stroke patients on a referral basis only: dietitians, radiotherapists, psychologists, orthoptists, podiatrists	These professional groups were chosen for inclusion as informants in this study because they are the core group of professionals who see all patients on a stroke unit on a daily basis. Clinicians who are referred individual patients will not have as strong a role in identification of a delirium and may not have specific expertise in working with patients post stroke
Any level of post-qualification experience	Pre-qualification students or unqualified staff	Pre-qualification and unqualified staff may not have the necessary expertise and training in identifying / dealing with stroke patients with a delirium

All clinicians who met the inclusion criteria were approached with intent to recruit them into the study. A total of 31 email responses were received as a result of the recruitment efforts described above. Of these, 10 were excluded as they did not meet the inclusion criteria (two doctors practising outside Scotland; one unqualified staff member; seven not in clinical contact with acute stroke patients in a hospital setting). Of the remaining 21, all were sent the information, consent and participant questionnaire, 16 returned these following up to three email reminders. Those who returned the paperwork were invited to log into the VLE having been provided with detailed instructions on how to do this (appendix 6.8). Following this stage, one participant (physiotherapist) withdrew from the study. The final number of recruited participants who entered the online discussions area successfully is 15, Table 22 (p.209) outlines the participant demographics.

Once the final number of participants was reached, a decision had to be taken regarding the composition of the groups. Finch et al. (2014) discussed homogeneity versus heterogeneity in focus group compositions, stating that while a degree of diversity within a group can aid discussion, too much of it can inhibit it. According to Finch et al. (2014) homogeneity within a group can facilitate disclosure, as participants can assume a shared understanding of terms and actions described. When groups are too heterogeneous, this can feel threatening to participants and it may inhibit disclosure (Finch et al. 2014). This was a determining factor in the composition of the groups, considering that focus groups usually involved six to eight participants (Finch et al. 2014). There were six OTs, three nurses, two PTs and five SLTs, and the decision was taken to have one group for OTs, one group for PT and SLT participants and one group for nurses. Despite the recruitment efforts, no doctors from Scottish health boards expressed an interest in the study. In an attempt to generate interest among doctors, a personal

connection was made via a colleague working in a Scottish stroke unit, who provided email contacts for other doctors working in the field. Three email approaches were made to these contacts, however, these emails were unanswered.

Table 22: Participant demographics

Group	ID	Band	Years of experience	Health Board	Unit size (n=beds)*
1	SLT1	8	18	NHS Greater Glasgow & Clyde	34
1	SLT2	8	16	NHS Greater Glasgow & Clyde	30
1	SLT3	8	20	NHS Greater Glasgow & Clyde	38
1	SLT4	6	4	NHS Greater Glasgow & Clyde	34
1	SLT5	7	20	NHS Lothian	16
1	PT1	6	10	NHS Greater Glasgow & Clyde	34
1	PT2	6	2	NHS Lothian	16
2	OT1	6	4	NHS Tayside	18
2	OT2	6	15	NHS Tayside	26
2	OT3	6	6	NHS Tayside	26
2	OT4	5	<1	NHS Tayside	18
2	OT5	6	1.5	NHS Greater Glasgow & Clyde	38
3	N1	5	3	NHS Forth Valley	30
3	N2	7	20	NHS Highlands and Islands	6
3	N3	6	3	NHS Lothian	22

* Information on stroke unit size obtained from ISD Scotland Report of Stroke Services (ISD Scotland 2014).

6.3 Data Analysis

The main phase of data collection using the online focus groups was conducted over two months, during which time the initial stages of the data analysis took place. The email exchange with nurses occurred once the AHP discussions had come to an end, by which time, the initial steps of the analysis had taken place. Having the data collection and analysis occur simultaneously enables the collection of data to be influenced by the analysis (Willig 2013, Charmaz 1995). This simultaneous process of data collection and analysis happened during the initial stages of open coding, which allowed the researcher to gain a sense of the data emerging. However, during the later stages of the analysis (focused coding and beyond) the researcher required a degree of immersion in the data that was not enabled by simultaneous data collection and analysis. The raw data generated by both the online focus groups and the email exchange with nurses were organised using N-Vivo© version 10.0 as a means of storing and categorising the data in the early stages of analysis. Holton (2007) was critical of the use of qualitative data analysis software such as N-Vivo©, stating that the software does not lend itself to the process of analysis required in classic GT research. However, Holton (2007) did acknowledge the power of such software programmes in archiving and retrieving large amounts of data, which is the way the software was used in this study. Indeed this is confirmed by Urquhart (2013), who suggested that software packages are helpful in managing large sets of data, rather than in conducting the data analysis itself.

According to Charmaz (2014), GT coding consists of at least two phases: the initial, open coding in which each segment of data is named, followed by selective coding which sorts and synthesises the codes generated in the initial phase so that the most

significant segments of data may emerge. The following sub-sections give an account of the process of coding as well as the overall stages of data analysis that were undertaken.

6.3.1 Open coding

The first stage of analysis consisted of line by line coding (Urquhart 2013, Charmaz 2014, Holton 2007): the data were read and re-read, and 'labels' or codes were attached to the text, in most cases, utilising words used by the participants themselves, thus ensuring that the codes were generated in-vivo (Charmaz 2014). This low-abstraction-level coding enabled the researcher to be confident that the codes generated in this stage remain true to the participants' experiences and free from the researchers own motives and biases (Willig 2013, Charmaz 2014). According to Holton (2007), line by line coding enables the researcher to be confident that every piece of the data is categorised, ensuring that no important parts of the data are missed. At this stage of the coding, the N-Vivo© software was invaluable as a repository for the raw data and it enabled the researcher to easily attach codes, and then retrieve these in the process of constant comparison as described below. Holton (2007) advised that at this stage the researcher ought to be as open as possible to what could emerge from the data, thus during this process 69 different codes were generated, many of which were descriptive and often anchored in the words used by participants themselves.

6.3.2 Focused coding

This stage, according to Urquhart (2013), occurs once there are no new open codes emerging from the data, thus the direction of analysis is clear, and decisions about which codes make the most analytical sense must be taken. Practically, this meant

examining the open, descriptive codes and exploring the ways in which these codes can be linked with one another (Willig 2013, Charmaz 2014). The codes identified in the open coding stage were sifted through, allowing for the most significant codes to emerge in the process, thus the focused coding phase synthesised the open codes generated in the stage above (Charmaz 2014). At this stage, N-Vivo© was again useful as 69 open codes were synthesised and grouped based on the content within. Charmaz (2014) pointed out that GT coding is not a linear process, and researchers will frequently find themselves revisiting codes generated in the initial phase, thus the data may be examined afresh, due to codes emergent in the focused coding phase. This is discussed further in section 6.3.5.

6.3.3 Theoretical coding

Theoretical coding follows on from focused coding and looks at the ways in which the focused codes relate to each other (Charmaz 2014). Charmaz (2014) described theoretical codes as integrative, lending shape to the focused codes gathered and enabling the researcher to tell a coherent story emerging from the data. According to Urquhart (2013) this is a crucial stage in theory development. While this study did not seek to generate theory, theoretical coding was used as a means of arriving at the final themes emergent from the data. Urquhart (2013) discussed the process of coding and creation of coding schemes, and proposed that researchers should come up with their own coding scheme rather than follow a prescribed matrix, since the coding ought to be true to the unique data and analytical scheme of each particular study. The coding scheme generated through the process of analysis is outlined in appendix 6.9. Urquhart

(2013) stressed the importance of being reflective when engaging in theoretical coding, a matter which is discussed further in the next section.

6.3.4 Memo writing

Throughout the process of the research, the author kept a written record of the process: codes, their justifications and the process of linking between the codes are all traceable, enabling the entire research process to be kept in check (Willig 2013). The N-Vivo© software was very useful at this stage as it enabled the researcher to write memos and attach these to relevant segments of the data and retrieve these quickly when required to look back at the process, as part of the constant comparison described in 6.3.5. Alongside the electronic memos stored in N-Vivo©, the researcher kept a reflexive diary. Urquhart (2013) defined reflexivity as "critical self-reflection" (p.70), a process which is crucial in keeping biases in check, reflecting upon the research process and maintaining an auditable trail of the entire research process (Willig 2013, Lempert 2007).

6.3.5 Constant comparison

Constant comparison is a process which occurred throughout every stage of the research as well as during the writing up of results; the researcher referred back to raw data, open coded data, focused codes and memos and ideas noted during the process. The process of constant comparison allowed the researcher not only to make sure that the data were coded appropriately, but also, for interpretation and deeper analysis to take place (Charmaz 2014, Holton 2007, Kelle 2007). Through the process of deep analysis, negative cases were highlighted. These cases were outliers which did not conform to the

overall trends that emerged in the data (Charmaz 2014). The way in which these were handled is described in the following section.

6.3.6 Negative case analysis

Willig (2013) regards negative case analysis as an important facet of quality in qualitative studies as the researcher explores the cases that do not fit as well with the trend of the data. Willig (2013) suggested that new insights may emerge through close examination of negative cases. Morse (2007) described negative cases as occurring when participants do not respond in the anticipated way. It is therefore important not to discard negative cases, but rather incorporate them into the analysis (Charmaz 2014, Morse 2007). Within the context of this study, this approach was utilised during the email conversations with nurse participants, who were asked to comment upon the differences in the ways in which participants responded to a description of delirium in a stroke patient. This led to a discussion around the nurses' perception of the knowledge and skill mix in the team of AHPs, confirming some of the differences highlighted by the process of initial analysis.

6.3.7 Theoretical saturation

Whilst Willig (2013) argues that theoretical saturation is more of a goal than a reality, it is important to note that coding of the data continued until no new categories were identified (Holton 2007). In other words, there were more and more instances of the same codes, but no new codes emerged (Urquhart 2013). The following page contains Figure 10, referred to earlier in relation to the data collection, but placed here in order to provide a depiction of the stages of data analysis as they related to this study.

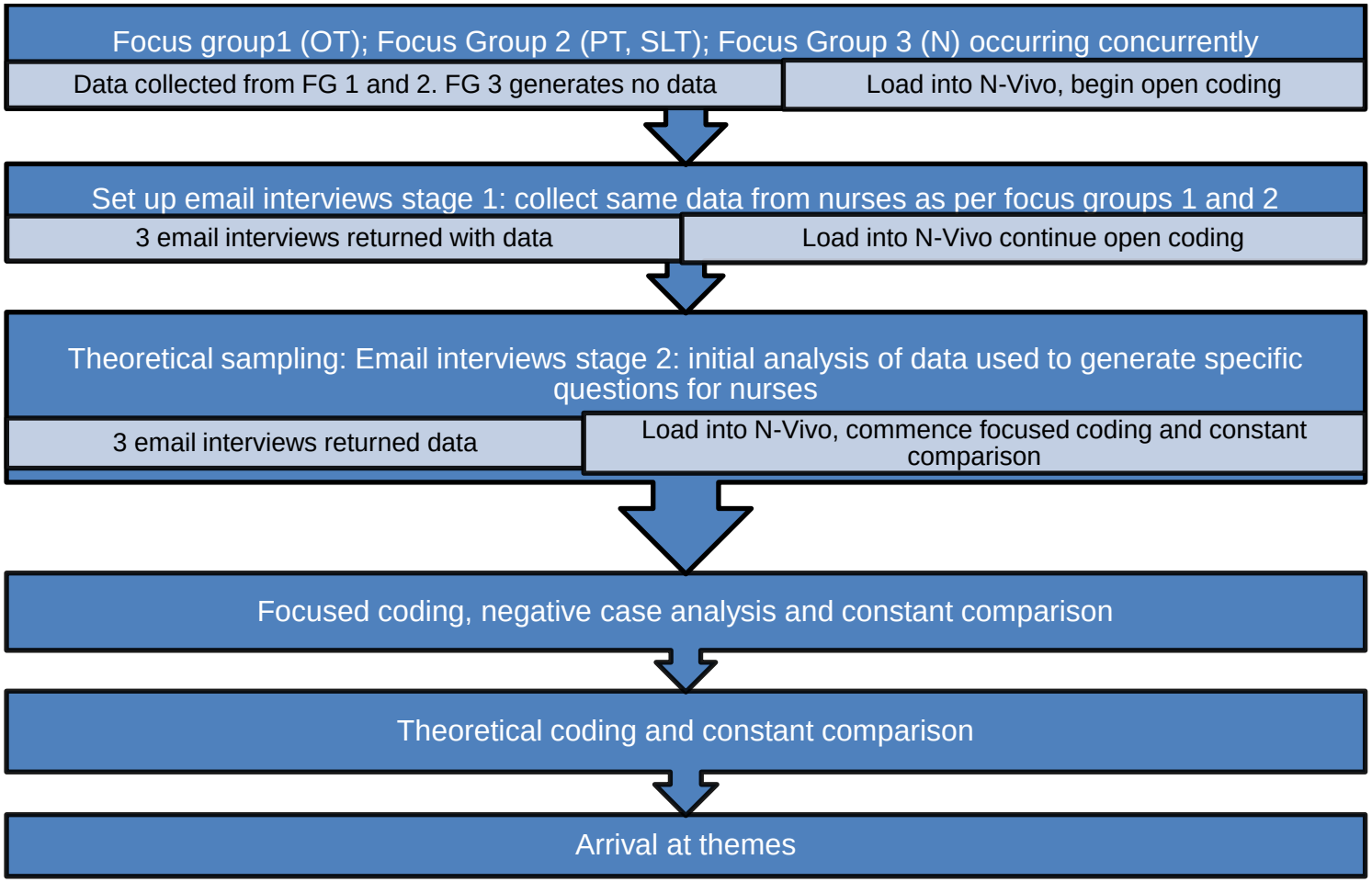

Figure 10: Data generation and stages of analysis

6.4 Findings

The online focus groups and email discussions generated a total of 84 posts yielding 7270 words set over 21 pages of script. The data analysis process described in section 6.3 led to the emergence of four themes. The following sections provide a detailed description of the themes, including verbatim extracts as well as making the links that highlight the relationships between the themes. When presenting extracts, the participant number will be given first, followed by the code and line from which the extract was taken, e.g.:

N1 [A2.32]: N1: the participant number as given in Table 22 (p.209)
A2: the code
.32: the line within that code where the extract appears

There was a considerable amount of medical jargon and abbreviations were used in the discussion. Where these required interpretation this was offered in square brackets and presented in normal text as opposed to the italicised quotes. Similarly, spelling or typographical errors were corrected and presented in square brackets following the original text.

6.4.1 Theme One: Uncertainty around symptom recognition

This theme depicts the process participants underwent in trying to work out the symptoms described in the case vignettes, particularly the hypoactive case details, since this case was somewhat vaguer in its presentation (appendix 6.1). The discussion was taken up with the participants trying to interpret the symptoms described, and various

suggestions as to what the symptoms manifested were offered. The presence of premorbid dementia was presumed, particularly when discussing the hypoactive case:

> *N1 [B13.2]: "I would think she has mild dementia and has been taken out of her familiar setting of home and this has knocked her off a bit"*
> *OT5 [B13.4]: "I would consider whether these are signs of early stages of dementia…"*
> *SLT2 [B13.20]: "This lady certainly appears to have cognitive decline and her drowsiness may be part of a dementia picture…"*

Other participants wondered whether the patient is experiencing low mood (OT2, OT3, OT4, OT5, PT2) and whether a lack of motivation and engagement in therapy sessions were resultant from a depressive illness and proposed to assess this further (SLT2, SLT4, PT2, OT2, OT4):

> *N2 [B12.4]: "This lady* [may] *be finding it difficult adapting to an acute ward, she might be disorientated, depressed as she does not understand what is going on."*
> *N3 [B12.2]: "It may be Mrs Bryan by not showing any interest in her surroundings, feels nothing can happen to her (fatalistic outlook, "once they get you into hospital etc", "won't be going home "" I'm 82" or what's the point?)"*
> *PT1 [B1.4]: "…Is it possible that some of the fatigue and apathy may also be a "normal" grieving response to the loss of function resulting from the stroke?"*

Several participants also wondered about the relationship between the symptoms described in the hypoactive case and fatigue or drowsiness:

> *PT1 [B11.16]: "…fatigue from the stroke itself may be responsible".*
> *OT5 [B11.6]: "I would be interested to know how much sleep she is getting at night, she may not be confused but may still be awake therefore causing the daytime drowsiness."*

Although the term 'delirium' was used by some participants at certain points in the discussion (presented in some extracts within theme two), there was a tendency to prefer the use of the more generic term 'confusion' rather than delirium *per se*. This led to a deeper exploration of the meaning of the term as participants were asked to

specify what they understood the term ‘confusion’ to mean, leading to a discussion around the usefulness of the term in practice:

> *OT4 [D3.4]: “…a person who is confused is not understanding the information they are gathering from the environment.”*
>
> *OT1 [D4.5]: “… I don't particularly like the word confused as I do find people are labeled [labelled] confused and can be sometimes written in medical notes as ‘?dementia’….Members of the MDT, family and patients often do not understand the different aspects of cognition but just identify the patient is confused.”*
>
> *OT5 [D4.8]: “I see confusion as the person not being able to make sense of the world around them - whatever feedback/input they are receiving isn't making sense and may be 'muddled up' in their mind….. We have patients who have language, processing or visual difficulties due to the stroke however they are described as 'confused'.”*
>
> *N2 [D4.1]: “[confusion] means very little, staff need to expand what why and how it affects them, it is often used as a word with little meaning attached”.*
>
> *N1 [D4.3]: “I think there needs to be more education at ward level about delirium and its causes. I think confused is too broad a term and doesn’t identify the reasons for the behaviours”.*
>
> *N3 [D1.5]: “I actually think the use of the word confused is like delirium - too vague. A person can appear unclear but they themselves are aware of where they are or they aware they are not expressing themselves/ or behaving as usual. ‘Confused’ tends to give the impression, someone is unaware of their behaviour and surroundings altogether…”*

It became clear during the analysis that those clinicians who reported they received delirium training were those who consistently referred to the term ‘delirium’. One participant openly discussed a lack of confidence in delirium recognition and offered this personal reflection:

> *SLT2 [C2.50] “*[delirium] *is definitely not something I am confident in recognising in patients and would more often mistake as cognitive impairment…”*

The two participants who discussed the training received on delirium and its identification offered the following:

N2 [B14.1]: "We certyainly [certainly] *are doing a lot of work at the moment with medical and nursing front line staff to recognise that it is a meidcal emergency* [medical emergency]*… we have worked very hard here to "Think delirium"".*

PT2 [B14.25]: "We had a very useful in-service on Delerium [delirium] *recently outlining what to look out for as compared to a longer-standing cognitive impairement* [impairment]*. We were told to look out for delerium* [delirium] *as an acute onset and fluctuating course with inattention and either disordered thinking or an altered level of consciousness. In-services like this help to raise awareness."*

This theme described the uncertainty around recognising a delirium, from initial thoughts around the reasons a patient may present as 'confused' to thoughts around the reasons why a patient may appear drowsy or lack motivation to engage with the therapy process. The participants offered insight into their own understanding of the term 'confusion' and how useful it is in describing the clinical picture. Some participants were critical of the use of the term 'confusion' as a vague or meaningless term, which does not offer an accurate depiction of the condition or underlying causes. Participants varied in the accuracy of language used, those who reported receiving delirium training seemed more confident in the use of the term 'delirium' in response to the symptoms depicted in the case vignettes.

6.4.2 Theme Two: Information gathering

During the process of trying to work out the symptoms described in the vignettes a strand of discussion developed around information gathering. Participants made a variety of suggestions of using screening tools, ranging from use of the Mini Mental State Examination (N2), the Addenbrook Cognitive Examination (ACE-III) (OT5) or the Montreal Cognitive Assessment (MoCA) (OT2, OT3). Other AHPs suggested carrying out assessments that are unique to their own profession, such as functional assessments

(OT1, OT2) or comprehension / language assessments (SLT4, SLT5). There were two suggestions for use of the 4AT: the first came from N2 in relation to the hypoactive delirium case. This was the only suggestion related to delirium screening for the hypoactive case. PT2 later discussed using the 4AT when the hyperactive delirium case was presented:

> *N2 [A31.1]: "On admission the 4AT screening for dementia/delirium should have been done, so you could track the changes."*
>
> *PT2 [A31.3]: "In the hospital I work in we use the 4AT screening tool for delerium* [delirium] *and cognitive impairment. This should be carried out on all patients on admission… I think you need to be careful using this measure particularly if you do not have a clear idea of whether there was a degree of cognitive impairment prior to admission."*

In discussing both case vignettes, many of the responses consisted of a report of an action or several actions the participants would take in response to the symptoms presented, as participants worked through the actions they would take to establish a clear clinical picture. These actions create a direct link with theme three on collaborative working, as professionals refer to and discuss matters with their colleagues. The actions proposed are seen in the context of the participants' own professional disciplines: the different professional roles emanate in the description of the actions to be taken: e.g. nurses were clearly interested in assessing any physiological changes and ensuring basic care needs are met (hydration, medication, bladder and bowel function):

> *N1 [A9.46]: "I would measure her observations including temperature I would also dip stick her urine looking for infection, check U & E's* [urea and electrolytes for assessing renal function] *and Liver function. I would be keeping a close eye on her throughout the day and night…I would also do bloods looking for possible infection and dehydration. I would also keep a check on bowel movements…"*

Participants were particularly interested in working out possible causes for the "confusion": OT1 and OT3 were interested to know whether a change in medication was

responsible, and OT2 made several references to checking with medical staff whether the symptoms depicted were “medication related”, SLT5 and N3 wondered whether the medication was taken at the correct time of day, PT2 wondered about any new medications which may have caused the overnight confusion. A further issue raised by many of the participants was related to whether the patients described in the vignette had an underlying infection, and wished to check inflammatory markers, particularly for a urinary tract infection (UTI) as seen in extract from N1 [A9.46] above. Similarly, the AHPs responded with a clear action to ask the medical team to review inflammatory markers to check for an underlying infection:

> *SLT4 [C1.2]: “I would be asking the medics about her inflammatory markers to check for any underlying infection particularly related to a UTI…”*

Once the discussion turned to examine the possibility of an infection, five participants raised the possibility of the symptoms manifested in the vignette as describing a delirium. This line of discussion did not persist outwith the context of exploring the possibility of an underlying infection and, as discussed in theme one, the language used subsequently was less accurate as ‘confusion’ was the preferred term to discuss the symptoms depicted in the case vignettes.

> *SLT5 [B4.25]: “I would still wonder if Mrs B. has hypoactive delirium and would ask the doctors for an infection screen, especially with her lack of fluids”.*
> *PT2 [B4.24]: “The medical staff may consider bloods to look at electrolyte imbalance or further imaging to look for an extension or new event. It could also be possible that this could be a post-stroke delirium.”*
> *OT2 [B4.13]: “…causes ? dehydration… ? delerium* [delirium]*? source of infection”.*
> *OT4 [B4.11]: “I would also speak with nursing staff if theres any possibility of a delirum [delirium] caused by infection.”.*

Theme two outlined the actions reportedly taken in the process of information gathering as the participants responded to a suspected delirium. The theme offers

some insight into the thought processes expressed by health professionals, who may come across a patient with the symptoms of a delirium. Some participants used the term ‘delirium’ in the context of seeking to establish whether there was an underlying infection. However, this did not seem to relate to the suggested cognitive assessment tools suggested by participants. Most of the assessment tools suggested were generic cognitive assessments, and the use of a delirium-specific screening tool was only mentioned by two of the participants.

6.4.3 Theme Three: Working in collaboration with others

The AHP participants all considered communicating with other team members as well as the next of kin as key to finding out about the symptoms manifested in the case vignettes. Participants stated they would liaise with the multidisciplinary team (MDT) on an ongoing basis, and all participants referred to nurses as key players in finding out more about the source of ‘confusion’. This is clearly corroborated by the nurses themselves, who described their role as central to the identification of physiological symptoms and behavioural changes associated with delirium. Throughout the discussions several insights into team working were offered, including suggestions of clearly defined roles, not only for the professionals on the team, but also, for the next of kin or family to be involved in the therapy sessions, as can be seen in the examples below.

All professionals participating in the study considered the role of the next of kin (participants used the abbreviation NOK) as instrumental in informing the history of the

patient and elucidating the clinical picture – particularly in establishing whether the patient had a pre-morbid cognitive decline, as typified in this response:

> *OT2 [A4.18]: "It would be valuable speaking to NOK to establish if there were episodes of this prior to admission."*

The role of the next of kin was discussed beyond acting as informants as many of the participants considered the next of kin to possess an important role in the success of therapy:

> *N2 [A4.4]: "Find out from family etc what is their normal pattern, and even encourage someone in, use stimulation as needed, use family to help engage".*
>
> *OT5 [A4.27]: "It may be good to involve her family in therapy to see if they can get her to engage.".*
>
> *PT2 [A4.53]: "I would…ask the family to fill out a 'This is Me' or similar booklet to include information about Mrs Bryan's life prior to the stroke. Staff awareness and use of this might help to orientate and comfort her." and later in the discussions: "I would consider inviting a family member to participate in the therapy session...".*
>
> *SLT4 [A4.62]: "I wonder if a family contact and a joint session with family may help with engagement. In the rehab ward this has often be a useful tool as pt's [patients] sometimes find it more engaging and stimulating with someone familiar there".*
>
> *SLT4 [A4.66] "Quite often as an SLT I'll meet with the family and give them advice re settling the pt [patient] using communication supports such as family photos etc."*
>
> *SLT5 [A4.69]: "…Could she be encouraged to join in any activities with other patients or perhaps her family could take her out for a short trip."*
>
> *PT1 [A4.71]: "In my unit the MDT readily involve family members to assist in our treatment sessions and this can work really well."*

The AHPs described their work within teams where there are clearly defined roles when it comes to the detection of delirium as typified in SLT4's perception:

> *[C2.37] "…the medics look to a medical cause for this through all their blood tests etc and it is the responsibility of the pt's* [patient's] *keyworker to liaise with the NOK to establish baseline and to ascertain whether this is an acute or more long standing problem."*

There were further insights into perceived professional roles around delirium identification as three participants discussed the differences in the knowledge base of team members as can be seen in extract SLT2 [C2.50] above, as well as:

> *N1 [C2.5]: "I think there is a big difference in the knowledge about delirium in post stroke patients. I find that the OT have more insight into it than the PT and SLT and the more junior the nurse the less knowledge they have about it. I feel that the PT and The SLT tend to only know about their specialist area and feel that it is more of a nursing/OT job to identify why the patient is mentally not quite right".*

> *N3 [C2.43]: "there does appear to be a gap for therapy staff but…it probably is still nursing staff who will report the delirium…due to the hours and numbers (more nurses than therapists)… If a patient is unwell or appears confused, OT /PT and SLT will defer therapy until the patient is able to participate so in most cases, the chances are it would be nursing staff…who would notice any confusion / delirium. There is a disparity between the different practitioners to recognise delirium…It may also be that each practitioner only really looked at* [a] *case from their own perspective."*

Other ideas were raised regarding professional roles and a perception from nurses around a collective responsibility of staff on the ward when it comes to delirium identification, as noted in extract N1 [D4.3] above as well as:

> *PT2 [C2.34]: "…as a physiotherapist I am not routinely carrying out formal screening for delirium we do note changes in behaviour and ability to participate in treatment and feed this back promptly to the MDT and document in the patient notes."*

> *N2 [C2.10]: "I think it's everyone's responsibility but realistically the screening is done by nursing staff … as part of the admission process and it's then ongoing..."*

Participants seemed to express a clear distinction of roles when it comes to delirium identification, with one participant being clear that the entire team should share the responsibility for delirium identification. There was a clear consensus in all participants as the role of family or next of kin, both as informants and as collaborators in

the treatment process, a matter which links with the last theme around the delivery of patient-centred care.

6.4.4 Theme Four: Delivering patient centred care

Throughout the process of discussing both case vignettes a very clear picture of all practitioners' values and regard for a patient's wellbeing clearly emerged. This theme links with the role of the family in supporting the patient's rehabilitation: the caring attitude of practitioners clearly came to the foreground in their wish to involve the family or next of kin. The theme also links with the actions that participants proposed to take in response, as can be seen from their comments. From the outset, many participants wondered whether the patients described in the vignettes had insight into their behaviour (OT1, OT2, OT4, OT5, N2) and whether they were aware of what was happening to them. Several participant placed an emphasis on the importance of discussing matters with the patient, so as to offer reassurance and comfort:

> *SLT5 [E4.16]: "Is she aware of where she is and what has happened or is she perhaps just scared?... with her declining memory does she know what has happened to her and what the future may hold. Even if she has been told she may not remeber* [remember] *or feel part of the process."*
>
> *N2 [E.24]: "I would keep a close eye on him and monitor the delirium, I would offer reassurance and try make him feel safe and cared for in his surroundings".*
>
> *N3 [E.26] "Explaining what has happened to him and why he is in hospital , explaining what is available and trying to reassure him as much as I can that he is safe, we want to help him , try to put his mind at ease, may help".*
>
> *OT2 [E.34]: "…important to discuss with patient any reason why she is feeling like this. What are her goals during her hospital admission? Perhaps she thinks she may not be able to return home and maybe depressed at being in hospital…"*
>
> *N3 [E4.3]: "I would ask her if there is anything worrying her , making her feel so tired and reassure her and encourage other patients if possible to interact with Mrs Bryan . Explaining what has happened and outlining what can happen and what can be done , may help Mrs Bryan understand better , what is going on".*

Further thoughts around the issue of perceived ‘confusion’ and the behaviour depicted in the case vignettes were offered:

> *OT5 [E2.3]: “What unseen stimuli is he responding to? is it distressing for him?”*
>
> *OT1[E1.17] : “why a person is deemed as confused, is it because they don't have their hearing aids in and cant [can’t] hear what is being asked of them…I would like to know why the patient shouted a [at] the physio, was he unsure where he was* go[ing] *therefor* [therefore] *scared.”*

There were also some suggestions of management from several participants, all of which place the patient at the very centre of the experience, demonstrating a basic ethos of caring and trying to achieve the best outcome:

> *N1 [E1.1]: “I would also do simple things like, encourage her Family to bring in her own clothes, take her out of the ward to the hospital cafe (if she is physically able) speak with her to see how she feels.”*
>
> *SLT4 [E.46]: “…ensuring the pt* [patient] *has their hearing aid, glasses, mobility aid etc is crucial. I've often seen on the ward that although the delirium is the presenting symptom a simple thing such as missing dentures or a staff member who looks like the pt's [patient’s] daughter is the actual cause for agitation.”*
>
> *SLT5 [E.39]: “I would like to see if she could be encouraged to eat and drink more if she was taken to a table to eat with others. Eating on your own by your bedside does not encourage an appetite or socialization.”*
>
> *PT2 [E.42]: “….ensure that mobility is gently encouraged and that adequate pain relief is available to allow this. Orientating the patient with a clock and familiar items may also help. Hearing aids and glasses should be in use if required..”*

Further references to placing the patient at the centre of the experience can be seen in theme three as participants make suggestions of involving the family in a variety of ways: from attempting to increase engagement in therapy as seen in OT5 [A4.27] and SLT4 [A4.62] or asking the family to fill in a “This is Me” booklet, that would allow the staff to get to know the patient better, particularly their life prior to the stroke as seen in the suggestion from PT2 [A4.53]. Suggestions for meeting with the family to explore the best

means of supporting communication with a patient came from SLT4 [A4.66] and simply involving the family in therapy sessions (PT1 [A4.71]) or asking the family to take the patient out for a short trip in order to encourage the patient SLT5 [A4.69]. All of these suggestions demonstrate a patient centred approach as well as a wish for the patient to achieve the best outcome of the interventions on offer.

6.5 Discussion

This section discusses the findings described above within the context of any available, relevant literature. As mentioned throughout the thesis, in the absence of relevant literature on delirium in acute stroke, literature from other relevant acute medical settings is referred to.

6.5.1 Understanding delirium and the importance of terminology

In this sample of participants, clinicians' understandings of delirium varied, particularly in response to the description of a hypoactive delirium. Lack of knowledge of delirium symptoms and lack of confidence in its identification are consistently reported in nursing and medical literature (Davis and MacLullich, 2009, Rice et al. 2011, Ryan et al. 2013). This is heightened in cases of hypoactive delirium (Bellelli et al. 2014b) or a delirium superimposed on dementia (Flanagan and Fick 2010), a matter which is reflected in the response participants had to the hypoactive case presentation. A study by McCrow et al. (2014) also confirmed this by using case vignettes to assess nurses' recognition of hypoactive versus hyperactive delirium and found higher rates of identification of the hyperactive delirium as represented in the case vignette they presented.

An important finding around the understanding of delirium is around the use of language: most of the clinicians tended to use tentative language to describe delirium symptoms, using the terms ‘confusion’ and ‘delirium’ interchangeably. This is reported in the literature in a variety of acute geriatric settings: Day et al. (2008) explored the constraints to best practice around delirium care. They found that although nurses understood the precipitating factors for developing a delirium they did not use the word ‘delirium’, rather they described behaviours and mental status. A review of case notes as part of the study by Day et al. (2008) confirmed this by revealing a near-absence of the word ‘delirium’ within patient notes, with the exception of patients who had been seen by a psychiatrist. Rice et al. (2014) confirm these findings through a mixed methods investigation into the reasoning applied by nurses as they attempt to recognise delirium in elderly patients. They describe the “casual conditions” which result in nurses recognising a delirium, these are determined based on a combination of intuition and clinical knowledge. Rice et al. (2014) reported that nurses equated the symptoms of delirium with ‘confusion’ and that despite the fact confusion was documented in a patient’s notes, this was not translated into the observable delirium features. Rice et al. (2014) concluded that delirium was under-recognised in their study.

Despite the lack of consistency around the use of the term delirium, the findings of this study indicate that the key principles of the initial management of delirium are followed even if accurate recognition is not achieved, namely, attempting to identify a physiological cause, reorientation and engaging with family and caregivers, actions that are all consistent with UK wide best practice guidelines (National Institute for Health and Care Excellence 2010, National Institute for Health and Care Excellence 2014, Healthcare Improvement Scotland 2014). This raises a question whether accurate recognition and clinicians’ use of language are indeed crucial in the management of

delirium. Teodorczuk et al. (2012) argued that the lay term ‘confusion’ is unhelpful since it is used interchangeably as both a symptom and a diagnosis. Others warned that the use of the term ‘confusion’ is misleading and erroneous and may lead to either misdiagnosis or mismanagement of delirium (Morandi et al. 2012, Teodorczuk et al. 2013, Fleet et al. 2015). Godfrey et al. (2013) found that the lack of accuracy in language denoted a lack of clarity regarding the distinctions between dementia and delirium and MacLullich et al. (2013) argued it is important to use ‘delirium’ as an umbrella term as a means of engaging and educating clinicians across the healthcare spectrum. Indeed, Ryan et al. (2013) and Godfrey et al. (2013) proposed that delirium is not a high diagnostic priority, yet there are clear reasons for delirium detection to be high on the priority of clinicians when considering the benefits of prevention and early intervention in terms of cost to the patient, families and healthcare systems as a whole (MacLullich et al. 2013). A further argument for arriving at an accurate diagnosis of delirium, as opposed to managing the symptoms of ‘confusion’ is the prognostic implications of developing the condition: for stroke patients increased morbidity, mortality and length of hospital stay are all associated with the development of delirium (Carin-Levy et al. 2012, Shi et al. 2012) as well as the increased risk of long term cognitive impairment (Melkas et al. 2012). Additionally, arriving at a definitive delirium diagnosis is crucial in the provision of best practice around its management, which is most effective when it is a multi-component intervention combining pharmacological and multidisciplinary non-pharmacological approaches (National Institute for Health and Care Excellence 2010, Morandi et al. 2013).

6.5.2 Delirium education

Only two clinicians in this study stated explicitly that they were trained to "Think Delirium", as per Healthcare Improvement Scotland initiative to help clinicians improve identification and initial management of the condition (Healthcare Improvement Scotland 2014). These participants appeared more confident in discussing the symptoms and appeared better able to recognise a delirium in a stroke patient. This is confirmed to a certain extent in the literature on the efficacy of education programmes in increasing delirium identification rates, albeit, none of these studies were conducted within a stroke setting: in a systematic review of 26 studies, Yanamadala et al. (2013) found that interactive, multi-strategy teaching programmes resulted in improved staff recognition of delirium as well as adherence to treatment protocols, although Yanamadala et al. (2013) found that overall, education programmes alone do not result in an improvement of delirium knowledge and skills. McCrow et al. (2014) reported on the short-term success of a web-based education programme in increasing recognition rates of delirium, albeit, these successes were not sustained at the follow up time point in this study. van de Steeg et al. (2015) reported the success of an online education programme in increasing knowledge and understanding of delirium, albeit, they did not explore the impact of this programme on day-to-day nursing practices or whether these results impact upon recognition rates (van de Steeg et al. 2015).

6.5.3 Team working including family and caregivers

This study sheds light on aspects of team working within the stroke unit when it comes to patients with delirium. Several issues have arisen: the divisions of roles within the team clearly emerged as well as a sense of distinction in the perceived knowledge

base between each professional group. The third issue to have emerged is the notion of the family or caregivers as an important part of the team, not only as informants but also as contributors to the therapeutic process. This also tied in with the ethos of patient centredness and collaboration which is discussed below.

The role of family or caregivers is recognised as part of multidisciplinary team interventions in the management of delirium, whether it is as informants (Healthcare Improvement Scotland 2014) or as participants in educational programmes (Siddiqi et al. 2007). Vidán et al. (2009) and Benedict et al. (2009) reported on interventions to prevent delirium in hospital settings: both programmes included family involvement in the interventions: Vidán et al.'s intervention included providing the family or caregivers a letter explaining about delirium and encouraging their presence on the ward (Vidán et al. 2009). Benedict et al. (2009) did the same, but also instructed the family or caregivers as to what they can do to help prevent delirium in their loved-one. Rosenbloom-Brunton et al. (2010) studied the feasibility of involving family in a delirium prevention programme for hospitalised older adults. The role of family members was to help with reorientation, cognitive stimulation and sensory functioning (vision and hearing). Their findings suggest that the intervention is feasible but the authors drew attention to the importance of building partnerships and positive therapeutic relationships in the nurse-caregiver-patient triad (Rosenbloom-Brunton et al. 2010). Martinez et al. (2012) also reported on the role of family or caregivers in a multicomponent intervention for preventing delirium in acute care settings. Family or caregivers were involved in two ways: the first was educating family members about delirium, the second was to involve family in reorientation of the patient. One of the findings of this study confirms this as all of these notions were raised by participants as they made repeated reference to family or next of kin as important contributors to the therapeutic process: from ensuring that sensory aids were present to

suggestions of taking the patient out and trying to encourage the patient in therapy sessions.

The literature reviewed in chapter II reported upon negative approaches towards patients with delirium in some hospital settings (Neville 2008, Dahlke and Phinney 2008, Kjorven et al. 2011). Additionally, chapter II discusses Schofield et al.'s (2012) findings on the way patients with delirium were regarded as disruptive and threatening as well as the lack of normal interaction between nurses and patients with delirium in their care. This study found nothing to confirm or refute this, rather, an ethos of patient centredness emanated throughout the discussions as inherent to participants' practice. The reported response to a patient with delirium revealed a caring, compassionate and holistic approach. It is possible that the methods of data collection in this study are responsible for this finding: this study relied on self-reporting of hypothetical actions as opposed to active observation of clinicians in practice. It is also possible that this finding relates to the culture and strong ethos of patient centredness and collaborative team work, which is a guiding principle in stroke units throughout NHS Scotland (Scottish Intercollegiate Guidelines Network, 2010).

6.5.4 With whom does responsibility lie?

The division of roles among some of the MDT members with regards to delirium identification is discussed in other hospital settings, since at the time of writing no studies reporting on this aspect of delirium care within a stroke setting were identified (appendix 2.1). In medical and elderly care settings, nurses are widely regarded as key players in delirium recognition due to the length of time they spend with patients and their ability to detect subtle behavioural changes (Hall et al. 2012, Dahlke and Phinney 2008, Fick et al.

2007). Ryan et al. (2013) suggested that nurses' prolonged contact and increased social engagement result in their noting different symptoms in comparison to doctors: nurses in their cohort tended to concentrate more on unusual behaviours, ability to communicate and inattentiveness, whereas doctors tended to rely on inattentiveness as the main feature of delirium (Ryan et al. 2013).

It is noteworthy that most of the existing research on delirium identification focuses on doctors and nurses. There are a number of studies on delirium education which include AHPs within their cohorts, however, none of these report on the specific competencies or roles of different professional groups in delirium identification and management (Foster et al. 2010, Bellelli et al. 2014b, Godfrey et al. 2013, Teodorczuk et al. 2013, McAiney et al. 2012). Occupational therapists are regarded as experts in cognitive assessment and their role in this area of stroke care is recognised in Scottish best practice guidelines (Scottish Intercollegiate Guidelines Network 2010). Indeed, one of the nurse participants in this study reflected upon the perceived skills and role in cognitive assessment, yet in discussing cognitive screening, the OT participants in this study did not mention delirium screening specifically, nor did they consistently use accurate language to discuss the symptoms of a delirium in a stroke patient.

In this study, the two participants who received delirium training discussed the use of the bedside tool, the 4AT. This tool is designed to be used by any professional in the team, as a means of triggering comprehensive diagnostic processes (Healthcare Improvement Scotland 2014). It is not the responsibility of nurses and AHPs to arrive at a formal diagnosis of delirium, however, screening for the condition is an important first step in arriving at a diagnosis. The 4AT is a tool which could potentially be useful in enabling all MDT members to recognise a delirium, leading to early diagnosis and effective management of the condition in stroke patients (Lees et al. 2013, Kutlubaev et

al. 2016). One of the nurse participants felt that it is everyone's responsibility to be able to recognise the symptoms of delirium, and indeed there is a clear argument that delirium recognition should be a shared concern for all members of the team: Godfrey et al. (2013) argued that every therapist should have an understanding not only of how and why a delirium develops, but also of their own role in recognition and prevention of the condition. Bellelli et al. (2014b) similarly argued that competence in delirium identification and management should pertain to all healthcare professionals caring for patients. The collaborative, patient-centred culture of practice in Scottish stroke units as suggested in this study, may well make this setting one in which the ideas of a shared responsibility for delirium detection, and 'ownership' (Teodorczuk et al. 2013) could be put into practice, possibly resulting in a more timely recognition of the condition.

6.5.5 Strengths and limitations of this study

To the best of the author's knowledge, at the time of writing this thesis, there were no other studies found which revealed the ways in which acute stroke unit staff understand and reportedly respond to delirium in their patients. Similarly, there were no studies identified which examine the role occupational therapists can play in delirium identification or prevention (appendix 2.1). Thus, one of the strengths of this study is in the exploration of a previously undescribed area of practice. A further strength of the study is in the inclusion of a variety of clinicians, exploring the perspectives of AHPs as well as nurses in establishing a picture of the workings of a stroke unit team when it comes to patients with suspected delirium. A relatively innovative study design and a rigorous approach to the process of data analysis enhanced confidence in these findings, as well as the representation of clinicians from a variety of settings.

However, this study was limited by its scale: a relatively small sample size restricted to Scottish services and a moderate amount of data generated from the discussions. It is recognised that online focus groups may well result in shorter, or one-line postings as compared with traditional face-to-face discussions (Lijadi and van Schakwyk 2015), this was observed to be the case for some participants in the study in a limited number of the postings. The data collected were, however, sufficient to allow analysis which produced an outcome approximating to data saturation (Willig 2013). Moreover, some writers have argued that the patterns of meaning found in online focus group discussions closely resemble those found in more traditional face-to-face interactions (Antaki et al. 2005, Guise et al. 2007).

It is possible that a degree of sampling bias affected this study, as recognised by Williams et al. (2012), choosing an online platform to collect the data may have influenced the demographics of the participants to those comfortable in engaging with a variety of online platforms. It is therefore possible that face-to-face focus groups may have resulted in a difference in the characteristics of participants recruited into the study. Furthermore, had a more popular platform (e.g. a social media discussion group) been chosen to host the discussions, it is likely to have made contributions easier for the participants. Lijadi and van Schakwyk (2015) reflected on the success of the use of Facebook as a means of collecting focus group data. It is however important to acknowledge that utilising a social media platform would have compromised the participants' anonymity, which may well have resulted in participants sharing different thoughts and reflections on their own practice. Lijadi and van Schakwyk (2015) reflected upon this point, stating that in online focus groups participants are often more free to express their true thoughts and feelings, behind the safety of a computer screen, more so when anonymised. A further reflection on the online platform is that it may have been at times taxing for participants who

required to access the forum from their homes due to firewall restrictions in NHS hospitals and it is possible that richer data would have been generated had the data collection method been different. Coyne et al. (2016) reflected upon this matter in relation to recruiting nurses into qualitative studies. They acknowledged that both recruitment and engagement of nurses in time-consuming research is difficult due to the many demands on nurses' time. For this reason, alongside the evidence of engagement in the study presented in this chapter, the researcher would have reservations about using an online platform for focus groups with clinicians. It is therefore likely that in future studies traditional methods of data collection would be utilised.

This study was also affected by a lack of balance in the professionals recruited into the study as there were more AHPs than nurses, and no doctors participated at all. Shaha et al. (2011) suggested strategies that may help in increasing recruitment of nurses into focus group studies. Shaha et al. (2011) discussed these suggestions in the context of traditional focus group methods, and raised an important approach for consideration in any future focus group research conducted with healthcare professionals: they recommended that personal contact with potential participants at the recruitment stage may help in gaining support and interest in the study (Shaha et al. 2011). On reflection, such an approach may have had an impact had the author been able to visit a few local hospitals in order to meet professionals and try to raise interest in the study. This is certainly an approach that would be considered in future as well as the consideration of carrying out traditional focus groups which may well result in more interest in the study. Both Shaha et al. (2011) and Coyne et al. (2016) suggested that the researcher must have not only flexibility but also an awareness of the limitations of the environment within which potential participant are working. It is felt that this issue was addressed adequately within this study, particularly demonstrated in the move to

include the nurses via email interviews rather than insisting they contribute to a platform they clearly were not engaging with successfully. Coyne et al. (2016) also suggested several ways of maximising recruitment and engagement in qualitative research, many of these were not relevant in the context of this study, however, one is worth noting: Coyne et al. (2016) suggested using existing contacts to gain access to nurses in practice in order to maximise recruitment. While this approach may well work in certain settings, it is worth noting that personal contacts were used when it came to trying to recruit doctors into this study, with no success. The study was certainly affected by the lack of doctors in the sample, the approach to recruitment did not reach foundation year doctors similar to the reflections in section 5.2.8 of chapter V. Email addresses for these doctors are not in the public domain and doctors in training tend to move between areas of practice fairly frequently (National Health Service 2014). It is anticipated that including doctors in the professional mix would have yielded different responses to the discussion and may have highlighted starker differences between medical or nursing groups and allied health groups.

A final potential limitation is in the use of vignettes to guide the discussions on a hypothetical case: Jenkins et al. (2010) cited this as a limitation of using vignettes where participants clearly respond differently to a hypothetical case as opposed to 'real life' situations. Indeed, Hughes and Huby (2004) warned that at times vignette methodology may restrict the depth of discussion as participants will stay within the constraints of the scenario depicted, thus they may be reluctant to discuss the ways in which they would respond had this scenario occurred in reality. Conversely, Jackson et al. (2015) regarded the use of vignettes in qualitative research as a strength in their ability to focus participants on context as well as capturing opinions and perspectives. It is possible that if the study was designed to incorporate an element of observation of practice that

different findings would have emerged in relation to the response of staff to a patient with delirium in their care. It is also possible that the use of vignettes within this study resulted in the moderate amount of data generated from the discussions. Despite the several limitations reflected upon, and although in future the researcher is likely to design a study rather differently, this study highlights an important aspect of clinical practice in stroke units which contributes to an understanding of the ways in which staff respond to and understand a delirium in a stroke patient.

6.6 Conclusions and implications for practice

This chapter details the third and final strand of data collection and analysis for this doctoral programme. Detailed methodological considerations were outlined in the chapter, including all the analytical steps which drew inspiration from the constructivist grounded theory approach (Charmaz 2014). The data were generated using hypothetical case vignettes as the triggers for discussion within online focus groups with allied health professionals and email exchanges with nurses working in acute stroke services throughout Scotland. Despite some of the limitations related to the scale of the study as well as the design utilised, it offers several insights into the ways in which staff on the MDT working in the acute stroke unit reportedly respond to a patient with delirium in their care. The findings suggest that the understanding of delirium varied among the professionals who took part, particularly when it came to recognising the manifestations of a hypoactive delirium. A further finding was around the use of terminology to describe a delirium: the word ‘confusion’ was frequently chosen as opposed to ‘delirium’. This did not seem to have an impact on the described actions participants would take in response to a delirium, as all of the actions reported were consistent with the principles of good

delirium management as per local and national guidelines (National Institute of Health and Care Excellence 2012, Healthcare Improvement Scotland 2014). While it is encouraging to observe this approach from clinicians, there are reasons why the use of accurate language to discuss and describe delirium is important: several authors argue that lack of accuracy in the choice of language is a barrier to correct identification (Morandi et al. 2012, Teodorczuk et al. 2013, Rice et al. 2014, Fleet et al. 2015). Additionally, using accurate language when it comes to delirium may help educate other staff members in the team (MacLullich et al. 2013), and finally, accurate use of language is crucial in allowing teams to be able to anticipate outcomes and long-term risks associated with delirium in acute stroke (Carin-Levy et al. 2012, Shi et al. 2012, Melkas et al. 2012).

A particularly encouraging finding of this study was the ethos of person centredness discussed by the participants who described their approach to the hypothetical scenarios as caring, compassionate and person centred. This stands in contrast to some of the reports in the literature around negative attitudes or marginalisation of patients with delirium in the acute care setting (Neville 2008, Belanger and Ducharme 2011, Teodorczuk et al. 2013, Clissett et al. 2014). This may be due to the strong ethos of person centredness and the strong culture of team work that are guiding principles in Scottish stroke units (Scottish Intercollegiate Guidelines Network, 2010). This potentially makes the stroke unit an area of practice which could herald a culture of ownership of delirium identification as a shared responsibility within the team (Godfrey et al. 2013, Teodorczuk et al. 2013, Bellelli et al. 2014b).

Whilst this study was not concerned with delirium education *per se*, there was some suggestion of its benefit as it seemed that within the sample of participants, those who received specialist delirium education in the past were able to discuss the symptoms

more confidently, identifying the action of screening using an appropriate delirium bedside tool. The results of this study, combined with empirical research on educational programmes for delirium identification (Yanamadala et al. 2013) could inform any future multidisciplinary educational programmes which would be specifically tailored to the staff working in acute stroke services.

Chapter VII

General Discussion

7.1 Introduction

This chapter is an overview and synthesis of the doctoral programme as a whole. The sections of this chapter discuss, in the context of the available literature, the overall messages that have emerged from the data collected in each strand of the doctoral programme. The chapter also provides an account of the contribution of this programme of research to the field of study as well as directions for future research.

7.2 The incidence, risk factors and impact of delirium in acute stroke

The most important finding of the systematic review and meta-analysis completed as the first strand of the doctoral programme was the identification of the incidence rate of delirium in the acute stroke setting as occurring in 28.1% of patients (95% CI: 22.9 to 33.2). This rate is consistent with the incidence of delirium found in elderly medical settings where it is reported to be between 20-29% (Inouye et al. 2014). At the time of the 2010 systematic review and meta-analysis going to press (Carin-Levy et al. 2012, appendix 7.1) this was the first study to attempt to provide an estimate of the rates of delirium in acute stroke. Shortly after this work was published, another systematic review and meta-analysis was published (Shi et al. 2012). The main aims of Shi et al.'s work

(2012) were to establish the incidence, risks, associated factors and clinical outcomes for people experiencing delirium in acute stroke. Shi et al. (2012) found that delirium affects 10%-30% of patients post stroke, but in their study, they did not attempt to synthesise the data regarding incidence specifically. The incidence of 28.1% found in the first strand of this programme of research fits within the upper end of the range discussed by Shi et al. (2012).

The systematic review and meta-analysis presented in chapter IV identified several of the risk factors associated with developing delirium in acute stroke: Older age, severe illness and pre-existing cognitive impairment have all been previously identified as risk factors for delirium in acute hospital settings (Young and Inouye 2007, National Institute for Health and Care Excellence 2010). More specifically to stroke patients, two of the studies included in the systematic review and meta-analysis incorporated a predictive model for developing delirium in acute stroke (Kostalova et al. 2012, Oldenbeuving et al. 2014). Older age, combined with infection, increased stroke severity and stroke type (PACI, TACI and haemorrhagic strokes) were found to be predictive of developing delirium in stroke patients (Kostalova et al. 2012, Oldenbeuving et al. 2014). These predictive models potentially enable staff to anticipate a delirium developing in stroke patients who fulfil these criteria, however, it should be noted that Kostalova et al. (2012) collected their data from a single, small (six bedded) stroke unit in the Czech Republic and Oldenbeuving et al. (2014) collected data from two stroke units in the Netherlands. It would be difficult to generalise their findings to the wider population since practice varies across different counties, and different populations may be affected by different risk factors. Indeed, in a large study (n=576) recently published by Lim et al. (2017), smoking was identified as an independent risk factor for developing delirium in

acute stroke (p=0.015; odds ratio=2.7; 95% CI 1.2 to 6.3), a factor not found by any of the studies included in the systematic review.

The role of medication in the development of delirium is documented in the general medical literature (Tune and Egeli 1999, Marcantonio et al. 2006, Young and Inouye 2007, Inouye et al. 2014, Ahmed et al. 2014). In the stroke literature, there is some interest in the link between the use of anticholinergic medication as a risk factor, however, only four of the studies included in the review found this to be an independent risk factor for delirium in acute stroke (Gustafson et al. 1991, Caeiro et al. 2004b, Kara et al. 2013, Miu and Yeung 2013). This association is inconclusive in the general hospital setting also (Moorey et al. 2016), suggesting the need to continue to explore this particular area of research.

The outcomes associated with developing delirium in the acute hospital setting are well established: increased length of hospital stay and increased mortality and morbidity are all documented (McCusker et al. 2003, Burns et al. 2004, Young and Inouye 2007, National Institute for Health and Care Excellence 2010, Witlox et al. 2010). This programme of research identified the same outcomes in stroke patients: those who experience delirium in the acute stage of stroke are more likely to have longer hospital stays, die in hospital within 12 months, more likely to have poorer functional outcomes and more likely to be discharged into a long term care facility. These finding are confirmed by Shi et al.'s systematic review on the same topic (2012) as well as in single studies not included in either systematic reviews (van Rijsbergen et al. 2011, Turco et al. 2013, Lim et al. 2017). These factors, taken together with the finding that delirium is found in around a quarter of acute stroke patients warrants attention due to the increased burden both on patients, families and healthcare providers (National Institute of Health and Care Excellence 2010, Leslie et al. 2011, O'Mahoney et al. 2011, Inouye et al. 2014).

Additionally, it is recognised that identifying patients at risk of delirium is an important way of preventing its development (Teodorczuk et al. 2012, Huber et al. 2012, Godfrey et al. 2013). The limitations of the systematic review and meta-analysis are explored in full in chapter IV, these are mainly related to search strategy, the use of the QUADAS (Whiting et al. 2003) as a critical appraisal tool and the degree of heterogeneity found in the meta-analysis component. Nevertheless, this review provides important information in highlighting the incidence of delirium as well as pinpointing the specific risk factors affecting stroke patients, thus providing clinically useful information to assist efforts of delirium prevention in this population.

7.3 Identifying delirium in research and clinical practice

An important finding of this doctoral programme is around the approach to delirium identification in research as well as clinical practice. The systematic review presented in chapter IV found a wide variation in the procedures employed by the various studies as they set out to identify delirium in stroke patients. Diagnostic tools varied widely, as did the timing of delirium assessment, from assessments being conducted once in the first two weeks of admission to the stroke unit (Mori and Yamadori 1987); delirium diagnoses reached by means of case-note reviews (Shih et al. 2007, Dunne et al. 1986, Schmidley and Messing 1984); studies assessing for delirium twice or more within the first week of admission (Oldenbeuving et al. 2011, Miu and Yeung 2013, Oldenbeuving et al. 2014) or delirium assessments being conducted more than once daily (Gustafson et al. 1991, Gustafson et al. 1993, Dahl et al. 2010, Mitasova et al. 2012, Naidech et al. 2013). There did not seem to be any pattern in the frequency and method of assessment in the way that it linked with the incidence rates identified, despite the

suggestion from McManus et al. (2007) that the frequency of delirium assessment corresponded with higher incidence rates found. In clinical practice, the timing of delirium assessment is key in achieving early identification, a matter which is regarded as a means of preventing the potentially serious consequences of the condition (Holly et al. 2013, O'Hanlon et al. 2013). It is therefore encouraging to note that much of the contemporary literature on the incidence of delirium in acute stroke describes delirium assessments taking place within the first few days of admission (Table 8, p.115). A further issue related to diagnostic procedures employed by the studies included in the review is around the exclusion of patients with pre-existing dementia and aphasia. Inouye et al. (2014) criticised this practice stating that exclusion of patients with pre-existing dementia inevitably results in an under-estimation of incidence rates. Indeed, it is encouraging to note that the studies published in subsequent years did not report the exclusion of stroke patients with premorbid dementia or aphasia for the purpose of evaluating the presence of delirium (Lees et al. 2013, Oldenbeuving et al. 2011, Mitasova et al. 2012, Kutlubaev et al. 2016, Melkas et al. 2012, Miu and Yeung 2013, Turco et al. 2013).

The issue of the tools used to diagnose delirium in stroke patients clearly emerged as problematic in this programme of research. At the time of completing the original systematic review and meta-analysis in 2010, the problem of lack of a consistent approach to delirium identification was confounded by the absence of specific guidance on how to screen for delirium in a stroke population as well as the lack of studies investigating the performance of bedside tools in a cohort of stroke patients. This matter has since been partly addressed with the expansion of the body of literature on the performance of delirium bedside tools in the acute stroke setting. Despite this, it is not yet possible to come to conclusions regarding the best approach to delirium identification in stroke patients since more recent studies continue to utilise diverse methods of delirium

identification, as demonstrated in the updated systematic review. This matter contributed to the substantial heterogeneity detected in the meta-analysis component, leading to the subgroup analysis based on the various tools utilised (as detailed in section 4.3.4.4).

The survey presented in chapter V of the thesis identified a similar problem: survey respondents cited a number of bedside tools that were used to detect delirium, not all of which were specifically designed to detect delirium [e.g. the AMT (Hodkinson 1972) and the MMSE (Folstein et al. 1975)]. Additionally, at the time of conducting the survey, none of the tools cited by participants had been validated for use in acute stroke, and respondents felt that the tools were not suitable for use with stroke patients, citing communication difficulties such as aphasia as well as the cognitive difficulties arising from the stroke. Since the survey results were published (Carin-Levy et al. 2013, appendix 7.2) four validation studies were identified (Mitasova et al. 2012, Lees et al. 2013, Kutlubaev et al. 2016, Infante et al. 2017), these give clinicians several options for their evidence-based decisions on the choice of bedside tool to use in the acute stroke setting. These findings of variability in the choice of tool, the timing and frequency of assessment and lack of certainty around the suitability of bedside tools for use in a stroke setting highlight the importance of establishing stroke-specific guidelines for the identification of delirium in practice. Klimiec et al. (2016) reiterated this in a recent, comprehensive review of what is known about delirium in acute stroke. They also called for the development of a simple, reliable tool which is adapted for patients with neurological conditions (Klimiec et al. 2016). Based on the psychometric performance of existing tools in stroke cohorts, this may not be necessary, since the CAM-ICU (Ely et al. 2001a) and the 4AT (Bellelli et al. 2014a) seem to perform well with stroke patients, based on single validation studies (Mitasova et al. 2012, Lees et al. 2013, Kutlubaev et al. 2016, Infante et al. 2017).

Rapp et al. (2000) discussed the issue of the clinical versus research practice in delirium identification. They stated that in the realities of clinical practice there often is not the time available to complete lengthy delirium assessments which utilise bedside tools. Indeed, other authors acknowledged that while best practice in delirium diagnosis is a combination of screening as well as full clinical assessment, time may be too tight in the clinical setting to allow completion of both (Schofield 2008, Schofield 2010, Inouye et al. 2014). This raised the question of whether the diagnostic processes identified in the the systematic review differ from the approach clinicians utilise in practice. The survey reported in chapter V of this thesis attempted to address this question among others. Despite this survey being affected by several important limitations related to design, coverage and generalisability, it still provides a useful snapshot of the practice of identifying delirium in the acute stroke setting at the time. The survey indicated that most stroke units either did not have a screening policy for the delirium identification in acute stroke, or the clinicians were unaware of such policy. The issue of sparse institutional policies regarding delirium screening is reported in European literature (Morandi et al. 2013, Steen et al. 2013). Other surveys of practice (reported in the paragraphs below) did not report on the presence or absence of delirium protocols within their survey. Confirming this point to an extent, in an opinion piece, Greysen (2015) is critical of the lack of attention to creating delirium policies within the American healthcare setting, despite the evidence available regarding the benefits and successes of prevention programmes. Within NHS Scotland, this matter has been addressed within recent years with the introduction of initiatives such as 'Think Delirium' by Healthcare Improvement Scotland (2014). Such initiatives to roll out delirium screening to the majority of patients over the age of 65 (Bond and Goudie 2015), taking a multidisciplinary approach to the use of the 4AT and raising awareness of the condition in acute hospital settings in

Scotland appear to have been well-received (Healthcare Improvement Scotland 2015). However, the guidance from Healthcare Improvement Scotland (2014) does not devote specific attention to screening patients with communication disorders or reduced consciousness as a potential area of difficutly in implementing this approach to routine screening. The survey reported in chapter V of the thesis was conducted prior to the implementation of the 'Think Delirium' initiative (Healthcare Improvement Scotland 2014), therefore it is not surprising that nearly half of respondents claimed they did not routinely screen for delirium in actue stroke, a matter which is confirmed in early surveys of practice in other geographical and clinical settings (Ely et al. 2004, Flagg et al. 2010, Steen et al. 2013).

The lack of consistency in the delirium diagnostic approaches identified in the systematic review and survey extend beyond the utilisaiton of bedside tools to the members of staff conducting delirium assessments. In the survey reported in chapter V, mainly doctors diagnosed delirium and this was achieved by means of clinical judgement, and in some cases combined with the use of a standardised tool. Overall the survey found that only a small number of respondents used tools to diagnose delirium in their practice. The lack of use of standardised tools to identify delirium is confirmed in a variety of countries and clinical settings (Salluh et al. 2009, Patel et al. 2009, Forsgren and Eriksson 2010, MacSweeny et al. 2010, Steen et al. 2013, Bellelli et al. 2014b, Elliot 2014, Sinvani et al. 2016). Several authors suggested that lack of clinician knowledge, reduced confidence and low levels of training are the main barriers to the use of standardised delirium assessment tools in the process of delirium identification (Devlin et al. 2008, Flagg et al. 2010, Wells et al. 2012, Morandi et al. 2013, Elliot 2014, Sinvani et al. 2016). This matter is also reflected in findings of the online focus groups presented in chapter VI which suggested a lack of confidence in recognising the symptoms of delirium,

particularly the hypoactive type, a matter which is consistent with literature on detection of delirium in the acute hospital setting (Fick et al. 2007, Flanagan and Fick 2010, Bellelli et al. 2014b, McCrow et al. 2014). A finding that perhaps related to lack of in-depth understanding of delirium which emerged from the focus group study was the inconsistent and somewhat tentative language used to discuss delirium in stroke patients as clinicians often referred to 'confusion' throughout the discussions. This is reported in other hospital settings (Day et al. 2008, Rice et al. 2014, Day and Higgins 2015) and is regarded by several authors as a misleading term which is considered as a barrier to correct identification and management of the condition (Day et al. 2008, Morandi et al. 2012, Godfrey et al. 2013, MacLullich et al. 2013, Teodorczuk et al. 2013, Fleet et al. 2015).

7.4 Multidisciplinary delirium education and team roles

While this thesis is not concerned with delirium education *per se*, elements of this issue have emerged in two strands of the thesis as the question of staff training arose both in the survey (chapter V) and the focus group findings (chapter VI). Most of the nurses who responded to the survey claimed that they do not diagnose delirium in practice because they were not trained to use delirium bedside tools. In the focus group study, two participants mentioned their attendance at a training session on delirium and they seemed more confident in recognising and discussing the symptoms. These participants were also singled out in their reference to the use of the 4AT as consistent with the 'Think Delirium' programme (Bellelli et al. 2014a, Healthcare Improvement Scotland 2014).

An important finding of the focus group study was on aspects of team working within the stroke unit when it comes to identifying patients with delirium. The division of

roles within the team, a distinction in perceived knowledge about delirium and the inclusion of the family or caregivers as an important part of the team are all presented in chapter VI. The difference in clinicians' roles in delirium recognition is discussed in other hospital settings: nurses are regarded as important contributors in delirium recognition due to the relatively prolonged contact with patients, and their ability to detect behavioural fluctuations both day and night (Fick et al. 2007, Dahlke and Phinney 2008, Hall et al. 2012, Ryan et al. 2013). Considering the key role nurses could play in delirium identification in stroke patients, it is disappointing that in the survey presented in chapter V, nurse participants reported lack of training on delirium identification. Clearly the survey was conducted prior to the rolling out of the 'Think Delirium' programme, and this aspect seems to have now been addressed as the reported rates of delirium recognition appear to have increased in the hospitals surveyed as part of the impact assessment carried out by Healthcare Improvement Scotland (2015). It is however worth noting that the impact report from Healthcare Improvement Scotland (2015) does not specifically mention the stroke setting since the interest is mainly across all acute care units throughout NHS Scotland. This distinction is important due to the previously noted difficulties in cognitive assessment of stroke patients (Lees et al. 2013, Lees et al. 2014). The difficulties in performing cognitive assessments in stroke patients may have implications on the involvement of AHPs in this area of practice: speech and language therapists could have an important role in assisting the accurate diagnosis of delirium in severely aphasic patients and occupational therapists, with their expertise in cognitive assessment of stroke patients (Scottish Intercollegiate Guidelines Network 2010) would have much to offer the team effort in delirium identification, as long as they have the confidence to engage with the process. Indeed, one of the issues than became clear in the analysis of the data presented in chapter VI is that the OT participants did not convey a sense of

understanding of the manifestations of a delirium in a stroke patient, suggesting that this may be an area to investigate again, to establish the extent to which educational programmes rolled out in NHS Scotland may have had an impact on AHP response to a delirium in patients in acute stroke.

7.5 A patient-centred approach to delirium in acute stroke

In their seminal text, Gerteis et al. (1993) outlined the key elements of patient-centred care: education and care co-ordination; good communication between staff and patient as well as among staff; ensuring patients' physical and emotional comfort as well as alleviation of fear and anxiety; and, involvement of family in the care of the patient. Elements of all of these emanated in the approach participants took to the patients described in the case vignettes used to generate the data presented in chapter VI. The family or caregivers have a recognised role in assisting clinical teams in the management of delirium as informants of premorbid function as well as participants in the therapeutic process (Vidán et al. 2009, Benedict et al. 2009, Rosenbloom-Brunton et al. 2010, Martinez et al. 2012, Healthcare Improvement Scotland 2014). Indeed, one of the key findings presented in chapter VI was around the ways in which clinicians would involve the family of the patient with delirium, from the finding out of information to actively participating in therapy sessions. This approach to care is strongly related to the aims of delivering patient-centred care (Gerteis et al. 1993, Zeitz et al. 2011, Kitson et al. 2013), as seen in the discussion in chapter VI. Clinicians participating in the focus groups also reported actions that were perceived as holding a caring, compassionate approach towards patients as well as a sense of interest in the patient's welfare and comfort. This is consistent with the ethos and culture in Scottish stroke services as patient centredness

is a guiding principle in stroke units throughout NHS Scotland (Scottish Intercollegiate Guidelines Network, 2010). Studies explored in section 2.8 of the literature review examined aspects of negative responses to patients with delirium, however, the focus group study could not confirm this in any way. This may be related to some extent to the ways in which the data were collected, as reflected upon in relation to the limitations of the focus group study. Yet, despite these limitations, the data did not suggest in any way negative responses from the participants towards patients with delirium in their care.

Team collaboration or effective team work and team communication are also important elements of patient centredness within the care of older people (Zeitz et al. 2011). This can be seen within the context of sharing responsibility for the care of patients with delirium, an issue raised in the discussion of chapter VI. Sharing responsibility is a matter which is discussed in contemporary literature in the field of delirium: Several authors argue for a team approach when it comes to recognition and prevention of delirium (Teodorczuk et al. 2012, Godfrey et al. 2013, Bellelli et al. 2014b, Schwartz et al. 2016). Another matter of importance in improving the care of patients with delirium is the notion of ownership identified by Teodorczuk et al. (2013). They perceived the lack of ownership over the care of a patient with delirium as a barrier to effective care, indicating that this affects the health service both at individual and organisational levels. The focus group study presented in chapter VI of this thesis would go further to suggest that the ownership is shared, as stated by one of the participants: “it’s everyone’s responsibility” (N2 [C2.10]). Indeed, Fisher et al. (2015) and Teodorczuk et al. (2013) called for education programmes on delirium to go beyond symptom recognition and rather be targeted towards promoting ownership. There is a shift in the delirium literature to move away from merely educating staff about delirium to calling for organisational change. Greysen (2015) referred to the ‘know-do-gap’ in organisational management

suggesting that despite mounting evidence of the scale of the problem, the cost to the organisation and the preventability of the condition, implementation is slow to follow. O'Hanlon et al. (2013) suggested that improving ward-level delirium care can be achieved by adopting brief and convenient screening procedures that allow for consistent and accurate identification of delirium, a matter which requires effective leadership. This is clearly the aim of the "Think Delirium" initiative (Healthcare Improvement Scotland 2014) however, there is some evidence of the slow implementation of this programme in Hendry's doctoral work (2017).

Teodorczuk et al. (2015) perceived good ward leadership to be conducive to good team work which leads to a more patient-centred approach in the care of the patient with delirium. Stroke units in the UK are established on the basis of their interdisciplinarity, they rely on effective teamwork and team communication as well as ongoing education of team members (Intercollegiate Stroke Working Party 2012). According to Clarke and Forster (2015) interdisciplinary teamwork goes beyond different professionals working together but rather it implies an accepting of responsibility of the group effort on behalf of the patients in their care. This collaborative, patient centred culture of practice in stroke services may well make this setting one in which the ideas of a shared responsibility of delirium detection, as well as 'ownership' (Teodorczuk et al., 2013) could be effectively put into practice.

7.6 Contribution to the field, implications for research and practice

This doctoral programme makes significant contributions to the field of delirium research by shining a spotlight on the area of delirium in acute stroke, specifically, the

scale of the problem as well as the ways in which multidisciplinary team members identify a delirium and respond to it in stroke services in Scotland. The systematic review and meta-analysis completed as the first strand of this programme of research was published in 2012 and has generated a fair amount of interest to date, with 41 citations (based on Google Scholar data) at the time of completing the thesis in June 2017. This publication (Carin-Levy et al. 2012, appendix 7.1) generated new knowledge in the incidence data presented in the meta-analysis, whereas the other components of the review acted as a synthesis of existing information on the risk factors for developing delirium in acute stroke and the negative outcomes associated with the condition. The updated systematic review is currently being prepared as a manuscript to be submitted for peer review in a leading stroke journal.

An aspect identified in the systematic review was the widely varying means of delirium identification utilised in the studies included in the review: different bedside tools, different timings and frequency of delirium assessment. Based on the findings of the review, there is no consensus over the ideal method of delirium identification, a matter discussed critically by Davis et al. (2013), who regarded this issue as a challenge to ascertaining delirium cases in research, and thus being able to accurately pinpoint the incidence of delirium in a population. Davis et al. (2013) regarded this aspect as an important direction for future delirium research. Being able to reach a consensus on the means by which delirium ought to be identified effectively in research would also carry implications for clinical practice. Within Scotland, there seems to be a consensus around the use of the 4AT as a rapid screen for delirium (Healthcare Improvement Scotland 2014). Its use is being rolled out beyond Scotland and interest in its potential in identifying delirium in a variety of medical settings has grown (Bellelli et al. 2014a, Hendry et al. 2016), particularly in cohorts of stroke patients (Kutlubaev et al. 2016, Infante et al. 2017).

This is a promising direction since the tool is designed for multidisciplinary use (Healthcare Improvement Scotland 2014). It would be very useful to continue to examine its use by nurses as well as allied health professionals within stroke services throughout the UK. More multidisciplinary research on the ways in which delirium is identified in stroke patients could potentially lead to delirium assessment being included as a recommendation in stroke best practice guidelines, a matter which to date has not received specific attention in the UK (Scottish Intercollegiate Guidelines Network 2010, National Institute for Health and Care Excellence 2013, Intercollegiate Stroke Working Party 2012).

This thesis makes a further original contribution to knowledge in the publication of the results of the survey of screening and diagnostic practices in Scotland (Carin-Levy et al. 2013, see appendix 7.2). This survey was limited in a variety of ways, previously reflected upon (section 5.5.4). However, the survey reveals information that is consistent with reports from other areas of practice and other populations. Interestingly, at the time of data collection, several emails from clinicians working outside of Scotland were received, suggesting that this exploration is important and should be extended beyond Scotland. This was not possible due to the scale of this doctoral programme (see section 5.5.4.4), however, it is a matter which could be rolled out upon completion of doctoral studies. A report of this survey was invited by the Scottish Stroke Nurses Forum and published in their 2014 newsletter (appendix 7.3) so that the information gleaned from the survey was shared with specialist stroke nurses. Disseminating the findings of this strand of the doctoral programme has certainly contributed to existing knowledge around the identification of delirium in stroke patients both in research and clinical practice.

The work carried out as the third strand of this programme of research also makes an original contribution to the field of delirium in acute stroke as it explores the ways in

which various healthcare staff reportedly respond to a patient with delirium in several stroke units in Scotland. Whilst there were some limitations related to the focus group design and the scale of the study, analysis of the data revealed that when faced with a patient exhibiting delirium symptoms, the actions proposed by staff were consistent with the guidelines on the management of delirium in acute hospital settings (National Institute of Health and Care Excellence 2010). While it was reassuring to note this, these actions were proposed in the absence of evidence of a deep understanding of the condition, particularly noted through the use of the lay term 'confusion' in most of the discussions about delirium. It was also noted that the hypoactive delirium posed challenges for staff attempting to identify the symptoms, a matter which is consistent with the literature on delirium (Bellelli et al. 2014b, McCrow et al. 2014). The two participants who received delirium training displayed greater confidence in their discussion of the symptoms of the condition and used more accurate language as well as being able to discuss an appropriate screening tool in response to the scenarios given. This suggests that stroke unit staff could benefit from tailored, multifaceted education programmes on delirium identification and management. However, it should be noted that recent contact with nurse clinical specialists in NHS Scotland revealed through conversation that despite implementation of the "Think Delirium" initiative successfully across a variety of hospital settings, delirium identification in stroke wards in which they worked continues to be problematic. Whilst this is merely anecdotal, it may suggest that more research in this area is warranted, attempting to identify whether barriers to delirium identification continue to affect this patient population despite widespread multidisciplinary education programmes. It is not known whether the training that has taken place in stroke units in Scotland addressed stroke-specific barriers to correct delirium identification, and given the uncertainty around the long-term success of such education programmes

(Yanamadala et al. 2013, McCrow et al. 2014) it would also be useful to evaluate the success of such programmes longitudinally, in a stroke specific setting.

A final original contribution made by the research conducted as part of this doctoral programme is on a discipline-specific note: repeated searches of the literature throughout the period of registration resulted in only two research papers dealing specifically with the contribution occupational therapists can make to the management of delirium (Schweickert et al. 2009, Álvarez et al. 2017), and none specifically on the identification of delirium by occupational therapists. This is surprising given that occupational therapists have been recognised by a national survey as the professional group who routinely assess cognition in stroke patients (Lees et al. 2014). The author plans to conduct a further analysis of the data related to the occupational therapy participants and to prepare this for publication within an occupational therapy specific journal. This would serve as a means of disseminating the information to the profession in the hope of establishing a firmer position for delirium research within the occupational therapy literature. Additionally, this may help to disseminate the importance of delirium as a clinical priority for which occupational therapists have a role in both its identification and its effective management (Álvarez et al. 2017).

Chapter VIII

Conclusion

The three studies presented in this thesis comprise a pragmatic, mixed methods programme of research on delirium in acute stroke. The first strand of the programme, a systematic review and meta-analysis, examined the incidence rates, means of identification, risk factors and outcomes associated with developing delirium in this population. The second strand, a web-based survey examined the ways in which doctors and nurses working in acute stroke services in Scotland identify a delirium in practice. The third and final strand was an online focus group study utilising a grounded analysis to explore how multidisciplinary team members understand and reportedly respond to delirium in acute stroke. Each strand of this programme of research was presented in a separate chapter, which included detailed methodological considerations, findings and corresponding discussions, drawing upon the available literature in the field of delirium in acute stroke, as well as delirium in other acute medical settings as required. This thesis addressed several gaps in the literature which were evident at the time of the programme commencing, some of which are now beginning to fill as interest in delirium in acute stroke grows. The question of the scale of the problem of delirium in acute stroke was addressed by the research undertaken in the first strand: several studies exploring the incidence of delirium in acute stroke, the risk factors and outcomes associated with delirium in this clinical area were available, but no systematic review or meta-analysis was available at the time. The findings of the systematic review and meta-analysis conducted as the first strand of this programme of research made a significant

contribution to the field at the time of first publication (Carin-Levy et al. 2012). The systematic review component synthesised data from 28 studies on delirium in acute stroke to clearly identify the risk factors for developing the condition as well as its serious consequences: increased length of hospital stay, increased mortality and increased morbidity are all identified in chapter IV of this thesis. A further finding of the systematic review was the wide variety of tools used as outcome measures in research in order to identify delirium in stroke patients. This led to the question of whether the same inconsistent approach applied in practice, a question addressed by the second strand of the programme, a web-based survey.

The survey presented in chapter V of the thesis explored the ways in which doctors and nurses across Scottish stroke services identify delirium. Despite its limitations, the survey revealed some important preliminary findings regarding the identification of delirium in Scottish stroke services: at the time of data collection no standardised protocols for identifying delirium existed. Furthermore, the survey revealed an inconsistent approach to the process of delirium identification. Additionally, the survey suggested a difference between the practice of doctors and nurses when it comes to delirium identification in this setting: the nurses who responded to the survey reported they did not diagnose delirium in practice, citing the lack of training in the use of delirium bedside tools (Carin-Levy et al. 2013). This led to the wish to explore the experiences of different healthcare professionals in acute stroke services when working with patients with delirium. The question was explored by qualitative means, using online focus groups as the third strand of this doctoral programme.

The qualitative exploration presented in chapter VI of the thesis used online focus groups with case vignettes and a grounded analysis which revealed a number of interesting findings regarding clinical practice in the area of delirium in acute stroke. The

findings of the third and final strand suggest inconsistent understanding of delirium across a variety of healthcare professionals. This was particularly noted in discussing a hypoactive delirium. In general, the lay term 'confusion' was favoured by respondents, a matter which is associated by some authors as a barrier to accurate identification of delirium (Day et al. 2008, Morandi et al. 2012, Teodorczuk et al. 2013, Rice et al. 2014, Fleet et al. 2015). Despite this, the findings of the third strand revealed that the principles of delirium management were followed, and a collaborative approach to teamwork and patient centredness emanated throughout the discussions.

The issue of education had peripherally emerged in both the survey and the focus group strands, despite not being amongst the aims of either study. It seemed that staff who were educated about delirium and its identification were confident in discussing the symptoms and citing appropriate screening tools (chapter VI) as opposed to nurses who felt they did not identify delirium in their practice because they were not trained to do so (chapter V). There is some evidence in the literature of the success of educational programmes (Yanamadala et al. 2013), but this is not in the stroke setting, where the identification of delirium is complicated by aphasia, cognitive deficit arising from stroke and reduced consciousness in some patients (McManus et al. 2007, Oldenbeuving et al. 2011, Lees et al. 2013). The exploration of any benefits of setting-specific staff education programmes would be an appropriate continuation of this programme of research, and other ideas for future research are offered in the general discussion of the thesis (section 7.6). However, it is possible that staff education alone will not resolve the difficulties of delirium identification in clinical practice (Jenkins et al. 2014, Hendry et al. 2016). It is suggested that education programmes need to come along with a cultural shift within organisations towards recognising delirium as a diagnostic priority within hospital settings (Dewar et al. 2013 Godfrey et al. 2013, Ryan et al. 2013), as currently being addressed

by Healthcare Improvement Scotland. This will allow staff the time and resources to be educated on the symptoms, precipitating factors, and means of identifying delirium so that its impact can be minimised through early identification and appropriate management (Teodorczuk et al. 2012, Huber 2012, Godfrey et al. 2013, O'Hanlon et al. 2013). The stroke unit is potentially an area in which this could be put into practice successfully due to the collaborative, patient-centred culture of practice in Scottish stroke units (Langhorne and Pollock 2002, Scottish Intercollegiate Guidelines Network 2010). It is anticipated that disseminating the findings of this doctoral programme would potentially lead to greater awareness of the condition amongst stroke unit team members so as to enable the ideas around a shared responsibility of delirium detection and management to be embedded into practice.

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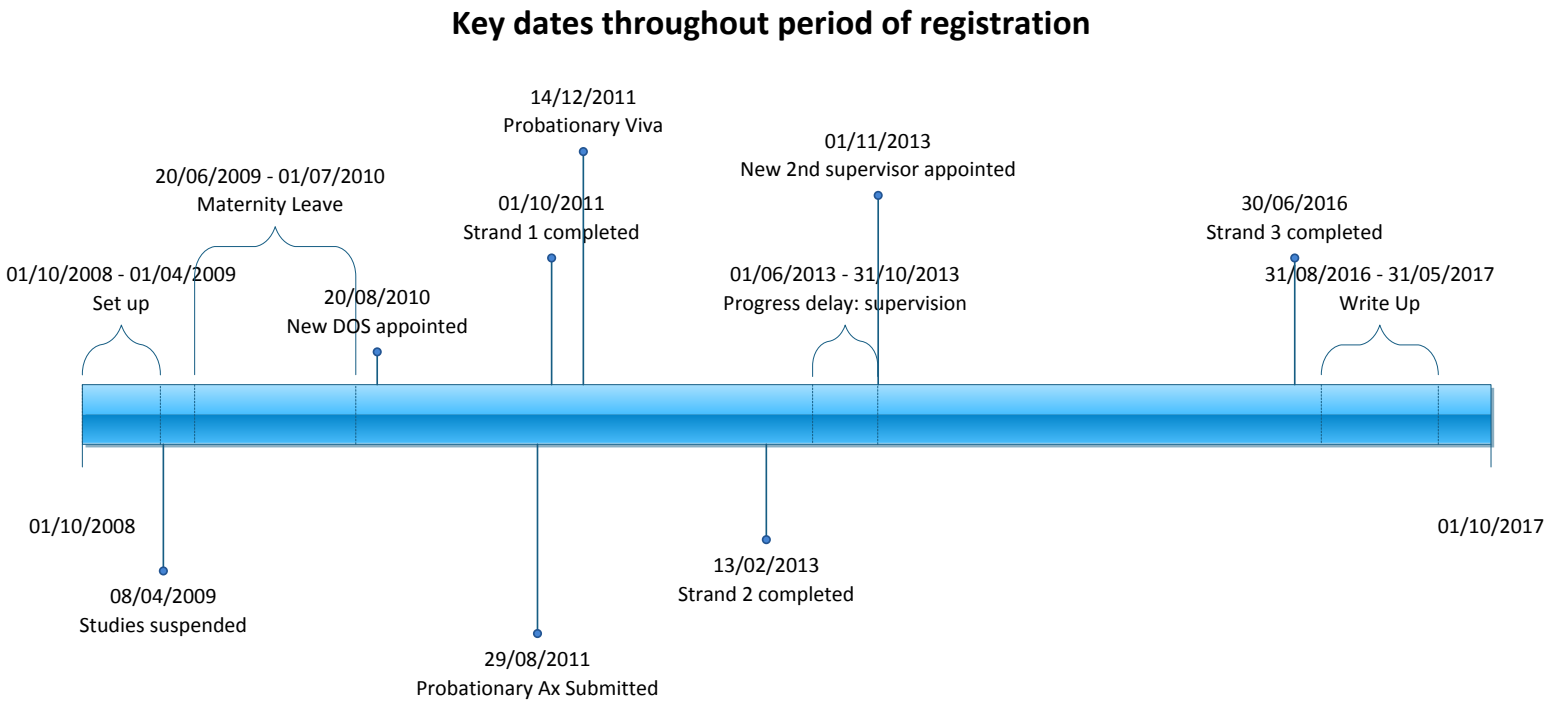
Appendices

Appendix related to chapter I

Appendix 1.1: Project timeline



Appendix related to chapter II

Appendix 2.1: Search strategy:

The last searches were performed in April 2017.

Table 1: Delirium identification in stroke patients

Database	Keywords	Hits	Duplicate	Retrv'd
Medline (via EBSCOhost)	Barriers (AND) Delirium (AND) Stroke patients: Delirium (AND) Identification (AND) Stroke patients: Delirium Identification (AND) Barriers (AND) Stroke: Delirium (AND) Screening (AND) Stroke: Delirium (AND) Recognition (AND) Stroke patients:	0 5 0 24 5		2 0 0
CINAHL (via EBSCOhost)	Barriers (AND) Delirium (AND) Stroke patients: Delirium (AND) Identification (AND) Stroke patients: Delirium Identification (AND) Barriers (AND) Stroke: Delirium (AND) Screening (AND) Stroke: Delirium (AND) Recognition (AND) Stroke patients:	0 4 0 12 1	3 2	0 0 0
PsychINFO (via EBSCOhost)	Barriers (AND) Delirium (AND) Stroke patients: Delirium (AND) Identification (AND) Stroke patients: Delirium Identification (AND) Barriers (AND) Stroke: Delirium (AND) Screening (AND) Stroke: Delirium (AND) Recognition (AND) Stroke patients:	0 4 0 12 1	2 2	0 0 0
AMED (via Ovid)	Barriers (AND) Delirium (AND) Stroke patients: Delirium (AND) Identification (AND) Stroke patients: Delirium Identification (AND) Barriers (AND) Stroke: Delirium (AND) Screening (AND) Stroke:	0 0 0 1 0		0

	Delirium (AND) Recognition (AND) Stroke patients:			
EMBASE (via Ovid)	Barriers (AND) Delirium (AND) Stroke patients: Delirium (AND) Identification (AND) Stroke patients: Delirium Identification (AND) Barriers (AND) Stroke: Delirium (AND) Screening (AND) Stroke: Delirium (AND) Recognition (AND) Stroke patients:	2 7 1 29 18	 1 1 	0 0 0 0 0

Table 2: Allied health professionals' roles mentioned in delirium literature

Database	Keywords	Hits	Duplicate	Retrv'd
Medline (via EBSCOhost)	Delirium (AND) Occupational Therapy Delirium (AND) Physiotherapy Delirium (AND) Speech and Language Therapy	20 34 1		1 1 0
CINAHL (via EBSCOhost)	Delirium (AND) Occupational Therapy Delirium (AND) Physiotherapy Delirium (AND) Speech and Language Therapy	12 9 1	3 1	0 1 0
PsychINFO (via EBSCOhost)	Delirium (AND) Occupational Therapy Delirium (AND) Physiotherapy Delirium (AND) Speech and Language Therapy	13 8 1	1 1	0 0 0
AMED (via Ovid)	Delirium (AND) Occupational Therapy Delirium (AND) Physiotherapy Delirium (AND) Speech and Language Therapy	1 0 0		1
EMBASE (via Ovid)	Delirium (AND) Occupational Therapy Delirium (AND) Physiotherapy Delirium (AND) Speech and Language Therapy	42 0 2	1	0 0

Appendix related to chapter III

Appendix 3.1: Extract from research journal

Choosing the Review Tool.
Diary Entry date: 23.2.2011

In the process of setting up the protocol for the systematic review, it was essential that a review tool would be used - and this process was a bit of a saga in itself. I agonised over this for many weeks and this held back the process of finalising the data extraction form.
I wanted a tool that would be:

(*) validated - so it had undergone rigorous analysis as to its feasibility for use in systematic reviews / assessment of methodological quality.
(*) used in research, the more widely used, the better - so that I could enter a the title of the tool as a search term in a literature data base and find out who else used it in a systematic review, and to what success. This was really quite important to me, as I wanted to have a sound justification for the tool that I used, and there is also something about "strength in numbers" (for me anyway, it's a comfort...)
(*) the tool had to be as relevant to what we are doing as possible, so this excluded checklists that look at intervention studies as these have far too many categories that are not applicable.
(*) I wanted a tool that gave me a definitive answer as to whether the study was strong or weak according to the number of items checked on the prescribed list.
So I started searching....
Gillian recommended various places to start my search, and also recommended the Downs and Black checklist.
I hit the books and the websites and found the following tools / checklist that caught my interest:
@ Downs and Black Checklist JECH 1998; 52;377-384 - I later tried to apply this tool, as described below.
@ The Effective Public Health Practice Project Quality Ax Tool for Quantitative Studies (EPHPP) - I also tried to apply this tool, as described below
@ The Centre for Evidence Based Mental Health www.ecbmh.com - Critical Appraisal Form for study of diagnosis - this tool just helped me formulate some of the questions I wanted to ask, but it didn't meet the other criteria set above, and thus I didn't use it.
@ The Newcastle-Ottawa Quality Assessment Scale for Case Control Studies - I couldn't find the necessary evidence regarding its validity, it seemed complicated to use and I couldn't find evidence of its use in other people's research.
@ The QUADAS tool for assessing methodological quality of diagnostic studies - this was the chosen one!
@ The STROBE statement checklist: the specific checklist for evaluating observational cohort case control studies - this is essentially a statement looking at the quality of reporting of studies, and again, it had many items that were not applicable to the types of studies in my review, and therefore I excluded it, but kept it on file, because it is very useful for general critique of studies.

....And there were many more, all of which I had to ignore, as the amount of data

and checklists out there is extraordinary so at some point I just had to stop looking for anything new and choose from the pool of items that I already had.

The first tool to be chosen was the EPHPP - it seemed clear, concise and gave me a straight answer: is this study strong, weak or moderate. I liked that. I applied it to a couple of studies and found that there were items that I couldn't score, because these items were regarding intervention studies. I therefore contacted the Canadians who work on the EPHPP project (still ongoing) and they reassured me that this is okay, I would just omit the items and score the rest, and thus I would get an overall score as to the strength of the study. Seemed straight-forward enough, however, the next hurdle was finding out who else has used the tool. A search of the research databases has shown that only 7 articles published (and cited in 3 large databases) actually cited this tool. These were not all articles that actually used the tool as I was intending, and the articles were not as recent as I would have liked.

The next tool I tried out was the Downs and Black Checklist. This one was much more widely cited and I thought that it would work well. However, it is a fairly lengthy checklist, and many of the items (at least half) were not applicable to our type of study, which meant that it seems pointless to use a tool that does not actually work for the purpose of my review.
I consulted Robert Rush, our in-house Statistician regarding adapting the tool to my purposes, and he very clearly said that I can adapt or create any tool I wanted, but unless I take it through the same rigorous validation process as the original tool had undergone, it won't have the same strength and validity. That seemed clear enough - the Downs and Black checklist was out.
We did go to the extent of piloting the data extraction forms with the Downs and Black checklist, and this confirmed that it wasn't really a tool we could use in this review.

So lastly, we decided to go with the QUADAS tool - because it met all my criteria for selection of a tool as listed above, other that the last one - the scoring system. I could live with that - I realised later that it was my own insecurity in determining the strength of a study, based on my own judgement that I was trying to shy away from, but actually, when it boiled down to it, I felt capable of commenting on strength after having read the study carefully and applied the QUADAS.
We then piloted the data extraction form for the second time, and all agreed that it works well, it is concise enough, it asks all the relevant questions and it allows me to make judgements about studies without a scale or definitive answer as in the EPHPP.

Appendices related to chapter IV

Appendix 4.1: Study Protocol

Delirium After Stroke – A Systematic Review

Updates for Sept. 2016 appear in red

1. BACKGROUND

Delirium (or acute confusional state) is a severe but potentially preventable disorder which is common among elderly hospital patients (Henon et al. 1999; Inouye et al. 1999), with a typical prevalence of 20-30% across a variety of settings (Siddiqi, House, and Holmes 2006). Delirium is associated with increased mortality, morbidity and length of hospital stay (McCusker et al. 2003; Young and Inouye 2007).
Delirium may be hyperactive (accompanied by overt psychotic symptoms and agitation); hypoactive (characterised by sedation); or mixed (i.e. both hypoactive and hyperactive). The hypoactive type can often be undetected or misdiagnosed as depression (Carson et al. 2004).
Delirium is found in up to 48% of patients soon after the onset of stroke, especially in those aged 65 and over and it is negatively associated with functional outcome and long-term survival (Mcmanus et al. 2007; Sheng et al. 2006). Only a small number of studies on delirium after stroke were identified through preliminary literature searches, however, these studies deal mainly with identification of precipitating factors such as lesion site or type of stroke (Caeiro et al. 2005; Shih et al. 2007) or with the incidence of this complication and its relationship to outcome (Caeiro et al. 2004; Henon et al. 1999; Sheng et al. 2006).
There does not seem to be a published systematic review on the topic of delirium following a stroke, additionally, there is currently no clear guidance on whether stroke patients should be screened for delirium, if so, the best way to screen for delirium or indeed on the multidisciplinary treatment recommendations for the condition. The National Institute for Clinical Excellence recently published their policy document regarding best practice in delirium (National Institute for Clinical Excellence 2010), however, there is no specific mention of stroke being a risk factor for developing delirium. The NICE guidelines on the management of stroke do not mention cognitive complications / consequences of stroke at all (National Institute for Health and Clinical Excellence 2008). The Scottish Intercollegiate Guidelines Network has not published any policy document on delirium, and in its document on stroke treatment, there is no specific mention of delirium as a complication of stroke – the word “confusion” is mentioned only once as a possible complication with no reference made to the best way to manage “confusion” (Scottish Intercollegiate Guidelines Network 2010). Taken together, it is clear that this lack of information and guidance on the screening and diagnosis of delirium after stroke may affect outcomes for this population and that this area warrants further research.

2. OBJECTIVES

To scope the literature on delirium post stroke using systematic review methodology to answer the following questions:

6. What is the incidence of delirium following a stroke?

7. How is delirium screened for and diagnosed in patients who have had a stroke?

8. What is the sensitivity and specificity, positive and negative predictive values of the screening / diagnostic tools when applied to a person who has had a stroke?

9. What is the feasibility of using the tools identified above applied to a person who has had a stroke, specifically considering language difficulties arising from the stroke?

10. What are the predictors of developing delirium after stroke and what is the impact of delirium on outcome post stroke?

3. METHODS

3.1 Criteria for considering published material for this review:

Types of studies: We will include all observational studies: Cross sectional, longitudinal, cohort studies and case control studies and case series (Petticrew and Roberts 2006). We will exclude single case studies all experimental designs and studies investigating treatment for delirium. We will exclude systematic reviews with or without a meta-analysis.

Types of participants: we will consider human only, adult (≥18 years) participants with stroke or subarachnoid haemorrhage (SAH) (Hatano 1976) who present to the hospital with a clear diagnosis of stroke or SAH, thus, studies presenting patients admitted due to delirium, where the cause was found to be neurological will be excluded from this review. We will exclude studies reporting on acquired brain injury or progressive neurological brain damage (e.g. multiple sclerosis, dementia). We will exclude *Delirium Tremens*.

Diagnostic criteria: Delirium must be diagnosed by established diagnostic criteria (ICD10, DSM3, DSM3R, DSM4, DSM5 or diagnostic tools based on these criteria such as CAM or DRS). Studies where the diagnostic process for delirium was unclear will be excluded.

Types of publication: We will consider only full publications and letters reporting on data, therefore conference proceedings and letters to the editor will be excluded. The following non-English languages will be included: Hebrew, French, German, Dutch, Spanish. Where identified, duplicate publications will be scrutinised and decisions on inclusion / exclusion taken within the team.

3.2 Search Methods for identification of studies

~~We will search the Cochrane Stroke Group Trials Register and the Cochrane Dementia and Cognitive Improvement Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*, latest issue),~~

We will search MEDLINE (1950 to present), EMBASE (1980 to present), CINAHL (1981 to present), PsycINFO (1840 to present), Web of Science. (see appendix for details of keyword combinations).

We will also search the following specialist databases: British Nursing Index (1985 to present), Physiotherapy Evidence Database (PEDro: http://www.pedro.org.au), OTseeker (http://www.otseeker.com)

In an effort to identify further published, unpublished, and ongoing trials, the following will be carried out:

(1) Search ISI proceedings for conference abstracts to allow us to contact authors to establish whether a publication of their results is due.

(2) Scan reference lists of identified studies and reviews.

3.2.1. Key words used / combinations: based on search strategies published in the Cochrane library for topics on both stroke and delirium, these are the key words that will be used in the search, with a combinations of all synonyms from a+b as follows:

a. **Stroke:** Stroke; Cerebrovascula / cerebral vascular + disorders / accident; Cerebral / cerebellar / brain + infarct / ischemia / thrombo* / emoboli* ; Subarachnoid; Brain attack.

b. **Delirium:** Delirium / deliri*; Acute confusion / confusional state; Acute + organic / psychoorganic + psycho/syndrome; Acute brain syndrome; Metabolic encephalopathy; Clouded state; Clouding of consciousness

4. DATA COLLECTION AND ANALYSIS

4.1 Study selection

Titles and abstracts identified from literature searches will be reviewed by lead author and obviously irrelevant work will be eliminated. This author will log all citations in an Include / Exclude database using an agreed form. The abstracts will then be reviewed by a second review author from the team, they will independently screen for relevance and inclusion criteria will be applied and any disagreement resolved by discussion with a third reviewer.

4.2 Data extraction and management

We will design and use data extraction forms to extract data from the studies which meet our inclusion criteria. These forms will be piloted on 3 studies to assess the quality of the form and amend any shortcomings. Three review authors will independently perform the data extraction to collect data on the study design, population, observation and outcomes. The following details will be recorded:

(1) Study design

(2) Sample characteristics, sample size, selection bias, drop-out rate, etc.

(3) Tool(s) used to screen for and diagnose delirium, their sensitivity and specificity, positive and negative predictive values and any comments the authors may have on the feasibility of use with participants who survived a stroke.

(4) The outcome measures used in the study and whether valid data exist regarding their psychometric properties.

(5) Analyses: statistical tests performed and their appropriateness for the study design.

4.3 Assessment of methodological quality

The included literature will be presented in tabular form to summarise their methodological quality. As the papers reviewed are expected to be of a variety of study designs, the assessment of their quality will occur according to published criteria: A published tool for the assessment of the quality of diagnostic test accuracy will be adopted (Whiting et al. 2003). This tool was chosen due to its relevance to this review as the main part of the review is to examine suitability of screening / diagnostic tools for delirium after stroke.

This tool was chosen due to its methodological strength, its ease of application and suitability for use in the evaluation of observational studies.

5. ANALYSIS OF FINDINGS

Depending on the types of studies that are identified, the data will be pooled, wherever possible to attempt to draw conclusions regarding the clinical implications of the finding of the studies so that the ultimate goal of identifying:

1. The incidence of delirium post stroke.

2. The most appropriate way to screened for and diagnose delirium in patients who have had a stroke.

3. The appropriateness, psychometric properties and feasibility of identified screening / diagnostic tools as applied to participants experiencing delirium after stroke.

References

Caeiro, L., Ferro, M., Claro, M. I., Coelho, J., Albuquerque, R. and Figueira, M. L. 2004. Delirium in acute stroke: a preliminary study of the role of anticholinergic medications. *European Journal of Neurology*, 11 (10), pp.699-704. Available from: http://search.ebscohost.com/login.aspx?direct=true&db=afh&AN=14603641&site=ehost-live

Caeiro, L., Menger, C., Ferro, J. M., Albuquerque, R. and Figueira, M. L. s. 2005. Delirium in acute subarachnoid haemorrhage. *Cerebrovascular Diseases (Basel, Switzerland)*, 19 (1), pp.31-38. Available from: http://search.ebscohost.com/login.aspx?direct=true&db=cmedm&AN=15528882&site=ehost-live

Carson, A., Zeman, A., Brown, T. and Sharpe, M.2004. Organic Disorders. In: Johnstone, E., D. Cunningham Owens, S. Lawrie, M. Sharpe and C. Freeman eds. *Companion to Psychiatric Studies*. 7 ed. Edinburgh: Churchill Livingstone, pp. 341-344.

Hatano, S. Experience from a Multicentre Stroke Register: a Preliminary Report. Bulletin of the World Health Organisation 54. 1976. World Health Organisation. 15-9-2010.
Ref Type: Electronic Citation

Henon, H., Lebert, F., Durieu, I., Godefroy, O., Lucas, C., Pasquier, F. and Leys, D. 1999. Confusional state in stroke: relation to preexisting dementia, patient characteristics, and outcome. *Stroke; A Journal Of Cerebral Circulation*, 30 (4), pp.773-779. Available from: http://search.ebscohost.com/login.aspx?direct=true&db=cmedm&AN=10187878&site=ehost-live

Inouye, S. K., Bogardus, S. T., Charpentier, P. A., Leo-Summers, L., Acampora, D., Holford, T. R. and Cooney, L. M. J. 1999. A multicomponent intervention to prevent delirium in hospitalized older patients. *New England Journal of Medicine*, 340 (9), pp.669-676. Available from: http://search.ebscohost.com/login.aspx?direct=true&db=psyh&AN=1999-10488-001&site=ehost-live

McCusker, J., Cole, M. G., Dendukuri, N. and Belzile, E. 2003. Does delirium increase hospital stay? *Journal of the American Geriatrics Society*, 51 (11), pp.1539-1546. Available from:

http://search.ebscohost.com/login.aspx?direct=true&db=cmedm&AN=14687382&site=ehost-live

Mcmanus, J., Pathansali, R., Stewart, R., Macdonald, A. and Jackson, S. 2007. Delirium post-stroke. *Age & Ageing*, 36 (6), pp.613-618. Available from: http://search.ebscohost.com/login.aspx?direct=true&db=afh&AN=28340566&site=ehost-live

National Institute for Clinical Excellence (2010). *Delirium: Diagnosis Prevention and Management*. NICE.

National Institute for Health and Clinical Excellence. Stroke: National Clinical Guidelines for Treatment amd Initial Management of Acute Stroke and Transient Ischaemic Attack (TIA). 2008. London, Royal College of Physicians.
Ref Type: Generic

Petticrew, M. and Roberts, H. 2006. *Systematic Reviews in the Social Sciences a practical guide*. Oxford: Blackwell Publishing.

Scottish Intercollegiate Guidelines Network. Management of Patients with Stroke: Rehabilitation, prevention and management of complications, and discharge planning. A National Clinical Guideline. 2010. NHS Quality Improvement Scotland.
Ref Type: Serial (Book,Monograph)

Sheng, A. Z., Shen, Q., Cordato, D., Zhang, Y. Y. and Yin Chan, D. K. 2006. Delirium within three days of stroke in a cohort of elderly patients. *Journal of the American Geriatrics Society*, 54 (8), pp.1192-1198. Available from: http://search.ebscohost.com/login.aspx?direct=true&db=cmedm&AN=16913984&site=ehost-live

Shih, H. T., Huang, W. S., Liu, C. H., Tsai, T. C., Lu, C. T., Lu, M. K., Chen, P. K., Tseng, C. H., Jou, S. B., Tsai, C. H. and Lee, C. C. 2007. Confusion or delirium in patients with posterior cerebral arterial infarction. *Acta Neurologica Taiwanica*, 16 (3), pp.136-142. Available from: http://search.ebscohost.com/login.aspx?direct=true&db=cmedm&AN=17966952&site=ehost-live

Siddiqi, N., House, A. O. and Holmes, J. D. 2006. Occurrence and outcome of delirium in medical in-patients: a systematic literature review. *Age And Ageing*, 35 (4), pp.350-364. Available from: http://search.ebscohost.com/login.aspx?direct=true&db=cmedm&AN=16648149&site=ehost-live

Whiting, P., Rutjes, A., Reitsma, J., Bossuyt, P. and Kleijnen, J. 2003. The development fo QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Medical Research Methodology*, 3 p.25.

Young, J. and Inouye, S. K. 2007. Delirium in older people. *BMJ (Clinical Research Ed)*, 334 (7598), pp.842-846. Available from: http://search.ebscohost.com/login.aspx?direct=true&db=cmedm&AN=17446616&site=ehost-live

APPENDIX

Keyword combinations used in database searching:

1. Stroke / post stroke / CVA
2. Cerebrovascula / cerebral vascular + disorders / accident / insult
3. Cerebral / cerebellar / brain + infarct / ischemia / thrombo* / emoboli*
4. Cerebral / brain / Subarachnoid + haemorrhage / hemorrhage
5. Brain attack
6. Delirium / deliri*
7. Acute confusion / confusional state
8. Acute + organic / psychoorganic + psycho/syndrome
9. Acute brain syndrome
10. Metabolic encephalopathy
11. Clouded state
12. Clouding of consciousness
13. 1 and 6-12
14. 2 and 6-12
15. 3 and 6-12
16. 4 and 6-12
17. 5 and 6-12

Appendix 4.2: Example of search record

Database: EMBASE Host: Ovid	Accessed: 9.9.16

Keywords	Limiters	Hits	Scanned titles for relevance: included	Duplicate or included in 2010	NR	Retrieve
1+6	Date of Publication: 2010-2016; Human only NOT Alcohol Surgery Heat stroke Limits as per protocol	382	17	14	365	3
Include: Kara et al. 2013 Kutlubaev et al. 2013. Delirium in the acute phase of stroke: Frequency and predisposing factors. Zhurnal Nevrologii i Psihiatrii imeni S.S. Korsakova. 113 (3) (pp 37-41) **Exclude:** Kosak et al. 2015 single case report in Turkish Makazaki et al. 2013 Retrospective analysis of the effectiveness of Yokukansan (Japanese herbal medicine, TJ-54) in the treatment of delirium following acute stroke. Neurological Surgery. 41 (9) (pp 765-771) [Japanese] Litvinenko et al. 2010 Efficacy and safety of rivastigmine (exelon) in the confusion syndrome in the acute phase of ischemic stroke. Zhurnal Nevrologii i Psihiatrii imeni S.S. Korsakova. 110 (11) (pp 36-41) [Russian]						
Keywords	**Limiters**	**Hits**	**Scanned titles for relevance: included**	**Duplicate or included in 2010**	**NR**	**Retrieve**
1 + 7		60	1 Kara et al. 2013 Turkish		59	0
1 + 8		2			2	0
1+9		8	0	0	8	0
1+10		0				0
1+11		1			1	0
2 + 6	Date of Publication: 2010-2016; Human only	32	2	2	30	0

	NOT Alcohol Surgery Heat stroke Limits as per protocol					
2 + 7		6	1	1	5	0
2 + 8		29	0		29	0
2+9		27	0		27	0
2+10		25			25	0
2+11		2	0		2	0
3+6		155	1	1	154	0
3+7		47	1			
Read and excluded: Jacquin et al. 2014 Post-stroke cognitive impairment: High prevalence and determining factors in a cohort of mild stroke. Journal of Alzheimer's Disease. 40 (4) (pp 1029-1038) [Not specific enough]						
3+8		2	0	0	2	0
3+9		45	0	0	45	0
3+10		38	0	0	38	0
3+11		3	0	0	3	0
4+6		67	1	0	66	1
Retrieved: Tsymbalov K.S., Fetkenhour D.R. 2016 Recognized homonymous hemianopsia and delirium during the admission examination leading to diagnosis and appropriate treatment of a new stroke. Neuropsychiatric Disease and Treatment. 12 (pp 1385-1388), 2016. Date of Publication: 14 Jun 2016.						
4+7		12	1	1	11	0
4+8		2	0	0	2	0
4+9		21	0	0	21	0
4+10		31	0	0	31	0
4+11		2	0	0	2	0
5+6		36	0	0	36	0
5+7		0	0	0	0	0
5+8		0	0	0	0	0
5+9		1	0	0	1	0
5+10		0	0	0	0	0
5+11		0	0	0	0	0

Appendix 4.3: Exclude / Include form

Reviewer:

Details of publication

Author/s

Source Journal Title: Year Volume Issue Pages

Include? Yes ☐ No ☐ Maybe ☐

Exclude?

Reason for Exclusion:

Not topic-specific: does not include delirium in stroke patients State topic:	
Language:	
N<2	
Conference proceedings	

Cross-checked Y ☐ N ☐

Final Decision and Comments

Appendix 4.4: Data Extraction form

Reviewer:
Details of publication

Brief title
Author
Journal title
Year

Language if not English:

Stated aim

Study type

Participants in Study
1. **Total number of participants in study**

2. **Was there an explanation of how sample size was arrived at?**

YES	NO

3. **Study population** (i.e. population to which study could be generalised)

4. **Country of study**

5. **Entry criteria for study**

6. **Exclusion criteria for study**

7. **Characteristics of participants**
   Age (e.g. mean, standard deviation, median, range)

   Gender

   Any other relevant participant information

Screening / Diagnostic Tools
Start of QUADAS tool –refer to Whiting et al (2003) for guidance
State reference standard:
State index test:

Item	Question	Yes	No	Un-clear
1.	Was the spectrum of patients representative of the patients who will receive the test in practice?	()	()	()
2.	Were selection criteria clearly described?	()	()	()
3.	Is the reference standard likely to correctly classify delirium?	()	()	()
4.	Is the time period between reference standard and index test short enough to be reasonably sure that the delirium did not change between the two tests?	()	()	()
5.	Did the whole sample receive verification of delirium using a reference standard of diagnosis?	()	()	()
6.	Did patients receive the same reference standard regardless of the index test results?	()	()	()
7.	Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard?)	()	()	()
8.	Was the execution of the index test described in sufficient detail to permit replication of the test?	()	()	()
9.	Was the execution of the reference standard described in sufficient detail to permit its replication?	()	()	()
10.	Were the index test results interpreted without knowledge of the results of the reference standard?	()	()	()
11.	Were the reference standard results interpreted without knowledge of the results of the index test?	()	()	()
12.	Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?	()	()	()
13.	Were uninterpretable / intermediate test results reported?	()	()	()
14.	Were withdrawals from the study explained?	()	()	()

End of QUADAS tool

8. State which tool/s was used to diagnose / screen for (or both) Delirium:

9. Are data related to sensitivity, specificity, positive / negative predictive value available?

10. Make comments on applicability of screening tool for persons with stroke if possible (e.g. were patients with language difficulties excluded?)

Outcome Measures

11. State the outcome measures recorded:

12. What were the time points at which these outcomes were recorded?

13. If more than one assessor was involved in outcome assessment was inter-rater reliability tested and satisfactory?

YES	NO

14. How many of the original sample were included in final outcome measures?

Statistical Methods

15. Describe all the statistical methods used

16. Was there adequate explanation of how missing data were addressed?

YES	NO

17. Were the statistical methods used appropriate?

YES	NO

Results

18. Numbers experiencing delirium after stroke

19. Factors associated with the development of delirium after stroke (state all described)

20. Factors associated with delirium and outcome (e.g. increased length of stay, discharge destination)

21. Authors conclusion(s)

22. Reviewers conclusions re strength of study

23. List any points that need to be clarified through contact with the authors

Appendix 4.5: PRISMA statement checklist

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Section/topic	#	Checklist item	Reported in which section?
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	NA
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	NA
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4.1.1
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4.1.2
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Appendix 4.1
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4.2.3

Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4.2.2
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 4.2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4.2.3
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4.2.5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Appendix 4.4
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	4.2.4
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	4.2.6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	4.2.6
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	4.2.6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	4.2.6
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	4.3.1

Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	4.3.2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table 10
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Table 8 Table 9
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Table 9 Figure 4
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Table 10
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Table 9 Figure 4
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	4.4.1 – 4.4.6
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	4.4.7
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	4.5

Appendices related to chapter V

Appendix 5.1: Survey Questions

Delirium in Acute Stroke: Survey of Diagnostic / Screening Procedures

Please note that when you click **CONTINUE** your answers are submitted and you cannot return to review or amend that page.

About you

1. Are you?

- ○ Doctor
- ○ Nurse

Please state your grade

2. Do you work with stroke patients?

- ◉ in a stroke unit
- ◉ in a ward with stroke beds
- ○ Both of the above

Please select the hospital you work in (list appears in alphabetical order)

Screening for Delirium (acute confusional state)

3. Does your ward have a policy on screening new patients for delirium (acute confusional state)?

- Yes
- No
- Not Sure

4. Do you routinely screen for delirium (acute confusional state) on admitting new patients to the ward?

- Yes
- No

5. Do you screen patients for delirium (acute confusional state) on a regular basis during admission?

- Yes
- No

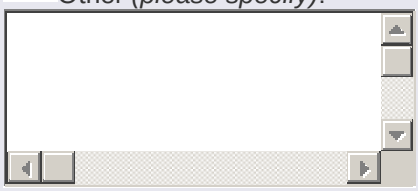
5.a Please state the frequency of screening of patient on the ward

- As the need arises
- Once weekly
- Twice weekly
- Fortnightly
- Other *(please specify)*:

Diagnosis of Delirium (acute confusional state)

6. How do you identify delirium (acute confusional state) in stroke patients?

- Standardised tool
- Clinical judgement
- Both
- I do not diagnose delirium in my practice
- Other *(please specify)*:



a. If you do NOT use a tool to diagnose delirium in stroke patients, which of the following best describes your practice?

- I diagnose delirium based on diagnostic criteria (e.g. DSM-IV or ICD-10)
- I diagnose delirium based on the symptoms presented
- I do not diagnose delirium in my practice
- Other *(please specify)*:

b. If you do NOT use a tool to either screen for or diagnose delirium in stroke patients, please tick the option which best describes your reasons for not doing so:

- I have not been trained to use a standardised tool
- I have been trained but am not confident in using a standardised tool
- I do not consider this important to my practice
- The tools are not suitable for stroke patients
- Lack of time

7. If you use a standardised tool, please indicate which one you use:

- Confusion Assessment Method
- Confusion Assessment Method for Intensive Care Unit (CAM-ICU)
- Delirium Rating Scale
- Delirium Symptom Interview
- Organic Brain Syndrome Scale
- Other *(please specify)*:

8. Do you think the tool/tools you use is suitable for a stroke population?

- Yes
- No
- Not Sure

Please elaborate on the reasons for your selection above:

Thank you for your time!

Many thanks for participating in this survey.

If you have any questions or comments regarding this survey or the topic it explores, please feel free to contact me at gcarin-levy@gmu.ac.uk

Appendix 5.2: NHS ethical approval

South East Scotland Research Ethics Service

Waverley Gate
2-4 Waterloo Place
Edinburgh
EH1 3EG

NHS Lothian

Name: Gail Carin-Levy
Address: School of Health Sciences
Queen Margaret University
Edinburgh
EH21 6UU

Date: 23/11/2011
Your Ref:
Our Ref: NR/1111AB22
Enquiries to: Alex Bailey
Direct Line: 0131 465 5679
Email: alex.bailey@nhslothian.scot.nhs.uk

Dear Gail,

Full title of project: Delirium in Acute Stroke: A survey of screening and diagnostic practice in Scotland

You have sought advice from the South East Scotland Research Ethics Service on the above project. This has been considered by the Scientific Officer and you are advised that, based on the submitted documentation (email correspondence and Protocol Survey.docx), it does not need NHS ethical review under the terms of the Governance Arrangements for Research Ethics Committees in the UK. The advice is based on the following:

- *The project is an opinion survey seeking the views of NHS staff on service delivery.*

If this project is being conducted within NHS Lothian you should inform the relevant local Quality Improvement Team(s).

This letter should not be interpreted as giving a form of ethical approval or any endorsement of the project, but it may be provided to a journal or other body as evidence that ethical approval is not required under NHS research governance arrangements. However, if you, your sponsor/funder or any NHS organisation feels that the project should be managed as research and/or that ethical review by a NHS REC is essential, please write setting out your reasons and we will be pleased to consider further. Where NHS organisations have clarified that a project is not to be managed as research, the Research Governance Framework states that it should not be presented as research within the NHS.

You should retain a copy of this letter with your project file as evidence that you have sought advice from the South East Scotland Research Ethics Service.

Yours sincerely,

Alex Bailey
Scientific Officer
South East Scotland Research Ethics Service

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Appendix 5.3: QMU ethical approval

The following is the last page of the ethics application made to QMU, signed and approved by Head of Division as per requirements:

36. For all applicants, send the completed form to your Head of Division or Head of Research Centre or, if you are an external researcher, submit the completed form to the Secretary to the QMU Research Ethics Panel. **You should not proceed with any aspect of your research which involves the use of participants, or the use of data which is not in the public domain, until you have been granted Ethical Approval.**

FOR COMPLETION BY THE HEAD OF DIVISION/HEAD OF RESEARCH CENTRE
Either

I refer this application back to the applicant for the following reason(s):

Name *(if you have an electronic signature please include it here)*

_____ Head of Division / Research Centre

Date _____

Please return the form to the applicant.

Or

Please tick **one** of the alternatives below and delete the others.

~~I refer this application to the QMU Research Ethics Panel.~~

~~I find this application acceptable and an application for Ethical Approval should now be submitted to a relevant external committee.~~

I grant Ethical Approval for this research. ✓

External ethical application has already been sought. See the attached Journal No 4 as appended to this application

Name *(if you have an electronic signature please include it here)*

Ian McMillan Acting Head of Division / ~~Research Centre~~

Date 8/02/2012

Please send one copy of this form to the applicant and one copy to the Secretary to the Research Ethics Panel, Quality Enhancement Unit, Registry.
Date application returned: _____

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Appendix 5.4: Email invitations and reminders

Dear Colleague,

Delirium in acute stroke: a survey of screening and diagnostic practice in Scotland.

My name is Gail Carin-Levy, I am a lecturer in Occupational Therapy, undertaking a PhD on delirium in acute stroke, concentrating on identification, knowledge and attitude of frontline staff.

I am contacting you today to request your participation in a very short survey (it will take **no more than 5 minutes** of your time). This survey aims find out how doctors and nurses screen for, identify and diagnose delirium (also known as 'acute confusional state') in patients admitted to hospital with stroke.

All data collected in this survey will be held anonymously and securely. We do not ask for or retain any personal data.

I would be very grateful if you could complete the online survey by following this link http://www.surveys.qmu.ac.uk/deliriumi_in_acute_stroke

If you would like more information about the survey or if you prefer a paper copy of the survey, please contact me via email: gcarin-levy@qmu.ac.uk or telephone: 0131 474 0000.
If you would like to contact my Director of Studies: Dr Kath Nicol knichol@qmu.ac.uk or at the above telephone number.

Many thanks in anticipation,

Gail Carin-Levy, Lecturer, Division of Nursing, Occupational Therapy and Arts Therapies, Queen Margaret University:

Appendices related to chapter VI

Appendix 6.1: Vignettes

Trigger Question	Vignette 1	Vignette 2
What are your initial thoughts?	Mrs Bryan is an 82 year old lady who was admitted recently with acute weakness of the left side of her face and her left arm. She was diagnosed clinically as having had a right sided infarct. Computed tomography (CT) of her brain confirmed a R hemisphere lacunar ischaemic stroke, as well as mild small vessel disease and generalised atrophy reported as consistent with her age. On the third night of her admission she became confused and restless, but this has resolved by morning.	Mr Arthur is an 82 year old man who was admitted recently with acute weakness of the left side of his face and his left arm. He was diagnosed clinically as having had a right sided infarct. Computed tomography (CT) of his brain confirmed a R hemisphere lacunar ischaemic stroke, as well as mild small vessel disease and generalised atrophy reported as consistent with his age. On the third night of his admission he became confused and restless, but this has resolved by morning.
• How do you interpret this? • What does this information add?	Discussion with family members reveals that they have become a little worried about her memory recently. In the last 6 months, Mrs Bryan has forgotten to pay a few bills, and the family had to help her with this. On the recommendation of the GP, the family have also arranged for her medication to be dispensed in blister packs via the local pharmacy.	Discussion with family members reveals that they have become a little worried about his memory recently. In the last 6 months, Mr Arthur has forgotten to pay a few bills, and the family had to help him with this. On the recommendation of the GP, the family have also arranged for his medication to be dispensed in blister packs via the local pharmacy.
What do you make of this?	The night time confusion seems to have resolved, but now, Mrs Bryan is rather drowsy by day and spends much of the time asleep. She doesn't seem to want to engage with physiotherapy during the day and appears apathetic.	The night time confusion continues, but now, Mr Arthur is also confused during the day. He recently shouted at one of the physios who tried to take him to the gym. Family members reported this is completely out of character.
This is all the information currently available to you. What's your view about the patient's mental state?	Due to Mrs Bryan's drowsiness, the nurses are concerned that she is not taking adequate fluids and IV fluids were commenced. It appears from the notes that Mrs Bryan has not had any bowel movements since admission.	Mr Arthur has not been taking adequate fluids and has commenced IV hydration. This is made complicated by his repeatedly pulling out the drip. One of nurses reported that Mr Arthur appeared at times to be responding to unseen stimuli.

Appendix 6.2: Ethical procedures

The following is the last page of the ethics application made to QMU, signed and approved by Head of Division as per requirements:

36. For all applicants, send the completed form to your Head of Division or Head of Research Centre or, if you are an external researcher, submit the completed form to the Secretary to the QMU Research Ethics Panel. **You should not proceed with any aspect of your research which involves the use of participants, or the use of data which is not in the public domain, until you have been granted Ethical Approval.**

FOR COMPLETION BY THE HEAD OF DIVISION/HEAD OF RESEARCH CENTRE
Either

I refer this application back to the applicant for the following reason(s):

Name *(if you have an electronic signature please include it here)*

_____ Head of Division / Research Centre

Date _____

Please return the form to the applicant.

Or

Please tick **one** of the alternatives below and delete the others.

~~I refer this application to the QMU Research Ethics Panel.~~

~~I find this application acceptable and an application for Ethical Approval should now be submitted to a relevant external committee.~~

✓I grant Ethical Approval for this research.✓

Name *(if you have an electronic signature please include it here)*

_____ Head of Division / ~~Research Centre~~

Date 14/02/2014

Please send one copy of this form to the applicant and one copy to the Secretary to the Research Ethics Panel, Quality Enhancement Unit, Registry.
Date application returned: _____

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The following is an email trail with Scientific Officer of NHS Lothian regarding exemption from full ethical review:

Carin-Levy, Gail

From: Bailey, Alex <Alex.Bailey@nhslothian.scot.nhs.uk>
Sent: 14 October 2013 10:25
To: Carin-Levy, Gail
Subject: RE: Qualitative Study of Practice: Delirium after stroke
Attachments: Governance Arrangements for Research Ethics Committees -- harmonised edition.pdf

Dear Gail,

We can no longer letters for staff-only studies as the matter is clearly covered in the Governance Arrangements for Research Ethics Committees (attached). You can send the attached to any journals etc. that are looking confirmation that NHS ethics approval isn't required.

Regards,

Alex

Alex Bailey
Scientific Officer
South East Scotland Research Ethics Service
Waverley Gate
Edinburgh
EH1 3EG
Phone: 0131 465 5679 (35679)

From: Carin-Levy, Gail [mailto:GCarin-Levy@qmu.ac.uk]
Sent: 14 October 2013 10:11
To: Bailey, Alex
Subject: RE: Qualitative Study of Practice: Delirium after stroke

Dear Alex,
Many thanks for your reply, this is very helpful.
The study is simply seeking the opinions of staff about issues related to the identification of delirium after stroke. I am not seeking to approach patients, carers or case records (or any of the issues your raised below).
I will require a letter of exemption (as you have kindly provided for my last study which was a Scottish wide online survey of practice) – when the protocol is finalised (next few weeks) I shall send it to you for approval – I hope this is OK.

I will contact Susan Shepherd separately to explore the need for R&D approval.

Many thanks for your advice,

Kind regards,
Gail

Gail Carin-Levy BSc (Hons)
Lecturer in Occupational Therapy
Level 1 (UG) Coordinator and Co-Admissions Tutor
School of Health Sciences, Queen Margaret University, Edinburgh EH21 6UU

1

Tel: 0131 4740000 say: "Gail Carin-Levy" when prompted by our automated system
email: gcarin-levy@qmu.ac.uk
 @gcarinlevy
www.qmu.ac.uk

From: Bailey, Alex [mailto:Alex.Bailey@nhslothian.scot.nhs.uk]
Sent: 10 October 2013 08:41
To: Carin-Levy, Gail
Cc: Shepherd, Susan
Subject: RE: Qualitative Study of Practice: Delirium after stroke

Dear Gail,

If the study involves NHS staff only then there is no requirement (policy-wise or legally) for NHS ethical review unless the study involves any of the following:

NHS patients (i.e. people identified through their involvement with the NHS, including services provided under contract with the private or voluntary sectors)
their carers
their tissue
NHS patient-identifiable data

people who lack the capacity to give informed consent to take part in the research
processing of confidential patient information without consent where this would otherwise breach confidentiality (England and Wales only)
material consisting of or including human cells, which has been taken from the living or the deceased (England and Wales only). Legally required, if it involves analysis of DNA in material from the living and consent for research not in place (UK-wide)
patients who are cared for in private and voluntary sector nursing homes (in England, Wales and Northern Ireland) and/or residents of residential care homes (in Northern Ireland only)
exposure to ionising radiation
medical devices that are not CE-marked or CE-marked devices that have been modified or are being used for a new purpose
investigational medicinal products
practising midwives conducting a clinical trial
protected information from the Human Fertilisation and Embryology Authority register

However, you should contact NHS Lothian R&D (copied in) as they may require R&D approval for the study.
If the study is health-related research then it will require a sponsor and ethical review as per The Research Governance Framework.

Regards,

Alex

Alex Bailey
Scientific Officer
South East Scotland Research Ethics Service
Waverley Gate
Edinburgh
EH1 3EG
Phone: 0131 465 5679 (35679)

From: Carin-Levy, Gail [mailto:GCarin-Levy@qmu.ac.uk]
Sent: 09 October 2013 16:39
To: Bailey, Alex
Subject: Qualitative Study of Practice: Delirium after stroke

Dear Alex,
I am in the process of writing up the protocol for a study which forms the 3rd strand of my PhD.
The study will be a multidisciplinary, online focus group evaluation of clinicians' knowledge about delirium after stroke. More specifically, I trying to explore the barriers to the timely and accurate identification of delirium after stroke.
I know that you need a protocol in order to decide whether this study will require full ethical approval, but I thought I would check first if you are OK about a draft (nearly completed) protocol – as the qualitative methods are not pinned down completely and all the recruitment forms (informed consent etc.) have not yet been written.
Obviously, if I am going for full ethical approval this will all be done but I wondered if you were happy to look at the protocol as it stands now in order to be able to decide whether full ethical approval will be required.
Your guidance is very much appreciated,
Best wishes,
Gail

Gail Carin-Levy BSc (Hons)
Lecturer in Occupational Therapy
Level 1 (UG) Coordinator and Co-Admissions Tutor
School of Health Sciences, Queen Margaret University, Edinburgh EH21 6UU
Tel: 0131 4740000 say: "Gail Carin-Levy" when prompted by our automated system
email: gcarin-levy@qmu.ac.uk
@gcarinlevy
www.qmu.ac.uk

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The information contained in this message may be confidential or

legally privileged and is intended for the addressee only. If you

have received this message in error or there are any problems

please notify the originator immediately. The unauthorised use,

disclosure, copying or alteration of this message is

strictly forbidden.

Appendix 6.3 Final grant report to CHSS

Minor Research Award

Final Report

Applicant(s) name(s):
Gail Carin-Levy
Address for correspondence, including email and daytime telephone number:
Queen Margaret University Drive, Edinburgh, EH21 6UU; E: gcarin-levy@qmu.ac.uk; T: 0131 4740000
Present employer and place of employment:
Queen Margaret University
Title of research and CHSS reference:
The barriers and facilitators to identification of delirium in stroke patients. Ref: Exec.17.04.14
Place of research:
Queen Margaret University, online platform
Actual date of end of study:
July 2015

Briefly outline the original proposal, including the layman's terms description.
Background: Delirium after stroke is associated with increased mortality, morbidity and length of hospital stay, it is therefore important to identify a delirium as early as possible. We explored how multidisciplinary team (MDT) members understand delirium following a stroke and what actions are taken when a patient develops delirium. Design: Utilising online focus groups and following the principles of grounded theory methodology the data were generated with the aid of two case vignettes. Coding and a constant comparative analytical approach were utilised in the data analysis. Sample: The plan was to recruit in the first round up to 20 Health Care Professionals (HCPs) and to organise them into profession specific groups, with a maximum of 6 participants per focus group. A provisional second round was planned for, entailing the recruitment of a maximum of 5 additional participants for theoretical sampling. Recruitment: Doctors, nurses, physiotherapist (PT), occupational therapists (OT) and speech and language therapists (SLT) working in stroke units across Scotland were targeted via a number of stroke specific research groups and associations. A pool of professionals who indicate their willingness to participate was created to allow purposive sampling to be used. HCPs of different grades, experience and geographic location were invited to participate. Ethics: this project was exempt from full ethical review by the South East Scotland Ethics Service and NHS Lothian R&D. The project was reviewed by Queen Margaret University Ethics Committee and ethical approval was granted.

Lay description: Delirium (acute confusion) is a serious psychiatric complication following a stroke: patients who experience delirium are likely to stay in hospital for longer and deteriorate in physical and mental health. Early identification of delirium is crucial in its management, yet it can be challenging to identify delirium in stroke patients due to language or cognitive difficulties resultant from the stroke. This study will explore the barriers to identification of delirium after stroke. This will inform the development of training programmes for healthcare staff to improve the rates of delirium identification, which may ultimately lead to improved outcomes for this population. (Word count: 340).

Outcome of Project:

Recruitment: Contact with potential participants was made via special interest groups and professional associations. Recruitment emails were sent as well as a publicity generated via social media (Twitter and Linked-In). Several clinicians emailed the lead researcher, indicating their willingness to participate. They were asked to complete a consent form and basic demographics questionnaire, based on this information the inclusion / exclusion criteria were applied. Fully qualified professionals currently employed by the National Health Service in a clinical capacity, working at least one session per week in an acute stroke environment were invited to participate.

Sample: 15 participants were recruited into the study, of which 13 made contributions to data collection. Two SLT participants did not contribute to any of the data collection process and were thus excluded.

Procedure: Two online focus group discussions were created: One group was for OTs, the other for PTs and SLTs (there were not enough participants from either PT or SLT to form their own groups). The nurses recruited (n=3) were unable to commit the time required to participate in the focus group discussions and therefore contributed via email interviews.

Data: data collection and analysis occurred simultaneously. The raw data generated by both the online focus groups and the email interviews were coded utilising N-Vivo (version 10.0). Rigorous analytical processes in line with grounded theory methodology were followed.

Findings: Five main themes were formed: Difficulty identifying delirium, the reported actions taken in response to symptoms, working within a team, the role of the next of kin, and, the patient at the centre of the experience. These were further synthesised to provide three areas for consideration:

- Understanding delirium: Participants' understanding of delirium varied: a minority of participants who received delirium training in the past were able to correctly identify symptoms and suggest relevant screening tools. Most participants did not identify a hypoactive delirium, interpreting the symptoms as dementia or depression and using tentative language to discuss delirium symptoms.

- Patient Centred Care: Participants demonstrated a caring and nurturing attitude, placing the patient at the centre of their stroke recovery experience.

The patient's insight into the confusion and their emotional wellbeing were a key concern, as was the regard for the next of kin as an important part of the MDT.

- Dynamics of Team Working: Participants placed an emphasis on the roles of MDT members as instrumental in working out the clinical picture: Nurses saw their role as identifying the symptoms as well as using an appropriate delirium screening tool (The 4AT). Allied health staff tended to defer to nurses and medical staff to take these actions.

Limitations: The study was limited by its scale, and clearly more research is required in this area to elaborate on our findings, preferably, including doctors in the group of participants. The online focus groups may have been at times taxing for participants who required access to the forum from their homes due to firewall restrictions in NHS hospitals.

Implications for patient care/health improvement: Early recognition of delirium is one of the most important means of minimising the effects of the condition but this is only possible if staff members are educated about the condition, and the best means of delirium screening. These findings offer important insights which could pave the way towards the creation of bespoke education programmes for MDT staff in acute stroke services. Increasing delirium awareness and recognition among MDT members in stroke units could lead to earlier delirium detection and potentially improve outcomes for this population.

Indications for further lines of research: These results will inform the creation of multidisciplinary education programmes which will be piloted and, pending the obtaining of funding, rolled out to stroke units around Scotland. Another potential line of research is to pursue the validation of a multidisciplinary screening tool for use with a stroke cohort. A further line of exploration is to determine the best approaches to AHP management of delirium in stroke patients, since the medical and nursing management of the condition is well documented in the general setting. (Word count: 670)

Dissemination

Full publications:
CARIN-LEVY, G., NICOL, K., VAN WIJCK, F., MEAD G.E., MCVITTIE C. Staff Response to Delirium in Acute Stroke: Knowledge, Awareness and Barriers to Early Identification Manuscript currently under review in *Age and Ageing*

CARIN-LEVY, G., NICOL, K., VAN WIJCK, F., MEAD G.E., MCVITTIE C. Occupational therapists' understanding of delirium in acute stroke: potential implications on patient outcomes. Manuscript being prepared for submission in OT specific journal (either *British Journal of Occupational Therapists* or *Occupational Therapy International*)

Conference presentations:
CARIN-LEVY, G., NICOL, K., VAN WIJCK, F., MEAD G.E., MCVITTIE C. Staff Response to Delirium in Acute Stroke: Knowledge, Awareness and Barriers to Early Identification. *UK Stroke Forum Conference*: Liverpool, December 2015.

CARIN-LEVY, G., NICOL, K., VAN WIJCK, F., MEAD G.E., MCVITTIE C. Staff Response to Delirium in Acute Stroke: Knowledge, Awareness and Barriers to Early Identification. *Scottish Stroke Allied Health Professionals Forum Conference*: Sterling, June 2015.

CARIN-LEVY, G., NICOL, K., VAN WIJCK, F., MEAD G.E., MCVITTIE C. Staff Response to Delirium in Acute Stroke: Knowledge, Awareness and Barriers to Early Identification. *European Stroke Conference*: Vienna, May 2015.

Break-down of costs / spending

Description	**Unit price**	**Total**
Study expenses to support participation of 15 HCPs.	£20.00	£300
Delivery	£4.95	£4.95
Unspent money: two participants (enclosed with this report).	£20	£40
Assistance to cover Eurostroke Conference registration fee, Vienna, May 2015 (as per email enclosed)	£195.05	£195.05
Total:		**£500**

Please find relevant receipts enclosed with this report.

Appendix 6.4: Participant Information Sheet and consent form

Queen Margaret University

EDINBURGH

Psychological difficulties in the acute stages of stroke

Information Sheet

You are being invited to take part in a study which forms part of a doctoral programme on psychological difficulties in acute stroke. This is a qualitative, online exploration of some of the psychological difficulties you may encounter in your day to day working in the acute stroke environment. Before you decide to take part, please read through this information sheet which will outline all the information required to allow you to take a decision about offering your time to this research project.

Q: Who can take part in the study?
The inclusion criteria for this study are:

- Currently employed in a clinical capacity
- Working at least 1 session or ½ day per week with acute stroke patients
- Any member of the multidisciplinary team
- Any level of post-qualification experience

The exclusion criteria are:

- Not employed in a clinical capacity
- Working fewer than 1 session or ½ day per week with acute stroke patients
- No access to the internet
- Students or non-qualified staff

Q: What will happen if I agree to participate?
If you agree to participate you will be asked to contribute an online focus group. These groups are asynchronous (i.e. NOT occurring in "real time") meaning that you can access the focus group discussion area at a time that suits you. The discussions will take place over 4-5 weeks. You will be exchanging information and ideas with members of your own profession. You will be emailed to let you know when new information is posted, and you may receive an email reminder if necessary (a maximum of two per week). It is possible that after one round of recruitment, you will be invited to participate in a shorter, on-off discussion to clarify any issues that may have arisen from the focus groups. You are under no obligation to agree to take part in either phase of the study.

Q: What are the security arrangements?
In order to participate you will need to register with a secure, online Virtual Learning Environment (VLE) and will be allocated a username and password. You will need to log in to the virtual boards every time you wish to access the discussions.
Only those who agreed to take part in the study will be given usernames and passwords to these boards, the discussion forums are not open to the public and cannot be reached through a search engine.

Q: Will I be participating anonymously?
Since you will be using a username, other participants will have no way of identifying you, as long as you do not reveal your own identity. Only the researcher will have access to the identities behind the usernames, however, these will not be used in any way other than linking your level of experience with the contributions you make during the analysis. This level of anonymity will be maintained throughout the project and when writing the results up for publication, any quotes included in the publication shall remain anonymous.

Q: Are there any risk associated with participation?
There are no known risks to participating in such a research project. This project received ethical approval from QMU's ethics committee.
Under the Department of Health guidelines for research governance this study does not require full ethical review as it does not meet any of the criteria for Requirements for Research Ethics Committee Review. This project was also exempt from an ethics application by the Research and Development department of NHS Lothian.

Q: Are there any incentives to participating?
Yes, taking part in this activity can form part of your CPD – if you are a physician, you can use this activity as "category 3: self certified activities". If you are a nurse or member of allied health professions, you are encouraged to reflect on what you have learnt from participating in this project. A reflective model will be sent to all participants on completion of the study. Additionally, those who take part in the study will be given a £20 Boots gift token as a note of appreciation for their time.

Further information:

- You will be free to withdraw from the study at any stage and you would not have to give a reason.
- The results may be published in a peer-reviewed journal and/or presented at a conference as appropriate.
- If you would like to contact an independent person, who knows about this project but is not involved in it, you are welcome to contact Dr Maria Giatsi Clausen. Her contact details are given below.

If you have read and understood this information sheet, any questions you had have been answered, and you would like to be a participant in the study, please now complete the consent form and return either by post (SAE enclosed) or by email to gcarin-levy@qmu.ac.uk

Contact details of the researcher

Name of researcher: Gail Carin-Levy

Address: Lecturer in Occupational Therapy, School of Health Sciences
Queen Margaret University, Queen Margaret University Drive
Edinburgh EH21 6UU
Email / Telephone: gcarin-levy@qmu.ac.uk / 0131 474 0000

Contact details of the independent adviser:

Name of adviser: Dr Maria Giatsi Clausen

Address: Lecturer in Occupational Therapy, School of Health Sciences
Queen Margaret University, Queen Margaret University Drive
Edinburgh EH21 6UU
Email / Telephone: mgiatsiclausen@qmu.ac.uk / 0131 474 0000

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Psychological difficulties in the acute stages of stroke

Please check / initial the following:

- ☐ I have read and understood the information sheet and this consent form. I have had an opportunity to ask questions about my participation.
- ☐ I understand that I am under no obligation to take part in this study.
- ☐ I understand that I have the right to withdraw from this study at any stage without giving any reason.
- ☐ I agree to participate in this study.

Name of participant: _____

Signature of participant: _____

Signature of researcher: _____

Date: _____

Name of researcher: Gail Carin-Levy

Address: Lecturer in Occupational Therapy, School of Health Sciences
Queen Margaret University, Queen Margaret University Drive
Edinburgh EH21 6UU

Email / Telephone: gcarin-levy@qmu.ac.uk / 0131 474 0000

Appendix 6.5: Anonymity instructions to participants

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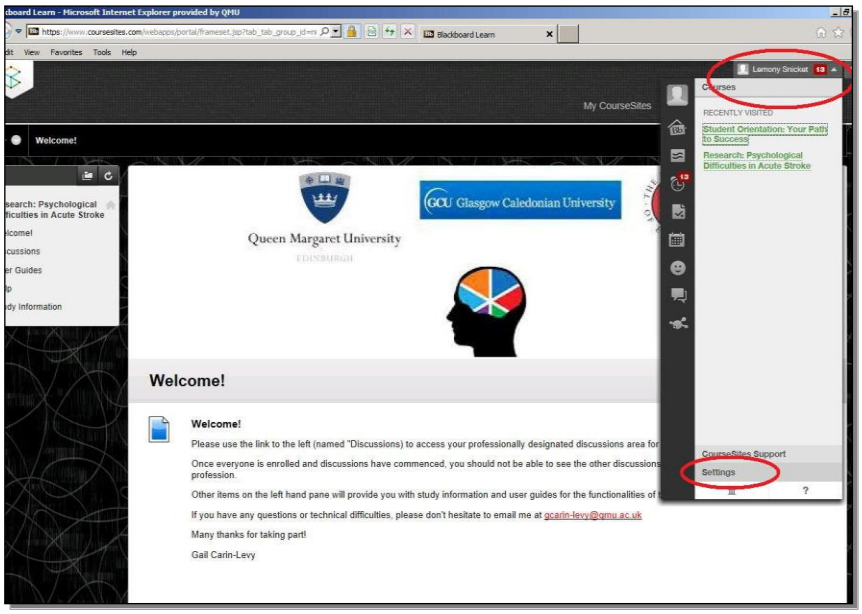
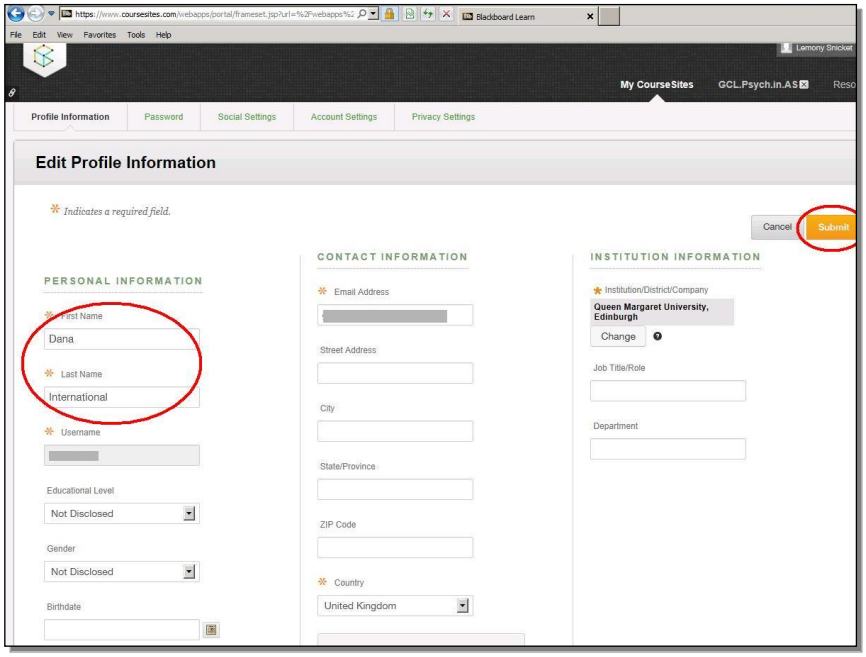
Anonymity in the Virtual Learning Environment

Once you are in the course, click on the "global navigation menu" – that is where your name appears, at the top R corner: once you do this a drop-down menu will open to make your screen look like this:



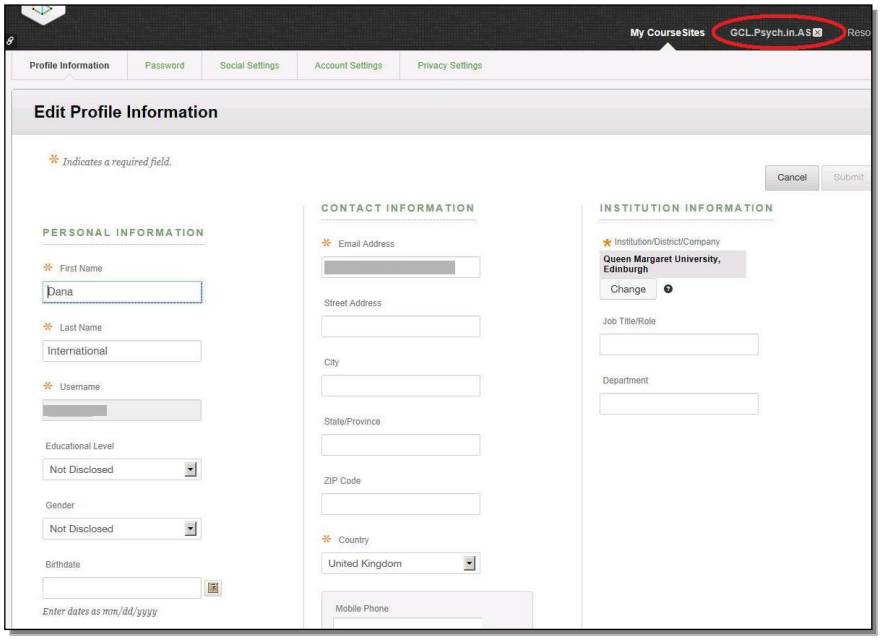
Select "Settings" (circled above in red).

Then select "Personal Information" and you should be taken to a screen that looks like this:



In the first name and last name fields (circled in red) change your real name to a made-up character and click the orange “submit” button.

Once you have done this, you can go back to the study area by clicking on the tab GCL.Psych.in.AS as circled in red below:



When this is done, all your posts will be in your new alias and your real identity concealed.

Appendix 6.6: Recruitment Advert

Psychological difficulties in the acute stages of stroke

- Do you work with acute stroke patients?
- Are you a Doctor, Nurse or AHP (list below)?
- Are you interested in taking part in an online study?

I am studying the ways in which professionals working with acute stroke patients identify psychological difficulties.

The study involves taking part in an online discussion group – you will take part anonymously, discussing matters with members of your professional group.

You can take part in your own time, from the comfort of your own home.

You are asked to participate in online discussions during a 4 week period, it should take **no more than 2 hours each week** (you can contribute more if you like!)

- **Benefits of participating:**
  1. Taking part in this study is acceptable as self-certified **CPD**.
  2. You will be offered a gift voucher to thank you for your time.

Interested?

Contact: Gail Carin-Levy, Lecturer in OT at Queen Margaret University:

gcarin-levy@qmu.ac.uk
0131 474 0000
@gcarinlevy

AHPs included in the study: OTs, Physiotherapists, Speech and Language Therapists

Appendix 6.7: Demographics Questionnaire

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Please complete the following basic information:

Name	
Profession	
Grade / Band	
Years of experience working in stroke services	
Ward (please delete)	Stroke Unit / Stroke beds on regular ward
Hospital	
How did you hear about the study?	
Please choose a screen name that will keep your identity concealed from other participants in the study	

Please return this sheet along with your completed consent form in the SAE enclosed with the study information.

Appendix 6.8: Registration and log on instructions

Psychological difficulties in the acute stages of stroke

Registration into the Virtual Learning Environment

Registering to use the VLE:
You will shortly receive an email invitation to join the virtual learning environment hosted by Blackboard Learn.
This invite will contain this link to the login page: https://www.coursesites.com/webapps/Bb-sites-course-creation-BBLEARN/pages/index.html

This link will take you to this page, where you should select "sign up as a student" in the top right hand box:

When you sign up, and every time you log in, you are given the option of using you social media account - I urge you **NOT to register or log in using your social media / Yahoo / Google** account as this will compromise your anonymity.

You will be taken to a registration screen, asking for a few details – please follow these instructions as this is the only way to guarantee your anonymity if you register with a username and keep referring to that name when interacting online with other users.

When asked for your first name, surname and email, only give the correct email address (no other users will be able to see it!) – choose a first name and surname that characterises you, e.g.

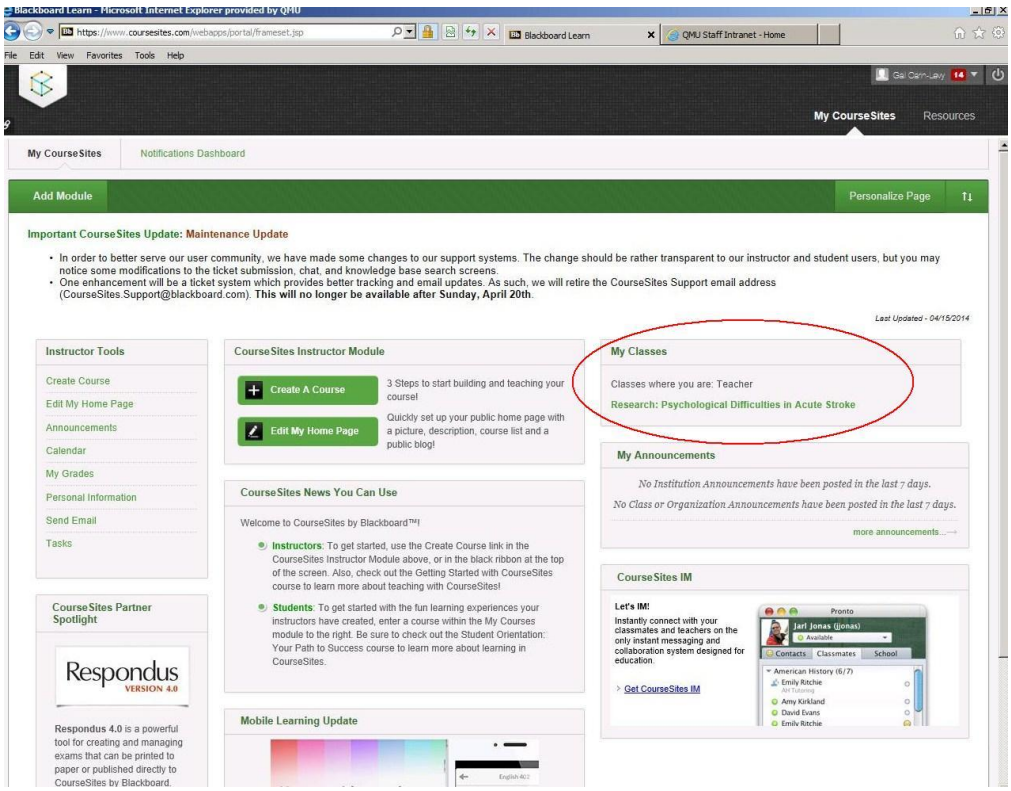
First name: Paisley
Last name: OT
Or

First name: Sailor
Last name: Physio

Your user name should be the same as the screen name you originally chose when filling in the paperwork for the study, so if you require a reminder of this screen name, simply let me know before you register.

I would advise that you keep your login details somewhere safe and accessible for the duration of the study.

How to access the study pages:
When you log in you get to a home screen that looks like this:



There is a lot of information you do not need (I apologise for this!) but you can access the study by looking under "**My Classes**" where you will find a link to "**Psychological Difficulties in Acute Stroke**" - click this link and it will take you straight to the relevant study pages.

Any difficulties, please just get in touch: gcarin-levy@qmu.ac.uk or call me on 0131 4740000
.

Appendix 6.9: Coding scheme and arrival at themes

Open codes	Focused codes	Theoretical code	Theme
Code A9 line 46: Keep a close eye day and night Code A2 line 2: Urine sample, bloods, medicines Code A4 line 4: Find out from family what normal pattern is	A9: Observations A2: Check inflammatory markers A4: Contact family or next of kin	A The actions taken in response	Information gathering
Code B2 line 3: further event in occipital lobe? Code B11 line 6: How much sleep is she getting? Code B13 line 20: Drowsiness as part of dementia Code D4 line 5: I don't particularly like the word confused	B2: A further neurological event? B11: Fatigue or sleep disorder B13: Looks like dementia	B Identifying delirium	Uncertainty around symptom recognition
Code C2 line 2: Ask OT for cognitive screen Code A36 line 4: I would do a MOCA Code C2 line 32: I don't routinely screen for delirium Code C3 line 5: Refer to liaison psychiatry Code C3 line 9: Ask medical team to check fluids Code A2 line 4: Make contact with family	C2: Professional roles C3: Referring to other professionals A4 Contact family or next of kin	C Working within a team	Working in collaboration with others
Code A2 line 4: Make contact with family Code A4 line 14: Get family to encourage fluids Code A4 line 4: Find out from family re normal pattern	A4: Contact family or next of kin	D The role of the next of kin	Delivering patient centred care
Code E4 line 12: Does he understand what has happened to him? Code E1 line 22: was she kept awake by others, causing her distress? Code E2 line 3: is he distressed by unseen stimuli?	E4: Patient insight E1: Environmental influences E2: Experience of hallucinations	E The patient at the centre of the experience	

Appendices related to chapter VII

Appendix 7.1: Publication of strand I work

J Neurol (2012) 259:1590–1599
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ORIGINAL COMMUNICATION

Delirium in acute stroke: screening tools, incidence rates and predictors: a systematic review

G. Carin-Levy · G. E. Mead · K. Nicol · R. Rush · F. van Wijck

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Abstract Delirium is a common complication in acute stroke yet there is uncertainty regarding how best to screen for and diagnose delirium after stroke. We sought to establish how delirium after stroke is identified, its incidence rates and factors predicting its development. We conducted a systematic review of studies investigating delirium in acute stroke. We searched The Cochrane Collaboration, MEDLINE, EMBASE, CINHAL, PsychINFO, Web of Science, British Nursing Index, PEDro and OT Seeker in October 2010. A total of 3,127 citations were screened, full text of 60 titles and abstracts were read, of which 20 studies published between 1984 and 2010 were included in this review. The methods most commonly used to identify delirium were generic assessment tools such as the Delirium Rating Scale ($n = 5$) or the Confusion Assessment Method ($n = 2$) or both ($n = 2$). The incidence of delirium in acute stroke ranged from 2.3–66%, with our meta-analysis random effects approach placing the rate at 26% (95% CI 19–33%). Of the 11 studies reporting risk factors for delirium, increased age, aphasia, neglect or dysphagia, visual disturbance and elevated cortisol levels were associated with the development of delirium in at least one study. The outcomes associated with the condition are increased morbidity and mortality. Delirium is found in around 26% of stroke patients. Difference in diagnostic and screening procedures could explain the wide variation in frequency of delirium. There are a number of factors that may predict the development of the condition.

Keywords Delirium · Acute stroke · Diagnosis and screening

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Introduction

Delirium (or acute confusional state) is a severe but potentially preventable disorder which is common among elderly hospital patients [1, 2], with reported prevalence of 20–30% across a variety of settings [3]. Delirium is associated with increased mortality, morbidity and length of hospital stay [4, 5]. Delirium may be hyperactive (accompanied by overt psychotic symptoms and agitation); hypoactive (characterised by sedation); or mixed (i.e. both hypoactive and hyperactive). The hypoactive type can often be undetected or misdiagnosed as depression [6].

Although stroke is a recognised predisposing factor for the development of delirium, there is currently no clear guidance on whether stroke patients should be routinely screened for delirium, no guidelines on the best way to screen for delirium and no multidisciplinary treatment recommendations for the condition [7, 8]. This is despite recent national guidance on the importance of early identification of delirium in hospital patients over the age of 65 presenting with significant illness [9]. Potentially, this means that delirium in acute stroke may be missed, particularly the hypoactive type [10].

There is, to our knowledge, no published systematic review on delirium after stroke. As a systematic review is

the least biased way of collating and examining evidence from the literature [11], we undertook a systematic review to determine the following in acute stroke:

1. The incidence of delirium, the patient-related factors associated with its development, and the association between developing delirium and outcome.
2. How best to screen for delirium, specifically, the feasibility of the screening tools, and their sensitivity and specificity.

Materials and methods

In October 2010 we searched Cochrane Stroke Group Trials Register and the Cochrane Dementia and Cognitive Improvement Group Trials Register, the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*, latest issue), MEDLINE (1950–), EMBASE (1980–), CINAHL (1981–), PsycINFO (1840–), Web of Science (1970–); British Nursing Index (1985–), Physiotherapy Evidence Database (PEDro) and OT Seeker for the systematic evaluation of evidence in occupational therapy practice. See appendix for keyword combinations used. Reference lists of identified articles were scrutinised to identify studies that were not identified by the electronic searches. Authors of published studies were contacted on two occasions for clarification and seeking out of further details.

Inclusion criteria

We included cross-sectional studies, longitudinal studies, cohort studies case control studies and case series. All adult participants (≥18 years) presenting as hospital inpatients with a clear diagnosis of stroke [12] or subarachnoid haemorrhage (SAH) were included. Full publications in English, Hebrew, French, German, Dutch or Spanish were considered for this review.

Exclusion criteria

We excluded conference proceedings, editorials, opinion pieces, review papers, letters, single case studies, case series of three patients or fewer, studies presenting patients admitted due to delirium (rather than stroke or SAH), studies reporting on acquired brain injury or progressive neurological brain damage (e.g. multiple sclerosis, dementia) or delirium tremens.

Study selection

Titles and abstracts identified from database searches were reviewed by one author (GCL) and obviously irrelevant work was eliminated. This author categorised all citations as either 'include', 'exclude' or 'possible' using an agreed paper form, the reasons for exclusion were also logged on this form. All abstracts of both included, possible and excluded studies were reviewed by the first author plus a second review author (FvW, GEM or KN) who independently screened for relevance and fulfilment of inclusion criteria. Disagreements were resolved by discussion with a third reviewer.

Data extraction and quality assessment

Paper data extraction forms were designed, piloted on three studies, revised and subsequently used to extract data from the studies which met the inclusion criteria. We extracted data on (1) year of publication, study design, and characteristics of study participants, (2) sample size, inclusion and exclusion criteria, (3) tools used to diagnose and or screen for delirium including any data provided regarding psychometric properties and the suitability of tool use with stroke patients. This was judged based on the necessity of the patient to be able to understand and use language in order to participate in the assessment, (4) number of patients who experienced delirium, predictors of developing delirium and outcomes associated with delirium in acute stroke. Our data extraction forms also incorporated the 14 item tool for the Quality Assessment of studies of Diagnostic Accuracy included in systematic reviews known as the QUADAS tool [13]. Each item in this checklist had been designed to assess the reliability of specific aspects of a study's methodology (see Table 1 for full details). Individual items are scored as 'yes', 'no' or 'unclear'. 'Yes' scores indicate that the methodology has minimised bias and increased reliability of the study outcomes while a high number of 'no' or 'unclear' scores question the reliability of the diagnostic procedure [13]. In some cases, we had to score 'non-applicable' due to the nature of some of the papers. When completing the QUADAS checklist, the Reference Standard was regarded as a clinical assessment of delirium using established diagnostic criteria [14] such as DSM-III [15], DSM-III-R [16], DSM-IV [17] or DSM-IV-R [18]. The index test was regarded as any delirium diagnostic or screening tool such as the Confusion Assessment Method (CAM) [19], the Delirium Rating Scale (DRS) [20], Organic Brain Syndrome (OBS) Scale [21] or the Mini Mental State Examination (MMSE) [22].

One review author (GCL) extracted all data and assessed quality and three other authors (GEM, FvW and KN) independently extracted the data from a third of the papers each. In instances where there were discrepancies in scoring QUADAS items, raters discussed the specific items

Table 1 QUADAS scores itemised per paper

Item/study	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Caeiro et al. [23] Journal of neurology	Y	Y	Y	Y	Y	Y	Y	Y	Y	NA	NA	Y	UC	Y
Caeiro et al. [31] European Journal of Neurology	Y	N	Y	Y	Y	Y	Y	Y	Y	NA	NA	Y	UC	UC
Caeiro et al. [32]	Y	Y	Y	Y	Y	Y	Y	Y	Y	NA	NA	Y	UC	Y
Dahl et al. [27]	Y	Y	Y	Y	UC	N	Y	Y	Y	N	N	Y	UC	N
Dostovic et al. 2008	N	Y	Y	NA	Y	Y	Y	N	N	NA	NA	UC	UC	UC
Dunne et al. [33]	Y	Y	UC	UC	UC	UC	UC	UC	UC	UC	UC	Y	N	N
Fassbender et al. [24]	Y	Y	Y	UC	UC	NA	NA	NA	N	NA	NA	Y	UC	UC
Gustafson et al. [30]	Y	Y	Y	Y	Y	Y	Y	Y	Y	UC	UC	Y	UC	UC
Gustafson et al. [29]	Y	Y	Y	Y	Y	Y	Y	N	Y	N	N	Y	N	UC
Henon et al. [2]	Y	Y	Y	UC	Y	Y	Y	Y	N	UC	UC	Y	UC	Y
Marklund et al. [37]	Y	Y	UC	UC	Y	NA	NA	NA	N	NA	NA	Y	UC	Y
McManus et al. [38] Age & Ageing	Y	Y	Y	NA	Y	Y	NA	Y	NA	NA	NA	Y	N	UC
McManus et al. [39]	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y	UC	Y
Mori and Yamadori [36]	Y	Y	UC	N	UC	Y	Y	Y	Y	UC	UC	Y	UC	UC
Nicolai and Lazzarino [35]	Y	N	UC	UC	UC	UC	Y	Y	N	UC	UC	Y	N	N
Oldenbeuving [40]	Y	N	Y	Y	Y	Y	Y	N	N	NA	N	Y	UC	Y
Sandberg et al. [25]	Y	N	Y	UC	Y	UC	Y	Y	N	UC	UC	Y	UC	N
Schmidley and Messing [44]	Y	Y	UC	UC	UC	Y	NA	NA	N	UC	UC	Y	UC	UC
Sheng et al. [26]	Y	Y	Y	UC	Y	Y	NA	NA	Y	NA	NA	Y	NA	Y
Shih et al. [34]	N	N	N	NA	Y	Y	NA	NA	N	NA	NA	Y	UC	NA

Items are scored: yes; no; unclear (UC); or non-applicable (NA)

QUADAS items: 1. Was the spectrum of patients representative of the patients who will receive the test in practice?; 2. Were the selection criteria clearly described?; 3. Is the reference standard likely to correctly classify the target condition?; 4. Is the time period between reference standard and index test short enough to be reasonably sure that target condition did not change between the two tests?; 5. Did the whole sample or a random selection of the sample receive verification using a reference standard of diagnosis?; 6. Did patients receive the same reference standard regardless of the index test result? 7. Was the reference standard independent of the index test?; 8. Was the execution of the reference standard described in sufficient detail to permit replication of the test?; 9. Was the execution of the index test described in sufficient detail to permit its replication?; 10. Were the index test results interpreted without knowledge of the results of the reference standard?; 11. Were the reference standard results interpreted without knowledge of the index test?; 12. Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?; 13. Were uninterpretable/intermediate test results reported?; 14. Were withdrawals from the study explained?

and reached agreement as to the definitive scores. Full scores for each paper are presented in Table 1.

Statistical analysis

Data on incidence were extracted from each study and a 95% confidence interval (CI) produced. These were combined in a meta-analysis to synthesise single descriptive statistics across the studies. To determine the pooled estimate, the DerSimonian and Laird random effects [14] meta-analytic approach was undertaken. Statistical heterogeneity was assessed using the Q statistic, with $p < 0.05$. The metan procedure in Stata version 9.2 was employed in the analysis and production of the associated Forest plot.

Results

A total of 3,127 citations were identified by one author (GCL), of which, 198 were retrieved for abstract and/or full text scrutiny. A total of 138 studies were rejected as per our inclusion/exclusion criteria, leaving 60 titles, the full texts of which were further scrutinised. Of these articles, a total of 40 were excluded due to not meeting our inclusion criteria leaving a total of 20 studies which met the inclusion criteria for this review. No new titles were identified from reference lists of the available studies.

Description of studies included in this review

All included studies originated from hospital-based cohorts, most of which stated that delirium assessments were conducted within 1 week of hospital admission (Table 2). The designs employed in the studies included in this review were prospective studies ($n = 11$), retrospective studies ($n = 3$) case controls ($n = 3$), one cross-sectional study, one pilot study of treatment intervention and one study which was described as "observational" (see Table 2).

Table 2 Description of studies included in the review

Study	Country	Study design	Stroke/SAH	Size (n =); age (years): mean (SD) range	Method of diagnosis	N experiencing delirium (%)	95% Confidence intervals*
Caeiro et al. [23]	Portugal	Prospective case control	Stroke	218; 57.3 (13); 24–86	DRS DSM IV criteria within 4 days	29 (13.3%)	8.8–17.8
							1.9–5.9
Caeiro et al. [31]	Portugal	Case control	Stroke	190; 63.6 (12.8); 33–84	DSM IV TR; DRS within 4 days	22 (11.5%)	7.0–16.1
Caeiro et al. [32]	Portugal	Prospective cohort	SAH	68; 55.5 (14.5); 27–86	DSM IV R; DRS daily for first 4 days	11(16%)	7.4–24.9
Dahl et al.	Norway	Prospective	Stroke	178; 73 (no further data)	CAM to screen; DSM criteria twice daily for 1 week	18[56]	5.7–14.5
Dostovic et al.	Bosnia and Herzegovina	Prospective	Both	223; 70.0 (11.3)	DRS R-98; DSM IV criteria within 4 days	59 (25.3%)	20.7–32.2
Dunne et al.	Australia	Retrospective	Both	387; 68; 20–91	DSM III	9 (2.3%)	0.8–3.8
Fassbender et al.	Germany	Prospective cohort	Stroke	23; 72; 39–89	DSM III R "in first days of admission"	9 (39%)	19.2–59.1
Gustafson et al. [30]	Sweden	Prospective cohort	Stroke	145; 73; 40–101	DSM III R; OBS Scale twice daily	69 (47.5%)	39.5–55.7
Gustafson et al. [29]	Sweden	Prospective case control	Stroke	83; 74.37 (8.1); 44–89	DSM III R; OBS Scale "several times daily"	35 (42%)	31.6–52.8
Henon et al.	France	Prospective cohort	Stroke	202; 75; 40–101	DSM IV; DRS	49 (24.3%)	18.4–30.2
Marklund et al.	Sweden	Observational	Stroke	88; 71 (11)	Diagnosis of "disorientation" on a 3 point scale on days 1 and 4	23 (26%)	16.9–35.3
McManus et al. [38]	UK	Prospective observational	Stroke	82; 66.4 (15.9); 24–97	CAM within 4 days	23 (28%)	18.3–37.7
McManus et al. [39]	UK	Prospective observational	Stroke	82; 66.4 (15.9); 24–97	CAM; DRS within 4 days	CAM: 23 (28%)	18.3–37.7
						DRS: 22 (27%)	17.2–36.4
Mori and Yamadori	Japan	Prospective	Stroke†	41; 68.2 (10.9); 18–85	Clinical Exam, MMSE within first week	25 (61%)	46.1–75.9
Nicolai and Lazzarino	Italy	Review of clinical records	Stroke	78; 71.7 (6); 65–85	Clinical Exam, MMSE	13 (16%)	8.4–24.9
Oldenbeuving et al.	The Netherlands	Pilot study of intervention	Stroke	527; 77; 53–86	CAM to screen, DRS for severity	62 (11.6%)	9.0–14.5
Sandberg et al.	Sweden	Cross sectional	Stroke	133; 77.1 (7.7)	DSM IV; OBS Scale	88 (66%)	58.1–74.2
Schmidley and Messing	USA	Retrospective case note review	Stroke†	46; aged 71 and 68 (data presented on 2 cases only)	Clinical assessment	2 (4.3%)	−1.5–10.2
Shang et al.	Australia	Observational 12 month follow-up	Stroke	156; 79.2 (6.7)	DSM IV criteria within 3 days	39 (25%)	18.2–31.8
Shih et al.	Taiwan	Retrospective case note review	Stroke‡	29; 65.55; 34–86	Clinical assessment	14 (48%)	30.1–66.5

* CIs were calculated by our own team rather than extracted from each study

† R MCA infarct only

‡ PCA infarct only

Diagnostic and screening tools used

A total of 12 studies reported applying established diagnostic criteria when assessing patients for delirium: Six (30%) studies applied DSM IV [2, 23–27], three (15%) studies applied DSM III-R [28–30], two studies applied DSM IV-R [31, 32], and one (5%) study applied DSM III [33]. Three studies referred to "clinical assessment" but did not detail any diagnostic guidelines [34–36], and one study referred to the diagnosis of "disorientation" using a simple three-point scale [37]. As for tools used to screen for delirium, of the 14 studies utilising such tools, five used the DRS or DRS R-98 [2, 23, 24, 31, 32]; two studies used the CAM [38]; two studies used both the DRS and the CAM [39, 40]; three studies used the OBS Scale [25, 29, 30] and two studies used the MMSE [35, 36]. See Table 2 for full details.

The DRS [20] and the CAM [19] are frequently used tools both of which are based on DSM criteria and have been designed to identify delirium in a variety of settings. The DRS is a tool comprising ten items, designed for use by medical staff with specific training [20]. The highest possible score is 32, with a cut-off score of ten indicating the presence of delirium, thus the DRS may be used to rate the severity of delirium [10]. Comprising of four features (acute onset and fluctuating course, inattention with either: disorganised thinking or altered level of consciousness) the CAM was developed for use by any health professional, it has high sensitivity, specificity and reliability and is easy to administer [19].

The Organic Brain Syndrome (OBS) Scale was developed for the evaluation of disturbance of awareness and orientation and other signs of confusion in the elderly [41]. Reportedly taking up to 1 h to complete [42], the OBS Scale consists of two subscales: OBS1 (16 items) for disorientation and OBS2 (39 items) for confusion. For both subscales, the severity of symptoms are ranked in a four-point ordinal scale from zero to three, where zero denotes a correct response and three denotes incorrect response. The Mini Mental State Examination (MMSE) [22] is a screening test of cognitive impairment.

One of the 20 studies included in this review reported data on sensitivity and specificity of the screening tools but this was not specific to stroke patients. However, all studies using either the DRS or the CAM referred to the original papers where data on sensitivity and specificity were available. There was no attempt in any of the studies to assess the suitability of using a generic delirium screening tool in acute stroke. A number of studies considered the challenge of using the above tools in acute stroke, as ten studies reported excluding patients with reduced consciousness [23, 27, 29, 30, 32, 33, 36–39] and four studies excluded patients with aphasia [24, 26, 29, 36]. Caeiro et al. [23, 31, 32] reported scoring zero in certain items of the DRS if patients had "language difficulties"; however, this term is somewhat vague. Henon et al. [2] considered the possibility of erroneously diagnosing demented or aphasic patients with delirium and report that patients had to score over 10 on the DRS. Gustafson et al. [30] referred to the use of clinical observation of rapid behavioural changes and disorientation on the ward as indicative of delirium in aphasic patients.

Evaluation of methodological quality

Studies which achieved the highest QUADAS scores tended to be those which utilised more than one method of identifying delirium in their cohort: a combination of a clinical assessment with the use of a screening tool [2, 23–25, 29–32] or two tools such as the CAM for detection and the DRS for severity of delirium [39, 40]. In studies which utilised only one method of identification of delirium items 7, 10 and 11 of QUADAS were removed and thus appear in Table 1 as "non-applicable" [13]. Item seven of the QUADAS was at times difficult to score as although the different tests utilised in practice are independent of each other, the DRS [20] and the CAM [19] are based on DSM diagnostic criteria and therefore one may argue that they are not entirely independent. Table 1 gives details of the scores given to each study as per QUADAS items.

Incidence of delirium in acute stroke and SAH

The overall incidence estimates of delirium in acute stroke and SAH is difficult to definitively establish due to the substantial heterogeneity observed ($\chi^2 = 587.49$, degrees of freedom = 19, $p = 0.000$). This is often the case for single group studies, with 99% of the variation in the point estimate being attributable to heterogeneity [43]. Due to this, we report only the results of the random effects approach: incidence of delirium was 26% with a 95% CI of 19–33% (Fig. 1). The frequency of delirium assessment also varied: ten studies applied diagnostic procedures once within the first week of admission [23, 24, 26, 28, 31, 32, 36–39] and three studies applied these more than once daily [29, 30, 38] with the rest of the studies not reporting on the time points at which delirium assessments were carried out (Table 2).

Risk factors for developing delirium in acute stroke

Risk factors were examined in 17 of 20 studies ($n = 478$ with delirium). The most frequently cited risk factors for developing delirium in the acute stage of stroke were the

following: older age [2, 23, 26, 27, 29, 30, 32]; specific symptoms resultant from the stroke (aphasia, neglect or dysphagia) [23, 26, 27, 31, 32, 38]; impaired vision [25–27, 38], either as a result of the stroke or pre-morbid visual disturbance, elevated cortisol levels [28, 29, 37] and drugs with anticholinergic effect [30, 31]. Eight studies ($n = 209$ with delirium) reported the association between lesion location and development of delirium: three studies found an association between right-sided lesions [33, 36, 44] and two for left-sided lesions [30, 34]. One study associated lesions of the posterior cerebral artery (PCA) with the development of delirium [35] while another reported a longer duration of delirium in patients with right hemisphere lesions, but the findings were not statistically significant [24]. Two studies [2, 27] found no significant association between lesion type or location with the development of delirium. Two studies [23, 26] found that delirium was most frequent and most severe following intracerebral haemorrhage, and two studies [26, 38] found an association between a total anterior circulation infarct (TACI) stroke and the development of delirium. The remaining studies did not investigate the association between lesion location or type and delirium.

Outcomes associated with delirium in acute stroke

Ten studies ($n = 331$ with delirium) related outcomes to the presence of delirium in acute stroke. All ten studies showed that those who experience delirium had unfavourable outcomes, with the other ten studies not reporting data on outcomes. It was consistently reported that patients who experienced delirium in the acute stage of stroke were more likely to have unfavourable outcomes such as increased hospital stay [23, 26, 29, 30, 38], increased mortality rates [23, 24, 26, 37, 38] and increased dependence: measured by rates of institutionalisation [26, 29, 38] or by means of standardised assessment of ability to perform activities of daily living [2, 23, 25–27].

Discussion

Incidence rates of delirium in acute stroke

Our meta-analysis finding of an incidence rate of 26% (95% CI 19–33%) of delirium in acute stroke is consistent with the rate of delirium found in other medical settings [3]. However, this result must be seen in the context of other findings of this review which relate to the variation in diagnostic and screening methods used to identify delirium after stroke. This variation and the varying methodological rigor, discussed below, are factors which may explain the wide range of incidence of delirium observed and the heterogeneity observed across the studies (Fig. 1).

Rigour of delirium diagnostic procedures

The rigor of diagnostic procedures across the studies included in this review must be seen in light of the decade the studies were conducted in. Three of the studies included in this review predate the development of validated delirium diagnostic or screening tools [33, 36, 44], one of which was a retrospective case note review and shall be discussed separately below [33]: Mori and Yamadori conducted a study investigating the presence of acute agitated delirium and ACS following right MCA infarcts. The authors state that mental state examinations were performed; however, there is no mention of diagnostic criteria used. Also, the MMSE was applied within 2 weeks; arguably, this time period is too long, as it is possible that cases of ACS were missed within that time period [36]. Schmidley and Messing do not explicitly refer to diagnostic criteria used; however, they do detail the definition of ACS which follows DSM III criteria [44].

Four of the studies included in this review conducted retrospective reviews of patient case notes to establish the incidence of delirium after stroke [33–35, 44]; while these methods are valid, the rigour of diagnostic procedures is impossible to critique as the reporting of these is lacking, perhaps understandably as the researchers did not conduct the delirium assessments. Other instances where we had difficulty commenting on the rigor of diagnostic procedures relate to lack of sufficient detail reported: Sandberg et al. conducted a study of sleep apnea and its relation to delirium, the scales used to diagnosed delirium are described; however, the frequency and timing of assessment are not detailed thus it is difficult to critique the methods beyond the choice of tools [25]. Dostovic et al. [24] and Fassbender et al. [28] also do not give sufficient details regarding the execution of the delirium assessments; thus it is difficult to judge the methods employed to diagnose delirium in their cohort. Marklund et al. [37] provided sufficient detail of their diagnostic protocol as they aimed to investigate the relationship of serum cortisol levels post stroke and relate these to the presence of disorientation. It is curious that they chose to investigate the presence of 'disorientation', which is a manifestation of delirium, but in itself, it does not constitute a medical or psychiatric condition and seen alone, it is not enough to determine a delirium diagnosis as per DSM criteria [15, 16, 18]. Marklund et al. [37] assessed 'disorientation' by means of a non-standardized three-point scale, the validity and sensitivity of which is unknown. Overall, it appears that in those studies where more rigorous assessment protocols were

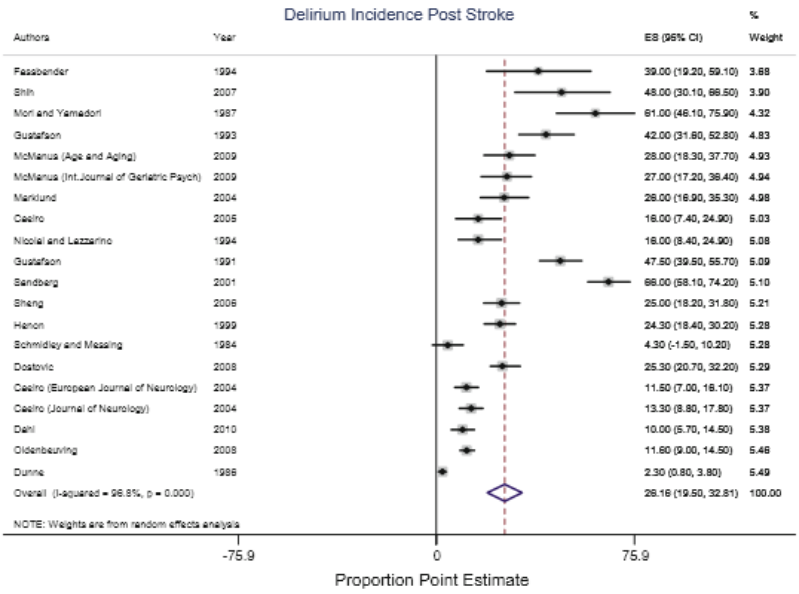

Fig. 1 Meta-analysis of incidence rates, the horizontal lines in the Forest plot represent the 95% confidence interval around the point estimate. The box around the point estimate is proportional to that of the study's weight in the analysis. The pooled estimate diamond is centred on the pooled estimate

followed, there is greater confidence in the incidence rates found.

The use of general delirium tool in a stroke cohort

An important finding of this review is the application of diagnostic tools developed for use in a general medical environment, within a stroke cohort. Among the studies included in this review, none had addressed the fact that the tools used were not specifically designed to detect delirium in a stroke cohort. The question regarding the suitability of the tools used to screen for delirium in stroke patients was asked by McManus et al. [10] as they offered some drawbacks for the use of both the CAM and the DRS in a stroke population, based mainly on language difficulties and the fluctuating nature of cognitive function within the acute phase of stroke. Albeit, McManus et al. [39] compared the CAM and the DRS in the acute stroke population and found that there was high level of agreement between the two screening tools and that there is a strong correlation between a low MMSE score and delirium in this setting. They concluded that the CAM is favourable due to its ease of use but cautioned that appropriate training is essential for use of either tool. Oldenbeuving et al. [45] also favour the CAM for use in a stroke cohort, despite the fact that it was not tested for use in this setting. The tool less frequently used by studies in this review is the OBS Scale. According to Bjorklund et al. [41] various studies have assessed the OBS scale's sensitivity to detecting a range of organic brain syndromes and found high inter-rater reliability. The OBS Scale has also been reported to show good responsiveness to cognitive symptoms in an elderly population [41] but there is no published reference to any psychometric properties of this tool [46]. A comparison between the OBS scale and the MMSE as applied to patients with dementia was carried out by Jensen et al. [47] and the two were found to have good agreement; however, the sample comprised of patients with dementia and the applicability of the OBS scale in a stroke setting is not described in the literature. The fourth tool reported in this review is the MMSE, a tool which has reported restrictions in the application in stroke due to its score being influenced by language, mood and sensory and motor function [10]. It seems clear that greater uniformity in the method and frequency of application of delirium assessment batteries would enable the

establishment of greater clarity on the incidence of delirium after stroke.

Sources of bias

Some of the studies we reviewed were limited by selection bias. Mori and Yamadori and Schmidley and Messing investigated the presence of ACS in MCA infarcts, reportedly due to the fact that the relationship between right hemisphere infarctions and ACS had been previously described [36, 44]. Similarly, Nicolai and Lazarino restricted their cohort to PCA territory infarcts; however, unlike the aforementioned studies, the presence of ACS in this type of infarct is not well documented in the literature, and indeed, they report a small number of new cases of PCA infarcts with ACS [35]. Another factor relevant to selection bias is exclusion criteria. A total of four studies excluded patients with aphasia [24, 26, 29, 36]. Aphasia has been reported in up to 38% of patients with acute stroke [48]; therefore it is possible that a substantial proportion of patients have been excluded from the study of incidence rates of delirium. Another point to note is that the CAM was validated for use with non-verbal patients in the intensive care environment (CAM-ICU) [49], it is therefore surprising that researchers chose to exclude patients with aphasia when there is a validated tool available for use with patients who are unable to communicate. A total of seven studies excluded patients with a history of dementia [24, 26, 33–36, 44], presumably to enable more accurate distinction between delirium and dementia; however, other authors have reported an association between pre-existing cognitive impairment and developing delirium in acute stroke [27, 30, 38]. Thus, by excluding this group of patients, the incidence rates of delirium would be potentially affected.

Risk factors and outcomes in delirium after stroke

Some of the risk factors for the development of delirium identified in this review are consistent with the general medical and geriatric literature. Older age, severe illness and visual impairment are established risk factors for delirium [5, 9, 50]. The importance of anticholinergic medication as precipitating factor for the development of delirium is documented in the medical literature [5, 51]; however, only two of the studies included in this review examined this as a risk factor for delirium in acute stroke. More specifically to stroke, a number of studies included in this review have found that a stroke in the territory of the middle cerebral artery (MCA) is a precipitating factor for the development of delirium, which has been reiterated by Caplan, who reviewed studies that we have excluded on the grounds that the presenting feature of the patients' admission was the delirium rather than stroke [52]. To the best of our knowledge, other stroke-specific factors highlighted in this review have not previously been discussed in the literature. As for outcomes associated with delirium after stroke, these are consistent with published literature, as it is well established that delirium is associated with an increased length of hospital stay and increased mortality and morbidity [4, 5, 9, 53].

Strengths, weaknesses and future research

To our knowledge, this is the first time the literature on delirium after stroke has been systematically reviewed. We are confident that our search strategy has identified all the available literature in the field, and we had followed a rigorous protocol when applying inclusion/exclusion criteria and during data extraction. We have applied a validated, rigorous checklist [13] for the quality assessment of included studies, which we believe has strengthened the review. However, the main restriction of this review stems from the substantial heterogeneity of the studies included. It was difficult to compare and group studies because of the wide variation in the way delirium was detected and the timing and frequency of delirium assessment. This has highlighted the importance of establishing delirium screening guidelines within stroke medicine, to enable an early identification, treatment and potential minimisation of the effects of the condition on patients and healthcare systems. We propose that an important direction for future research lies in either adapting an existing screening tool for the use within a stroke cohort, or the development of a new tool, specifically designed to be used with patients after stroke.

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Conflicts of interest There are no conflicts of interest to disclose.

Appendix

Key words used in searches and their combinations:

Stroke: stroke; cerebrovascula/cereb.ral vascular + disorders/accident; cerebral/cerebellar/brain + infarct/ischemia/thrombo*/emoboli*; subarachnoid; brain attack

Delirium: delirium/deliri*; acute confusion/confusional state; acute + organic/psychoorganic + psycho/syndrome; acute brain syndrome; metabolic encephalopathy; clouded state; clouding of consciousness.

(1) Stroke/post stroke/CVA
(2) Cerebrovascula/cerebral vascular + disorders/accident/insult
(3) Cerebral/cerebellar/brain + infarct/ischemia/thrombo*/emoboli*
(4) Cerebral/brain/subarachnoid + haemorrhage/hemorrhage
(5) Brain attack
(6) Delirium/deliri*
(7) Acute confusion/confusional state
(8) Acute + organic/psychoorganic + psycho/syndrome
(9) Acute brain syndrome
(10) Metabolic encephalopathy
(11) Clouded state
(12) Clouding of consciousness
(13) 1 and 6–12
(14) 2 and 6–12
(15) 3 and 6–12
(16) 4 and 6–12
(17) 5 and 6–12

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Appendix 7.2: Publication of strand II work

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Hindawi

Research Article

Delirium in Acute Stroke: A Survey of Screening and Diagnostic Practice in Scotland

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Aims. To survey the use of delirium screening and diagnostic tools in patients with acute stroke across Scotland and to establish whether doctors and nurses felt the tools used were suitable for stroke patients. *Methods.* An invitation to participate in a web-based survey was e-mailed to 217 doctors and nurses working in acute stroke across Scotland. Descriptive statistics were used to report nominal data, and content analysis was used to interpret free text responses. *Results.* Sixty-five responses were logged (30% return rate). 48% of the respondents reported that they routinely screened newly admitted patients for delirium. Following initial screening, 38% reported that they screened for delirium as the need arises. 43% reported using clinical judgment to diagnose delirium, and 32% stated that they combined clinical judgment with a standardised tool. 28% of the clinicians reported that they used the Confusion Assessment Method; however, only 13.5% felt that it was suitable for stroke patients. *Conclusions.* Screening for delirium is inconsistent in Scottish stroke services, and there is uncertainty regarding the suitability of screening tools with stroke patients. As the importance of early identification of delirium on stroke outcomes is articulated in recent publications, validating a screening tool to detect delirium in acute stroke is recommended.

1. Introduction

Delirium is a common neuropsychiatric condition affecting 20–30% of elderly patients across most hospital settings [1]. In acute stroke, the incidence of delirium reported by individual studies ranges from 10% [2] to 48% [3], and meta analyses recently performed placed the incidence around 26%–28% [4, 5]. Delirium is associated with increased mortality, morbidity, and length of hospital stay [5–8], and it has been strongly associated with development of cognitive impairment in the long term in the general medical setting [9, 10]. In acute stroke, recent studies have clearly demonstrated that patients who develop delirium are more likely to die within 12 months, have poorer functional outcomes, and are at higher risk of developing dementia [4, 5, 11, 12]. There are calls in the literature for clinicians to place an emphasis on early identification of delirium in stroke patients, using a tool validated specifically for this population, as early intervention may minimise the aforementioned unfavourable outcomes [5, 13, 14]. The most recent guidance published in the United Kingdom (UK) by both the National Institute for Health and Clinical Excellence (NICE) and the Royal College of Physicians (RCP) do not mention delirium as a specific complication of stroke [15, 16]; however, both refer to cognitive impairment and inattention. The word "confusion" is mentioned in the Scottish Intercollegiate Guidelines Network document "Management of Patients with Stroke" (SIGN 118), but there is no specific guidance about how to screen for or manage this "confusion" [17]. Clinical guidelines from other English speaking countries were examined for comparison: Australian guidelines [18] do not mention delirium in stroke patients; American Heart Association (AHA) guidelines mention delirium in the context of screening for psychiatric sequelae to stroke in the end of life care [19]; Canadian

guidelines were the most detailed, and they contained a clear message about the importance of delirium as a complication in acute stroke. This was discussed in relation to screening for cognitive impairment or a change in cognitive function, and there is a clear call to screen patients at risk, using a validated screening tool [20]. Screening for delirium in other clinical settings is considered important across several countries. Clinical guidelines published in the UK [7], United States of America [21], Australia [22], and Canada [23] all guide clinicians to screen for delirium in services which are known to have a high prevalence of the condition. This is in order to ensure that delirium is not missed or misdiagnosed and thus to decrease the length of hospital stay and the unfavourable outcomes and ultimately generate cost savings for the organization [7, 23]. As for the method of diagnosis, the UK and Canadian documents specifically recommend the use of the Confusion Assessment Method (CAM) [24] as the diagnostic tool of choice.

2. Description of Screening/Diagnostic Tools

Our systematic review [4] identified a number of tools commonly mentioned in the literature; however, the most frequently cited are the Delirium Rating Scale (DRS) [25] and the CAM [24], both of which are based on the American Psychiatric Association diagnostic and statistical manual (DSM) criteria and designed to identify delirium across a variety of medical settings. The DRS was designed to be used by medical staff with specific training [25]. It comprises of 10 items, the highest possible score is 32, with a cut-off score of ten indicating the presence of delirium, thus it is a useful tool to rate the severity of delirium [13]. The CAM comprised four features (acute onset, fluctuating course, and inattention with either disorganised thinking or altered level of consciousness); it was originally developed for use by any health professional, and it has high sensitivity, specificity, and reliability and is easy to administer [24]. Other tools mentioned in the literature are the mini mental state examination (MMSE) [26]: it is a screening test for cognitive impairment and not specifically designed for the detection of delirium [27]; nonetheless, it seems to be used in some studies as a means of identifying delirium in a stroke patient [4]. Levkoff et al. [27] provide a useful review of instruments available for the detection of delirium in hospital patients.

In summary, a variety of screening and diagnostic tools for the detection of delirium exist; screening for delirium is important in a variety of settings, but there is no clear guidance about how, when, and how often to screen patients for delirium after stroke. Although studies of delirium in acute stroke describe how delirium is identified [4], it is unclear what happens in clinical practice; namely, how delirium is identified and diagnosed and by whom. The literature from the general medical/geriatric settings gives an indication that, in practice, delirium is under-recognised, and staff do not routinely use screening tools in daily practice [28, 29].

The aims of this web-based survey were to investigate the use of delirium screening and diagnostic tools in patients with acute stroke. We sought to identify whether and if so, how doctors and nurses across Scotland screen for and diagnose delirium in acute stroke.

The survey explored the following questions:

(i) Is delirium screened for in routine clinical practice?

(ii) How often does screening for delirium in acute stroke take place and what is the method of screening and or diagnosis in clinical practice?

(iii) Who is most likely to identify delirium in acute stroke?

(iv) Which delirium identification tools (if any) are used?

(v) What are clinicians' views about the suitability of screening tools as they are used within acute stroke care?

3. Methods

3.1. Survey Questionnaire. The Bristol Online Survey Tool was used to set up, collect, and subsequently analyse the survey data. This tool is widely used by universities and other public bodies in the UK [30]. Web surveys are inexpensive; they increase the ease of administration for the research team and allow data to be analysed as soon as it is logged on the online survey tool [31]. Web-based surveys yield the same findings as paper surveys in terms of content [32, 33] although online surveys may yield a slightly lower response rate [34]. We attempted to maximise response by keeping the length of the survey as short as possible, maintaining a clear structure, and using clear language [34]. A scrolling design (rather than the questions set over several webpages) was chosen to maximise ease of use and minimise potential technical difficulties. This design is reputed to increase response rate as it reduces the time taken to complete the survey [35]. Survey questions were constructed based on published guidance on effective question writing [36] and effective design for web-based response options such as minimising "drop down boxes" as they are burdensome to respondents [37]. Following questionnaire development, the survey tool was distributed to three clinicians: a stroke physician, a stroke nurse specialist, and a psychiatrist. This process was used to check for language, structure, and sequence of the questions presented [38], but no data were collected during this process. Two minor difficulties related to the ambiguity of questions were identified and rectified prior to the survey being distributed among stroke clinicians practising throughout Scotland.

3.2. Sample and Recruitment. The survey was distributed to 217 clinicians (doctors and nurses) working in the acute stroke setting in Scotland by the administrators of the British Association of Stroke Physicians (BASP) and the Scottish Stroke Research Network (SSRN), and the first author contacted all (n = 114) members of the Scottish Stroke Nurses Forum (SSNF) directly. The first author cross checked the complete distribution lists of SSRN and SSNF and removed duplicate names and email addresses. The BASP database was not shared with the first author; therefore, it was not possible to check for duplicates with other databases, and

Table 1: Respondent characteristics.

Characteristics	$n = 65$ (%)
Profession	
Doctors	36 (53.7)
Nurses	29 (43.3)
Grade	
Consultant	24 (36.9)
Senior trainees (doctors)	12 (18.4)
Senior nurse (band 7 and above)	14 (21.5)
Main grade nurse (band 6 and below)	15 (23.0)
Main practice area	
Specialist stroke unit	47 (72.3)
General hospital ward	8 (12.3)
Both of the aforementioned	10 (15.4)
No. of patients admitted to respondents' workplace each year [39]	
>500	15 (23)
250–500	39 (60)
100–250	7 (10.7)
<100	4 (6.1)

we were informed by the administrator that the approximate number of BASP members in Scotland is 60. The initial invitations were sent by email in July 2012. Two further email reminders were sent two weeks apart, in August 2012. In order to be able to calculate response rate as accurately as possible, respondents were asked not to disseminate the email invitation among their colleagues.

3.3. Data Analysis. Descriptive statistics were used to report nominal data. Free text comments were analysed by the first author using qualitative content analysis methodology: the first author read and reread the words used in the responses and then classified them into small sets of categories or codes of shared meaning. The codes were counted to determine how frequently they appear within the text responses and patterns relating to the key themes emerged [39–41]. Data regarding size of stroke unit and number of stroke beds of all hospitals across Scotland were obtained via Information Service Division Scotland [42]; these are presented in Table 1 to categorise respondent characteristics.

3.4. Ethics. This study did not require ethical approval as it an opinion survey seeking the views of NHS staff on service delivery. A letter of confirmation was obtained from the South East Scotland Research Ethics Service. Ethical approval was gained from Queen Margaret University.

4. Results

Sixty-five (30%) responses were received following an initial email and two reminders. A total of 36/90 (40%) of doctors replied; 29/127 (23%) of nurses replied. The characteristics of the respondents are summarised in Table 1.

4.1. Screening for Delirium. In response to the question: *"Does your ward have a policy on screening new patients for delirium?"*, 21/65 (32%) respondents selected "yes," 35 respondents (53.5%) replied "no," and 9 respondents (14%) responded "unsure." In response to the question: *"Do you routinely screen for delirium on admitting new patients to the ward?,"* 31(48%) selected "yes" and 34 (52%) selected "no." The following question: *"Do you screen patients for delirium on a regular basis during admission?"* yielded the same result, with 31 (48%) selecting "yes" and 34 (52%) selecting "no." Of the 31 respondents who selected "yes," 25 (81%) reported screening "as the need arises"; two (6.5%) selected "once weekly"; and four (13%) selected "other" and provided a short text explanation: two respondents stated that screening occurred during ward rounds or if a concern is raised by a staff member. One respondent stated that they screened daily, and, one respondent stated that they screened on admission (which answers the original question: "*Do you routinely screen for delirium on admitting new patients to the ward?*").

4.2. Diagnostic Methods. In response to the question: *"How do you normally diagnose delirium in stroke patients?,"* 28 respondents (43%) reported applying their clinical judgement, two respondents (3%) reported using a standardised tool, and the remaining respondents reported combining clinical judgement with the application of a standardised tool ($n = 21$, 32.3%). Two respondents selected "other": one reported using *"AMT* (abbreviated mental test) *and urine testing and observations"* and the other reported using the CAM [24] to diagnose delirium. Twelve respondents (18.5%), all of whom were nurses, stated that they do not diagnose delirium in their practice and selected the option *"I have not been trained to use a standardised tool"*. Table 2 summarises these results.

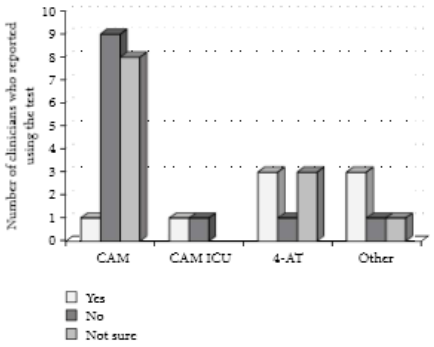
4.3. Clinicians' Choice of Diagnostic Tool. Table 2 outlines the structure of the questions relating to the choice of diagnostic tool. Free text comments made in response to the question on clinicians' choice of diagnostic tool revealed that six (9%) respondents used a tool developed by a local collaboration between Liaison Psychiatry and Geriatrics known as "4AT" [43]. Four respondents reported using either the abbreviated mental test (AMT) [44] or the MMSE [26].

4.4. Suitability of the Diagnostic Tool in a Stroke Population. Respondents were asked *"Do you think the tool you use is suitable for a stroke population?."* A total of 52 (80%) of the 65 respondents answered this question. Seven respondents selected "yes" (13.5%), 16 respondents selected "no" (31%), and the remaining 29 selected "not sure" (56%). Figure 1 cross-references those who selected their tool of choice with clinicians' opinion regarding suitability for stroke patients. 15 (23%) participants gave free text comments. The majority ($n = 8$; 53%) of comments related to the difficulty using a generic screening tool with persons who experience communication difficulties such as receptive or expressive aphasia. Four respondents questioned the validity of the tool in a stroke population and discussed in particular cognitive

Table 2: Questions regarding diagnostic practices and tools utilised.

Question	Doctors $n = 36$	Nurses $n = 29$
How do you normally diagnose delirium in stroke patients?		
Standardised tool	1 (2.7%)	1 (3.4%)
Clinical judgement	22 (61%)	6 (20.6%)
Both the aforementioned	13 (36.1%)	8 (27.5%)
I do not diagnose delirium in my practice	0	12 (41.3%)
Other	0	2 (6.8%)
If you use a tool to diagnose or screen for delirium in stroke patients, please indicate which tool you use		
CAM	11 (30%)	7 (24.1%)
CAM-ICU	2 (5.5%)	0
DRS	0	0
Delirium symptom review	1 (2.7%)	0
Organic brain syndrome scale	0	0
Other	8 (22.2%)	4 (13.7%)
No response	14 (38.8%)	18 (62%)

CAM: confusion assessment method.
CAM-ICU: confusion assessment method for intensive care unit.
DRS: delirium rating scale.



CAM: confusion assessment method
CAM-ICU: confusion assessment method for intensive care unit
4-AT: the 4-A test [40]

Figure 1: Is the tool you use suitable for use in stroke patients?

or *"neurological abnormalities"* arising from the stroke. One respondent felt that the tool they used had *"reasonable face validity,"* and one further respondent advocated the use of the CAM [24].

5. Discussion

Our survey results highlight a number of key findings that reveal current delirium diagnostic and screening practice in Scottish stroke services. Most stroke units either did not have a screening policy for the identification of delirium in acute stroke, or the clinicians were unaware of such policy. Almost half of respondents to this survey stated that they did not routinely screen for delirium in acute stroke. The diagnosis of delirium was reportedly made mainly by doctors, in most cases by means of clinical judgement and in some cases combined with the use of a standardised tool. Interestingly, the majority (41%) of nurses who responded to this survey ($n = 12$) claimed that they do not diagnose delirium in their practice, citing lack of training to use a standardised tool as the main reason for this. This finding supports the findings of a survey of nurses across intensive care and general medical/surgical units which highlights that nurses have only modest confidence levels in identifying delirium in clinical practice [45]. Other authors have reported infrequent use of standardised tools for the screening and/or diagnosis of delirium: nurses reportedly rely largely on clinical judgement when it comes to diagnosing delirium. In these studies, the clinicians surveyed had recognised the importance of delirium as an underdiagnosed condition of potentially serious consequences; however, routine screening and utilisation of standardised observation tools were still the exceptions in a variety of studies [45–47]. Surveys of doctors highlight similar concerns. A survey of Brazilian critical care physicians found that less than 15% of respondents used validated delirium assessment tools [48]. An American survey of ICU clinicians found that despite the belief that the literature supported routine screening for delirium, only 40% of respondents did so, and of those, only a small number used specific delirium screening tools [49]. Furthermore, a finding from a survey of junior doctors working in a variety of medical settings in the UK revealed that the fundamental cause of under-recognition and undertreatment of delirium lies in the lack of knowledge of the diagnostic criteria and standardised screening tools [50].

Within our own survey, a small number of respondents reported using a variety of tools to diagnose delirium in their practice, citing tools which have not been validated for the use in acute stroke [26, 43]. Some studies found a degree of usefulness in detecting cognitive changes using the AMT [44] and the MMSE [26] which might be due to delirium [51–53]; however, these tools are not specifically designed to detect delirium [27, 49, 54]. Some of our respondents reported difficulties in using diagnostic tools in stroke patients because of aphasia. Our systematic review highlights that previous studies have excluded patients with aphasia from their cohorts for the same reason [4]. In our survey, only two respondents reported using the CAM-ICU, which might increase the proportion of patients with language difficulties who may be assessable [55] as the CAM-ICU does not rely on language for the diagnosis of delirium [49, 56]. This tool has recently been validated for use in stroke patients, demonstrating high sensitivity, specificity, overall accuracy, and inter-rater reliability [14, 57]. Various

authors, in both nursing and medical literature are calling for clinicians to take a key role in the identification of delirium in practice, advocating the use of validated instruments to facilitate accurate and timely recognition, leading to prompt treatment and better outcomes for patients [5, 14, 28, 58].

Our response rate was 30%, a rate lower than a number of surveys (both online and traditional) of delirium identification published within the last five years [46–48, 50]. Our response rate seems to be influenced by the notable difference between doctors and nurses response to our invitation to participate: only 23% of nurses approached actually completed the survey. Eley et al. [59] identified the main barrier to nurses' access to computers in the ward environment as lack of time due to other demands of the job. This may be a reason why the response rate from the nurses in this survey was comparatively low.

6. Strengths, Limitations, and Future Research

We were keen to explore practice within Scotland only at this stage, and we would plan to roll out the same survey throughout the UK. Our response rate was moderate but consistent with the literature on online surveys return rates [34, 60]. Other surveys examining delirium identification utilised a variety of methods of survey distribution which yielded better response rates, for example, using a combined approach of both paper and online options [47] or using the traditional postal questionnaire design [46, 50]. We were keen to be able to calculate our response rate; therefore, we used convenience sampling and approached specific individuals in the clinical field and avoided snowballing, but this may have introduced a selection bias. Nevertheless, our data are of interest because this is, to the best of our knowledge, the first survey of diagnostic and screening practice in relation to delirium in acute stroke services in the UK. Our survey contributes to a growing body of knowledge on delirium in acute stroke. This field of research is steadily growing as more publications are generated on the various aspects of identification [14, 52] and potential treatment [61, 62] of the condition.

It was interesting to note the inconsistent screening and diagnostic practice identified by this survey, which is perhaps related to the lack of guidance or policy regarding screening and diagnosis of delirium in stroke. It would be beneficial for UK best practice guidelines in stroke care [15, 17] to incorporate information on delirium and perhaps consider establishing a standardised way of identifying the condition in this population. This would require further research to be conducted, not only to validate a tool to detect delirium in stroke patients, but also to establish the most effective time intervals for screening patients. Another avenue for further research is to identify the barriers to regular and effective screening for delirium across all members of the multidisciplinary team. In light of the fact that both this survey and others have identified the need for training and increasing awareness of delirium among staff working with stroke patients, we would like to reiterate the importance of this and call for more staff to become familiar with the risk factors and outcomes associated with delirium. Increasing the amount of correctly identified cases of delirium may lead to better outcomes for these patients and may yield cost benefits to the organisation [7].

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Appendix 7.3: Report published in the 2014 SSNF newsletter

Delirium in acute stroke: A survey of screening and diagnostic practice in Scotland

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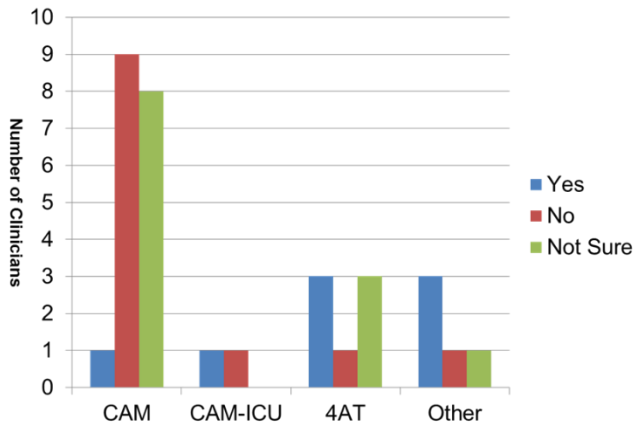
Background and aims: Delirium is a serious complication following a stroke, affecting 26%-28% of patients (Carin-Levy et al. 2012, Shi et al. 2012) and associated with increased mortality, morbidity and length of hospital stay (McCusker et al. 2003, McCusker et al. 2002, National Institute for Health and Care Excellence 2010). Screening for delirium is considered important in various hospital settings (Schuurmans et al. 2001), yet it is unclear how, when and how often to screen patients for delirium after stroke. The aims of this project were to:

- Survey the use of delirium screening and diagnostic tools in patients with acute stroke across Scotland.
- Establish whether doctors and nurses felt the tools they used were suitable for stroke patients.

Method: In 2012, an invitation to participate in a web-based survey was e-mailed to 217 doctors and nurses working in acute stroke across Scotland via the British Association of Stroke Physicians (BASP), the Scottish Stroke Research Network (SSRN), and the Scottish Stroke Nurses Forum (SSNF). Descriptive statistics were used to report nominal data and content analysis was used to interpret free text responses.

Results: Sixty five responses were logged (30% return rate). 48% of respondents reported they routinely screened newly admitted patients for delirium. Following initial screening, 38% reported they screened for delirium as the need arises. 43% reported using clinical judgment to diagnose delirium and 32% stated they combined clinical judgment with a standardised tool. 28% of clinicians reported they used The Confusion Assessment Method however, only 13.5% felt it was suitable for stroke patients (figure 1).

Figure 1: Is the tool you use suitable for use in stroke patients?



CAM: Confusion Assessment Method; CAM-ICU: Confusion Assessment Method for Intensive Care Unit; 4-AT: The 4 A test

Discussion: Our survey results highlight a number of key findings that reveal current delirium diagnostic and screening practice in Scottish stroke services. Some of our findings are consistent with other authors: infrequent use of standardised delirium screening tools was reported in studies of both nurses and doctors across a variety of medical settings (Flagg et al. 2010, Forsgren and Eriksson 2010, Davis and MacLullich 2009, Salluh et al. 2009). A small number of own survey respondents reported using a variety of tools to diagnose delirium in their practice such as The 4-A Test (Bellelli et al. 2014) and the Mini Mental State Examination (MMSE), neither of which have been validated for use in acute stroke. Some of our respondents reported difficulties in using diagnostic tools in stroke patients because of aphasia, consistent with findings of a systematic review of screening tools to detect delirium after stroke (Carin-Levy et al. 2012).
Conclusion: Screening for delirium is inconsistent in Scottish stroke services and there is uncertainty regarding the suitability of screening tools with stroke patients. Various authors, in both nursing and medical literature are calling for clinicians to take a key role in the identification of delirium in practice, advocating the use of validated instruments to facilitate accurate and timely recognition, leading to prompt treatment and better outcomes for patients (Shi et al. 2012, Mitasova et al. 2012).

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The full version of this paper is published as an open-access paper and can be downloaded here: http://www.hindawi.com/journals/isrn.stroke/2013/620186/cta/

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