Psychological Sequelae of Stroke: Examining Emotionalism Maintaining Factors and the Prevalence of Stroke-Induced Post-Traumatic Stress Disorder.

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Thesis Portfolio Abstract

Background: Every two seconds, someone in the world sustains a stroke, yet research on the emotional consequences of stroke remains rather in its infancy. As such, stroke survivors and their carers must be advised regarding the treatment and prognosis of emotional difficulties, such as post-traumatic stress disorder (PTSD) and emotionalism, in the absence of robust evidence.

Methods: To examine the prevalence of PTSD after stroke or transient ischemic attack (TIA), an updated systematic review and meta-analysis was conducted. Subgroup analyses and meta-regression were used to explore high heterogeneity between the studies included in the review. To examine psychological factors related to emotionalism after stroke, empirical analyses of pre-existing data that was collected during a large, longitudinal cohort study (Testing for Emotionalism After Recent Stroke, TEARS) were undertaken. A series of logistic regression analyses were used to explore associations between demographic variables (age, sex, stroke type), psychological variables (anxiety, depression, cognition, daily functioning and emotionalism) measured at 2-weeks after stroke, and the presence of emotionalism at 6- and 12-months after stroke.

Results: A total of 18 studies (N =1815) were examined in the systematic review and meta-analysis. The pooled prevalence estimate of PTSD after stroke was 18% (95% CI= 14-23%). Subgroup analyses and meta-regression revealed that prevalence was significantly higher in studies including only stroke (in comparison with mixed stroke and TIA samples), and studies assessing PTSD using a self-report measure (in comparison to clinical interview). This accounted for 22% of the heterogeneity between studies. The empirical study (N = 228) found that emotionalism and anxiety at baseline (2-weeks after stroke), were associated with a greater likelihood of experiencing emotionalism at 6- or 12-

months. Younger age and worse cognitive impairment at baseline (2-weeks after stroke) were associated with a greater likelihood of drop-out from the TEARS study before the 6- and 12-month assessments.

Conclusions: The papers presented in this thesis demonstrate that PTSD and emotionalism are commonly experienced following stroke, both in the acute stages and later in the recovery journey. Given the impact of such emotional difficulties on rehabilitation and societal reintegration, is it clear that further exploration of the constructs related to the development and maintenance of these conditions is crucial in progressing towards much needed, evidence-based non-pharmacological interventions.

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Chapter 1: Introduction to Thesis Portfolio

Stroke is a condition characterised by sudden neurological disturbance, as a result of blocked (ischemic) or ruptured (haemorrhagic) blood vessels (NICE, 2020). Stroke is one of the leading causes of death and disability worldwide (Feigin et al., 2017). Whilst mortality rates following stroke are decreasing, advances in medical treatment and a growing, ageing population has meant that more people are living with its devastating effects (GBD 2016 Stroke Collaborators, 2019). What is more, the incidence of stroke is estimated to increase by 60% per year until 2035, with the number of stroke survivors more than doubling in that time in the UK alone (King et al., 2020). Given this vast increase, and associated costs to health and social care, it is vital that research is up-to-date to appropriately inform clinical practice guidelines.

Mood Difficulties following Stroke

The psychological effects of stroke are variable and wide-ranging. Carota and Bogousslavsky (2009) identified four key domains in which psychological difficulties may present after stroke: (i) affective and mood disorders, such as depression and anxiety, (ii) behavioural and personality changes, such as apathy, anger and irritability, (iii) cognitive impairment, and (iv) disorders of perception and identity of the self, others and places.

Stroke can be a hugely challenging event for the patient and those around them. Sudden loss of functioning, coupled with fear of death and disability makes it unsurprising that emotional difficulties are encountered by many. Persistent emotional problems are common in both patients with minor and severe strokes (Moran et al., 2014), even continuing 5-years after the index stroke event (Lincoln et al., 2013). This presents several challenges to rehabilitation and achieving optimum patient outcomes. Firstly, those experiencing significant mood or emotional problems after stroke may experience difficulties in completing rehabilitation programmes. It

may be that an individual finds it difficult to initiate or self-direct recommended treatment (Skidmore et al., 2010), lacks motivation to engage in treatment or make the necessary lifestyle changes required to achieve optimal functioning (Kutlubaev & Hackett, 2014), fears injury or further damage to health (Ferro & Santos, 2020), or is simply too fatigued to participate (Nicholson et al., 2017). Secondly, mood difficulties have been associated with increased mortality (Zhang et al., 2020) and poorer adherence to treatments aimed at preventing repeat stroke (Kronish et al., 2012). Finally, those experiencing significant mood problems after stroke are far more likely to encounter restrictions in the course of societal reintegration and social participation (de Graaf et al., 2020). Not only does this have various implications for the quality of life of the patient following stroke, but further impacts those around them, increasing caregiver burden (Minshall et al., 2019). It is clear that mood and emotional difficulties after stroke require careful consideration in planning rehabilitation efforts.

Thus far, the majority of research into mood disorders after stroke have focused on depression and anxiety. However, comprehensive rehabilitation requires consideration of the lesser expected psychological sequalae, such as post-traumatic stress disorder and emotionalism (Lincoln et al., 2011). This thesis focuses on these lesser examined aspects. More specifically, the prevalence of post-traumatic stress disorder following stroke and psychological variables associated with post-stroke emotionalism.

Post-traumatic Stress Disorder

Post-traumatic stress disorder (PTSD) is a mental health condition which can occur in response to actual or perceived threat of death, serious injury or adverse life events. PTSD comprises four key symptomatic clusters (American Psychiatric Association, 2013). Firstly, symptoms of intrusion are experienced, such as intrusive

memories, flashbacks or nightmares, meaning that the individual persistently re-experiences the traumatic event. Secondly, the individual makes several attempts to avoid trauma-related stimuli (either external reminders, or trauma-related thoughts and feelings). Thirdly, negative alterations in cognition or mood occur, such that the individual experiences negative thoughts or feelings after the traumatic event. This may present as overly negative thoughts/assumptions about oneself or the world, negative affect, decreased interest in activities, difficulty experiencing positive emotion or difficulty recalling features of the traumatic event. Finally, the individual experiences alterations in arousal and reactivity. In other words, they may become hypervigilant to any source of potential threat, may experience difficulty concentrating or sleeping, may engage in risky behaviours and demonstrate irritability or aggression.

As a sudden, unexpected event that may lead to death or severe disability, stroke is considered to be a traumatic event by many stroke survivors (Crowe et al., 2016). A growing body of clinical evidence has illustrated that PTSD occurs commonly as a result of stroke (Garton et al., 2017), however, post-stroke PTSD has only gained recognition in the past 20 years (Sembi et al., 1998). Furthermore, literature examining the prevalence, development and maintenance of post-stroke PTSD is inconsistent, with many reporting contradictory findings. As such, much remains unknown about PTSD following stroke.

Emotionalism

Emotionalism (also termed emotional lability, emotional incontinence, pathological laughing and crying, pseudobulbar affect) is characterised by increased emotional expression (usually crying, or sometimes laughing), which is unpredictable and beyond the control of an individual (House et al., 1989). This leads to emotional reactions which are incongruent with personal experiences. At times,

emotional reactions may be triggered by appropriate stimuli, for example crying after hearing difficult news, however such reactions are often disproportionate to the circumstance. On other occasions, laughter or crying may occur in an uncontrolled way when a situation is not objectively sad or humorous (Kim & Choi-Kwon, 2000).

Estimates of emotionalism prevalence after stroke vary, largely depending on the timing and method of assessment, but is reported to be around 20% (Gillespie et al., 2016). Initially, emotionalism was thought to originate from specific neuroanatomical regions, for example the frontal lobes, cerebellum and thalamus (Engelman et al., 2014; Parvizi et al., 2009; Girotra et al., 2018). However, a lack of social support and worse functioning (Choi-Kwon et al., 2012), irritability (Ferro et al., 2010), cognitive intrusions (Eccles, 1999), personality factors and maladaptive coping skills (Carota & Bogousslavsky, 2018) have been found to be related to the development and maintenance of emotionalism. It may therefore be that emotionalism does not simply reflect damage to specific neural pathways, but also the psychological effects of stroke.

The role of psychological factors in the pathogenesis of emotionalism after stroke requires further evaluation, to appropriately inform its guidance and treatment. Despite the prevalence and implications of emotionalism after stroke, it is strikingly under-researched. Consequently, knowledge of the development, persistence and maintenance of post-stroke emotionalism over time is limited. Individuals experiencing emotionalism (and their carers) must therefore be advised regarding its prognosis on the basis of sparse scientific evidence.

Summary of Thesis Project

This thesis portfolio examines two common, but underresearched psychological sequalae of stroke: PTSD and emotionalism. Chapter 2 presents a systematic review and meta-analysis assessing the prevalence of PTSD after stroke.

This paper provides an updated estimate of the prevalence of stroke-induced PTSD, which was originally published in 2013 by Edmundson and Colleagues, and highlights the varying methods and timing of PTSD assessment used amongst studies. Suggestions are made with regards to achieving consensus on the best method for identifying stroke-induced PTSD, and regarding further research into differences in PTSD prevalence based on subtypes of stroke. Chapter 3 presents a bridging chapter, which is used to link the papers written in Chapters 2 and 4.

Chapter 4 presents an empirical research paper, examining the presence of emotionalism in the first year after stroke and potential psychological factors associated with such presence. This was achieved through secondary analyses of data collected within a wider, longitudinal cohort study of post-stroke emotionalism: Testing for Emotionalism After Recent Stroke (Broomfield et al., 2020). Consideration is also made for demographic and psychological factors that may contribute to drop-out in longitudinal stroke research. Recommendations are made regarding further longitudinal research examining psychological factors related to post-stroke emotionalism, with the inclusion of patient and public involvement. Recommendations for the development and testing of non-pharmacological interventions for emotionalism after stroke are also discussed. Chapter 5 provides additional results of regression and correlational analyses which are not reported in Chapter 4.

The final chapter of this thesis portfolio presents a discussion and critical evaluation. This integrates the findings of the systematic review and meta-analysis, and the empirical research paper. Associations with wider literature are discussed with implications for both clinical practice and research. References can be found at the end of Chapters 2, 4, and 7 and all appendices are included at the end.

Chapter 2: Systematic Review and Meta-Analysis

Prevalence of Post-Traumatic Stress Disorder following Stroke and TIA: An Updated Systematic Review and Meta-Analysis.

Written for publication to: *Stroke* (see Appendix A for author guidelines)

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Abstract

Background and Purpose: It is recognised that post-traumatic stress disorder (PTSD) is higher in stroke survivors than the general population, however, there is little consensus on its exact prevalence. This review aimed to provide an updated systematic review and meta-analysis of observational studies examining the prevalence of PTSD after stroke and integrate the results with those reported previously. In addition, this review sought to further examine subgroups within the data, such as the prevalence of PTSD per subtype of stroke.

Methods: Multiple databases were searched in August 2020. After independent screening and data extraction, 9 new studies were combined with the 9 studies included in the previous review, to form a combined dataset of 18 studies, including 1815 participants. All studies were assessed for quality.

Results: The overall prevalence of PTSD after stroke was 18% (95% CI [14, 23%]). Heterogeneity was high between studies. Unlike the previous review, no significant difference was found in PTSD prevalence based on the timing of assessment. Prevalence rates were higher for individuals who experienced stroke and were assessed by self-report measure, accounting for 22% of heterogeneity.

Conclusions: This review confirms that PTSD is experienced by around 1 in 5 stroke survivors and is sustained after 12-months. Further research would greatly benefit from consensus regarding the optimum method for assessing PTSD after stroke. Further exploration of stroke subtypes and severity impacting the onset and maintenance of PTSD would also be beneficial.

Keywords: assessment, meta-analysis, prevalence, PTSD, stroke, rehabilitation

Prevalence of Post-Traumatic Stress Disorder following Stroke and TIA: An Updated Systematic Review and Meta-Analysis.

Mood difficulties are common following stroke, with around one third of survivors reporting emotional problems[1]. Whilst the prevalence and development of stroke-induced depression and anxiety are well documented[2,3], far less is known about the development of Post-Traumatic Stress Disorder (PTSD) after stroke. Characterised by symptoms of cognitive intrusions, avoidance, altered affect and arousal[4], PTSD can be triggered by life-threatening medical events[5]. Due to its unexpected, uncontrollable onset, and potentially life-threatening nature, experiencing a stroke may leave survivors at particular risk of developing symptoms of PTSD. However, PTSD that is specifically triggered by stroke has only gained formal recognition over the past 20 years[6] and hence, continues to be an underresearched and poorly understood area.

The potential effects of stroke-induced PTSD are wide-ranging. For example, it is frequently acknowledged that PTSD after stroke is associated with poorer quality of life and worse functional outcomes[7-11], although the exact mechanisms of this relationship are unclear. Theoretically, it is possible that several aspects of PTSD symptoms hinder rehabilitation efforts, or contribute to poorer engagement in functional rehabilitation. For example, intrusive thoughts and memories may put extra demand on the already limited cognitive resources of many stroke survivors. This may make it more difficult for the individual to fully process their traumatic experience. In addition, those experiencing stroke-induced PTSD may try to avoid physical and emotional reminders of their stroke, impeding attempts at societal reintegration. Alternatively, it may be that the localisation or severity of stroke contributes to a higher level of disability, in turn contributing to an increased presence of PTSD[12].

It is equally possible that the presence of stroke-induced PTSD contributes to poorer adherence to preventative treatments and increased mortality. For example, Kronish and colleagues[13] found that a large percentage of stroke survivors were not compliant with medications prescribed to prevent future stroke or Transient Ischemic Attack (TIA). They hypothesised that the self-management of illness may serve as a distinct association with the traumatic triggering event, hence contributing to an avoidance of medications. Alternatively, nonadherence to medication may be related to forgetfulness as a result of cognitive impairment, or may be related to different beliefs held regarding medication by those with elevated PTSD symptoms, such as a perceived lack of control over the health difficulty that triggered the onset of PTSD symptoms[14]. Although such mechanisms have yet to be confirmed, these findings present an important consideration for treatment planning after stroke.

Alongside limited evidence to account for why PTSD worsens stroke outcomes, there is little consensus regarding the prevalence of PTSD following stroke and TIA. Whilst it is consistently acknowledged that the prevalence of PTSD is higher in stroke survivors than in the general population[7, 8, 12, 13, 15-25], the literature is cluttered with varying estimates and mixed results[26]. It is therefore difficult to accurately assess needs within healthcare systems[27]. Incidence rates have ranged between 4-37% with the only known meta-analysis[25] concluding that around 1 in 4 stroke survivors experience PTSD symptoms within the first year post index event. In an effort to untangle variability amongst the data and reach greater consensus regarding the prevalence of stroke-induced PTSD, it is important that the most up-to-date evidence is examined.

In 2013, Edmondson and colleagues[25] reviewed the available evidence to provide an estimated prevalence of PTSD induced by stroke or TIA, however several studies have been published since then, which are potentially relevant. In addition,

Edmondson and colleagues highlighted several limitations which could be addressed through an updated review. Firstly, most of the available data in the 2013 review had only examined stroke-induced PTSD in relatively small sample sizes. The authors noted that over half of their overall data came from one study, potentially skewing the results. Secondly, they recognised that the mean age of their sample was lower than that of the wider population of stroke survivors and so may not be generalizable to older survivors. Thirdly, whilst Edmondson and colleagues reported that all of the studies included in their review were considered to meet their minimum criteria for quality, the procedure used to arrive at this conclusion was unclear. For example, it is unclear what constituted their minimum criteria and if quality was assessed by one or several individuals. Furthermore, it is not clear how each study performed against their quality assessment. An updated review could potentially address these issues, leading to a more current prevalence estimate on the basis of a larger sample size, thus increasing precision and bolstering confidence in the conclusions drawn.

Finally, Edmondson and colleagues noted the need for further subgroup exploration within the data. They identified that a large proportion (64%) of heterogeneity was explained by the length of time between stroke or TIA and PTSD assessment (greater or less than 12-months after the index event). They also noted that prevalence rates appeared to vary on the basis of the type of PTSD assessment (i.e. self-report measure or clinical interview). It would be useful for clinical practice to examine whether such conclusions continue to present amongst more contemporary data. In addition, Edmondson and colleagues noted that they were unable to ascertain any differences between the prevalence of PTSD induced by either stroke or TIA due to a lack of data. According to Kiputh and colleagues[29], PTSD should be examined separately in stroke and TIA to ascertain whether the traumatic experience of sudden-onset neurological symptoms, or residual impairment

following stroke, is more associated with the onset of PTSD symptoms. Given the temporary nature of TIA, it could be plausible that the prevalence of PTSD is less in TIA populations, however the presence of other mood disorders such as anxiety and depression appears to be similar amongst the two cohorts of patients[30]. It is therefore also conceivable that the same is found for PTSD. More research examining PTSD amongst individuals with TIA has been conducted since the 2013 review[16, 18, 28], allowing for further exploration of prevalence rates according to both conditions.

This systematic review therefore aimed to integrate and examine data from the 2013 review with the data published since, in order to provide an updated prevalence estimate of PTSD induced by stroke or TIA. This review was completed in accordance with the following research questions:

1. What is the prevalence of PTSD induced by stroke or TIA?
2. What are the methods used to assess PTSD after stroke or TIA?
3. Are there differences in the prevalence of PTSD between individuals who have experienced stroke and individuals who have experienced TIA?

Methods

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[31] guidelines (see Appendix B for PRISMA checklist). The review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO), registration: `CRD42020192317 (accepted 28/08/2020).

Search Strategy

All studies that provided a prevalence estimate of stroke or TIA-induced PTSD, published since the previous review in 2013, were identified. Search terms from the previous review were revised and used to search the following electronic databases: PubMed, AMED database, CINAHL, PsycINFO, ProQuest database and

The Cochrane Library. Databases were searched from February 2013 to August 2020 with all searches completed on 1st August 2020. Search terms were developed as two strings (to represent stroke or TIA and to represent PTSD) and were combined using AND. See Appendix C for full electronic search strategy. Search terms to represent stroke or TIA for PubMed were: ((stroke).ti,ab OR (stroke*).ti,ab OR (CVA).ti,ab OR (cerebrovascular*).ti,ab OR ((brain OR vascular OR lacunar OR venous OR cerebral OR isch?mic) adj2 (accident* OR infarct* OR event* OR attack*)).ti,ab OR TIA.ti,ab). Search terms to represent PTSD for PubMed included: (("traumatic stress disorder").ti,ab OR (ptsd).ti,ab or (post-traumatic).ti,ab OR (posttraumatic).ti,ab OR (post adj traumatic).ti,ab OR (traumatic adj stress).ti,ab). Terms were adjusted for the other databases. In addition, reference lists of the relevant studies were scanned for further potential studies. All titles and abstracts were independently screened by the authors ET (all title and abstracts) and SF (50% randomly selected proportion) to identify any potentially eligible articles. Full text articles were obtained of those identified and were inspected to determine eligibility by the same independent reviewers. Any disagreements were resolved by discussion.

Inclusion/Exclusion Criteria

Studies were included if they were undertaken in populations of individuals with a clinical diagnosis of haemorrhagic or ischemic stroke or TIA and assessed symptoms of PTSD using either a validated self-report measure or clinical interview. No limits were set for study location or time since stroke. Studies were excluded based on the following criteria:

- Paediatric stroke (defined as <18 years of age at time of stroke)
- Design: studies which were not observational, cohort or cross-sectional
- Unclear/uncertain clinical diagnosis (e.g. no formal diagnosis of stroke or TIA)

- Studies in which data was not separated across neurological conditions and/or psychiatric presentations (e.g. stroke combined with traumatic brain injury, or PTSD combined with depression)
- Studies not available in English
- Qualitative studies

Data Extraction

A study-specific extraction proforma was develop and piloted prior to data extraction (see Appendix D). Information was extracted on study characteristics (numbers of participants, study location), design (sampling method, setting, exclusion criteria), assessment of stroke/TIA and PTSD (method of stroke diagnosis, PTSD assessment measure, time since stroke, PTSD prevalence) and patient characteristics (age, gender, stroke type). The main outcome was crude PTSD prevalence, determined using either clinical cut-off scores from self-reports measures, or clinical interviews in the included studies. Extracted data is summarised in Table 1. All data extraction was completed by ET and checked by SF.

Quality Assessment

The procedure used to assess quality, and overall quality ratings in the 2013 review were unclear. To ensure consistency for this update, the quality of all studies included in the 2013 review and in this current update was assessed using the Quality Assessment Tool for Observational Cohort and Cross-sectional Studies[32] (QATOCCS; see Appendix E). The QATOCCS is a 14-item measure which requires the rater to assess key concepts, for example: “Was the research question or objective in this paper clearly stated?”. Each item may be answered “yes”, “no”, “cannot determine”, “not reported” or “not applicable” allowing the rater to summarise and critically appraise each study based on the responses. Supplementary guidance is provided which assists the rater in determining each response and the overall rating

of "good", "fair" or "poor". There are no fixed guidelines regarding overall quality, which is formed on the basis of the rater's judgement of the risk of bias identified from the responses. For this review, item 8 ("For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?") was considered not applicable, due to the dichotomous nature of stroke/TIA diagnosis. Item 8 was therefore not considered when forming judgements of the quality of each study. The overall rating given to each study was influenced by the studies ability to answer the questions set out in this review. A second rater (SF) also assessed the quality of a randomly selected 50% of the included studies using the QATOCCS. Any disagreements in quality rating were resolved through informal discussion.

Analysis plan

The studies reported in the 2013 review were combined with those identified in the current update. All data analysis was conducted using the "Metafor" package[33] in R 4.0.3[34]. The prevalence of stroke-induced PTSD for each study was calculated and then pooled to give an overall prevalence estimate. A random effects model was used to account for high heterogeneity identified by the I^2 statistic and double arcsine transformation was used to stabilise variance, preventing the confidence intervals of studies with low prevalence falling below zero[35]. Sensitivity analysis was also conducted due to high heterogeneity between studies.

Subgroup analyses that were planned *a priori* included the length of time between the index stroke event and PTSD assessment, the method by which PTSD was assessed (clinical interview vs. self-report measure) and the type of stroke experienced by the included sample (stroke, TIA, or both). Due to insufficient data, the impact of stroke subtypes, such as ischemic or haemorrhagic, on PTSD

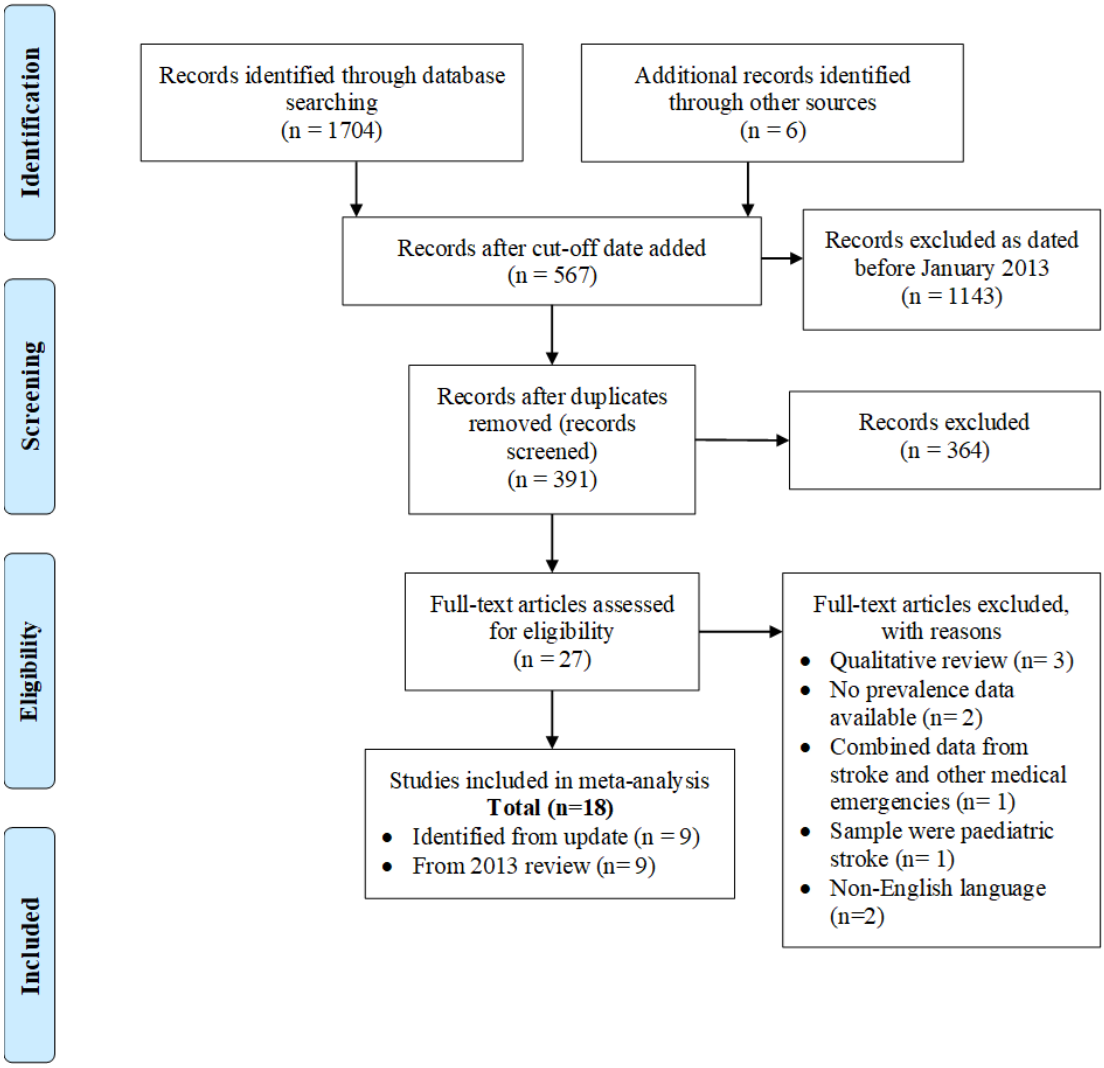
prevalence could not be analysed. Forest plots were created as a means of graphically summarising the results, including 95% confidence intervals of each study and overall prevalence estimates. Meta-regression analyses were used to assess differences between subgroups. Visual inspection of funnel plots was conducted to assess for potential publication bias.

Results

The search from January 2013 to August 2020 identified 391 potential studies, of which 9 met the inclusion criteria for this review (see Figure 1). The following results are based on the combined data set of 18 studies, containing 9 studies from the original review[6, 13, 15, 17, 21, 22, 24, 36, 37] and 9 studies identified for the update[7, 8, 12, 16, 18-20, 23, 28].

Figure 1

Search strategy flowchart



Study Characteristics

A total of 1815 participants were included across 18 studies. The sample size varied widely across studies (range: 27-535) , the mean age of participants was 67 years (*SD* = 7.60) and 53.4% were men. All studies were either cross-sectional (9) or prospective longitudinal cohort (9) in design. Most participants had been recruited in person whilst in hospital (8) or when visiting outpatient clinics (4), with the remaining identified through medical records (1), through participation in another trial (1), using a combination of the above methods (2), or recruitment methods were not reported (2). The included studies were conducted in ten countries: UK (5), USA

(3), France (2), Germany (2), Norway (1), Switzerland (1), Croatia (1), The Netherlands (1), Brazil (1) and China (1).

Table 1

Characteristics of Studies Included in the Prevalence of Stroke-induced PTSD Updated Review

Source	N	Study Location	Male (%)	Mean Age (years)	Stroke Type	Time since Stroke (months)	PTSD Measure	Clinical Interview (Y/N)	PTSD Prevalence (%) [95% CI]	Quality rating
Bruggiman, 2006	49	Switzerland	67	51	Stroke NOS	1-12	IES	N	31 [23-41]	Fair
Favrole, 2013	40	France	65	52	Ischemic stroke or TIA	1-6	IES	Y	25 [1-8]	Fair
Field, 2008	81	UK	53	71	Stroke NOS	3	PDS	N	37 [27-48]	Good
Garton, 2020	108	USA	50	57	Haemorrhagic stroke	12	PCL	N	7 [3-13]	Fair
Grosse-Holz, 2020	61	Germany	62	70	TIA	3	PDS	N	25 [14-37]	Good
Jiang, 2020	64	China	62	56	Haemorrhagic stroke	12	IES	Y	24 [14-36]	Good
Kronish, 2012	535	USA	41	63	Stroke NOS and TIA	1-60	PCL	N	18 [15-21]	Fair
Letamendia, 2012	27	France	63	64	Stroke NOS	1	PCL	N	4 [0-19]	Fair

Source	N	Study Location	Male (%)	Mean Age (years)	Stroke Type	Time since Stroke (months)	PTSD Measure	Clinical Interview (Y/N)	PTSD Prevalence (%) [95% CI]	Quality rating
Marques, 2020	70	Brazil	60	55	Ischemic stroke	1-6	PCL	N	19 [10-30]	Fair
Merriman, 2007	102	UK	56	73	Stroke NOS	1-12	PDS	N	30 [22-40]	Fair
Noble, 2008	105	UK	43	53	Haemorrhagic stroke	3-13	PDS	N	31 [23-41]	Good
Rutovic, 2019	85	Croatia	62	64	Ischemic stroke	3	PCL	N	13 [7-22]	Fair
Sagen, 2009	104	Norway	59	65	Ischemic stroke	4	SCI	Y	3 [1-8]	Fair
Sembi, 1998	61	UK	NR	66	Stroke NOS or TIA	1-18	CAPS	Y	10 [4-20]	Poor
Stein, 2018	55	USA	45	63	Ischemic stroke	6-12	PCL	N	11 [4-22]	Fair
Utz, 2019	84	Germany	54	69	TIA	12	PDS	N	8 [3-16]	Good
Visser-Meily, 2013	94	The Netherlands	18	55	Haemorrhagic stroke	36	IES	N	26 [17-36]	Fair
Wang, 2011	90	UK	48	75	Stroke NOS	1-3	PDS	N	30 [21-41]	Good

Key: CAPS= Clinician Administered PTSD Scale[38]; IES= Impact of Events Scale[39]; NOS= Not Otherwise Specified; NR= Not Reported; PCL= PTSD Checklist[40]; PDS= Posttraumatic Stress Diagnostic Scale[41]; SCI= Structured Clinical Interview[42]; TIA= transient ischemic attack

Assessment of PTSD after Stroke

The timing of PTSD assessment varied widely amongst studies (range: 1-60 months post ictus). Most of the studies assessed PTSD within the first year (15), whereas others assessed PTSD within 18 months (2), at 3 years (1) and up to 5 years (1) after stroke. PTSD was assessed using clinical interview (either alone or in combination with a screening measure) in 4 studies. Two of these studies[19, 37] used clinical interview alone to diagnose PTSD, whilst the other two studies[6, 16] determined the presence of PTSD using a self-report measure and then confirmed diagnosis and assessed severity/complexity using clinical interview. The remaining 14 studies used a self-report measure only. Table 1 shows the measure used in each study. Whilst such measures were not developed specifically for use within stroke populations, they are widely used to assess PTSD following a wide range of potentially traumatic medical events, including stroke[43].

Prevalence of PTSD after Stroke

The overall prevalence of PTSD following stroke or TIA was 18%, 95% CI [14, 23%] across the 18 studies included in this review (see Figure 2 for forest plot). The prevalence rates reported by individual studies varied greatly (range: 3-37%) and there was significant heterogeneity between studies (I^2 = 85%, τ^2 = 0.0148, p = < .01).

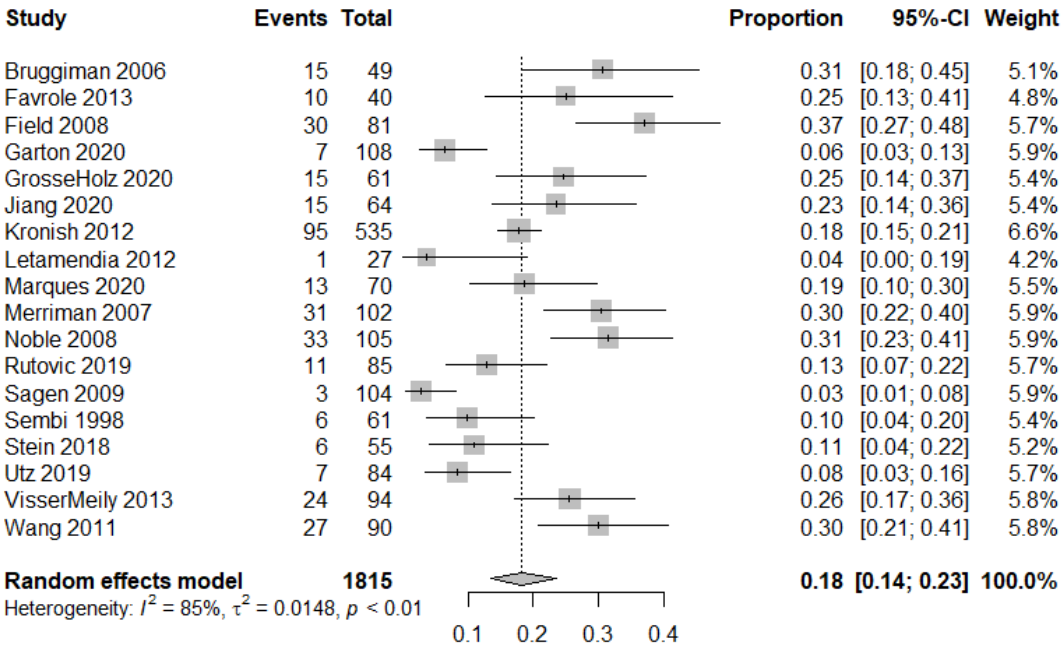
Sensitivity Analysis

As a result of the high heterogeneity found between studies, a sensitivity analysis was conducted. Each study was removed consecutively, to highlight any significant impact on the overall prevalence of stroke-induced PTSD. Prevalence estimates were found to be between 17%, 95% CI [13, 22%] and 20%, 95% CI [15, 24%], which indicated that no one study considerably impacted the pooled prevalence estimate. This meant that the one study rated as “poor” in terms of quality

was deemed not to impact the findings and hence, included in the analyses reported here.

Figure 2

Forest Plot of Pooled Prevalence Data



Subgroup Analyses

To further examine the high heterogeneity between studies, subgroup and meta-regression analyses were used. In accordance with the 2013 review, subgroups were assessed based on the time between stroke and the PTSD assessment (< 12-months and > 12-months), and the type of assessment used (clinical interview or self-report measure). In addition, the prevalence of PTSD across different subtypes of stroke (i.e. stroke, TIA or both) was assessed.

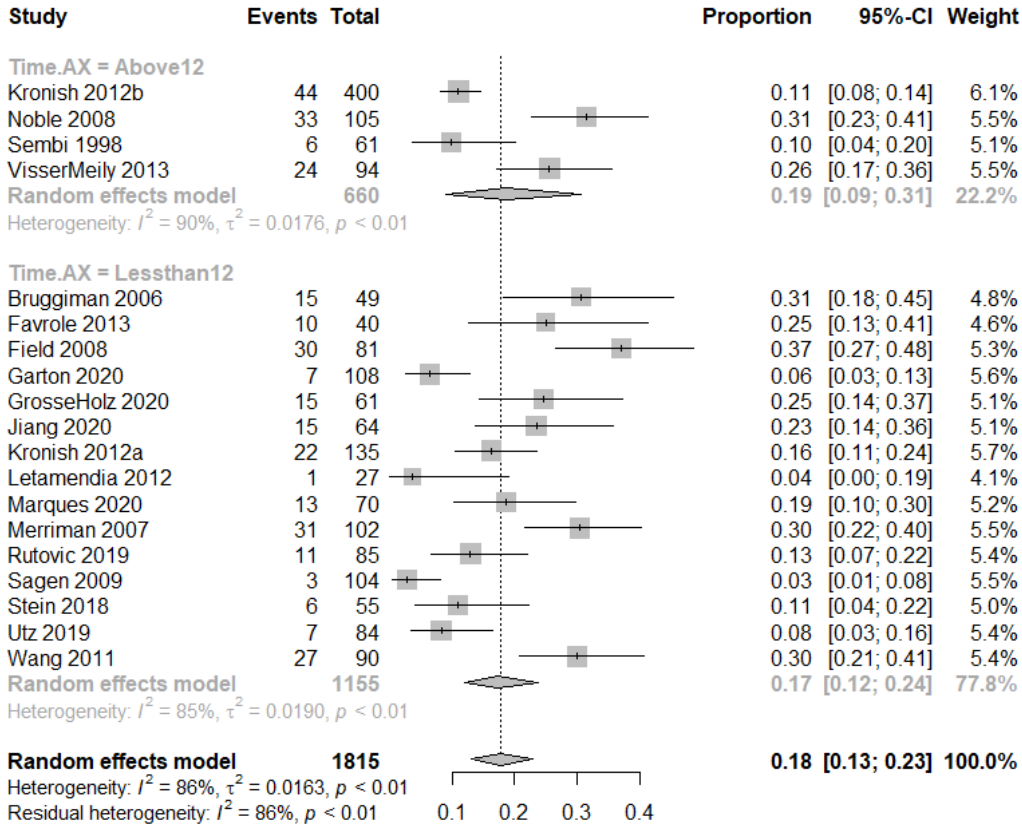
Timing of Assessment

The time between the occurrence of stroke and PTSD assessment varied greatly across the 18 studies included in this review (range: 1-60 months). The 2013 review highlighted that the timing of the PTSD assessment (either within or later

than 12-months after stroke) explained substantial heterogeneity across the studies (64%). Therefore, the data for this review was split into two subgroups; PTSD assessment completed within 12-months of stroke or PTSD assessment completed later than 12-months after stroke. As one study[13] assessed PTSD between 1-60 months, their data was split into the number of participants assessed within 12-months of the index stroke event, and those assessed later than 12-months after the index event, in accordance with the 2013 review. The aggregate prevalence estimate in the 15 studies which assessed PTSD within 12-months of stroke was 17%, 95% CI [12, 24%] in comparison to 19%, 95% CI [9, 31%] in the studies that assessed PTSD later than 12-months after stroke (see Figure 3 for forest plot). Meta-regression analyses indicated that there was no significant difference between the estimated PTSD prevalence when assessed within 12-months, or longer than 12-months after the index stroke (*OR*= .93, 95% CI [.68, 1.26], *p*= .65).

Figure 3

PTSD Prevalence in Studies Assessing PTSD > 12 Months after Stroke and < 12 Months after Stroke

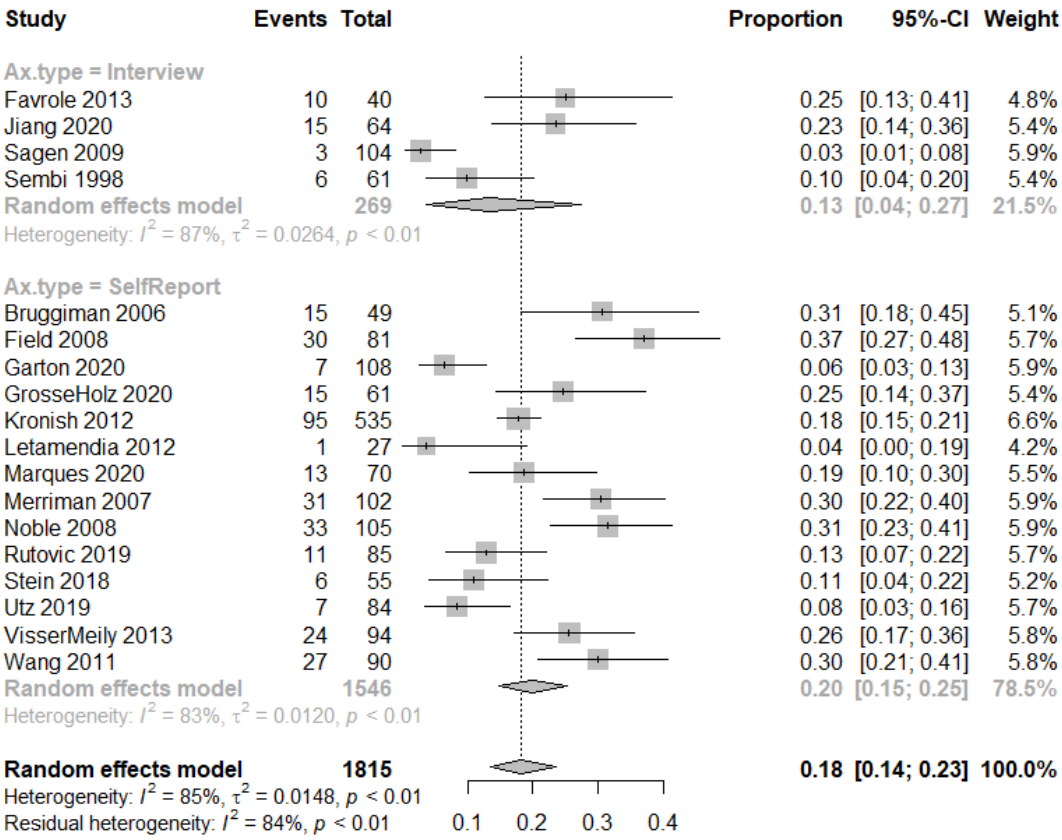


Assessment type

In accordance with the 2013 review, aggregate estimates were also produced per the type of PTSD assessment used (clinical interview or self-report measure). The aggregate prevalence estimate in the 4 studies using clinical interview was 13%, 95% CI [4, 27%] compared to 20%, 95% CI [15, 25%] in those studies assessing PTSD using a self-report measure alone (see Figure 4 for forest plot). Meta-regression analyses indicated that there was a significant difference between the estimated PTSD prevalence in these subgroups, with prevalence rates likely to be higher in studies assessing PTSD using a self-report measure (*OR* = 1.62, 95% CI [1.11, 2.41], *p* = .01).

Figure 4

PTSD Prevalence in Studies Assessing PTSD using Clinical Interview compared to Studies using Self-report Measures



Stroke subtype

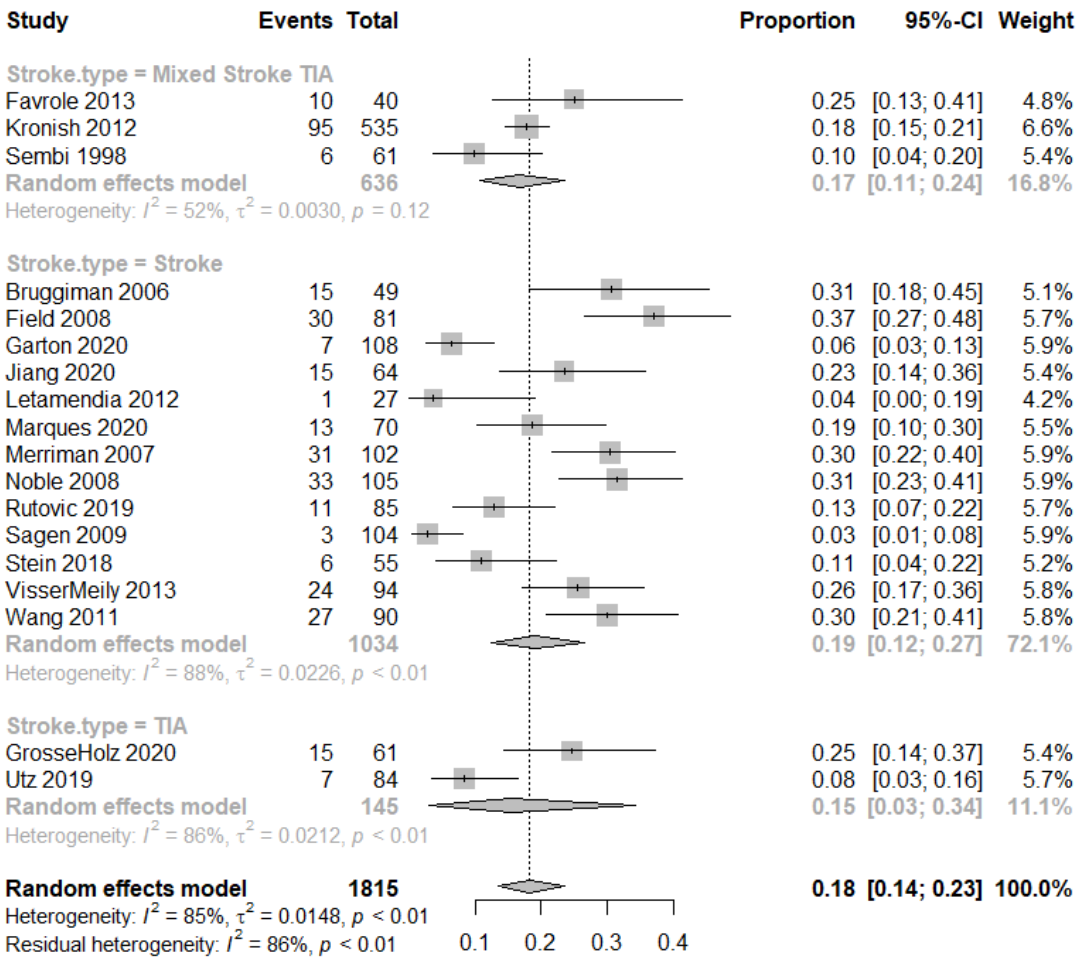
The type of stroke experienced by participants also varied across studies. Most studies included only those who had experienced stroke and excluded TIA (13), with around half of those further distinguishing between ischemic and haemorrhagic stroke. Other studies included those who had experienced either a stroke or TIA (3) or only included individuals who had experienced TIA (2). Subgroup differences were therefore examined based on the inclusion criteria regarding the type of stroke experienced by participants (i.e. stroke only, mixed sample of stroke and TIA, or TIA only). The aggregate prevalence estimate in the studies only including stroke was 19%, 95% CI [12, 27%] in comparison to 17%, 95% CI [11, 24%] in the studies

including both stroke and TIA, and 15%, 95% CI [3, 34%] in the studies only including TIA (see Figure 5 for forest plot). Meta-regression analyses indicated a significant difference in PTSD prevalence between the studies only including stroke, in comparison to the studies including a mixed sample of stroke and TIA, with prevalence rates likely to be higher in samples only assessing individuals with stroke (*OR* = 1.79, 95% CI [1.36, 2.37], *p* = < .001). No significant difference was found between studies only including stroke and only including TIA (*OR* = 1.20, 95% CI [.67, 2.08], *p* = .63).

In the final regression model, the self-report method of assessment and sample including stroke only, explained 22% of the heterogeneity in PTSD prevalence rates.

Figure 5

PTSD Prevalence in Studies including Samples of Stroke only, Mixed Stroke and TIA, or TIA only



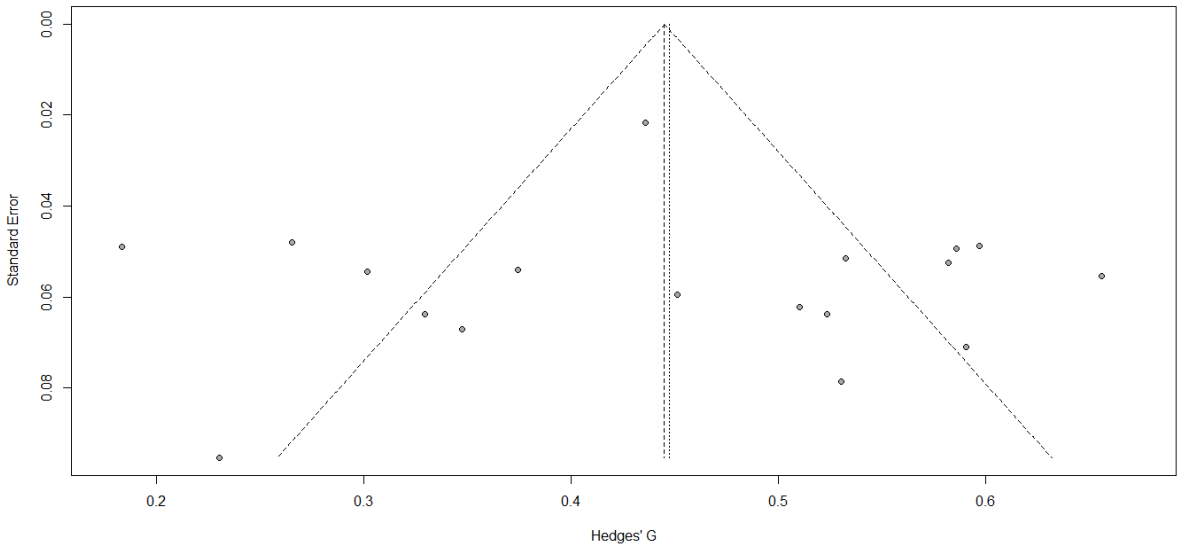
Quality and Bias

The quality of studies included in this review varied (see Table 1 for a summary of quality ratings). Lower quality ratings were most frequently related to sample size or low participation rate. No studies were excluded on the basis of quality rating. Most studies were rated "fair" in terms of quality (11), with 6 rated as "good" and one study rated as "poor". Cohen's Kappa was used to determine inter-rater agreement between the two raters (ET and SF), for each of the items rated in the QATOCCS. There was "good" agreement[44] between the two raters (κ = .66, p = < .001).

A funnel plot and Egger's test were used to assess for publication bias (see figure 6). Visual inspection of the plot showed some asymmetry, however this could have been attributed to the high heterogeneity amongst the studies included in this review. The Egger's test indicated that there was no evidence of significant publication bias (*intercept* = .262, *p* = .88).

Figure 6

Funnel Plot to Assess for Publication Bias



Discussion

This systematic review and meta-analysis aimed to provide an updated estimate of PTSD following stroke or TIA. The pooled prevalence of PTSD after stroke or TIA was 18%, 95% CI [14, 23%], confirming that PTSD prevalence is higher in stroke survivors than in the general population (around 3% in the UK[45]). This mirrors prevalence findings in other psychiatric disorders following stroke, such as depression and anxiety[2,3].

The pooled prevalence in this study was higher than that found in the 2013 review (13%), however the authors suggested that two underlying prevalence estimates existed based on the timing of PTSD assessment in their review (23%

prevalence in the first 12-months after stroke, compared to 11% where PTSD was assessed later than 12-months after the index stroke). In contrast with the 2013 review, there was no significant difference in PTSD prevalence rates according to the timing of assessment, with 17%, 95% CI [12, 24%] prevalence in the first year after stroke and 19%, 95% CI [9, 31%] prevalence after the first year. This difference in findings could be attributed to an increase in the number of studies and more contemporary data included in the current review. Alternatively, this may reflect a pattern of change generally in how PTSD presents after stroke, which could not be further explored within the scope of this review. Nonetheless, these findings indicate that PTSD symptoms are sustained over time in survivors of stroke or TIA, beyond the acute phase in which high distress may be deemed an initial reaction to the stroke, hospital treatment, or discharge. Given the significant impact of stroke-induced PTSD on long-term functional outcome and quality of life[7-11], there is a clear need to continue assessing for PTSD later in the recovery journey. Of course, this would be dependent on local service resources, but perhaps screening could be included as part of the patient's annual stroke review to identify those who may require further input at the later stages. Clinical guidelines could be a good way of specifying the most appropriate screening measure and intervals at which PTSD assessment after stroke should be undertaken.

In the current review, prevalence rates were significantly higher in studies assessing PTSD using a self-report measure alone (20% prevalence, 95% CI [15, 25%]), in comparison to the studies assessing PTSD using clinical interview (13% prevalence, 95% CI [4, 27%]). This confirms the previously reported pattern of lower rates of PTSD when assessed by clinical interview[25] and again, replicates patterns seen in depression and anxiety after stroke[2,3]. These findings continue to pose an interesting question regarding the accuracy by which self-report measures reflect

psychiatric disorders in research and clinical practice. In other words, whether scores are reflective of clinical PTSD, or could be attributed to the myriad of challenges faced by stroke survivors, such as adjustment difficulties, avoidance, sleep disturbance or irritability. Nonetheless, self-report measures continue to provide brief tools that are useful in identifying those that may require further input, particularly within stretched healthcare systems. Perhaps, an appropriate approach could be to conduct a follow-up diagnostic clinical interview for those individuals scoring around the cut-off threshold on a self-report measure (i.e. those who are in borderline ranges or are not clearly "yes/no" in terms of scores). This would allow a finer focus on differential diagnoses of other factors that give rise to post-traumatic stress symptoms and clinical PTSD.

In the current review, prevalence rates also varied by the type of stroke experienced by participants (i.e. stroke only, mixed stroke and TIA, or TIA only). PTSD prevalence was significantly higher in studies including stroke only (19% prevalence, 95% CI [12, 27%]), in comparison to studies including a mixed sample of stroke and TIA survivors (17% prevalence, 95% CI [11, 24%]). Prevalence was slightly lower again in those studies assessing PTSD after TIA alone (15% prevalence, 95% CI [3, 34%]), although this difference did not reach statistical significance. It should be noted however, that very few studies assessed PTSD following TIA only and the confidence interval was wide (3-34%). Therefore TIA only data represented a small proportion (8%) of the overall sample and there is limited confidence regarding the precise prevalence in TIA samples. This may be why a significant difference was found between stroke and mixed samples, but not stroke and TIA only samples, and hence, the conclusions drawn should be viewed with this in mind.

To date, this is the first known review comparing PTSD prevalence by the different types of stroke experienced by participants across individual studies. The small range of prevalence estimates across the three groups could indicate that PTSD is common following either stroke or TIA, like other mood disorders such as anxiety and depression[30]. However, the significant difference found in prevalence amongst studies only including stroke survivors could be suggestive of an association between the typically higher severity/nature of symptoms, treatment and/or degree of disability in stroke and the development of PTSD. Further exploration of these differences is needed to confirm such hypotheses.

Strengths and Weaknesses of Included Studies

This updated review included 18 studies, 9 of which were included in the 2013 review. The quality of the studies included varied, with studies including only TIA or only stroke tending to be rated more highly[17-19, 22, 24, 28]. Lower quality ratings were most frequently associated with low sample sizes or a low participation rate, suggesting that some studies may have been underpowered and not fully representative of stroke/TIA survivors. Furthermore, some studies did not sufficiently report important information, such as the proportion of men and women[6], the method of recruitment[12], the proportion of individuals recruited at different time points[6, 13], or the type of stroke experienced by participants[6, 13, 15, 17, 21, 24, 36]. Whilst the studies included in this review focused on PTSD *as a result* of stroke or TIA, most did not include historical data such as prior psychiatric difficulties. It is therefore difficult to ascertain the potential influence of any pre-existing difficulties on the findings. Future research should, where possible, include a range of demographic information and consider the impact of potential confounding variables in reporting results.

The majority of studies in this review included self-selecting samples, recruited through inpatient settings and outpatient clinics. Given that the symptoms of PTSD may contribute to avoidance or reluctance to engage in rehabilitation efforts and preventative treatments[11-13], it must be considered whether those experiencing PTSD symptoms may also be less likely to engage in research opportunities examining such symptoms. Furthermore, the majority of studies excluded those with severe language or cognitive difficulties. The prominence of communication difficulties, such as aphasia and dysarthria is high[46] (64%), as is moderate, persisting cognitive impairment[47] (38%) after stroke. It is therefore possible that the conclusions drawn are not fully reflective of the wider population of stroke survivors, particularly those experiencing greater levels of impairment. Future research exploring the prevalence of PTSD amongst stroke survivors must address this problem.

Finally, as noted above, 14 out of 18 studies used a self-report measure alone to assess PTSD. This is surprising given the impact of cognitive impairment and communication difficulties on an individual's ability to recall and report information. Whilst such measures provide useful tools for screening those that may require further input, reliance on self-report measures alone may lead to an inaccurate estimation of prevalence. For example, Lees and Colleagues[48] noted that even in "medically-stable" stroke survivors, over half of participants required assistance from the researcher to complete a self-report screen of anxiety and depression, raising questions as to the accuracy of self-report measures, particularly in the acute phases of stroke. In addition, a range of measures and cut-off scores were used across the different studies included in this review, which may have contributed to the high heterogeneity found. This further highlights a clear need for consensus around the optimal method of both assessing and reporting PTSD after stroke.

Strengths and Weaknesses of the Current Review

This updated review included 18 studies, giving an overall sample of 1815 across Europe, USA, South America, and Asia. This adds to the location demographic of the 2013 review, which was limited to Europe and the USA only, and provides a promising indication that the assessment of PTSD after stroke is gathering pace across different continents and cultures.

By combining the data from the 2013 review and the current update, the sample size increased by 37%, improving precision in estimates and meaning that the largest study[13] in the 2013 review no longer represented half of the overall sample. However, data pooling in this review used the cut-offs reported in each study to determine PTSD prevalence, meaning that a combination of methods and reporting rates were used to determine overall prevalence. The increase in sample also allowed for further data pooling and subgroup analysis, however some estimates were based on small sample sizes (e.g. those studies only including TIA), and there was high heterogeneity between studies. In addition, planned analyses examining PTSD prevalence across subtypes of stroke (e.g. ischemic or haemorrhagic) could not be completed due to insufficient data.

Although regression analyses highlighted the impact of stroke sample and assessment measure as explaining some of the heterogeneity found, over 60% of heterogeneity could not be explained by the analyses. This may be reflective of the combination of methods and reporting rates used in studies, methodological issues within the studies themselves or an additional factor not identified within this review. The combination of methods and reporting rates was also highlighted within the 2013 review and hence, the benefits of an increased sample size and further data pooling were considered to outweigh this problem.

This review used several methods aimed at reducing bias. For example, multiple databases were searched allowing for a wide range of articles to be screened for eligibility. This included searching for grey literature through the ProQuest database, although no unpublished studies were included in the final review. There is of course, the possibility that despite thorough searching, some articles were missed or further research has been published since this review. Furthermore, as the current searches only included those published since the date of search completion for the 2013 review (31st January 2013), there is also the possibility that relevant articles that were published prior to 2013 were not included in either review. Screening, data extraction and quality ratings were conducted by two raters independently, thus decreasing subjectivity and improving reliability. Potential articles were not excluded on the basis of quality; however this may have contributed to the high heterogeneity found.

Clinical Implications

This updated review confirms that the prevalence of PTSD is high following stroke or TIA and is sustained over time, similar to other psychiatric disorders[2,3]. There is a clear need to continue screening for PTSD symptoms later in the recovery journey, particularly when considering the impact of PTSD on functioning and quality of life[7-11]. It should be noted however, that there is a distinct lack of studies examining interventions aimed at treating PTSD after stroke, meaning that any decisions made regarding treatment must be made in the absence of robust evidence.

In addition, this review highlights the common occurrence of PTSD following both stroke and TIA. Differences found between the participant samples only including stroke survivors and those including both stroke and TIA survivors suggests that the severity of the stroke experienced may contribute to a higher risk of developing PTSD. Nonetheless, the prevalence of PTSD found in samples only

assessing individuals following TIA was still much higher than the general population (15% prevalence, 95% CI [3-34%]). This suggests that TIA survivors may also benefit from preventative methods and treatment of PTSD, to avoid longer-term difficulties. Due to service pressures however, TIA survivors are not routinely seen by specialist stroke psychology services and hence, it may be that the needs of this particular population are frequently unmet. Although suggestions have been made as to interventions focused on coping skills for this particular group[28], a lack of robust evidence again precludes evidence-based decisions regarding treatment being made.

Implications for Research

As noted, it would be most advantageous for consensus to be reached regarding the best approach and tool for screening PTSD after stroke, with consensus also around the threshold for diagnosis. This would provide a more robust indication of PTSD following stroke and lead to greater consistency across research studies and clinical practice. In turn, this may contribute to less heterogeneity between studies and provide a more accurate estimate of prevalence. This could potentially be achieved through receiver-operated characteristic (ROC) analysis of studies using both clinical interview and self-report measures.

In addition, further assessment of PTSD following TIA would be advantageous. As noted above, several studies either exclude TIA or do not distinguish between stroke and TIA in the reporting of results. The data regarding PTSD prevalence is therefore blurred in terms of stroke severity. Furthermore, this review highlights the high occurrence of PTSD following TIA, although this conclusion is drawn on the basis of data from only two studies and thus may not fully reflect the population of TIA survivors. Similarly, further studies reporting prevalence per subtypes of stroke (e.g. ischemic, haemorrhagic) would provide a

useful addition to the current literature and allow for further exploration of the impact of stroke subtype on PTSD prevalence.

Finally, it would be useful to gain a greater understanding of the experiences associated with the onset or persistence of PTSD following stroke. Whilst this review has provided a useful update of prevalence data, it is not yet known which aspects of the stroke experience tend to contribute to the development and/or maintenance of PTSD. For example, whether the sudden onset of medical symptoms, sudden loss of function, experiences during acute hospital care, or ongoing difficulties are more associated with PTSD. Qualitative research could provide much-needed contributions to exploring this, whilst also providing a vital insight into the most useful interventions for when PTSD is identified.

Conclusions

This review confirms the high rates of PTSD following stroke or TIA, with around 1 in 5 survivors experiencing symptoms. This review also confirms that PTSD symptoms are sustained over time, beyond what may be considered an initial reaction to the onset of symptoms and discharge from hospital. Unfortunately, there was high heterogeneity between studies, which could only be partially accounted for. The findings indicate that those experiencing a stroke and assessed using a self-report measure are more likely to show PTSD symptoms. Further studies would greatly benefit from consensus regarding the most robust method for assessing PTSD after stroke or TIA and further exploration of stroke subtypes/severity impacting the onset and maintenance of PTSD. Whilst further research examining the prevalence of PTSD after stroke does little to address the continued lack of evidence regarding the best treatment options for when PTSD is identified, it is clear that in the meantime, stroke services should continue to screen for PTSD after stroke and TIA, including later in the recovery journey.

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Conflict of Interest

None.

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Chapter 3: Bridging Chapter

The current chapter provides a bridge between the systematic review and meta-analysis presented in Chapter 2, and the empirical paper presented in Chapter 4. A summary of the findings from the systematic review and meta-analysis presented in Chapter 2 is provided. Theoretical links between post-traumatic stress disorder (PTSD) and emotionalism are made, with key emphasis on clinical similarities found between the two conditions. An overview of the empirical paper is then provided, with information regarding the decision-making process that led to changes being made to the proposed statistical analyses.

Summary of Systematic Review and Meta-Analysis

The systematic review and meta-analysis reported in Chapter 2 identified a high prevalence of PTSD following stroke (18%), which was maintained beyond 12-months after the index event. Two key factors were identified as contributing to higher prevalence of PTSD after stroke. Firstly, prevalence was higher when assessed by self-report measure, as opposed to diagnostic clinical interview. This appears to mirror a general pattern in the assessment of psychiatric disorders following neurological change (e.g. Whelan-Goodinson et al., 2009). Secondly, prevalence of PTSD varied by the type of stroke experienced by participants in the studies (i.e. sample including stroke only, mixed stroke and transient ischemic attack (TIA), or TIA alone). Studies including individuals who had experienced a stroke, but excluding individuals with TIA, were more likely to report higher prevalence of PTSD. This could suggest an association between the nature or severity of stroke, treatment or length of stay in hospital, or the degree of disability following stroke, and the likelihood of developing PTSD symptoms, given that these factors are usually worse following stroke in comparison with recovery from TIA. Such

association requires further examination however, for any firm conclusions to be drawn.

PTSD and Emotionalism: Theoretical Links

As noted in Chapter 1, both PTSD and emotionalism following stroke have only begun to receive attention within the literature over the past 20-30 years (Sembi et al., 1998; House et al., 1989). Although considered separate psychiatric conditions, theoretical links have been drawn between them. For example, Calvert and Colleagues (1998) assessed psychological associations with emotionalism in 448 stroke survivors and found that irritability was associated with the presence of emotionalism at one-month after stroke. They highlighted irritability as a common feature of both PTSD and emotionalism, suggesting either overlap or similarity between the two conditions. Furthermore, they noted that in both conditions, the patient experiences "recurring, uncontrollable emotionally charged mental events" (p. 929), with the only difference being that in PTSD, the individual experiences reliving symptoms, whereas such events in emotionalism are reported as precipitants.

Subtle similarities have been highlighted elsewhere, for example Eccles and Colleagues (1999) noted that stroke survivors with emotionalism experience intrusive thoughts regarding their stroke. Furthermore, they highlighted the role of avoidance in maintaining the presence of emotionalism. Again, both of these factors are key symptoms of PTSD. Whilst they recognised that emotionalism is not necessarily a direct manifestation of PTSD, they did note the possibility that both conditions could be related to an abnormality in processing emotionally important stimuli, perpetuated by an avoidant coping style.

More recently, a systematic review examining psychological correlates of emotionalism across neurological disorders was conducted (Fitzgerald et al., submitted). Interestingly, avoidance, irritability and intrusion were all found to be

predictors of emotionalism after neurological change, thus providing some support for the theoretical links noted above.

Emotionalism was originally postulated as a neurobiological condition, most commonly related to lesion location (Colamonico et al., 2012; Nieuwenhuis-Mark et al., 2008) and serotonergic pathways (Ahmed & Simmons, 2013). As such, it was considered to be distinct from psychological correlates. However, overlap between symptoms of emotionalism and other psychological disorders, such as symptoms of PTSD, anxiety and depression, coupled with low quality evidence for pharmacological treatment of emotionalism (Allida et al., 2019), has led to more recent examination of the relationship between emotionalism and other psychological variables. Thus far, research has largely focused on associations between emotionalism and depression after stroke, hence, further exploration of other psychological correlates is needed to inform potential psychological models and the treatment of emotionalism.

Overview of Empirical Paper

The pathophysiological causes of emotionalism after stroke have received much speculation. As noted, further exploration of potential psychological predictors of emotionalism after stroke is needed. The empirical paper presented in Chapter 4 reports the results of exploratory data analysis of the predictive nature of several demographic and psychological variables (age, sex, stroke classification, anxiety, depression, cognition, functioning), in the presence of emotionalism at three timepoints (2-weeks, 6-months and 12-months after stroke). The predictor variables noted are also considered in relation to study drop-out between baseline assessment (2-weeks) and the 6-month or 12-month assessment. Data for these analyses were collected during a larger study assessing emotionalism after stroke (Testing for Emotionalism After Recent Stroke; TEARS; Broomfield et al., 2020).

Modifications made to statistical analysis plan for empirical paper

When the research design for this thesis portfolio was initially proposed, data collection for TEARS was still in progress and hence, it was difficult to develop a concrete analysis plan. Initially, it was expected that the trajectory of emotionalism and the psychological variables noted above would be conducted using a longitudinal trajectory modelling method, such as latent class growth analysis. Following completion of data collection however, it became apparent that such analysis would not be possible.

Firstly, when this thesis project was proposed, the diagnostic accuracy and psychometric properties of the two emotionalism measures designed as part of TEARS (TEARS diagnostic interview and TEARS questionnaire) had not yet been established. The TEARS diagnostic interview produces a categorical outcome, thus could not be used in trajectory modelling due to the assumption of a continuous outcome. In addition, the optimum cut-off for the TEARS questionnaire was established as 2 or above (out of a possible score of 16). The majority of participants scored 0, which meant that the assumption of distributional normality between outcome and time was also violated (Broomfield et al., 2020).

Secondly, attrition across the timepoints in TEARS was high, with only 116 out of 228 participants having complete data at all timepoints. The potential risk of bias in trajectory modelling was therefore high, due to the loss of several data. Hence, it was deemed more informative for future research and clinical practice to explore the predictive nature of psychological variables with outcomes relating to emotionalism and also drop-out from the research. To achieve this, a series of logistic regression analyses were used, predicting 6-month and 12-month outcomes (no emotionalism, presence of emotionalism or loss to follow-up) from the demographic and psychological variable data collected at baseline.

Chapter 4: Empirical Research Paper

Predicting the Presence of Post-Stroke Emotionalism using Psychological Factors in the First Year After Stroke

Written for publication to: *Stroke* (see Appendix A for author guidelines)

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Abstract

Background and Purpose: Emotionalism is a commonly experienced consequence of stroke, leading to difficulties engaging in rehabilitation and societal reintegration. Post-stroke emotionalism (PSE) has received little attention amongst the literature and as such, its development and maintenance is poorly understood. This paper aimed to explore potential psychological constructs related to emotionalism in the first year after stroke. More specifically, which psychological factors measured in the acute phase of stroke (within 2-weeks) could predict the likelihood of emotionalism being experienced later in the recovery journey.

Methods: This paper reports secondary quantitative analyses of data collected as part of a large, longitudinal cohort study: Testing for Emotionalism After Recent Stroke. Data from 228 participants were used to explore associations between baseline PSE, anxiety, depression, cognition, daily functioning and demographic characteristics, and the presence of emotionalism at 6- and 12-months after stroke. Associations between these variables and loss to follow-up were also explored.

Results: Emotionalism was experienced by stroke survivors across the first year after stroke (27% at 2-weeks, 20% at 6-months and 15% at 12-months after stroke). Regression analyses showed that PSE and anxiety at baseline were associated with greater likelihood of experiencing PSE later in the recovery journey. Younger age and worse cognitive impairment were associated with drop-out from the TEARS study at 6- and 12-month assessments.

Conclusions: Emotionalism is commonly experienced after stroke and is maintained beyond the acute phase of stroke recovery. There is an association between anxiety and PSE across time, thus suggesting a link between the two conditions. Further

robust research into the maintenance of PSE over time is crucial in developing much needed, clinically-effective interventions of a non-pharmacological nature.

Keywords: emotionalism, impact, longitudinal research, psychological factors, stroke

Predicting the Presence of Post-Stroke Emotionalism using Psychological Factors in the First Year After Stroke

Emotionalism is a commonly-experienced consequence of neurological changes, estimated to affect 10-20% of stroke survivors[1], yet is strikingly underresearched. Post-Stroke Emotionalism (PSE) has vast implications for the rehabilitation and everyday life of stroke survivors. For example, it is known to cause distress, embarrassment, and fear, leading to decreased involvement and quality of social participation, and to inhibit progress in rehabilitation[2]. Furthermore, whilst already difficult post-stroke[3], reintegration into occupational and societal roles may be worsened by the presence of difficult emotional symptoms such as PSE[4]. Finally, PSE may be misinterpreted as an understandable reaction to physical changes after stroke, or as separate psychiatric difficulties, such as depression[5]. Indeed, whilst depression may co-occur with PSE, the negative beliefs prominent in depression are rarely shown in those with PSE alone[6]. Therefore, individuals experiencing PSE may feel considerably misunderstood and reluctant to seek help.

Literature examining the causes and maintenance of PSE has largely focused on biological factors, such as specific neuroanatomic regions or neurotransmitters[7-9] however, no definitive picture has been confirmed. PSE management guidelines have remained unchanged for some time, suggesting distraction and anti-depressant medication are the only treatment options[10]. This does little to serve those who may not want, or be able, to take antidepressant medication. Furthermore, the latest review examining medication in the treatment of PSE[11] concluded that the effectiveness that had been reported was based on very low-quality evidence.

Despite there being no proven non-pharmacological treatments for PSE, and no published trials examining interventions in the absence of medication for PSE, some psychological techniques have been highlighted within the literature, such as

relaxation and distraction[12, 13]. Furthermore, we know that non-pharmacological approaches are used in routine clinical practice. Gillespie and colleagues[14] recently conducted a survey of clinicians working in inpatient stroke services and identified several non-pharmacological intervention approaches that were perceived as effective for PSE. Specifically, offering reassurance, discussing goals, education, normalising the experience, relaxation, and environmental changes were reportedly used frequently. The authors further noted that the techniques identified as being most frequently used were also perceived by clinicians as the most effective. In addition, they highlighted the perceived expectation that clinicians *should* offer non-pharmacological methods of treatment. Whilst there is clearly a need for robust evidence examining the clinical effectiveness and acceptability of such approaches, these findings indicate that non-pharmacological approaches are regularly considered and employed in practice.

Surprisingly then, there is little research examining psychological constructs which may contribute to the development and maintenance of PSE, although several theoretical conceptions are noteworthy. Deficits in cognitive functioning (attention and executive skills) may contribute to difficulties regulating emotion, given the overlap in neuroanatomical regions deemed responsible for these skills[15]. In addition, co-occurring psychiatric difficulties may serve to maintain the presence of PSE. For example, a plausible association between PSE and post-traumatic stress disorder has been noted[16, 17], due to overlaps in symptomatology (e.g. recurrent, uncontrollable emotion and avoidant behaviours). Additionally, those experiencing co-morbid depression and/or anxiety may be pre-occupied with grief and feel apathetic towards rehabilitation, or may avoid situations that could help their progress[18].

Theoretically, it is likely that a combination of several psychological factors may contribute to the development and maintenance of PSE. These have yet to be

examined longitudinally however, or in great detail. This distinct lack of evidence precludes the development of much needed evidence-based, non-pharmacological interventions targeting PSE. A crucial first-step in progressing the evidence-base is further in-depth exploration of potential psychological constructs relating to PSE.

Recently, qualitative investigations have sought to improve current psychological knowledge of PSE experiences. McAleese and Colleagues[19] hypothesised that an individual's beliefs surrounding emotionalism would affect their ability to cope with the condition. Based on semi-structured interview data gathered from 18 stroke survivors with PSE, four themes emerged which captured participants' experiences of living with the condition: (i) Spontaneous and uncontrollable emotional reactions, (ii) Incongruence, (iii) Social reactions, and (iv) Convalescence. As expected, those expressing negative, inflexible assumptions regarding emotionalism were more distressed, and each theme echoed the vast implications of avoidance, social isolation, and embarrassment on recovery.

Fitzgerald and Colleagues[22] also sought to capture the PSE experience qualitatively, using longitudinal interview data from 100 stroke survivors who had experienced PSE (collected at 2-weeks, 6-months and 12-months after stroke). Three key themes emerged from their data, encompassing "in the moment" aspects (characteristics and triggers of PSE, and elements related to control), "ways of coping" (e.g. acceptance, avoidance, cognitive and behavioural attempts at symptoms management, help from others), and "impact" of PSE (including changes to self, distress, embarrassment, uncertainty and attempts at making sense of experiences). Notably, their findings identified several changes in the PSE experience over time; increased barriers to control and difficulty regulating emotions, increased avoidance, embarrassment and distress in the latter stages of recovery (12-months after stroke), highlighting the need for PSE to be investigated in a longitudinal fashion.

The themes captured within the qualitative investigations cited above highlighted key difficulties experienced by stroke survivors more generally, for example the grief associated with loss following stroke[20], but also difficulties unique to the emotionalism experience, such as the discrepancy between internal emotions and external expression, and perceptions of self-control. Such findings emphasise key differences between emotionalism and other key psychiatric disorders that may be experienced after stroke, such as depression. Again, this highlights the need for an improved understanding of PSE, in order to accurately inform treatment planning which has thus far, been primarily based on interventions developed for other psychiatric disorders.

In summary, there is a clear need for increased understanding of the psychological correlates and maintaining factors of PSE. Firstly, to appropriately inform the conceptualization of PSE and secondly, to encourage the implementation of high-quality studies examining the effectiveness of current and novel non-pharmacological treatments. Ultimately, this will better inform clinical guidance into PSE management and allow patients experiencing PSE (and their carers) to receive more comprehensive, evidence-based support. A recent, large-scale longitudinal cohort study examining PSE over several timepoints (Testing Emotionalism After Recent Stroke [TEARS][21]) has been conducted, with the aim of exploring the prevalence, impact, neurological and psychological characteristics of PSE. The psychological experiences and impact of PSE have been examined qualitatively from the data gathered (Fitzgerald et al., unpublished manuscript[22]). This paper, therefore, aimed to analyse the data collected using quantitative methodology, to explore PSE and potential associated psychological factors within the first year of stroke.

Research Questions

This paper aimed to address the following research questions:

1. What are the sample characteristics, with regards to PSE and potentially relevant psychological variables (mood, cognition, and functioning), of the stroke survivors who participated in the Testing Emotionalism After Recent Stroke (TEARS) study?
2. Are there differences in personal characteristics (e.g. age, sex, type of stroke) and psychological variables (mood, cognition, functioning) between those who experience PSE immediately following stroke and those who do not?
3. Which personal characteristics (e.g. age, sex, type of stroke) and psychological variables (mood, cognition, functioning) measured at baseline, are associated with an increased probability of PSE at baseline (2-weeks), 6-months, and 12-months after stroke?
4. Which personal characteristics (e.g. age, sex, type of stroke) and psychological variables (mood, cognition, functioning) measured at baseline, are associated with an increased probability of drop-out from the TEARS study?

Method

Design

The current paper is a secondary analysis of data collected as part of the TEARS study[21], focusing on quantitative exploration of the psychological variables included in the original study. Ethical approval was granted for TEARS and subsequent analyses by Scotland A Research Ethics Committee (REC reference= 14/SS/1103, IRAS ID= 157483). TEARS was also registered with the Scottish Stroke Research Network (NRS Ref. NRS15/157483). Ethical approval for the current study was granted by The University of East Anglia Faculty of Medicine and Health Sciences Research Ethics Committee (Reference: 2019/20-043).

Testing Emotionalism After Recent Stroke (TEARS) Study

TEARS was one of the first studies to examine PSE prevalence and neuropsychological correlates over several timepoints. It aimed to develop the first definitive description of PSE prevalence, including impact, neurological and psychological characteristics. In the study, stroke survivors completed a range of assessments relating to stroke, including PSE, completion of daily activities, language, mood, cognition, quality of life and carer burden (see Measures section below). Assessments were conducted at 2-weeks, 6-months, and 12-months after the index stroke event and completed by stroke nurses on the hospital wards, pre-trained by NB. The primary objective of TEARS was to determine the precise prevalence of PSE diagnosed in survivors at each timepoint. The secondary objectives included determining the impact, neurological and psychological characteristics of PSE, of which this paper contributes towards.

Participants

All participants were stroke survivors who participated in TEARS. No further recruitment or direct contact with participants was required for the purposes of this study. The TEARS recruitment process took place between October 2015 and October 2018. Participants consented to participate in TEARS, and for their data to be used in subsequent analyses.

A total of 277 stroke survivors were recruited at baseline (within 2-weeks of stroke), across nine NHS hospital sites in Scotland. Recruitment, determination of capacity, and all assessments were completed by a team of pre-trained Scottish Stroke Research Network Nurses, at site. Lacking capacity did not preclude individuals from participation if a nearest relative/Welfare Guardian could consent on their behalf.

Inclusion criteria for TEARS was as follows:

- Able to give written informed consent, or informed consent given from the nearest relative/Welfare Guardian for patients who cannot consent themselves
- Male or non-pregnant female >18 years of age
- Clinical diagnosis of ischemic or haemorrhagic stroke, first ever or repeat

Exclusion criteria for TEARS was as follows:

- Subarachnoid haemorrhage, other extra axial bleeds or suspected stroke where an alternative diagnosis including Transient Ischemic Attack is likely
- Severe concurrent medical condition that would prevent participation in study procedures (e.g. cardiac failure with severe pulmonary oedema) or with life expectancy <3 months
- Lack of spoken English
- Evidence of severe distressing behaviours secondary to stroke/dementia which in the opinion of referring clinical team precluded participation/testing.

Scores from 233 participants were available but due to missing data, the total number of participants included in the current study was 228. These were all participants who completed the diagnostic interview for PSE (Testing Emotionalism After Recent Stroke-Diagnostic Interview) at baseline (2-weeks) assessment.

Measures

Emotionalism

1. **Testing Emotionalism After Recent Stroke- Diagnostic Interview (TEARS-IV[21], see Appendix F).** TEARS-IV is a semi-structured diagnostic interview, developed on the basis of well-established and widely recognised PSE diagnostic criteria[23] and is the best available standardised assessment of PSE. TEARS-IV comprises sections on post-stroke crying and post-stroke laughter (screen questions, case characteristics, frequency, and impact), for example “What have your emotions and emotional expression, in particular

crying, been like since the stroke?". The administering clinician is required to classify the individual within one of four categories: (i) No evidence of post-stroke emotionalism, (ii) Post-stroke emotionalism, crying component only, (iii) Post-stroke emotionalism, laughter component only, (iv) Post-stroke emotionalism, crying and laughter components. For the purposes of this study, the outcome of the TEARS-IV was treated as a binomial categorical variable (yes/no), and was used to determine whether the presence of PSE for each participant at each assessment time point.

2. **Testing Emotionalism After Recent Stroke-Questionnaire (TEARS-Q[21], see Appendix G).** TEARS-Q is a brief, self-report measure of PSE, constructed based on post-stroke tearful emotionalism diagnostic criteria: (i) increased tearfulness, (ii) crying comes on suddenly, with no warning (iii) crying not under usual social control, (iv) crying episodes occur at least once weekly. TEARS-Q consists of eight questions, each rated on a 5-point Likert scale (Strongly agree, agree, unsure, disagree, strongly disagree). The instructional set orients respondents to focus on changes to crying since their stroke, in the past two weeks. The first two questions: (i) "I feel more tearful in the past two weeks than before the stroke", and (ii) "I have actually cried more in the past two weeks than before the stroke" are used as stop/continue questions. Ratings of "Strongly Agree" give a score of 2 and "Agree" gives a score of 1, whilst all other ratings give a score of 0. Scores from each question are summed to give an overall score out of 16. TEARS-Q is shown to have acceptable psychometric properties, for example good internal consistency (Cronbach's $\alpha = 0.87$); acceptable discriminant validity (mean score difference of -7.18 between those diagnosed with PSE from those without); coherent scale dimensionality (one factor accounts for 57% of item

response variance), and diagnostic accuracy using a cut-off point of 1.5[21]. Scores of 2 or above are therefore considered to indicate the presence of emotionalism.

Functional Outcome: The Barthel Index of Activities of Daily Living

Functional Outcome was assessed using The Barthel Index of Activities of Daily Living[24]. The Barthel Index is a widely-used measure of performance in activities of daily living, such as grooming, feeding and mobility. Each of the ten items generates a score between 0-3, to give an overall score out of 20. Lower scores indicate higher dependence on others for assistance. The Barthel Index is shown to have good psychometric properties (reliability, concurrent validity and responsiveness), and is validated for use in stroke populations[25].

Mood: Hospital Anxiety and Depression Scale (HADS[26])

Symptoms of anxiety and depression were assessed using the HADS. The HADS is commonly used in routine clinical practice to determine levels of anxiety and depression experienced by patients. There are 14 items in total, split into two subscales: 7 items assessing anxiety symptoms, e.g. “I get sudden feelings of panic”, and 7 items assessing depressive symptoms, e.g. “I still enjoy the things I used to enjoy”. Each item generates a score between 0-3, to give a total score out of 21 for each subscale. A score of > 8 on either subscale denotes considerable symptoms of anxiety or depression. The HADS has yielded good psychometric data for detecting the presence of depression within stroke populations and was found to be the only effective tool for identifying anxiety post-stroke[27]. For the purposes of this study, the depression and anxiety subscales were treated as separate, continuous variables.

Cognition: Abbreviated Mental Test[28] (AMT)

At baseline, cognition was assessed using the AMT. The AMT is a brief assessment tool, initially developed to identify the presence of dementia. Since its

development, the AMT has been widely-used in a range of clinical settings to identify the presence of cognitive impairment. The AMT consists of ten questions, such as "What is the time to the nearest hour". Each question answered correctly gives one point, which is totalled to give an overall score out of ten. Overall scores of 8 or less are considered to indicate cognitive impairment. The AMT has been shown to be a valid tool, with good specificity for screening cognitive impairment in acute medical settings[29].

Procedure

All outcome data was collected and returned in CRF format to the Robertson Centre for Biostatistics, Glasgow Clinical Trials Unit, University of Glasgow (RCB). The data were entered onto a database by the RCB team, who managed all data queries. The final locked dataset (containing anonymised data) was uploaded to a secure, password-protected server, from which data were downloaded for the purposes of this study. All data analysis was completed by the first author (ET). Consultancy and advice regarding statistical analyses was provided by the TEARS study statistician (RW).

Analysis Plan

To address research questions 1 and 2, descriptive statistics of the data collected at baseline were generated and summarised. The data was inspected to confirm that assumptions for the subsequent analyses were met. Descriptive data was then grouped by the presence of PSE at baseline (i.e. diagnosed PSE at baseline vs. no PSE at baseline), and compared using the "tableone" function in R[30]. For categorical variables, data was summarised using frequencies and percentages, with chi-square comparisons between those with and without emotionalism. For continuous variables, data were either summarised using means and standard deviations, or median and inter-quartile ranges where variables were not normally

distributed. To assess for significance between the groups, unadjusted t-tests were used where parametric assumptions had been met, and Mann Whitney-U tests were used where parametric assumptions were violated. The variables which were approaching significance at the 10% level between the two groups were taken forward into regression analyses.

To address research questions 3 and 4, a series of logistic regression analyses were used. Firstly, a binominal logistic regression was used to assess associations between the personal characteristics (sex, age, stroke type), psychological variables (anxiety, depression, cognition, and functioning) and PSE diagnosis at baseline. Secondly, multinomial regression analyses were used to assess which of the variables measured at baseline predicted outcomes at 6- and 12-months. The three possible outcomes in each multinomial regression were: (i) No PSE at timepoint, (ii), PSE present at timepoint, (iii) Lost to follow up. No PSE at that timepoint was modelled as the reference category. The variables measured and shown to be approaching significance at baseline were entered into the model as predictor variables, with the first regression model assessing outcome at 6-months post-stroke, and the second regression model assessing outcome at 12-months post-stroke. In both analyses, model fit was assessed using the Likelihood Ratio Test and the Cox and Snell R^2. The model was adapted on the basis of these values and those variables showing as most significant, until optimal model fit was achieved (i.e. systematic model building). Group differences between those who remained in the study and those who dropped out of the study between the baseline and 12-month assessments were also compared using the "tableone" function in R[30]. As noted above, unadjusted t-tests were used where parametric assumptions had been met, and Mann Whitney-U tests were used where parametric assumptions were violated.

Power Calculation

According to Peduzzi[31], a minimum sample for sufficient power in logistic regression can be derived using the number of variable and positive cases ($N = 10k/p$, where k = the number of predictor variables and p = the proportion of positive cases). This formula was used to generate suggested minimum sample sizes here. For the first, binomial regression (baseline predictors, baseline PSE), assuming a medium effect, alpha level of .05, 5 predictor variables and number of positive cases (i.e. those diagnosed with PSE at baseline), a minimum sample of 185 was required to achieve sufficient power (80%). For regressions 2 and 3 (multinomial regressions analysing baseline predictors of outcome at 6- and 12-months), the same formula was used, with the number of positive outcomes considered as the number of participants who remained in the study at each time point. Both calculations revealed that a minimum sample of 100-125 were required to achieve sufficient statistical power (80%) to detect a medium effect. As this current study is a secondary data analysis, power ultimately depended on the sample size in the original TEARS study. The total sample was 224 and hence, the analyses were considered to be sufficiently powered.

Results

Descriptive Statistics and Group Differences

Descriptive statistics of the demographic and psychological variables are shown in Table 1 below. In total, 228 stroke survivors had completed the TEARS diagnostic interview at baseline and were included in the current study. The mean age of participants at the time of stroke was 65 years (SD = 14.5) and 98 (43%) of participants were female. Most participants had achieved at least a secondary school level of education (80%). The majority of participants had experienced infarction stroke (91%) and 62 participants (27%) presented with PSE at baseline, based on the outcome of the diagnostic interview.

Table 1

Descriptive statistics and group differences of demographic characteristics and psychological variables of stroke survivors at baseline assessment, for individuals with and without PSE

Characteristic	Levels	No PSE Diagnosis	PSE Present	Total Cohort	P
Number of Participants		166	62	228	
Age at Stroke	Mean (*SD*)	67.06 (14.23)	59.68 (13.99)	65.05 (14.51)	.001**
Sex	Female (%)	65 (39.2)	33 (53.2)	98 (43.0)	.079*
	Male (%)	101 (60.8)	29 (46.8)	130 (57.0)	
Education	Primary (%)	3 (1.80)	2 (3.22)	5 (2.19)	.433
	Secondary (%)	101 (60.84)	46 (74.19)	147 (64.47)	
	University (%)	28 (16.87)	7 (11.29)	35 (14.03)	
	Other (%)	24 (14.46)	7 (11.29)	31 (13.60)	
Stroke type	Infarction (%)	150 (90.4)	59 (95.2)	209 (91.67)	.474
	Haemorrhage (%)	15 (9.0)	3 (4.8)	18 (7.89)	

Characteristic	Levels	No PSE Diagnosis	PSE Present	Total Cohort	P
Oxford Classification of Stroke	Total Anterior Circulation Stroke	8 (4.8)	2 (3.2)	(4.39)	.614
	Partial Anterior Circulation Stroke	59 (35.5)	17 (27.4)	76 (33.33)	
	Lacunar Stroke	53 (31.9)	26 (41.9)	79 (34.65)	
	Posterior Circulation Stroke	40 (24.1)	14 (22.6)	54 (23.68)	
TEARS-Q Score	Median (IQR)	0.00 (0.00)	8.00 (6.00)	0.00 (5.00)	<.001**
Barthel Activities of Daily Living Index	Median (IQR)	19.00 (5.00)	18.00 (8.00)	18.00 (6.00)	.226
HADS Depression	Median (IQR)	3.00 (4.00)	5.00 (7.00)	3.00 (4.00)	<.001**
HADS Anxiety	Median (IQR)	4.00 (6.00)	8.00 (8.00)	5.00 (7.00)	<.001**
AMT (cognition)	Mean (*SD*)	7.91 (1.00)	7.63 (1.10)	8.02 (1.25)	.167*

SD = standard deviation, IQR = inter-quartile range, PSE = Post-Stroke Emotionalism, TEARS-Q = Testing for Emotionalism After Recent Stroke Questionnaire, HADS = Hospital Anxiety and Depression Scale, AMT = Abbreviated Mental Test
*approaching significance at $\alpha = .10$ and therefore carried forwards into regression analyses
**significant at $\alpha = .05$

Of the 228 participants, 224 had also completed TEARS-Q, with an average score of .59 (*SD* = 1.81) in the group without PSE, compared to an average score of 7.77 (*SD* = 4.80) in the group presenting with PSE. There was a significant difference in TEARS-Q score between the two groups ($p = < .001$). At an alpha level of .05, significant differences were also found between the group with and without PSE for age at stroke ($p = .001$), HADS depression scores ($p = < .001$), and HADS anxiety scores ($p = < .001$).

Outcomes at 6-months and 12-months

For the purposes of this study, PSE data from the 6- and 12-month follow-up assessments were categorised into three possible outcomes: (i) No PSE, (ii) PSE present, or (iii) Lost to follow-up. Table 2 summarises the outcome data at 6- and 12-months, grouped by PSE diagnosis at baseline. In total, 148 participants completed assessment at 6-months, of which 30 (20.1%) presented with PSE. A total of 80 participants (35.1%) were lost to follow up at the 6-month time point. At 12-months, a total of 109 participants completed the assessment, of which 17 (15.6%) presented with PSE. At the 12-month timepoint, a further 39 (17%) participants were lost to follow up.

Table 2

Summary of the Outcome Data at 6- and 12-month assessment time-points, grouped by individuals with and without PSE at baseline

Timepoint	Level	No PSE at baseline (%)	PSE present at baseline (%)	Total (%)	P
Outcome at 6-months	No PSE	95 (57.23)	23 (37.10)	118 (51.75)	<.001**
	PSE present	12 (7.23)	18 (29.03)	30 (13.16)	
	Lost to follow-up	59 (35.54)	21 (33.87)	80 (35.09)	
Outcome at 12-months	No PSE	73 (43.98)	19 (30.64)	92 (40.35)	.121
	PSE present	10 (6.02)	7 (11.29)	17 (7.46)	
	Lost to follow-up (total)	83 (50.00)	36 (58.06)	119 (52.19)	

PSE = Post-Stroke Emotionalism
**significant at α = .05

Regression Analyses

1. Baseline predictors and baseline PSE

A binomial regression analysis was used to assess the probability of PSE presence at baseline, as predicted by demographic (age and sex) and psychological variables (depression, anxiety, cognition, functioning, and TEARS-Q emotionalism score) also measured at baseline. Level of education, stroke type and Oxford Classification of stroke were removed prior to the model being fitted, on the basis of the group difference analyses noted above. Cognition and daily functioning were removed from the final model, as they were considered not to contribute to the probability of PSE occurring at baseline. The final model is summarised in Table 3.

The model indicated that baseline TEARS-Q (emotionalism) score was positively related to PSE at baseline (*OR* = 1.65, 95% CI [1.43, 1.90], *p* = < .001) and was statistically significant. In other words, the higher the TEARS-Q score, the more likely it was for individuals to be diagnosed with PSE at baseline. The size of effect was deemed "small", based on Chen and colleagues[32] suggestion that a small effect size is an odds ratio of < 1.5, and a large effect is an odds ratio of > 5.

Depression at baseline was negatively related to baseline PSE, but with little evidence of association (*OR* = .975, 95% CI [.846, 1.123], *p* = .723). This meant that those with higher depression scores were less likely to be diagnosed with PSE at baseline, however this did not reach statistical significance in the model.

Anxiety at baseline was positively related to baseline PSE, but with little evidence of association (*OR* = 1.095, 95% CI [.971, 1.123], *p* = .139). This meant that those with higher anxiety scores were more likely to be diagnosed with PSE at baseline, however this did not reach statistical significance in the model.

Age at the time of stroke was negatively related to baseline PSE, with little evidence of association (*OR* = .977, 95% CI [.946, 1.009], *p* = .155). This meant that

those who were older at the time of stroke were less likely to be diagnosed with PSE at baseline, however this did not reach statistical significance in the model.

In addition, sex was positively related to baseline PSE, but with little evidence of association (*OR* = 1.558, 95% CI [.594, 4.082], *p* = .367). This meant that males were more likely to be diagnosed with PSE at baseline, however this also did not reach statistical significance in the model.

Overall, the variability in PSE diagnosis at baseline, explained by the five predictor variables, was 65% (R^2 = .656). The model correctly predicted 94.8% of cases where PSE was present, and 75.0% of cases where PSE was not present, giving an overall percentage correct prediction rate of 89.3%.

Table 3

Binomial regression model for predicting the probability of PSE presence at baseline from demographic and psychological variables also measured at baseline

Variable	B	Standard Error	Wald	Exp (B)	95% Confidence interval for Exp (B)	P
TEARS-Q (emotionalism)	.501	.072	48.601	1.650	1.434-1.900	< .001**
HADS Depression	-.026	.072	.126	.975	.846-1.123	.723
HADS Anxiety	.091	.062	2.187	1.095	.971-1.236	.139
Age	-.024	.017	2.023	.977	.946-1.009	.155
Sex (male)	.443	.492	.813	1.558	.594-4.082	.367
Constant	-2.096	1.261	2.765	.123		.096

B = coefficients, Exp (B) = Odds Ratio, TEARS-Q = Testing for Emotionalism After Recent Stroke Questionnaire, HADS = Hospital Anxiety and Depression Scale
**significant at α = .05

2. Baseline predictors and outcome at 6-months

Multinomial regression analysis was used to assess the relationship between personal demographics (age, sex, stroke type) and psychological variables (anxiety, depression, functioning, cognition, and emotionalism), with outcomes at 6-months after stroke. The three potential outcomes were: (i) No PSE at 6-months, (ii) PSE present at 6-months or (iii) Lost to follow-up. No PSE at 6-months was entered into the model as the reference category. The TEARS-IV (diagnostic interview) outcome was used as a measure of baseline emotionalism, as opposed to the TEARS-Q score. This was because TEARS-IV is considered the gold standard of diagnostic emotionalism assessment. Sex and stroke type were removed from the final model as they were deemed not to contribute to either outcome. The final model is summarised in Table 4.

The final model indicated that age was negatively associated with PSE at 6-months (*OR* = .971, 95% CI [.940, 1.002], *p* = .063) and also negatively associated with loss to follow-up at 6 months (*OR* = .972, 95% CI [.950, .994], *p* = .015). The association between age and loss to follow-up reached statistical significance at an alpha level of .05, and was "small" in effect[32]. In other words, participants who were older were significantly less likely to drop out of the study at 6-months.

Depression at baseline was negatively associated with PSE at 6-months (*OR* = .874, 95% CI [.745, 1.026], *p* = .099) and was also negatively associated with loss to follow-up at 6-months (*OR* = .894, 95% CI [.881, 1.099], *p* = .771). This meant that individuals with higher depression scores at baseline were less likely to be diagnosed with PSE at 6-months and also less likely to drop out of TEARS before the 6-month assessment. Depression at baseline did not reach statistical significance at an alpha level of .05 in association with either outcome.

Anxiety at baseline was positively associated with PSE at 6-months (*OR* = 1.137, 95% CI [1.013, 1.040], *p* = .029) but negatively associated with loss to follow-up at 6-months (*OR* = .946, 95% CI [.865, 1.034], *p* = .219). The association between baseline anxiety and PSE at 6-months was significant at an alpha level of .05, and was "small" in effect[32]. This meant that individuals scoring higher for anxiety at baseline were significantly more likely to be diagnosed with PSE at 6-months.

Daily functioning (as measured by the Barthel Index) at baseline was negatively associated with PSE at 6-months (*OR* = .923, 95% CI [.819, 1.040], *p* = .186) and also negatively associated with loss to follow-up at 6-months (*OR* = .958, 95% CI [.879, 1.044], *p* = .329), but with little evidence of association. This meant that those who showed higher levels of functioning (and were therefore considered more independent in daily activities) were less likely to be diagnosed with PSE at 6-months and also less likely to drop-out from TEARS before the 6-month assessment. Daily functioning did not reach statistical significance at an alpha level of .05 for an association between daily functioning and either outcome at 6-months.

Cognition (as measured by the AMT) was negatively associated with PSE at 6-months (*OR* = .936, 95% CI [.796, 1.101], *p* = .424) and also negatively associated with loss to follow-up (*OR* = .893, 95% CI [.801, .997], *p* = .043). The association between baseline cognition and loss to follow-up 6-months was statistically significant at an alpha level of .05, and was "small" in effect[32]. This meant that those with higher AMT scores (and therefore less cognitive impairment) were less likely to drop-out from TEARS before the 6-month assessment.

Emotionalism at baseline was positively associated with PSE at 6-months (*OR* = .240, 95% CI [.091, .629], *p* = .004) and also positively associated with loss to follow-up at 6-months (*OR* = .710, 95% CI [.333, 1.516], *p* = .376). The association

between PSE at baseline and PSE at 6-months was statistically significant at an alpha level of .05, and was "small" in effect[32]. This meant that individuals who were diagnosed with PSE at baseline, were significantly more likely to be diagnosed with PSE at 6-months.

Table 4

Multinomial regression model assessing the relationship between age, depression, anxiety, functioning, cognition and emotionalism at baseline, and outcome at 6-months after stroke

Outcome	Variable	B	Standard Error	Wald	Exp (B)	95% CI for Exp (B)	P
PSE present	Age	-.030	.016	3.447	.971	.940-1.002	.063
at 6-months	HADS Depression	-.135	.082	2.723	.874	.745-1.026	.099
	HADS Anxiety	.128	.059	4.739	1.137	1.013-1.276	.029**
	Barthel Index	-.081	.061	1.750	.923	.819-1.040	.186
	AMT (cognition)	-.066	.083	.640	.936	.796-1.101	.424
	TEARS-IV outcome (No PSE at baseline)	-1.428	.492	8.410	.240	.091-.629	.004**
Lost to	Age	-.028	.012	5.921	.972	.950-.994	.015**
follow-up	HADS Depression	-.016	.056	.084	.984	.881-1.099	.771
	HADS Anxiety	-.056	.046	1.509	.946	.865-1.034	.219
	Barthel Index	-.043	.044	.953	.958	.879-1.044	.329
	AMT (cognition)	-.113	.056	4.087	.893	.801-.997	.043**

Outcome	Variable	B	Standard Error	Wald	Exp (B)	95% CI for Exp (B)	P
	TEARS-IV outcome (No PSE at baseline)	-3.42	.387	.782	.710	.333-1.516	.376

B = coefficients, Exp (B) = Odds Ratio, PSE = Post-Stroke Emotionalism, TEARS-IV = Testing for Emotionalism After Recent Stroke Interview, HADS = Hospital Anxiety and Depression Scale, AMT = Abbreviated Mental Test
**significant at α = .05

3. Baseline predictors and outcome at 12-months

Multinomial regression analysis was used to assess the relationship between personal demographics (age, sex, stroke type) and psychological variables (anxiety, depression, functioning, cognition, and emotionalism), with outcomes at 12-months after stroke. The three potential outcomes were: (i) No PSE at 12-months, (ii) PSE present at 12-months or (iii) Lost to follow-up. No PSE at 12-months was entered into the model as the reference category. TEARS-IV (diagnostic interview) outcome was used as a measure of baseline emotionalism, as opposed to the TEARS-Q score, due to being considered the gold standard method of assessment. Depression and stroke type were removed from the final model as they were deemed not to contribute to either outcome. The final model is summarised in Table 5.

The final model indicated that age was negatively associated with PSE at 12-months (*OR* = .945, 95% CI [.901, .992], *p* = .022) and also negatively associated with loss to follow-up at 12-months (*OR* = .969, 95% CI [.94, .991], *p* = .006). The association between age and both outcomes at 12-months reached statistical significance at an alpha level of .05, and was "small" in effect[32]. In other words, participants who were older were significantly less likely to be diagnosed with PSE at 12-months, and significantly less likely to drop-out of TEARS before the 12-month assessment.

Sex was positively associated with PSE at 12-months (*OR* = 5.547, 95% CI [1.302, 23.631], *p* = .020) and also positively associated with loss to follow-up at 12-months (*OR* = .316, 95% CI [.742, 2.564], *p* = .309). The association between male sex and PSE at 12-months reached statistical significance at an alpha level of .05, and was "large" in effect[32]. This meant that male participants were significantly more likely to be diagnosed with PSE at 12-months

Anxiety at baseline was positively associated with PSE at 12-months (*OR* = 1.258, 95% CI [1.102, 1.437], *p* = .001) but negatively associated with loss to follow-up at 12-months (*OR* = .980, 95% CI [.909, 1.058], *p* = .610). The association between anxiety at baseline and PSE at 12-months reached statistical significance at an alpha level of .05, and was "small" in effect[32]. This meant that individuals scoring higher for anxiety at baseline were significantly more likely to be diagnosed with PSE at 12-months.

Daily functioning (as measured by the Barthel Index) at baseline was negatively associated with PSE at 12-months (*OR* = .995, 95% CI [.853, 1.160], *p* = .947) and also negatively associated with loss to follow-up at 12-months (*OR* = .911, 95% CI [.843, .984], *p* = .018). The association between daily functioning at baseline and loss to follow-up at 12-months reached statistical significance at an alpha level of .05, and was "small" in effect[32]. This meant that those who showed higher levels of functioning (and were therefore considered more independent in daily activities) were significantly less likely to drop-out from TEARS before the 12-month assessment.

Cognition (as measured by the AMT) was negatively associated with PSE at 12-months (*OR* = .956, 95% CI [.741, 1.232], *p* = .727) and also negatively associated with loss to follow-up at 12-months (*OR* = .858, 95% CI [.763, .964], *p* = .010). The association between baseline cognition and loss to follow-up at 12-months reached statistical significance at an alpha level of .05, and was "small" in effect[32]. This meant that those with higher AMT scores (and therefore less cognitive impairment) were significantly less likely to drop-out from TEARS before the 12-month assessment.

Emotionalism at baseline was positively related to PSE at 12-months (*OR* = .634, 95% CI [.159, 2.532], *p* = .519) and also positively related to loss to follow-up

at 12-months (*OR* = .784, 95% CI [.374, 1.643], *p* = .519), with little evidence for association at an alpha significance level of .05.

Table 5

Multinomial regression model assessing the relationship between age, sex, anxiety, functioning, cognition and emotionalism at baseline, and outcome at 12-months after stroke

Outcome	Variable	B	Standard Error	Wald	Exp (B)	95% CI for Exp (B)	P
PSE present	Age	-.057	.025	5.261	.945	.901-.992	.022**
at 12-months	Sex (male)	1.173	.739	5.369	5.547	1.302-23.631	.020**
	HADS Anxiety	.230	.068	11.466	1.258	1.102-1.437	.001**
	Barthel Index	-.005	.078	.004	.995	.853-1.160	.947
	AMT (cognition)	-.045	.130	.122	.956	.741-1.232	.727
	TEARS-IV outcome (No PSE at baseline)	-.456	.707	.416	.634	.159-2.532	.519
Lost to	Age	-.032	.012	7.417	.969	.946-991	.006**
follow-up	Sex (male)	.322	.316	1.035	1.380	.742-2.564	.309
	HADS Anxiety	-.020	.039	.260	.980	.909-1.058	.610
	Barthel Index	-.094	.039	.260	.911	.843-.984	.018
	AMT (cognition)	-.154	.060	6.652	.858	.763-.964	.010**

Outcome	Variable	B	Standard Error	Wald	Exp (B)	95% CI for Exp (B)	P
	TEARS-IV outcome (No PSE at baseline)	-.243	.377	.416	.784	.374-1.643	.519

B = coefficients, Exp (B) = Odds Ratio, PSE = Post-Stroke Emotionalism, TEARS-IV = Testing for Emotionalism After Recent Stroke Interview, HADS = Hospital Anxiety and Depression Scale, AMT = Abbreviated Mental Test
**significant at α = .05

Group Differences: Participants who remained in the study compared to those lost to attrition at the 12-month assessment

In total, 109 participants were assessed at baseline, 6- and 12-months, with 119 participants lost to attrition between baseline and the 12-month assessment. Group differences were compared between those who remained in the study and those lost to attrition, and are summarised in Table 6 below.

Table 6

Descriptive statistics and group differences of demographic characteristics and psychological variables of stroke survivors at baseline assessment, for individuals who remained in the study and individuals lost to attrition at 12-months.

Characteristic	Levels	Remained in Study	Lost to Attrition at 12-months	Total Cohort	P
Number of Participants		109	119	228	
Age at Stroke	Mean (*SD*)	66.28 (12.77)	63.93 (15.91)	65.05 (14.51)	.224
Sex	Female (%)	48 (44.0)	50 (42.0)	98 (43.0)	.862
	Male (%)	61 (46.0)	69 (48.0)	130 (57.0)	
Stroke type	Infarction (%)	103 (94.5)	106 (89.1)	209 (91.67)	.271
	Haemorrhage (%)	6 (5.5)	12 (10.1)	18 (7.89)	
Oxford Classification of Stroke	Total Anterior Circulation Stroke	2 (1.8)	8 (6.7)	10 (4.39)	.032**
	Partial Anterior Circulation Stroke	43 (39.4)	33 (27.7)	76 (33.33)	

Characteristic	Levels	Remained in Study	Lost to Attrition at 12-months	Total Cohort	P
	Lacunar Stroke	42 (38.5)	37 (31.1)	79 (34.65)	
	Posterior Circulation Stroke	19 (17.4)	35 (29.4)	54 (23.68)	
TEARS-Q Score	Median (IQR)	0.00 (4.00)	0.00 (5.00)	0.00 (5.00)	.272
Barthel Activities of Daily Living Index	Median (IQR)	19.00 (4.00)	18.00 (8.00)	19.00 (6.00)	.005**
HADS Depression	Median (IQR)	3.00 (5.00)	3.00 (4.00)	3.00 (4.00)	.231
HADS Anxiety	Median (IQR)	5.00 (7.00)	5.00 (8.00)	5.00 (6.00)	.388
AMT (cognition)	Mean (*SD*)	9.02 (2.44)	7.81 (3.41)	8.38 (3.05)	.003**

SD = standard deviation, IQR = inter-quartile range, PSE = Post-Stroke Emotionalism, TEARS-Q = Testing for Emotionalism After Recent Stroke Questionnaire, HADS = Hospital Anxiety and Depression Scale, AMT = Abbreviated Mental Test
**significant at $\alpha = .05$

Of the 228 participants, 119 were lost to follow-up between baseline and 12-month assessment. In comparing those who remained in the study with those who did not, significant differences were found between the two groups for three variables. At an alpha level of .05, significant differences were found between Oxford Stroke Classification (p = .032), Barthel (daily functioning) scores (p = .005) and AMT (cognition) scores (p = .003).

Discussion

Of the 228 stroke survivors who participated in TEARS, 27% presented with PSE at baseline assessment (2-weeks post-stroke). This mirrors the findings of the only systematic review examining PSE prevalence[1]. Exploration of several demographic (age, sex, stroke type, classification) and psychological (depression, anxiety, cognition, daily functioning) variables between those who were presenting with PSE at baseline, and those who were not, revealed key differences between these groups. Significant group differences were found at baseline assessment for age at the time of stroke, anxiety, and depression. On average, those presenting with PSE at baseline were younger and had greater symptoms of anxiety and depression. This coincides with previous reports that suggest PSE may co-occur with symptoms of anxiety and depression[5, 6].

In addition, significant group differences were found regarding 6-month outcome (PSE at 6-months, No PSE at 6-months, or lost to follow-up), between those presenting with PSE and baseline and those who were not. A significant difference was not however, found between these groups with regards to outcome at 12-months. As TEARS is one of the first studies exploring PSE and psychological variables over several timepoints, such findings are important for the planning of future research. Attrition rate was far higher between baseline and 6-months, than 6- and 12-months, providing a possible explanation as to why the differences in outcome were found at

6-months but not 12-months. Group differences (of baseline variables) were also assessed between those who remained in the study at the 12-month assessment and those who were lost to follow-up. Significant differences were found between stroke classification (Oxford Classification system), Barthel (daily living) scores, and cognition scores. This may suggest that the type of stroke (and associated features) could impact continued participation in research. However, in the total cohort, there were far fewer individuals classified as experiencing a "Total Anterior Circulation" stroke in comparison to the other three categories, which may have also contributed to the difference noted here. The group differences found for daily functioning and cognition between those who remained in the study and those who dropped out mirrors the findings of the regression analyses detailed below. In short, such analyses suggested that those with less independence in daily functioning and worse cognitive functioning were more likely to drop-out from the TEARS study.

The predictive probability of demographic and psychological variables at baseline were explored using a series of regression analyses. With regards to PSE at baseline, the greatest predictor of PSE (as diagnosed by TEARS-IV) was emotionalism (as measured by TEARS-Q). This was expected, given that the two variables measure the same construct, and that TEARS-Q has been found to be an acceptable measure for diagnosing tearful PSE[20]. No other baseline variables (age, sex, depression, anxiety, cognition and daily functioning) were found to be significant predictors of PSE at baseline, however, the overall model (integrating emotionalism, depression, anxiety, age and sex) explained 69% variability in PSE at baseline, and correctly predicted 89% of instances. This provides some support for the idea that emotionalism may arise with, or be maintained by, a combination of psychological factors.

At 6-months after stroke, the prevalence of PSE was 20%, suggesting that 1 in 5 stroke survivors will experience PSE beyond what is considered the acute phase of stroke recovery. This appears to mirror prevalence findings in the prior PSE systematic review cited above[1] and also the prevalence of other psychiatric problems after stroke, such as depression[33], anxiety[34] and PTSD (see Chapter 2). PSE at 6-months was most associated with two psychological variables measured at baseline: emotionalism and anxiety. Although significant, the effect sizes for emotionalism and anxiety were "small". Firstly, this suggests that those who experienced PSE at baseline were more likely to also experience it at 6-months after stroke. This could reflect a pattern of maintenance over time, suggesting that targeted treatment for PSE may be useful in the first 6-months after stroke. In addition, those who experienced higher symptoms of anxiety at baseline were more likely to experience PSE at 6-months. This provides some support for the links drawn between anxiety symptoms and PSE previously[16-18]. Furthermore, avoidance and uncertainty were highlighted as key PSE maintaining factors derived from the qualitative data of TEARS[22] and also previous qualitative reports[19]. Given that avoidance and uncertainty are also key components of anxiety, it appears that such findings are mirrored when examining quantitative data collected from standardised assessment measures.

Loss to follow-up at 6-months was most associated with age and cognition. Again, the effects sizes of the significant associations between loss to follow-up and age, and cognition were "small". Specifically, those who were younger and less cognitively able were more likely to drop-out from the TEARS study. There could be several reasons for this. Firstly, return to occupational and societal roles is a primary goal of stroke rehabilitation, particularly for younger stroke survivors[36]. It may therefore be that those of working age were busy working towards occupational reintegration and either felt that they did not have sufficient time to continue in the

research, or that it was of much lower priority. Secondly, informal feedback given during the TEARS study indicated that participants felt there were great amounts of measures to complete at each assessment timepoint. Whilst this provided a wealth of data regarding PSE and other psychological constructs, completion of such measures may have been burdensome, particularly for those experiencing cognitive difficulties. Finally, it is possible that higher cognitive impairment experienced as a result of stroke was due to the stroke being more severe in nature. Perhaps therefore, these individuals were also experiencing more severe physical effects of stroke and were therefore engaging their efforts more into other, competing rehabilitation priorities.

At 12-months after stroke, 15.6% of stroke survivors presented with PSE, highlighting that approximately 1 in 6 continue to experience emotionalism a considerable amount of time after the index stroke event. Again, this appears to mirror prevalence findings in the prior PSE review[1] and also the prevalence of other psychiatric problems after stroke, such as depression[33], anxiety[34] and PTSD (see Chapter 2). PSE at 12-months was most associated with anxiety at baseline, and also two demographic variables (age and sex). The size of the associations between PSE at 12-months and anxiety, and age, were both "small" in effect, whereas the size of association between sex and PSE at 12-months was "large". Specifically, those experiencing higher levels of anxiety at baseline were more likely to experience PSE at 12-months, further supporting the idea of a link between symptoms of anxiety after stroke and the maintenance of PSE[16-18, 22]. As noted above, it may be that those experiencing symptoms of anxiety and/or PSE are likely to be avoidant of rehabilitation and social reintegration. Perhaps such avoidance is key in maintaining both of these psychological difficulties after stroke, for example by preventing habituation to the social and cognitive consequences of either condition.

In addition, those who were male and younger at the time of stroke were more likely to experience PSE at 12-months. Previous research has highlighted that those who are younger more frequently experience PSE[17], as is the case with other psychiatric disorders after stroke[36, 37]. Literature examining depression and anxiety in different age groups of stroke survivors have suggested several hypotheses that may be relevant here. For example, Broomfield and Colleagues[36] noted that increased rates of post-stroke anxiety in younger survivors is consistent with general epidemiological trends. Furthermore, they noted that experiencing stroke at a time of life when individuals may be caring for young families or need to work full-time, coupled with the expectation of good health at a younger age may be particularly challenging psychologically. Such hypotheses are entirely plausible in stroke survivors experiencing PSE, particularly given the noted links between PSE and anxiety, and the impact of PSE on rehabilitation and societal reintegration (e.g. distress, embarrassment, avoidance).

The finding that males were more likely to experience PSE at 12-months is interesting and contradicts most prior research. The effect size was "large", suggesting a clinically meaningful association between sex and PSE at 12-months. However, this may be related to the data available at the 12-month assessment, for example only 4 women presented with PSE at the 12-month assessment, compared to 13 men (see Chapter 5 for further details), potentially inflating the magnitude of the association. At both the baseline and 6-month assessments, the number of men and women diagnosed with PSE at each timepoint was more comparable (29 men and 33 women at baseline, and 16 men and 14 women at 6-months). It is not possible to determine whether the disparity noted was due to recovery of PSE in females, or to drop-out from the study, however, this could be examined in future research. Alternatively, this finding could be related to another factor, such as stigma or

attitudes towards help-seeking in men experiencing psychological difficulties after stroke[38]. Again, further research is needed to confirm this hypothesis.

With regards to loss to follow-up at 12-months, age, cognition and daily functioning were most associated with drop-out from TEARS. The size of the associations between loss to follow-up at 12-months and age, cognition, and daily functioning were all "small" in effect. In addition, analyses of group differences between those who remained in the study and those who dropped-out between baseline and 12-months showed that there were significant differences between the groups for stroke classification (according to the Oxford Stroke Classification System), cognition, and daily functioning.

Like the findings at 6-months, those who were younger and less cognitively able were more likely to drop-out from TEARS. Again, this could be related to reintegration with occupational and societal roles or finding the number of assessment measures burdensome. As noted, loss to follow-up may be related to higher severity of stroke or disability, or indeed the clinical features of the type of stroke experienced. This idea is supported by the finding that those with worse daily functioning (and therefore less independence) were more likely to drop out from the study before the 12-month assessment. It may be that those relying more heavily on others for support with daily tasks were more likely to experience difficulties in participation, or may have moved to a care facility and were therefore more difficult to contact for follow-up.

Limitations

This paper provided an in-depth exploration of PSE and other psychological variables measured in the acute phase of stroke (within 2-weeks), and associations between such variables and emotionalism later in the recovery journey. However, several limitations are noteworthy. Firstly, the conclusions drawn were heavily

reliant on the data available. As noted, attrition rate in TEARS was high, with less than half (48%) of the participants assessed at baseline continuing the study through to the 12-month assessment. Power calculation analyses suggested that the sample size was sufficient for the analyses (assuming a medium effect, α-level of .05 and power of 80%, per Peduzzi and colleagues[31]), however a larger sample would have given more confidence in the findings, particularly as the size of the effects noted were mostly "small". In addition, group differences were found between those who remained in the study and those who did not (for stroke classification, cognition and daily functioning), and regression analyses showed that those with worse cognitive functioning and worse daily functioning were more likely to drop out before the 12-month assessment. However, it is not possible to ascertain if other factors that could have been relevant later in the recovery journey, or related to the TEARS study itself, could have also contributed to study attrition.

Potentially, those who were lost to follow-up could have been experiencing more severe symptoms of PSE and were therefore more likely to discontinue the research. This may have implications for the data that are reported here, for example, PSE prevalence may be higher than was observed in this study. Consistent with this hypothesis, qualitative reports[19, 22] highlight that those experiencing PSE are more likely to avoid situations which could trigger PSE. Discussing PSE experiences could therefore be a situation which is keenly avoided. Of course, it is not possible to confirm this hypothesis in the current study. Although potential associations with drop-out in TEARS were explored here, reasons for loss to follow-up (e.g. unable to contact, death, withdrawal) were not recorded in the main study. This would have provided a crucial insight into the challenges faced by participants and researchers in the completion of longitudinal research and where possible, should be reported in future studies.

Secondly, variability in PSE at all timepoints (baseline, 6-months and 12-months) was only partially accounted for in the analyses noted above. It may therefore be that other demographic variables (e.g. ethnicity, employment, location, marital status) that were not included here may have contributed to PSE at the varying timepoints. In addition, psychological variables, such as distress and social functioning were not measured at baseline, but were assessed at the 6- and 12-month assessments in TEARS. Given the theoretical links drawn between PTSD and PSE[16, 17], and also social support and PSE[19, 22], it is possible that such factors impact the presence and/or maintenance of PSE.

Finally, several limitations of the TEARS study warrant consideration. For example, there is a possibility of sampling bias, due to non-consecutive admissions to each ward. The population included in TEARS were younger than the average age of stroke occurrence and stroke severity was mostly classed as minor-moderate. In addition, recruitment was limited to Western Scotland and hence, the generalisability of such findings must be carefully considered. Finally, all measures, including both the TEARS-IV and the TEARS-Q, were administered by the same person, at the same time. Administering both measures of emotionalism in one sitting may have led to carryover, inflating the association between the two. Furthermore, administering several other measures is likely to have been tiring for participants and may have contributed to the high attrition rate noted. Unfortunately also, there was minimal patient and public involvement (PPI), for TEARS during study design, which potentially could have highlighted acceptability issues in the planning and development stages.

Clinical Implications

This paper has highlighted the high prevalence of PSE in the acute stages of stroke recovery, maintained over time within the first year of stroke. It is therefore

clear that PSE should be screened later in the stroke recovery journey when patients are more likely to be back in community settings. As TEARS-Q was a significant predictor of emotionalism and has shown to have good psychometric properties[21] it is appropriate to use this brief tool as a way of identifying those that may require further input. Potentially, this could be undertaken during stroke annual reviews.

In addition, anxiety at baseline was associated with PSE at both 6- and 12-months after stroke, suggesting links between the two conditions. Although the size of these effects were "small", the qualitative analyses of TEARS data[22] highlighted that key features of anxiety (e.g. avoidance and uncertainty) were particularly meaningful in their PSE experience. Associations between symptoms of anxiety and PSE may therefore be particularly pertinent in clinical practice. Perhaps, the inevitable avoidance that is used to cope with both of these conditions actually inhibits progress through preventing habituation to their social and cognitive consequences. In other words, PSE could be thought of as a disorder of fear of crying, maintained by avoidance. This coincides with suggestions that PSE is not purely a neurological condition, thus further highlighting the need for robust examination of non-pharmacological treatments. Overall, whilst the individual, significant effect sizes shown in these results were small, the overall regression model for 6-month and 12-month outcomes accounted for a good amount of variance (42-63%), supporting the idea that PSE is best conceptualised in terms of multiple risk/maintain factors, as would be consistent in considering a psychological therapy model. It may be that PSE interventions incorporating well-established skills and techniques from the treatment of anxiety would be beneficial. PSE clearly continues to be a problem for many stroke survivors, which may compound physical and cognitive effects of stroke as well as continue to impede rehabilitation efforts, and developing evidence-based, non-pharmacological treatments is a critical next step.

Implications for Research

As noted, the findings presented in this paper are from exploratory analyses and as such, there is a clear need for further, robust investigation of the psychological correlates and contributors to PSE. This would improve current knowledge and has the potential to inform model development capturing the PSE experience. As noted, it would be beneficial for future research to incorporate PPI, potentially improving the quality and relevance of any proposed studies. In addition, the Health Research Authority suggests that PPI can contribute to recruitment and retention in research, which would be highly beneficial.

Given the findings presented in this paper, it is clear that research of a longitudinal nature is key to developing a greater understanding of PSE and should be considered in future research. In conjunction, it would be advantageous for any reasons given for loss to follow-up to be recorded, to gain a better understanding of the challenges faced in completion of such research. As noted, age and cognition were associated with drop-out at both the 6- and 12-month assessments in this study. It may therefore be worth exploring such factors in greater detail when planning future studies.

Conclusions

Emotionalism is commonly experienced after stroke and is maintained beyond the acute phase of stroke recovery. This paper highlighted the association between anxiety and PSE across time, thus suggesting a link between the two conditions. Given the impact of PSE on rehabilitation and societal reintegration, further research into psychological contributors to the development and maintenance of PSE is crucial. Not only would this improve the current knowledge and understanding of PSE, but it is likely to lead to more successful development of much needed, clinically-effective non-pharmacological treatments.

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Conflict of Interest

None.

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STROBE Checklist

Please see Appendix H for STROBE checklist (required for submission of empirical research paper).

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Chapter 5: Additional Analyses and Results

This chapter outlines additional statistical analyses and the findings, which were not reported in the empirical paper in Chapter 4. The primary focus of the empirical paper was in-depth exploration of the baseline data collected during TEARS, and the predictive value of such variables in relation to the outcomes at 6- and 12-months. In TEARS, additional psychological variables (psychological distress, social functioning, and an alternative measure of cognition) were measured at the 6-and 12-month assessments. The measures used to assess these variables are described in further detail below.

Firstly, descriptive statistics of the available data for the 6- and 12-month assessments are presented. Then, results of logistic regression analyses, examining the predictive association between psychological variables and post-stroke emotionalism (PSE) measured at the 6- and 12-month assessments are presented. Finally, bivariate correlational analyses were used to explore associations between psychological distress and PSE (as described previously in Chapter 3). The results are discussed, with recommendations made for future research.

Additional Measures at 6- and 12-months

In addition to the psychological variables measured at baseline (emotionalism, anxiety, depression, functioning and cognition), the following variables were measured at 6- and 12-month assessments.

Psychological Distress

In TEARS, psychological distress was measured at 6- and 12-months after the index stroke event, using the Impact of Events Scale-Revised (IES-R; Weiss & Marmar, 1996). The IES-R is a 22-item, self-report measure assessing levels of distress following stressful events. Three subscales are included (avoidance, intrusion and hyperarousal), reflecting the diagnostic criteria for Post-Traumatic Stress

Disorder (PTSD). Respondents are required to rate on a 5-point Likert scale (0= not at all- 4= extremely), how distressed they have been by each of the difficulties listed, e.g. "Any reminder brought back feelings about it". Items within each subscale are averaged to generate a total mean score between 0-12. Higher scores indicate higher levels of distress. As demonstrated in Chapter 2, the IES-R is frequently used as a measure of PTSD in stroke populations and has demonstrated good psychometric properties (Creamer et al., 2003).

Social Functioning

In TEARS, social functioning was measured at 6- and 12-months after the index stroke event, using the Social Ties Checklist (STC; Starr, Robinson & Price, 1983). The STC is a brief, 10-item questionnaire, in which individuals are asked to respond in a yes/no format to questions aimed at examining the degree of social involvement, e.g. "Do you regularly talk to or spend time with family members? (at least an hour a week)". Each "yes" response does not generate a score and each "no" response generates a score of 1, hence lower scores indicate higher levels of social participation. The STC has been used within stroke populations, with good reported reliability and validity (Starr *et al.,* 1983).

Cognition

As discussed in Chapter 4, cognition was measured at the baseline assessment in TEARS using the Abbreviated Mental Test (Hodkinson, 1972). At the 6- and 12-month assessments however, cognition was assessed using the Montreal Cognitive Assessment (MoCA; Nasreddine *et al.,* 2005). The MoCA is widely-used in routine clinical practice as a screening tool for cognitive impairment, validated for use in stroke populations (Cumming et al., 2013). It is conducted by clinicians and briefly assesses several cognitive domains, including orientation, attention, language, recall and executive functioning. Each cognitive domain is assessed using specific tasks,

such as confrontational naming, for which an overall score out of 30 is generated. Scores below 26 are indicative of cognitive impairment.

Statistical Assumptions

For all analyses completed in Chapter 4 and here, parametric assumptions were checked. For the logistic regression analyses, independence of observations was confirmed, as none of the variables in each regression model included repeated or matched data. Multicollinearity of the continuous predictor variables was checked using correlations, and the tolerance and variance inflation factor statistics. The statistics analysing multicollinearity were all below a level considered problematic, thus satisfying this assumption. Finally, linearity between the independent variables and log odds was checked by entering an interaction term for each variable and its log-transformed variable into the model. All interaction terms were not significant, thus satisfying this assumption.

For the correlation analyses described in this chapter, normality was checked using Q-Q plots. The assumption of normality for TEARS-Q data at both 6- and 12-months was violated and so a non-parametric alternative (Spearman's Rho) was used. In addition, bootstrapping was used to generate robust confidence intervals.

Results

6-month Analyses: Descriptive Statistics

A total of 148 participants completed the 6-month assessment. Descriptive statistics of the psychological variables measured, grouped by the presence or absence of PSE at the 6-month assessment (determined by the outcome of the TEARS diagnostic interview) are shown in Table 1.

Table 1

Descriptive statistics of demographic characteristics and psychological variables of stroke survivors at 6-month assessment

Characteristic	Levels	No PSE Diagnosis	PSE Present	Total Cohort
Number of Participants		118 (79.73)	30 (20.27)	148
Age at Stroke	Mean (SD)	67.15 (13.95)	60.12 (12.70)	65.71 (13.95)
Sex	Female (%)	53 (35.81)	14 (9.46)	67 (45.27)
	Male (%)	65 (43.91)	16 (10.81)	81 (54.73)
TEARS-Q Score	Median (IQR)	0.00 (0.00)	7.00 (11.00)	0.00 (1.00)
Barthel Activities of Daily Living Index	Median (IQR)	20.00 (1.00)	19.00 (4.00)	20.00 (2.00)
HADS Depression Score	Median (IQR)	4.00 (5.00)	7.00 (6.00)	5.00 (5.00)
HADS Anxiety Score	Median (IQR)	4.00 (7.00)	9.00 (9.00)	5.00 (8.00)
MoCA Cognition Score	Median (IQR)	27.00 (5.00)	26.00 (4.00)	27.00 (5.00)
IES-R Psychological Distress Score	Median (IQR)	2.00 (12.00)	14.00 (31.00)	4.00 (17.00)
Social Ties Checklist Score	Median (IQR)	4.00 (3.00)	4.00 (2.00)	4.00 (2.00)

SD = standard deviation, IQR = inter-quartile range, PSE = Post-Stroke Emotionalism, TEARS-Q = Testing for Emotionalism After Recent Stroke Questionnaire, HADS = Hospital Anxiety and Depression Scale, MoCA= Montreal Cognitive Assessment, IES-R= Impact of Events Scale-Revised

6-month Analyses: Logistic Regression

A binomial regression analysis was used to assess the probability of PSE presence at 6-months, as predicted by demographic (age and sex) and psychological variables (depression, anxiety, cognition, functional outcome, psychological distress, social functioning and TEARS-Q emotionalism score) also measured at 6-months. Preliminary checks confirmed that assumptions for logistic regression were met. Variables were entered into the model using the block enter method. The regression model is summarised in Table 2.

The model indicated that 6-month TEARS-Q (emotionalism) score was negatively related to PSE at 6-months (*OR* = 1.329, 95% CI [1.154, 1.532], *p* = < .001). This was statistically significant at an alpha level of .05, and was "small" in effect. This meant that the presence of PSE at 6-months, as measured by the TEARS-Q screening questionnaire, made it more likely for individuals to be diagnosed with PSE at 6-months, as diagnosed by the TEARS-IV diagnostic interview.

For all other variables in the model (depression, anxiety, daily functioning, psychological distress, social functioning, cognition, age and sex), there was little evidence of association with PSE at 6-months (*p*= > .05).

Table 2

Binomial regression model for predicting the probability of PSE presence at 6-months from demographic and psychological variables also measured at 6-months

Variable	B	Standard Error	Wald	Exp (B)	95% Confidence interval for Exp (B)	P
TEARS-Q (emotionalism)	.285	.072	15.472	1.329	1.154-1.532	.000**
HADS Depression	.070	.102	.479	1.073	.879-1.310	.489
HADS Anxiety	.084	.090	.880	1.088	.913-1.297	.348
Barthel (daily functioning)	-.020	.114	.032	.980	.783-1.226	.859
IES-R (distress)	.012	.021	.342	1.012	.972-1.055	.559
STC (social functioning)	-.284	.205	1.919	.753	.504-1.125	.166
MoCA (cognition)	-.141	.103	1.856	.869	.710-1.064	.173
Age at stroke	-.028	.024	1.427	.972	.928-1.018	.232
Sex (male)	-.032	.628	.003	.969	.283-3.316	.232
Constant	3.545	3.723	.907	34.644		.341

B = coefficients, Exp (B) = odds ratio, *SD* = standard deviation, IQR = inter-quartile range, PSE = Post-Stroke Emotionalism, TEARS-Q = Testing for Emotionalism After Recent Stroke Questionnaire, HADS = Hospital Anxiety and Depression Scale, IES-R = Impact of Events Scale-Revised, STC = Social Ties Checklist, MoCA = Montreal Cognitive Assessment
**significant at α = .05

Overall, the variability in PSE diagnosis at baseline, explained by the eight predictor variables, was 50% (R^2 = .509). The model correctly predicted 50% of

cases where PSE was present, and 95% of cases where PSE was not present, giving an overall percentage correct prediction rate of 85.8%.

6-month Analyses: Correlation

As noted in Chapter 3, subtle links have been made previously between PTSD and emotionalism. As such, a bivariate correlation was conducted to examine the association between psychological distress at 6-months (as measured by the IES-R) and emotionalism at 6-months (as measured by the TEARS-Q).

There was a positive correlation, that was small in effect, between psychological distress and PSE at 6-months, which was statistically significant (r = .233, 95% CI [.065, .397], p = .007). This meant that higher IES-R scores were associated with higher TEARS-Q scores at the 6-month timepoint.

12-month Analyses: Descriptive Statistics

A total of 109 participants completed the 12-month assessment in TEARS. Descriptive statistics of the psychological variables measured, grouped by the presence or absence of PSE at the 12-month assessment (determined by the outcome of the TEARS diagnostic interview) are shown in Table 3.

Table 3

Descriptive statistics of demographic characteristics and psychological variables of stroke survivors at 12-month assessment

Characteristic	Levels	No PSE Diagnosis	PSE Present	Total Cohort
Number of Participants		92 (84.40)	17 (15.60)	109
Age at Stroke	Mean (SD)	68.19 (12.37)	54.80 (9.50)	66.28 (12.85)
Sex	Female (%)	44 (40.37)	4 (3.67)	48 (44.04)
	Male (%)	48 (44.04)	13 (11.93)	61 (56.00)
TEARS-Q Score	Median (IQR)	0.00 (0.00)	7.00 (12.00)	0.00 (0.00)
Barthel Activities of Daily Living Index	Median (IQR)	20.00 (1.00)	20.00 (1.00)	20.00 (1.00)
HADS Depression Score	Median (IQR)	4.00 (4.00)	8.00 (8.00)	5.00 (5.00)
HADS Anxiety Score	Median (IQR)	4.00 (6.00)	10.00 (5.00)	5.00 (7.00)
MoCA Cognition Score	Median (IQR)	27.00 (4.00)	26.00 (3.00)	27.00 (4.00)
IES-R Psychological Distress Score	Median (IQR)	1.00 (12.00)	30.00 (44.00)	1.00 (16.00)
Social Ties Checklist Score	Median (IQR)	5.00 (2.00)	5.00 (2.00)	5.00 (3.00)

SD = standard deviation, IQR = inter-quartile range, PSE = Post-Stroke Emotionalism, TEARS-Q = Testing for Emotionalism After Recent Stroke Questionnaire, HADS = Hospital Anxiety and Depression Scale, MoCA= Montreal Cognitive Assessment, IES-R= Impact of Events Scale-Revised

12-month Analyses: Logistic Regression

A binomial regression analysis was used to assess the probability of PSE presence at 12-months, as predicted by demographic (age and sex) and psychological variables (depression, anxiety, cognition, functional outcome, psychological distress, social functioning and TEARS-Q emotionalism score) also measured at 12-months. Preliminary checks confirmed that assumptions for logistic regression were met. Variables were entered into the model using the enter method. The regression model is summarised in Table 4.

The model indicated that 12-month TEARS-Q (emotionalism) score was positively related to PSE at 12-months (*OR* = 1.534, 95% CI [1.142, 2.061], *p* = .004), and was "small" in effect. This was statistically significant at an alpha level of .05. This meant that the presence of PSE at 12-months, as measured by the TEARS-Q screening questionnaire, made it more likely for individuals to be diagnosed with PSE at 12-months, as diagnosed by the TEARS-IV diagnostic interview.

For all other variables in the model (depression, anxiety, daily functioning, psychological distress, social functioning, cognition, age and sex), there was little evidence of association with PSE at 12-months (*p* = > .05).

Table 4

Binomial regression model for predicting the probability of PSE presence at 12-months from demographic and psychological variables also measured at 12-months

Variable	B	Standard Error	Wald	Exp (B)	95% Confidence interval for Exp (B)	P
TEARS-Q (emotionalism)	.428	.150	8.092	1.534	1.142-2.061	.004**
HADS Depression	.321	.184	3.046	1.378	.961-1.977	.081
HADS Anxiety	.116	.165	.499	1.123	.813-1.551	.480
Barthel (daily functioning)	.096	.337	.080	1.100	.568-2.131	.777
IES-R (distress)	-.003	.034	.006	.997	.933-1.066	.938
STC (social functioning)	-.017	.299	.003	.984	.548-1.767	.956
MoCA (cognition)						
Age at stroke	-.067	.058	1.320	.935	.834-1.049	.251
Sex (male)	2.155	1.367	2.486	8.628	.592-125.694	.115
Constant	-5.035	9.112	.305	.007	.581	

B = coefficients, Exp (B) = odds ratio, *SD* = standard deviation, IQR = inter-quartile range, PSE = Post-Stroke Emotionalism, TEARS-Q = Testing for Emotionalism After Recent Stroke Questionnaire, HADS = Hospital Anxiety and Depression Scale, IES-R = Impact of Events Scale-Revised, STC = Social Ties Checklist, MoCA = Montreal Cognitive Assessment
**significant at α = .05

Overall, the variability in PSE diagnosis at baseline, explained by the eight predictor variables, was 73% (R^2 = .734). The model correctly predicted 73.3% of

cases where PSE was present, and 98.9% of cases where PSE was not present, giving an overall percentage correct prediction rate of 95.2%.

12-month Analyses: Correlation

Bivariate correlation was conducted to examine the association between psychological distress at 12-months (as measured by the IES-R) and emotionalism at 12-months (as measured by the TEARS-Q).

There was a positive correlation, that was "small" in effect, between psychological distress and PSE at 12-months, which was statistically significant (r = .277, 95% CI [.086, .479], p = .004). This meant that higher IES-R scores were associated with higher TEARS-Q scores at the 12-month timepoint.

Summary of Additional Analysis Findings

At both the 6- and 12-month assessments, the only significant predictor of PSE was TEARS-Q score. This may be expected, given that both TEARS-Q and TEARS-IV were measures of emotionalism. TEARS-Q has been shown to demonstrate acceptable psychometric properties to diagnose tearful emotionalism after stroke (Broomfield et al., 2020), which this finding supports. Although several other psychological variables were included in the model which had been shown in Chapter 4 to predict *future* presence of PSE (e.g. anxiety, age and sex), the same was not found for predicting at each time point separately here. There could be several reasons for this.

Firstly, the sample included in these analyses was much smaller, with only those who had self-selected to continue in TEARS at 6- and 12-months included. Given the number of variables included in the model, it is likely that the current analyses were underpowered and therefore may not accurately reflect associations between the variables at each time point. Secondly, these results may be reflective of a pattern of change over time that could not be uncovered by the analyses here. For

example, perhaps anxiety at baseline is associated with later development of PSE, but is less likely to co-occur. Further exploration of such hypotheses is needed to draw any firm conclusions. Thirdly, more psychological variables were available in the 6- and 12-month data (e.g. psychological distress and social functioning), which were not included in baseline analyses. The addition of such variables may have masked potential associations between other variables and PSE, or weakened the association to a point of non-significance. Finally, although only one of the predictor variables were significant at each time point, the overall regression models at each timepoint were significant, and predicted a high number of PSE cases correctly. It may therefore be that rather than distinct psychological variables being more associated with PSE, a combination of psychological factors are more likely to contribute to the development and/or maintenance of PSE. Again, further exploration of such factors, ideally with a much larger sample size, is needed to confirm such hypotheses.

Correlation analyses were used to assess for an association between PTSD and PSE. At both the 6- and 12-month timepoints, there was a weak, positive correlation between PTSD and PSE, which was statistically significant. Like previous research (e.g. Calvert et al., 1999; Eccles et al., 1999; Fitzgerald et al., submitted), this suggests that there is an association between higher symptoms of PTSD and PSE. Of course, correlational analyses cannot imply causation and notably, psychological distress was not found to be a significant predictor of PSE in the regression analyses reported above. It may therefore be that rather than distress contributing directly to the presence of PSE, they are more associated in terms of an aetiological link. For example, it may be that the significant results found here are related to symptoms of irritability or avoidance being experienced with both

conditions, as noted previously. Clearly, further robust examination of potential links between PTSD and PSE are warranted, to provide a more definitive picture.

Chapter 6: Thesis Discussion and Critical Evaluation

This final chapter provides an overview of the main findings from the systematic review and meta-analysis reported in Chapter 2, and the empirical paper reported in Chapter 4. The findings from both papers are integrated, with reference made to previous literature. The strengths and weaknesses of both papers are considered, with recommendations made for future research. The clinical implications of both papers are also explored. Finally, reflections on the process of completing this thesis portfolio are provided.

Main Findings

Systematic Review and Meta-Analysis

The systematic review and meta-analysis presented in Chapter 2 aimed to provide an updated prevalence of post-traumatic stress disorder (PTSD) after stroke or transient ischemic attack (TIA). A systematic review and meta-analysis of stroke-induced PTSD was previously conducted (Edmondson et al., 2013). This review sought to combine and update the previous findings, including exploration of the methods used to assess PTSD, the length of time between the index stroke event and PTSD assessment, and differences in prevalence between stroke and TIA. Subgroup analyses and meta-regression were used to identify significant differences between the types of assessment used (self-report measure vs. clinical interview), the timing of assessment (< 12-months vs. > 12-months) and type of stroke (stroke vs. mixed samples vs. TIA). There was high heterogeneity between the studies and so a random effects model was used, and a sensitivity analysis was conducted.

After screening and data extraction, 9 new studies were identified and combined with the 9 studies included in the 2013 review. The overall weighted pooled prevalence of PTSD after stroke was 18%, 95% CI [14, 23%], indicating that PTSD is commonly experienced following stroke or TIA. The pooled prevalence

found in this review was higher than that found in the 2013 review (13%), however their review suggested two underlying prevalence rates based on the timing of assessment. Unlike the previous review, subgroup analysis and meta-regression indicated that there was no significant difference in PTSD prevalence based on the timing of assessment (< 12-months or > 12-months after stroke). Whilst concrete conclusions regarding this difference cannot be drawn, it is possible that the increased number of studies, sample size or more contemporary data included in this review contributed to variation in the findings. The findings of both reviews, however, do highlight the persistence of PTSD over time, beyond the acute phase of stroke recovery.

In addition, the analyses revealed a significant difference between prevalence rates depending on the type of assessment measure used; PTSD prevalence was higher when assessed using a self-report measure than when assessed by clinical interview. A similar pattern was highlighted in the 2013 review and has also been commonly highlighted with regards to assessing other psychiatric difficulties, such as anxiety and depression in neurological populations (e.g. Whelan-Goodinson et al., 2009; Medeiros et al., 2020; Knapp et al., 2020). Given the frequency of this problem, it begs the question as to whether self-report measures provide an accurate reflection of clinical symptomatology, particularly after neurological injury. Ideally, psychological difficulties following stroke should be assessed via diagnostic clinical interview however, this is unrealistic given the limited time and resources available within healthcare systems. For now, self-report measures can at least highlight those individuals that may require further psychological input or indeed, further, more detailed diagnostic assessment.

Finally, prevalence of PTSD varied per the type of stroke experienced by study participants. In those studies only including stroke, but excluding TIA,

prevalence was significantly higher (19%, 95% CI [12, 27%]) than studies including mixed samples of stroke and TIA (17%, 95% CI [11, 24%]). The prevalence of PTSD in studies only including TIA (15%, 95% CI [3, 34%]) was slightly lower again, although this difference did not reach statistical significance. It is likely that the small proportion of studies (and much smaller sample) of TIA survivors influenced these findings. Nonetheless, the significant difference noted between stroke samples and mixed samples of stroke and TIA, may suggest an association between the severity of stroke and development of PTSD. As stroke is often physically disabling, requires more intensive treatment and has a much longer recovery time than TIA, it may be that some aspect of the stroke itself or hospital admission increases the likelihood of PTSD development. Alternatively, aspects of the recovery journey, such as avoiding reminders of the stroke may contribute to PTSD development and/or maintenance. It is beyond the scope of this thesis to determine any firm conclusions around the mechanisms behind elevated PTSD presence after stroke, but such findings warrant further input. Perhaps this could be explored through qualitative research, to capture lived experiences.

The small range of prevalence between these groups indicated that PTSD is common following both stroke and TIA, similar to other psychiatric disorders such as anxiety and depression (Broomfield et al., 2014). Given the rapid recovery and discharge following TIA, coupled with pressured healthcare resources, these individuals are often not seen by psychology services. It is therefore possible that the needs of TIA survivors are frequently unmet with regards to psychological wellbeing.

In interpreting the findings noted, it is important to consider the high heterogeneity between the studies included. The differences in prevalence rates for individuals who had experienced a stroke and were assessed using a self-report

measure accounted for 22% of heterogeneity, however around 60% was still unaccounted for. Several factors may have contributed, for example, the range of assessment measures and cut-offs used across studies to determine PTSD, methodological issues within the studies themselves, or an additional factor that could not be identified. Whilst a degree of heterogeneity is likely in meta-analyses (Imrey, 2020), a degree of caution is required when interpreting the findings.

Empirical Paper

The empirical research paper presented in Chapter 4 aimed to explore associations between demographic variables (e.g. age and sex), psychological factors (e.g. anxiety, depression, cognition and daily functioning) and the presence of post-stroke emotionalism (PSE). More specifically, which psychological factors measured in the acute phase of stroke (within 2-weeks) predicted the likelihood of emotionalism being experienced later in the recovery journey (6- and 12-months after stroke). Associations between such variables and loss to follow-up were explored. This was achieved through secondary analyses of data from 228 participants who participated in the Testing for Emotionalism After Recent Stroke study (TEARS; Broomfield et al., 2020). TEARS was a large, longitudinal cohort study examining PSE over several timepoints (2-weeks, 6-months and 12-months after stroke). TEARS aimed to develop the first definitive description of PSE prevalence, including impact, neurological and psychological characteristics.

In the analyses conducted here, group differences between those with and without emotionalism at baseline (as measured using the TEARS diagnostic interview) were compared using t-tests and Mann Whitney-U tests. Significant differences were found between: (i) emotionalism at baseline, with those diagnosed with PSE on the TEARS interview showing a higher average score on the TEARS questionnaire, (ii) age at the time of stroke, with those diagnosed with PSE at

baseline being on average, younger in age, (iii) anxiety at baseline, with those diagnosed with PSE showing higher average anxiety scores, and (iv) depression at baseline, with those diagnosed with PSE at baseline showing higher average depression scores. These findings could be suggestive of associations and/or common co-morbidities between psychiatric disorders after stroke (anxiety, depression and emotionalism). This idea appears to fit with prior research highlighting common co-occurrences of emotionalism and other psychiatric conditions after stroke (e.g. Almhdawi et al., 2020).

To examine the predictive associations between demographic variables (e.g. age, sex, stroke type), psychological factors (e.g. emotionalism, anxiety, depression, cognition and daily functioning), and PSE at baseline, 6- and 12-months, a series of logistic regressions were used. Firstly, binomial logistic regression was used to explore baseline variables and baseline PSE. In the final model, emotionalism, depression, anxiety, age and sex accounted for 65% of the variability in baseline PSE. The model correctly predicted 94.8% of cases where PSE was present, and 75.0% of cases where PSE was not present, giving an overall percentage correct prediction rate of 89.3%. The only significant predictor was emotionalism, as measured by the TEARS questionnaire. This was mirrored in the additional analyses presented in Chapter 5, whereby the TEARS questionnaire score measured at 6- or 12-months was the only significant predictor of emotionalism (measured by the TEARS interview) at the same timepoint. Given that the TEARS questionnaire has been shown to demonstrate acceptable psychometric properties (Broomfield et al., 2020), these findings suggest that it is a suitable method of screening and potentially diagnosing PSE.

Secondly, multinomial logistic regressions were used to explore associations between personal demographics (age, sex, stroke type) and psychological variables

(anxiety, depression, functioning, cognition, and emotionalism), with outcomes at 6-months and 12-months after stroke. The three potential outcomes were: (i) No PSE, (ii) PSE present, or (iii) Lost to follow-up, with "No PSE" entered into the model as the reference category.

Anxiety and emotionalism at baseline were significant predictors of PSE at 6-months. Those with emotionalism at baseline and higher anxiety scores at baseline were more likely to experience emotionalism at 6-months. This could represent a pattern of maintenance of PSE over time, whilst also providing support for the links made previously between anxiety and PSE (e.g. Eccles et al., 1999; Calvert et al., 1998; Almhdawi et al., 2020). In addition, these findings could be related to overlap in key components of PSE and anxiety. For example, recent qualitative analyses (McAleese et al., 2019; Fitzgerald et al., submitted) highlighted a key role of uncertainty and avoidance in PSE, which are also common features in anxiety disorders.

At 12-months, age, sex and anxiety at baseline were significant predictors of PSE at 12-months. Those who were younger, male, or highly anxious at baseline were more likely to be diagnosed with PSE at 12-months. Again, this supports the idea that anxiety could be associated with the maintenance of PSE (e.g. Eccles et al., 1999; Calvert et al., 1998; Almhdawi et al., 2020). As noted, avoidance could be key in maintaining both of these conditions, potentially through preventing habituation to the social and cognitive symptoms experienced. In addition, the finding that younger stroke survivors were more likely to experience PSE at 12-months could also be a factor of both conditions. Prior research has highlighted that anxiety after stroke is more common in younger survivors (Broomfield et al., 2014). Broomfield and Colleagues hypothesised that this was associated with the psychological challenges faced by experiencing a stroke at a time in life when health is expected to be good,

and survivors may be raising a family or need to continue working full-time. Such ideas are entirely plausible in stroke survivors experiencing PSE, particularly given the noted links between PSE and anxiety, and the impact of PSE on rehabilitation and societal reintegration (e.g. distress, embarrassment, avoidance).

With regards to loss to follow-up, age and cognition were significant predictors of loss to follow-up at both 6- and 12-months. In addition, daily functioning was a significant predictor of drop-out from TEARS before the 12-month assessment. Those who were younger and were more cognitively impaired were more likely to drop-out from TEARS. This could correspond with younger stroke survivors concentrating their efforts on returning to occupational and societal roles (Edwards et al., 2018). Given that informal feedback from TEARS indicated that the amount of measures completed at each timepoint was quite burdensome, it fits that those who were busy with other rehabilitation efforts found research participation too taxing. Perhaps, for those who were less cognitively able, the challenge in completing a myriad of assessments was even more demanding. Furthermore, drop-out from TEARS could have been related to the severity of stroke or higher levels of disability as a result of stroke. Those with worse daily functioning were likely to have experienced more severe stroke, hence the increased need for support/reliance on others. Perhaps, these individuals experienced particular difficulties with participation, could have been difficult to contact or indeed, suffered further strokes or died. Unfortunately, reasons for loss to follow-up were not recorded as part of the main TEARS study, therefore it is difficult to draw any firm conclusions regarding such hypotheses.

The meta-analysis (Chapter 2) highlighted the high prevalence of PTSD after stroke (around 18%), particularly in those diagnosed with stroke and assessed by self-report. PTSD was sustained over time, beyond 12-months after the index stroke

event. The empirical paper highlighted a comparable prevalence of PSE, again sustained beyond the acute phase of stroke recovery. The empirical paper also identified several potential psychological maintaining factors of PSE which could also be relevant in the maintenance of PTSD after stroke (e.g. anxiety and avoidance). Whilst this may be due to an overlap in symptomatology (e.g. recurrent and uncontrollable episodes of emotion, avoidant responses to stroke; House et al., 1989), it is important to consider a potential aetiological link between the two.

The limitations that influence the conclusions drawn from both papers require consideration. Therefore, the meta-analysis and empirical paper will be critically evaluated, before the implications of both papers are discussed in further detail.

Critical Evaluation

Both studies summarised above contribute to the current, sparse evidence base examining PTSD and emotionalism after stroke. Previously, exploration of PTSD grouped by stroke subtype (e.g. stroke, mixed samples or TIA) had not been conducted using meta-analytic methods. The meta-analysis therefore provided an updated pooled prevalence of PTSD after stroke, whilst also extending previous research into factors that may influence the likelihood of PTSD prevalence. Additionally, support for links between PTSD and PSE have been highlighted, and further evidence regarding the development and maintenance of PSE has been discussed. Previously, in-depth exploration of psychological factors related to PSE over time had not been conducted. This study therefore provides a suitable platform from which to continue developing the evidence-base regarding PSE.

The meta-analysis extended the review conducted in 2013 in many ways. Firstly,

This meta-analysis extended the location demographic of included studies to include South America and Asia in addition to Europe and the USA. Secondly, by combining

the data from the 2013 review with this update, the sample size increased by 37%, improving precision estimates and meaning that the overall sample was no longer mostly acquired from a single study. Thirdly, the increase in sample size also allowed for further exploration of subgroups (i.e. stroke vs. TIA). However, data pooling in this review used the cut-offs reported in each study to determine prevalence, meaning that a combination of methods and reporting rates were used to determine overall prevalence. Furthermore, some subgroup comparisons were based on small sample sizes, and there was high heterogeneity between the studies which could only be partially accounted for. The high heterogeneity noted may have been a result of combining the methods used to assess and report prevalence, or methodological issues within the studies themselves. As this was also highlighted as a limitation of the 2013 review, the benefits of an increased sample and further data pooling were seen to outweigh this limitation.

In addition, this meta-analysis used several methods aimed at reducing bias. For example, screening, data extraction and quality ratings were conducted by two raters independently, of the papers included in the 2013 review and also the current update. Subjectivity was therefore reduced and the reliability of the review was improved. In addition, articles were not excluded on the basis of quality, although this may have contributed to the high heterogeneity noted. Finally, multiple databases were searched, including those allowing for grey literature to be found, although no unpublished studies were included in the final review. There is of course however, the possibility that despite thorough searching, some articles were missed or further research has been published since this review.

With regards to the empirical paper, several limitations are also notable. Firstly, this study relied on the data available from TEARS, and attrition rates were high between the timepoints of the original study. This study therefore may have

been underpowered and any interpretations should be made with this in mind. Unfortunately, reasons for loss to follow-up were not recorded in TEARS and so only hypotheses can be offered. It would be hugely advantageous for research studies to record such details, so that these can be considered in the planning and development of further research. Secondly, variability in PSE at baseline, 6-months and 12-months could only be partially accounted for in the analyses conducted for this study. It may therefore be that other demographic (e.g. ethnicity, location, marital status) or psychological variables (e.g. social support or distress at baseline) contribute to the development and/or maintenance of PSE, but could not be explored here.

Finally, several limitations of the TEARS study warrant consideration. There is a possibility of sampling bias (e.g. due to inconsistent ward admissions). In addition, the population included in TEARS were younger than the average age of stroke occurrence and most strokes were rated as either minor or moderate. The generalisability of the findings must therefore be queried. All measures, including both the TEARS-IV and the TEARS-Q were administered by the same person, at the same time. As noted previously, administering both measures of emotionalism in one sitting may have led to carryover and hence inflation of an association between the two. Furthermore, administering several measures in one sitting is likely to have been burdensome for participants and may have contributed to the high attrition rate. Potentially, consultation with patient and public involvement during the planning stages of TEARS could have highlighted and resolved this issue, ensuring that the measures and procedures were acceptable to stroke survivors.

Clinical Implications

The findings from both the meta-analysis and empirical paper provide important implications for clinical practice and service development. The high

prevalence of both PTSD and PSE is comparable to the prevalence of other, more commonly assessed psychiatric difficulties, such as anxiety and depression (Medeiros et al., 2020; Knapp et al., 2020). This highlights the need for services to screen for PTSD and PSE following stroke, particularly later in the recovery journey (i.e. beyond the acute phase of recovery in which such conditions may be considered natural reactions to the myriad of challenges faced by stroke survivors). Within stroke rehabilitation, key goals often focus on physical recovery and return to work (Edwards et al., 2018). Given the impact of PTSD or PSE on rehabilitation (e.g. extra demand on limited cognitive resources, fear of participating in physical rehabilitation, avoidance of stroke reminders, increased fatigue), it is clear that the lesser-acknowledged psychological distress and emotional difficulties should be considered by clinical teams when planning and evaluating treatment. Whilst TEARS-Q presents an acceptable screening measure for PSE (Broomfield et al., 2020), there is little consensus around the optimum measure to use for screening PTSD in stroke survivors. The meta-analysis identified several screening measures and cut-off points used in practice, which undoubtedly contributed to the heterogeneity found. It would be most advantageous for agreement to be achieved regarding PTSD screening after stroke. From the meta-analysis, it appeared that the Impact of Events Scale (IES; Weiss & Marmar, 1996) was most commonly used. Given that the IES has also been found to show acceptable psychometric properties for use in the stroke population (Creamer et al., 2003), perhaps the IES could be recognised as the typical PTSD screening tool in stroke services.

The meta-analysis also highlighted the common occurrence of PTSD following TIA, however, due to services pressures and restricted resources, TIA survivors are not routinely seen by specialist stroke psychology services. It may therefore be that the needs of this particular population are frequently unmet. Whilst

it is unrealistic to suggest that stretched stroke services begin to also screen for mood difficulties following TIA, key commissioning partners, such as local Clinical Commissioning Groups and NHS England, should be aware of such findings in the development of future services.

The empirical paper highlighted associations between anxiety and PSE. Elsewhere, associations between anxiety and PTSD after stroke have been noted (e.g. Stein et al., 2018; Goldfinger et al., 2014; Favrole et al., 2013). Clearly, there is overlap between PTSD and emotionalism (e.g. Calvert et al., 1998; Eccles et al., 1999; Fitzgerald et al., submitted), and perhaps, symptoms associated with anxiety are the key link between the two conditions. For example, irritability that coincides with PTSD and anxiety could occur as a result of uncontrolled emotion in PSE. Those experiencing symptoms of anxiety may avoid situations that present any reminder of their stroke, in turn preventing habituation to the social and cognitive consequences of PTSD or PSE.

Nonetheless, difficulties unique to the PSE experience, such as the discrepancy between internal emotions and external expression, mean that when screening for mood difficulties after stroke, PSE should be differentiated from PTSD or anxiety. Otherwise, it is difficult to capture an individual's experiences idiosyncratically, thus preventing tailored rehabilitation planning. Identification of difficulties is not enough however, as access to effective therapies is needed to prevent and/or treat symptoms of PTSD and PSE. As noted, there is little evidence for interventions aimed at either stroke-induced PTSD or PSE, thus impeding any evidence-based decisions regarding treatment from being made. Perhaps, as a starting point, well-established skills and techniques highlighted within treatment for anxiety after stroke could be explored in the treatment of PTSD and/or PSE,

including for example, psychoeducation, avoidance reversal, cognitive restructuring, or graded exposure (e.g. Chun et al., 2018).

Implications for Research

In regards to PTSD after stroke, consensus is needed regarding the optimum method of assessment and clinical threshold. Not only would this provide a more robust indication of PTSD after stroke, but also lead to greater consistency and therefore accuracy in prevalence estimates. Potentially, a range of studies using self-report measures and clinical interviews could be analysed using receiver-operated characteristic analysis, to determine ideal methodologies to be used in clinical practice and research going forwards. In addition, as noted in Chapter 2, data regarding the prevalence of PTSD after different subtypes of stroke is limited. Given the differences in pathogenic origin, severity and symptoms between ischemic and haemorrhagic stroke, it could be that one subtype of stroke particularly lends itself to the development of PTSD. Future research would therefore benefit from distinguishing between types of stroke to provide evidence to support or refute such hypotheses. Finally, it would be useful to utilise the richness of data gathered through qualitative research in capturing the stroke-induced PTSD experience. As yet, it is not known which aspects of stroke contribute to the development and/or maintenance of PTSD, for example the sudden onset of physical symptoms, experience of hospital care or ongoing difficulties following discharge. Qualitative research could therefore provide a hugely beneficial insight into PTSD after stroke, in turn contributing to useful intervention techniques where PTSD is identified.

In regards to PSE, there is a clear need for further exploration of the psychological factors that may contribute to PSE development and/or maintenance. Research into the specific barriers and facilitators to participating in rehabilitation for those with PSE would be useful in extending the knowledge regarding PSE impact. It

would be most advantageous for such research to be conducted in a longitudinal fashion, to further capture how the PSE journey changes over time, and where in said journey, interventions would be most beneficial. To aid intervention development, it would be useful to progress a biopsychosocial model of the PSE experience, however research into PSE remains in its infancy and hence, requires further evidence.

Potentially, such a model may encompass the neurobiological correlates cited above (e.g. Rabins & Arciniegas, 2007; Carota & Calabrese, 2013; Kim, 2016), as a means of providing psychoeducation regarding the impact of stroke on the brain and associated mood and emotional difficulties. In addition, it would be important to incorporate the psychological associations with PSE found here and in previous qualitative research (McAleese et al., 2019; Fitzgerald et al., manuscript in preparation). For example, the overlap between symptoms of anxiety and PSE (e.g. uncertainty, avoidance and heightened distress) and key consideration for potential coping skills/interventions (e.g. increased awareness of the range of PSE triggers, graded exposure to avoided situations, cognitive restructuring of negative beliefs related to emotionalism and associated distress and embarrassment, and potentially, acceptance based approaches aimed at instilling compassion towards the self and PSE experiences). Ultimately, future model development relies on the planning and completion of robust research studies examining such potential hypotheses.

As noted in Chapter 4, patient and public involvement in the planning of future research may be helpful in reducing attrition from longitudinal studies, therefore should be considered in future research. Co-production would also be vital in the development of psychological interventions for PSE, and we can take heed of the wider stroke literature here. For example, Rowe and Colleagues (2019) undertook comprehensive consensus process in the development of core outcome sets for visual assessment after stroke. Consisting of a 3-round Delphi survey and consensus

meeting, key stakeholders including stroke survivors, carers, clinicians and researchers were involved in all aspects of the process and hence, consideration for a range of individuals who may benefit from standardised core outcome sets in visual assessment were integrated. Using such an approach in the development of PSE interventions would be ideal, bringing together individuals with lived experience of PSE, clinicians and expert academics to co-produce a feasible and acceptable psychological treatment for PSE.

Reflections on the Process of Completing this Thesis Portfolio

My primary reflections centre around the benefits and limitations of conducting secondary analyses of pre-existing data. A key advantage of this was access to a large dataset, which had been collected longitudinally and would have been far beyond the remit of a ClinPsyD thesis. Data collection for TEARS took place over several years, and so access to this data provided a unique opportunity for this thesis. If this project had included any data collection, it would likely have been affected by the ongoing Covid-19 pandemic and had to be changed as a result. As this project did not require any further recruitment or contact with participants, it could continue as planned, proving hugely advantageous when considering the time constraints for conducting ClinPsyD theses. However, not having an active role in the data collection process may have limited my ability to consider contextual depth in interpretation of the findings, for example in exploring attrition rates in TEARS.

In addition, a wide range of assessments had been undertaken at each timepoint in TEARS, meaning that a range of hypotheses could have been tested as part of this project. Whilst providing an extensive snapshot of emotionalism after stroke, I had no control over the study design or which measures were administered at each timepoint. As such, it was difficult to directly compare some variables over time. For example, cognition was assessed using a different measure at baseline, in

comparison to 6- and 12-months, and additional psychological constructs (distress and social participation) were measured at 6- and 12-months, but not at baseline. It would have been useful for there to be more consistency in the assessments conducted at each timepoint.

Furthermore, the measures of emotionalism developed during TEARS (questionnaire and diagnostic interview) had not yet been evaluated in terms of psychometric properties at the planning stages of this thesis project. As a result (and after many failed attempts using my limited knowledge of complex statistical analyses), the analysis plan for this project was amended. Whilst there was initial disappointment that the originally planned analyses could not be undertaken, it provided a useful learning experience in the iterative processes involved in conducting research.

Whilst undertaking the analyses and write-up of this project, my clinical training placement was in an inpatient neuropsychology service, including acute stroke rehabilitation. I found that the carry-over between this project and my experiences on placement provided an invaluable opportunity for learning. For example, I had never witnessed emotionalism in a clinical setting before this placement, but found that the knowledge gained over the course of this project helped me to identify potential emotionalism and differentiate it from other psychiatric disorders after stroke. Likewise, working with individuals who were experiencing emotionalism as part of placement helped me to keep in mind their lived experiences when writing this project.

Finally, a key regret that I have with regards to this project is the lack of patient and public involvement (PPI). This was identified as a key limitation of the original TEARS study and hence, I had planned to include PPI in the analysis and write-up of this project, to ensure that it reflected lived experiences of emotional

difficulties after stroke. I had been in contact with the Stroke Association during the planning stages of this project, for assistance in identifying potential PPI collaborators. However, I neglected to follow-up with them on any progress made and the deadline for this project soon arrived. Given the opportunity again, I would certainly make PPI involvement a higher priority for completing this project.

Overall Conclusions

The meta-analysis and empirical papers presented in this thesis add to the current knowledge and understanding of post-traumatic stress disorder (PTSD) and emotionalism after stroke (PSE). It is clear that both PTSD and PSE are experienced frequently by stroke survivors, both in the acute phases of stroke and later in the recovery journey (e.g. 12-months after the index stroke event). The meta-analysis showed that stroke-induced PTSD was higher when participants had experienced stroke (in comparison to mixed samples of stroke and TIA), and when assessed by self-report measure. However, the literature examining this phenomenon is encumbered by variability in the methods used to assess PTSD and the thresholds used to determine PTSD presence. As such, future research and clinical practice would benefit from achieving consensus regarding the optimum approach and tool for assessing PTSD in stroke survivors.

The empirical project highlighted associations between symptoms of anxiety and PSE in the first year after stroke. Perhaps, the inevitable avoidance that is used as a means of coping with anxiety or PSE acts as a key maintaining factor, inhibiting progress through preventing habituation to the social and cognitive consequences of either condition. In other words, PSE could be considered a disorder of fear of crying, maintained by avoidance. Given the impact of PSE on rehabilitation and societal reintegration, further examination of the psychological constructs related to

PSE development and maintenance is crucial in progressing towards much needed, evidence-based non-pharmacological interventions.

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Appendices

A- Stroke Journal Guidelines for Authors

B- PRISMA Checklist for Systematic Review Paper

C- Systematic Review Electronic Search Strategy

D- Systematic Review Data Extraction Proforma

E- Quality Assessment Tool for Observational Cohort and Cross-sectional Studies (QATOCCS) with Guidance

F- TEARS Diagnostic Interview Schedule

G- TEARS Questionnaire

H- STROBE Checklist for Empirical Paper

I- Confirmation of Ethical Approval for Thesis Project

Appendix A: Author Guidelines for Submission to *Stroke*

New Submissions

To submit your manuscript online, please visit the journal's online manuscript submission site (http://stroke-submit.aha-journals.org), and follow the instructions for creating an author account and submitting a manuscript. Access can also be gained by visiting *Stroke* online at https://www.ahajournals.org/journal/str and selecting the Online Submissions button. If you have any questions about the online submission process, contact the Editorial Office by e-mail at stroke@strokeahajournal.org.

Basic and Translational Science

Research includes animal experiments, cell studies, biochemical, genetic and physiological investigations, and studies on the properties of drugs and materials. It also includes the development and improvement of analytical procedures, imaging procedures, gene sequencing, and the development of biometric procedures.

Authors are required to submit an online checklist requesting reporting of randomization procedures, blinding, a priori definition of inclusion and exclusion, etc. After selecting a Basic Science article type in the submission system, the form becomes available to complete as part of the submission process. If the manuscript is accepted, the form will be published as supplementary material. See "Reporting Standards for Preclinical Studies of Stroke Therapy" (Stroke. 2016;47:2435-2438) for more information.

Clinical Science

Clinical research involves interactions with patients, diagnostic clinical materials or data, or populations in any of the following areas: (1) disease mechanisms (etiopathogenesis); (2) bi-directional integrative (translational) research; (3) clinical knowledge, detection, diagnosis and natural history of disease; (4) therapeutic interventions including clinical trials of drugs, biologics, devices and instruments; (5) prevention (primary and secondary) and health promotion; (6) behavioral research; and (7) health services research, including outcomes, and cost-effectiveness.

Population Science

Epidemiology is the science that investigates the patterns, causes, and effects of health versus disease in populations or patient cohorts. This involves, but is not limited to: (1) quantification and control of morbidity and mortality; (2) high-throughput “omics” and deep DNA sequencing; (3) longitudinal observations; (4) natural experiments (Mendelian randomization); (5) validation of potential disease-causing mechanisms identified in experimental studies and generating hypotheses for mechanisms to be tested in experimental studies; (6) use of “big data”, registries and “eHealth platforms”; and (7) systems biology and pathway analysis for integrating clinical with molecular data.

Submitted manuscripts must not contain material previously published, except as an abstract, and must not be under consideration for publication elsewhere, in whole or

in part. Manuscripts should conform to "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" (N Engl J Med. 1991; 324:424-428).

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As of January 1, 2020, all corresponding authors of article accepted to AHA Journals will be required to link an ORCID iD to their profile in the AHA Journal submission system.

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Initial Review Process

Submitted manuscripts will be evaluated initially by an associate editor or consulting editor. During initial review, the associate editor will determine whether the manuscript is appropriate for a full review based on the quality, originality, scientific rigor and data presentation/analysis of the manuscript. In some instances, the associate editor may reach out to a second reviewer (generally an assistant editor or invited reviewer with topic-related expertise) for a triage review. It is anticipated that approximately 50% of the submitted manuscripts will undergo formal review and 50% will be rejected without evaluation by external reviewers. This policy reflects the stringent requirements for the acceptance of manuscripts submitted to *Stroke.*

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The editors invite submission of manuscripts that have major importance to the scientific community. To be considered for expedited publication, an article must be unique and contain information that could make a significant difference in medical practice or constitute an important advance in basic knowledge. The authors must clearly state reasons for the request in the cover letter. If the editors agree that an article should be an expedited publication, they will arrange an accelerated review and, if accepted, accelerated publication.

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To avoid actual or perceived conflict of interest, the journal uses consulting editors to handle certain manuscripts. For more details, see the Conflict-of-Interest Procedures.

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Please upload a cover letter that includes the following statement: “All authors have read and approved the submitted manuscript, the manuscript has not been submitted elsewhere nor published elsewhere in whole or in part, except as an abstract (if relevant).” The authors may include the names of up to 3 reviewers whom they do **not** want to evaluate their submission. The editor ultimately decides who reviews the manuscript. Lastly, please note any potential overlapping content submitted or accepted to another journal or conference.

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- Text, including Introduction, Methods, Results, Discussion and Summary/Conclusions
- Acknowledgments
- Sources of Funding
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 Confidence intervals should be reported instead of P values for estimated parameters, such as odds ratios and relative risks; P values should be reported only for relevant analytic tests. Authors are encouraged to avoid the pitfalls associated with the misuse of P values as measures of significance. Please refer to "The ASA's Statement on p-Values: Context, Process, and Purpose." *The American Statistician.* 2016.70;2: 129-133. http://dx.doi.org/10.1080/00031305.2016.1154108.
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 Consult the AMA Manual of Style: A Guide for Authors and Editors, 10th ed, Oxford: Oxford University Press; 2007, for style.
 Consult current issues for additional guidance on format.

Checklists

Reporting guidelines will be required for the following study designs. Please upload a completed copy of the relevant checklist to the manuscript submission area as a related file.

- Basic Science submissions: Authors are required to submit an online checklist requesting reporting of randomization procedures, blinding, a priori definition of inclusion and exclusion, etc. After selecting a Basic Science article type in the submision system, the form becomes avialable to complete as part of the submission process. If the manuscript is accepted, the form will be published as supplementary material. See Reporting Standards for Preclinical Studies of Stroke Therapy" (*Stroke*. 2016;47:2435-2438) and NIH principles and guidelines for reporting preclinical research http://www.nih.gov/about/reporting-preclinical-research.htm.
- CONSORT guidelines for Randomized Controlled Trials http://www.consort-statement.org/
- STROBE (& MOOSE) guidelines for observational studies http://www.strobe-statement.org/, with use of the RECORD extension for studies that use routinely collected health data (e.g., disease registries, eMR, administrative data)
- PRISMA (& MOOSE) guidelines for systematic reviews and meta-analyses http://www.prisma-statement.org/
- STARD guidelines for studies of diagnostic accuracy https://www.equator-network.org/reporting-guidelines/stard/

- MIAME checklist for genomic and proteomic studies http://fged.org/projects/miame/
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Abstract

 Do not cite references in the abstract.
 Limit use of acronyms and abbreviations.
 Be concise (**300** words, maximum).
 The abstract should have the following headings:
 Background and Purpose (description of rationale for study)
 Methods (brief description of methods)
 Results (presentation of significant results)
 Conclusions (succinct statement of data interpretation)
 When applicable, include a fifth heading: "Registration" Please list the URL, as well as the Unique Identifier, for the publicly accessible website on which the trial is registered. If the trial is not registered, please indicate the reason in the heading.

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Abbreviations

Please create a list of nonstandard abbreviations and nonstandard acronyms used in the manuscript text. The list should be included in the manuscript and placed after the abstract, before the Introduction. The list should be entitled "Non-standard Abbreviations and Acronyms." Its content will not count toward the word limit. *Stroke* follows AMA style for standard and non-standard abbreviations and acronyms (http://www.amamanualofstyle.com). Abbreviations should only be used on words or phrases that are repeated more than 5 times in the article. All abbreviations and acronyms should be expanded upon first use in the text, and thereafter the abbreviation/acronym should be used.

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 The following are typical main headings: Materials and Methods, Results, Discussion, and Summary.
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 Prevention of bias is important for experimental stroke research (see Macleod et al, *Stroke*.2009;40:e50-e52). For studies where the primary objective is the preclinical testing of therapies, the following checklist items must be adhered to and clearly documented in the manuscript:
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Confidence intervals should be reported instead of P values for estimated parameters, such as odds ratios and relative risks; P values should be reported only for relevant analytic tests. Authors are encouraged to avoid the pitfalls associated with the misuse of P values as measures of significance. Please refer to "The ASA's Statement on p-Values: Context, Process, and Purpose." *The American Statistician.* 2016.70;2: 129-133. http://dx.doi.org/10.1080/00031305.2016.1154108.

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Acknowledgments

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Book reference: Schermerhorn ML et al. Carotid Artery Stenting. Fischer JE, Bland KI, Callery MP, eds. In: Mastery of Surgery. Wolters Kluwer Health/Lippincott Williams & Wilkins; 2007.

Website reference: Stroke Death Rates, Hispanics Age 65+. Quick Maps of Heart Disease and Stroke. National Center for Chronic Disease Prevention and Health

Promotion, Division for Heart Disease and Stroke Prevention. https://www.cdc.gov/dhdsp/maps/national_maps/stroke65_hispanics.htm. Accessed July 26, 2019.

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 The combined total number of figures and tables is limited to 6 (3 for Brief Reports). Each figure may contain up to 6 panels (i.e., parts A to F) and must conform to the requirements for figures described below.
 Authors should be pleased with the figure submission quality before submission. We recommend that you print the figure at its final publication size to check the quality.
 Figures should be submitted as high-resolution TIFF or EPS files. PowerPoint files are discouraged because elements within the figure (such as axis labels) may shift location or drop out during conversion. Further, do not create figures in Powerpoint because even if you convert to a different file type, the resolution will be too low for publication. JPEG, Word, PPT, and Excel files should not be used. See **Artwork and Table Guidelines** (PDF) for instructions for creating high-quality digital art.
 Figures should be supplied at the highest resolution possible for optimal clarity. Color figures should be at least 300 dpi; halftones, 600 dpi; and line art, 1200 dpi.
 Figures should be submitted at the final publication size. Please note that most figures will be sized at 1 column wide. Dimensions for figures are:

- 1 column: 3.25 inches wide (8 cm or 19.5 picas)
- 2 columns: 6.80 inches wide (17.272 cm or 40.8 picas)

 Color figures should be in RGB (red/green/blue) mode. If a figure is supplied in CMYK (cyan/magenta/yellow/black) mode, there may be a shift in the appearance of colors, especially fluorescents. Figures that will appear in black and white should be submitted in black and white.
 For line and bar graphs and pie charts, ensure that the colors/lines/symbols used for the different sets of data are easily distinguishable. Hair lines are hard to reproduce as are lines that are too thick, as they may make it hard to distinguish between the coordinates.
 Graphs and charts should have a white background.
 Labels for panels should be uppercase letters (A, B, C, D, E, F) in boldface Arial or Helvetica.
 Multipart figures may have no more than 4 panels (i.e., A, B, C, D, E, F).
 Multipart figures may be set at 2 columns across the page and should be laid out horizontally if appropriate.

 Use the same font (typeface) throughout the figure. Sans serif fonts, such as Arial and Helvetica, work best.
 Use the largest font size possible without distorting the figures. Text for super- or subscripts should be no smaller than 6 points.
 Whenever possible, all text within a figure should be the same size. If this is not possible, the font size should vary by no more than 2 points.
 Label units of measure consistently with the text and legend. Follow the AMA for unit abbreviations.
 Incorporate figure keys into the legend rather than including them as part of the figure whenever possible.
 Avoid heading/Title on the figure. Title information should be included in the figure legends.
 Any abbreviations or symbols used in the figures must be defined in the figure or figure legend.
 Follow AMA 9th edition for footnote style in legends.
 If the figure is reprinted/adapted from another source, please provide a permission letter and include the source in the legend as noted above.
 Supply a scale bar with photomicrographs.
 Authors are responsible for the cost of printing color illustrations. Authors are also responsible for obtaining from the copyright holder permission to reproduce previously published artwork.
 See AMA, 10th edition, Section 4.2 for more information on figures.

Graphic Abstract

Updated October 2020: The intent of the graphic abstract is to provide readers with a succinct summary of the study in a form that facilitates its dissemination in presentations. It can be submitted on first submisison, but is an absolute requirement for revision submissions of Basic and Translational Science Original submissions and **starting January 2021** for Clinical and Population Science Original submisisons.

 A single figure panel/diagram/cartoon.
 Emphasize the new findings in the paper and clinical implications.
 Size: The submitted document should be no larger than 18 cm (7 inches) square.
 Font: Prefer a san serif font that is no less than 12 point. Use the largest font size possible without distorting the figure.
 A legend of no more than 50-100 words is optional.
 Do not include tabular items; all content should be graphical.
 Please upload as Supplemental Material as a JPG file format. This is separate from the single Supplemental PDF containing additional manuscript content noted below.

Supplemental Material

 This optional section provides an opportunity for authors to present supporting materials to the manuscript. The manuscript appears both in the print version and online, whereas Supplemental material are independent from the manuscript and appear only online in the format submitted by the authors. Supplemental material undergoes peer review and must be submitted simultaneously with original submissions.

 Any collaborators who need to be cross-referenced in PubMed should be listed either as authors or, for study groups, in the main manuscript file as an Appendix. This information is included in the word count. If contributors do not need to be listed as authors or cross-referenced in PubMed, then they may be included in a PDF Supplemental Material File.
 The guidelines below should be used for supplemental material:
 Material to be published as an online only supplement should be uploaded online as a single PDF. An exception to this would be if the online supplement is a video file (.mov, .AVI, .mp4, .m4v, .mp4v) or an Excel file that contains too much material (e.g., hundreds of rows and columns that cross muliple pages) to convert to PDF and still be easily readable.
 The supplemental material should have a title page with the label of SUPPLEMENTAL MATERIAL above the title. The supplemental material to be included in this PDF is as follows: Supplemental Methods, Supplemental Tables, Supplemental Figures and Figure Legends, and Supplemental References. If applicable, the legends for the Video files should also be included in this PDF.
 The supplement should be single-spaced.
 Supplementary Materials should NOT include a separate reference list and all citations in the Supplemental Materials should be included in the main reference list.
In the manuscript text, following the Acknowledgments, Sources of Funding, & Disclosures section, please include a list of the supplemental materials with a callout to any references that are in the Supplemental Material only, for example:

- Supplemental Materials
- Expanded Materials & Methods
- Online Figures I – IV
- Online Video I
- Data Set
- References 34-39

 Number supplementary figures and tables as Figure I, Figure II, Table I, Table II, etc.
 Place the supplemental figure legend underneath the corresponding figure.
 When referring to online-only material in the print version of the manuscript, use the phrase “please see https://www.ahajournals.org/journal/str”
 Supplemental Material appears only online and will not appear in reprints of the article. The Editorial Office is not responsible for converting files to PDF.

Appendix B: PRISMA Checklist for Systematic Review Submission

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 3-5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 6
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 7
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 6-7
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 6-7
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 8
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 8
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 8
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 8
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 8-9
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 9-10
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 8
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 9-10
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 9
	13d	Describe any methods used to synthesize results and provide a	Page 9-

Section and Topic	Item #	Checklist item	Location where item is reported
		rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	10
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 9-10
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 9-10
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 19
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 9-10
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 10-11
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 11
Study characteristics	17	Cite each included study and present its characteristics.	Page 13
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page 13
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Page 13
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 24
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Pages 14-19
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Pages 14-19
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Page 14
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page 19
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Page 19
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 21-22
	23b	Discuss any limitations of the evidence included in the review.	Page 22-23
	23c	Discuss any limitations of the review processes used.	Page 23-24
	23d	Discuss implications of the results for practice, policy, and future research.	Pages 24-26
OTHER INFORMATION			
Registration	24a	Provide registration information for the review, including register name and registration number, or state that the review	Page 6

Section and Topic	Item #	Checklist item	Location where item is reported
and protocol		was not registered.	
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 6
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 27
Competing interests	26	Declare any competing interests of review authors.	Page 27
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 10

Appendix C: Full Electronic Search Strategy for Systematic Review

Search Terms

Database	Search String 1 (PTSD)	And/ Or	Search String 2 (Stroke or TIA)
Pubmed	((“traumatic stress disorder”).ti,ab OR (ptsd).ti,ab or (post-traumatic).ti,ab OR (posttraumatic).ti,ab OR (post adj traumatic).ti,ab OR (traumatic adj stress).ti,ab)	**AND**	((stroke).ti,ab OR (stroke*).ti,ab OR (CVA).ti,ab OR (cerebrovascular*).ti,ab OR ((brain OR vascular OR lacunar OR venous OR cerebral OR isch?mic) adj2 (accident* OR infarct* OR event* OR attack*)).ti,ab OR TIA.ti,ab)
AMED	As Pubmed above	**AND**	As Pubmed above
CINAHL	TI (“ptsd” OR “post-traumatic” OR “posttraumatic” OR “post traumatic” OR “traumatic stress” OR “stress disorder”)	**AND**	TI (stroke OR stroke* OR “CVA” OR cerebrovascular* OR “(brain OR vascular OR lacunar OR venous OR cerebral OR isch?mic) adj2 (accident* OR infarct* OR event* OR attack*)” OR “TIA”)
PsychInfo	As Pubmed above	**AND**	As Pubmed above
ProQuest	ALL (ptsd OR post-traumatic OR	**AND**	ALL (stroke OR stroke* OR “CVA” OR

	posttraumatic OR "traumatic stress" OR "stress disorder"). Search limited to dissertations and thesis.		cerebrovascular* OR isch?mic OR "TIA"). Search limited to dissertations and thesis.
The Cochrane Library	(("traumatic stress disorder").ti,ab,kw OR (ptsd).ti,ab,kw or (post-traumatic).ti,ab,kw OR (posttraumatic).ti,ab,kw OR (post adj traumatic).ti,ab,kw OR (traumatic adj stress).ti,ab,kw)	**AND**	((stroke).ti,ab,kw OR (stroke*).ti,ab,kw OR (CVA).ti,ab,kw OR (cerebrovascular*).ti,ab,kw OR ((brain OR vascular OR lacunar OR venous OR cerebral OR isch?mic) adj2 (accident* OR infarct* OR event* OR attack*)).ti,ab,kw OR TIA.ti,ab,kw)
N.B. ti= title, ab= abstract, ALL= anywhere except full text, kw= keywords			

Appendix D: Data Extraction Proforma for Systematic Review and Meta-Analysis

Source: Author/ year/ title	PTSD prevalence (%)	PTSD prevalence (n)	Total sample size (*N*)	PTSD measure used to establish diagnosis	Clinical Interview conducted? Y/N	Type of stroke experienced by participants	Time between stroke and PTSD assessment (months)	Mean age of sample (*SD*)	Location of study	Male (total number and %)	Study type (e.g. cross-sectional or cohort)	Recruited from? E.g. In hospital/ outpatient clinic
Example: Bruggiman 2006. Chronic posttraumatic stress symptoms after non-severe stroke	31	15	49	IES	N	First non-severe stroke	1-12months	51 (16.2)	Switzerland	33 (67)	Cross-sectional	NR

Appendix E: Quality Assessment Tool for Observation Cohort and Cross-sectional Studies (Blank)

Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies

Criteria	Yes	No	Other (CD/NR/NA)
1. Was the research question or objective in this paper clearly stated?			
2. Was the study population clearly specified and defined?			
3. Was the participation rate of eligible persons at least 50%?			
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			
5. Was a sample size justification, power description, or variance and effect estimates provided?			
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?			
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?			
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?			
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
10. Was the exposure(s) assessed more than once over time?			

11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
12. Were the outcome assessors blinded to the exposure status of participants?			
13. Was loss to follow-up after baseline 20% or less?			
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?			

*CD, cannot determine; NA, not applicable; NR, not reported

Quality Rating (Good, Fair or Poor)	
Rater 1 initials	
Rater 2 initials	
Additional Comments	

Guidance for Using QATOCCS as a Method of Assessing Quality.

Guidance for Assessing the Quality of Observational Cohort and Cross-Sectional Studies

The guidance document below is organized by question number from the tool for quality assessment of observational cohort and cross-sectional studies.

Question 1. Research question

Did the authors describe their goal in conducting this research? Is it easy to understand what they were looking to find? This issue is important for any scientific paper of any type. Higher quality scientific research explicitly defines a research question.

Questions 2 and 3. Study population

Did the authors describe the group of people from which the study participants were selected or recruited, using demographics, location, and time period? If you were to conduct this study again, would you know who to recruit, from where, and from what time period? Is the cohort population free of the outcomes of interest at the time they were recruited?

An example would be men over 40 years old with type 2 diabetes who began seeking medical care at Phoenix Good Samaritan Hospital between January 1, 1990 and December 31, 1994. In this example, the population is clearly described as: (1) who (men over 40 years old with type 2 diabetes); (2) where (Phoenix Good Samaritan Hospital); and (3) when (between January 1, 1990 and December 31, 1994). Another example is women ages 34 to 59 years of age in 1980 who were in the nursing profession and had no known coronary disease, stroke, cancer, hypercholesterolemia, or diabetes, and were recruited from the 11 most populous States, with contact information obtained from State nursing boards.

In cohort studies, it is crucial that the population at baseline is free of the outcome of interest. For example, the nurses' population above would be an appropriate group in which to study incident coronary disease. This information is usually found either in descriptions of population recruitment, definitions of variables, or inclusion/exclusion criteria.

You may need to look at prior papers on methods in order to make the assessment for this question. Those papers are usually in the reference list.

If fewer than 50% of eligible persons participated in the study, then there is concern that the study population does not adequately represent the target population. This increases the risk of bias.

Question 4. Groups recruited from the same population and uniform eligibility criteria

Were the inclusion and exclusion criteria developed prior to recruitment or selection of the study population? Were the same underlying criteria used for all of the subjects involved? This issue is related to the description of the study population, above, and you may find the information for both of these questions in the same section of the paper.

Most cohort studies begin with the selection of the cohort; participants in this cohort are then measured or evaluated to determine their exposure status. However, some cohort studies may recruit or select exposed participants in a different time or place than unexposed participants, especially retrospective cohort studies–which is when data are obtained from the past (retrospectively), but the analysis examines exposures prior to outcomes. For example, one research question could be whether diabetic men with clinical depression are at higher risk for cardiovascular disease than those without clinical depression. So, diabetic men with depression might be selected from a mental health clinic, while diabetic men without depression might be selected from an internal medicine or endocrinology clinic. This study recruits groups from different clinic populations, so this example would get a "no."

However, the women nurses described in the question above were selected based on the same inclusion/exclusion criteria, so that example would get a "yes."

Question 5. Sample size justification

Did the authors present their reasons for selecting or recruiting the number of people included or analyzed? Do they note or discuss the statistical power of the study? This question is about whether or not the study had enough participants to detect an association if one truly existed.

A paragraph in the methods section of the article may explain the sample size needed to detect a hypothesized difference in outcomes. You may also find a discussion of power in the discussion section (such as the study had 85 percent power to detect a

20 percent increase in the rate of an outcome of interest, with a 2-sided alpha of 0.05). Sometimes estimates of variance and/or estimates of effect size are given, instead of sample size calculations. In any of these cases, the answer would be "yes." However, observational cohort studies often do not report anything about power or sample sizes because the analyses are exploratory in nature. In this case, the answer would be "no." This is not a "fatal flaw." It just may indicate that attention was not paid to whether the study was sufficiently sized to answer a prespecified question– i.e., it may have been an exploratory, hypothesis-generating study.

Question 6. Exposure assessed prior to outcome measurement

This question is important because, in order to determine whether an exposure causes an outcome, the exposure must come before the outcome.

For some prospective cohort studies, the investigator enrolls the cohort and then determines the exposure status of various members of the cohort (large epidemiological studies like Framingham used this approach). However, for other cohort studies, the cohort is selected based on its exposure status, as in the example above of depressed diabetic men (the exposure being depression). Other examples include a cohort identified by its exposure to fluoridated drinking water and then compared to a cohort living in an area without fluoridated water, or a cohort of military personnel exposed to combat in the Gulf War compared to a cohort of military personnel not deployed in a combat zone.

With either of these types of cohort studies, the cohort is followed forward in time (i.e., prospectively) to assess the outcomes that occurred in the exposed members compared to nonexposed members of the cohort. Therefore, you begin the study in the present by looking at groups that were exposed (or not) to some biological or behavioral factor, intervention, etc., and then you follow them forward in time to examine outcomes. If a cohort study is conducted properly, the answer to this

question should be "yes," since the exposure status of members of the cohort was determined at the beginning of the study before the outcomes occurred.

For retrospective cohort studies, the same principal applies. The difference is that, rather than identifying a cohort in the present and following them forward in time, the investigators go back in time (i.e., retrospectively) and select a cohort based on their exposure status in the past and then follow them forward to assess the outcomes that occurred in the exposed and nonexposed cohort members. Because in retrospective cohort studies the exposure and outcomes may have already occurred (it depends on how long they follow the cohort), it is important to make sure that the exposure preceded the outcome.

Sometimes cross-sectional studies are conducted (or cross-sectional analyses of cohort-study data), where the exposures and outcomes are measured during the same timeframe. As a result, cross-sectional analyses provide weaker evidence than regular cohort studies regarding a potential causal relationship between exposures and outcomes. For cross-sectional analyses, the answer to Question 6 should be "no."

Question 7. Sufficient timeframe to see an effect

Did the study allow enough time for a sufficient number of outcomes to occur or be observed, or enough time for an exposure to have a biological effect on an outcome? In the examples given above, if clinical depression has a biological effect on increasing risk for CVD, such an effect may take years. In the other example, if higher dietary sodium increases BP, a short timeframe may be sufficient to assess its association with BP, but a longer timeframe would be needed to examine its association with heart attacks.

The issue of timeframe is important to enable meaningful analysis of the relationships between exposures and outcomes to be conducted. This often requires

at least several years, especially when looking at health outcomes, but it depends on the research question and outcomes being examined.

Cross-sectional analyses allow no time to see an effect, since the exposures and outcomes are assessed at the same time, so those would get a "no" response.

Question 8. Different levels of the exposure of interest

If the exposure can be defined as a range (examples: drug dosage, amount of physical activity, amount of sodium consumed), were multiple categories of that exposure assessed? (for example, for drugs: not on the medication, on a low dose, medium dose, high dose; for dietary sodium, higher than average U.S. consumption, lower than recommended consumption, between the two). Sometimes discrete categories of exposure are not used, but instead exposures are measured as continuous variables (for example, mg/day of dietary sodium or BP values).

In any case, studying different levels of exposure (where possible) enables investigators to assess trends or dose-response relationships between exposures and outcomes–e.g., the higher the exposure, the greater the rate of the health outcome. The presence of trends or dose-response relationships lends credibility to the hypothesis of causality between exposure and outcome.

For some exposures, however, this question may not be applicable (e.g., the exposure may be a dichotomous variable like living in a rural setting versus an urban setting, or vaccinated/not vaccinated with a one-time vaccine). If there are only two possible exposures (yes/no), then this question should be given an "NA," and it should not count negatively towards the quality rating.

Question 9. Exposure measures and assessment

Were the exposure measures defined in detail? Were the tools or methods used to measure exposure accurate and reliable–for example, have they been validated or are they objective? This issue is important as it influences confidence in the reported

exposures. When exposures are measured with less accuracy or validity, it is harder to see an association between exposure and outcome even if one exists. Also as important is whether the exposures were assessed in the same manner within groups and between groups; if not, bias may result.

For example, retrospective self-report of dietary salt intake is not as valid and reliable as prospectively using a standardized dietary log plus testing participants' urine for sodium content. Another example is measurement of BP, where there may be quite a difference between usual care, where clinicians measure BP however it is done in their practice setting (which can vary considerably), and use of trained BP assessors using standardized equipment (e.g., the same BP device which has been tested and calibrated) and a standardized protocol (e.g., patient is seated for 5 minutes with feet flat on the floor, BP is taken twice in each arm, and all four measurements are averaged). In each of these cases, the former would get a "no" and the latter a "yes."

Here is a final example that illustrates the point about why it is important to assess exposures consistently across all groups: If people with higher BP (exposed cohort) are seen by their providers more frequently than those without elevated BP (nonexposed group), it also increases the chances of detecting and documenting changes in health outcomes, including CVD-related events. Therefore, it may lead to the conclusion that higher BP leads to more CVD events. This may be true, but it could also be due to the fact that the subjects with higher BP were seen more often; thus, more CVD-related events were detected and documented simply because they had more encounters with the health care system. Thus, it could bias the results and lead to an erroneous conclusion.

Question 10. Repeated exposure assessment

Was the exposure for each person measured more than once during the course of the study period? Multiple measurements with the same result increase our confidence that the exposure status was correctly classified. Also, multiple measurements enable investigators to look at changes in exposure over time, for example, people who ate high dietary sodium throughout the follow up period, compared to those who started out high then reduced their intake, compared to those who ate low sodium throughout. Once again, this may not be applicable in all cases. In many older studies, exposure was measured only at baseline. However, multiple exposure measurements do result in a stronger study design.

Question 11. Outcome measures

Were the outcomes defined in detail? Were the tools or methods for measuring outcomes accurate and reliable–for example, have they been validated or are they objective? This issue is important because it influences confidence in the validity of study results. Also important is whether the outcomes were assessed in the same manner within groups and between groups.

An example of an outcome measure that is objective, accurate, and reliable is death–the outcome measured with more accuracy than any other. But even with a measure as objective as death, there can be differences in the accuracy and reliability of how death was assessed by the investigators. Did they base it on an autopsy report, death certificate, death registry, or report from a family member? Another example is a study of whether dietary fat intake is related to blood cholesterol level (cholesterol level being the outcome), and the cholesterol level is measured from fasting blood samples that are all sent to the same laboratory. These examples would get a "yes." An example of a "no" would be self-report by subjects that they had a heart attack, or self-report of how much they weigh (if body weight is the outcome of interest).

Similar to the example in Question 9, results may be biased if one group (e.g., people with high BP) is seen more frequently than another group (people with normal BP) because more frequent encounters with the health care system increases the chances of outcomes being detected and documented.

Question 12. Blinding of outcome assessors

Blinding means that outcome assessors did not know whether the participant was exposed or unexposed. It is also sometimes called "masking." The objective is to look for evidence in the article that the person(s) assessing the outcome(s) for the study (for example, examining medical records to determine the outcomes that occurred in the exposed and comparison groups) is masked to the exposure status of the participant. Sometimes the person measuring the exposure is the same person conducting the outcome assessment. In this case, the outcome assessor would most likely not be blinded to exposure status because they also took measurements of exposures. If so, make a note of that in the comments section.

As you assess this criterion, think about whether it is likely that the person(s) doing the outcome assessment would know (or be able to figure out) the exposure status of the study participants. If the answer is no, then blinding is adequate. An example of adequate blinding of the outcome assessors is to create a separate committee, whose members were not involved in the care of the patient and had no information about the study participants' exposure status. The committee would then be provided with copies of participants' medical records, which had been stripped of any potential exposure information or personally identifiable information. The committee would then review the records for prespecified outcomes according to the study protocol. If blinding was not possible, which is sometimes the case, mark "NA" and explain the potential for bias.

Question 13. Follow up rate

Higher overall follow up rates are always better than lower follow up rates, even though higher rates are expected in shorter studies, whereas lower overall follow up rates are often seen in studies of longer duration. Usually, an acceptable overall follow up rate is considered 80 percent or more of participants whose exposures were measured at baseline. However, this is just a general guideline. For example, a 6-month cohort study examining the relationship between dietary sodium intake and BP level may have over 90 percent follow up, but a 20-year cohort study examining effects of sodium intake on stroke may have only a 65 percent follow up rate.

Question 14. Statistical analyses

Were key potential confounding variables measured and adjusted for, such as by statistical adjustment for baseline differences? Logistic regression or other regression methods are often used to account for the influence of variables not of interest.

This is a key issue in cohort studies, because statistical analyses need to control for potential confounders, in contrast to an RCT, where the randomization process controls for potential confounders. All key factors that may be associated both with the exposure of interest and the outcome–that are not of interest to the research question–should be controlled for in the analyses.

For example, in a study of the relationship between cardiorespiratory fitness and CVD events (heart attacks and strokes), the study should control for age, BP, blood cholesterol, and body weight, because all of these factors are associated both with low fitness and with CVD events. Well-done cohort studies control for multiple potential confounders.

Some general guidance for determining the overall quality rating of observational cohort and cross-sectional studies

The questions on the form are designed to help you focus on the key concepts for evaluating the internal validity of a study. They are not intended to create a list that you simply tally up to arrive at a summary judgment of quality.

Internal validity for cohort studies is the extent to which the results reported in the study can truly be attributed to the exposure being evaluated and not to flaws in the design or conduct of the study–in other words, the ability of the study to draw associative conclusions about the effects of the exposures being studied on outcomes. Any such flaws can increase the risk of bias.

Critical appraisal involves considering the risk of potential for selection bias, information bias, measurement bias, or confounding (the mixture of exposures that one cannot tease out from each other). Examples of confounding include co-interventions, differences at baseline in patient characteristics, and other issues throughout the questions above. High risk of bias translates to a rating of poor quality. Low risk of bias translates to a rating of good quality. (Thus, the greater the risk of bias, the lower the quality rating of the study.)

In addition, the more attention in the study design to issues that can help determine whether there is a causal relationship between the exposure and outcome, the higher quality the study. These include exposures occurring prior to outcomes, evaluation of a dose-response gradient, accuracy of measurement of both exposure and outcome, sufficient timeframe to see an effect, and appropriate control for confounding–all concepts reflected in the tool.

Generally, when you evaluate a study, you will not see a "fatal flaw," but you will find some risk of bias. By focusing on the concepts underlying the questions in the quality assessment tool, you should ask yourself about the potential for bias in the study you are critically appraising. For any box where you check "no" you should ask, "What is the potential risk of bias resulting from this flaw in study design or

execution?" That is, does this factor cause you to doubt the results that are reported in the study or doubt the ability of the study to accurately assess an association between exposure and outcome?

The best approach is to think about the questions in the tool and how each one tells you something about the potential for bias in a study. The more you familiarize yourself with the key concepts, the more comfortable you will be with critical appraisal. Examples of studies rated good, fair, and poor are useful, but each study must be assessed on its own based on the details that are reported and consideration of the concepts for minimizing bias.

Appendix F: Testing for Emotionalism After Recent Stroke Diagnostic Interview (TEARS-IV)

Testing for Emotionalism After Recent Stroke-Case Interview (TEARS-IV)

******SWITCH ON DIGITAL RECORDER NOW******

A. Introduction

Hello. Stroke can sometimes cause changes to emotions (that is, how we feel inside) or emotional expression (that is, how we show our emotions - in particular through crying and laughter). In this interview, I am going to ask some screening questions first about crying, then about laughter, to see if this has been a problem for you since the stroke. If it has, I will also ask you some more detailed questions, is that OK?

B. Post-Stroke Crying: Screen Questions

OK, so first I am going to ask you some YES/NO questions about crying since the stroke.

(i) Have you felt more tearful **in the past two weeks** than before the stroke?

◯NO ◯YES***

(ii) Have you actually cried more **in the past two weeks** than before the stroke, not just felt like it?

◯NO ◯YES***

***** If response is YES on <u>either</u> item (i) or item (ii), complete sections C-E.***

If response is NO to both items (i) and (ii), go to section F.

C. Post-Stroke Crying: Case Characteristics

I will now ask you more about your emotions since the stroke and about how you express those emotions especially in tears - any changes to these, how this affects you and what you do.

If any questions are especially upsetting and you do not wish to continue, please say.

I will record your responses on this sheet, to help me remember. I will also record the interview using this hand held digital recorder. Is that Okay?

To start, let's talk about your emotions and emotional expression, in particular crying, since the stroke, in more detail.

I. What have your emotions and emotional expression, in particular crying, been like since the stroke?

Prompt: So have you changed in any way then? What is that like? Does it make sense, this idea of how we feel inside being different sometimes from how we express our feelings?

II. Have you been more tearful since the stroke than you were beforehand?

Prompt: What is that like? Can you say how often? Was this a pattern just following the stroke, but not now? Can you tell me more?

III. Have you actually cried more in the past month? (not just felt like it?)

Prompt: You said sometimes. How often is that? What is that like? Can you tell me more?

IV. What are the crying episodes actually like? Does the weepiness come suddenly, at times when you aren't expecting it? Suddenly means with only a few minutes no warning, not after several minutes trying to control yourself.

Prompt: Does that happen?

What is that like?

How often does that happen?

If you have episodes of crying, do you tend to sob loudly?

Can you tell me more?

V. If you feel the tears coming on, or if they have started, can you control yourself to stop them?

Prompt: So can you sometimes put it off by trying to control it? What helps?

So for instance, have you been able to stop yourself crying in front of other people? What did you do?

What was that like? Can you tell me more?

OK, thinking again about the past two weeks:

has the crying come on suddenly, with only a few seconds or no warning?

◯NO ◯YES

has the crying occurred at times you were not expecting it?

◯NO ◯YES

has the crying come on even if you did not feel sad at the time?

◯NO ◯YES

And again thinking about the past two weeks:

when the crying occurred, could you control yourself to stop it?

◯NO ◯YES

did the crying come on in situations you would not have cried in before the stroke?

◯NO ◯YES

D. Frequency and Impact of Crying

OK, now I am going to ask more about the frequency and impact of the crying episodes

Thinking about the past two weeks:

(i) Exactly how often have you experienced crying episodes?

◯ rare- less than once per week

◯ sometimes- at least once per week

◯ often- several times per week but less than every day

◯ very often- more than once per day

(ii) Approximately how long have the crying episodes lasted?

◯ just a few seconds

◯ up to one minute

◯ several minutes

◯ ten minutes or more

(iii) How distressing have you found the crying episodes?

◯ minimal/not distressing

◯ moderately distressing

◯ very distressing

◯ very severely distressing

◯ unsure

(iv) How embarrassing have you found the crying episodes?

◯ minimally/not embarrassing

◯ moderately embarrassing

◯ very embarrassing

◯ very severely embarrassing

◯ unsure

(v) Again, thinking about the past two weeks, have any of the following events set off/triggered the crying episodes:

Happy news item	◯NO	◯YES
Sad news item	◯NO	◯YES
Distressing news item	◯NO	◯YES
Emotional news item	◯NO	◯YES
Sentimental news item	◯NO	◯YES
Having happy memories in mind	◯NO	◯YES
Having sad memories in mind	◯NO	◯YES
Having distressing memories in mind	◯NO	◯YES
Having emotional memories in mind	◯NO	◯YES
Having sentimental memories in mind	◯NO	◯YES
Talking about the stroke	◯NO	◯YES
Talking about crying since the stroke	◯NO	◯YES
A kind word from others	◯NO	◯YES

Have any factors not listed here set off the crying episodes, please specify:

(vi) Again, thinking of the past two weeks, have the crying episodes stopped you from doing anything?

◯NO ◯YES

If Yes, which three activities has the crying episodes most stopped you doing (e.g. meeting new people, meeting familiar people, going out, answering the telephone?)

Specify:

1.

2.

3.

(vi) Thinking of the past two weeks, have crying episodes caused you to avoid people or situations?

◯NO ◯YES

(vii) Specifically due to your crying episodes, have you avoided any of the following situations?

Speaking to/seeing family	◯NO NOT AVOIDED	◯YES AVOIDED
Speaking to/seeing close friends	◯NO NOT AVOIDED	◯YES AVOIDED
Speaking to/seeing acquaintances	◯NO NOT AVOIDED	◯YES AVOIDED
Speaking to people you do not know	◯NO NOT AVOIDED	◯YES AVOIDED
Speaking to health professionals	◯NO NOT AVOIDED	◯YES AVOIDED
Speaking on the telephone	◯NO NOT AVOIDED	◯YES AVOIDED
Going into shops	◯NO NOT AVOIDED	◯YES AVOIDED
Going into restaurants	◯NO NOT AVOIDED	◯YES AVOIDED
Going to parties, receptions	◯NO NOT AVOIDED	◯YES AVOIDED
Going to public places (cinema, theatre, transport)	◯NO NOT AVOIDED	◯YES AVOIDED

(viii) Which three situations have you **most avoided** because of the crying episodes?

Specify:

1.

2.

3.

E. Coping Strategies for Crying

OK, now I am going to ask what you and others do to cope with the crying episodes.

Thinking about the crying episodes in the past two weeks:

(i) Have you used any of the following strategies to try and stop/limit the crying episodes?

Looking away	◯NO ◯YES
Hiding behind a book or newspaper	◯NO ◯YES
Leaving a room	◯NO ◯YES
Trying to think of something else	◯NO ◯YES
Controlling your breathing	◯NO ◯YES
Trying to relax	◯NO ◯YES
Counting to ten	◯NO ◯YES
Covering your face with your hands	◯NO ◯YES

If Yes, can you describe which three main methods you use most:

1.

2.

3.

(iii) Of the strategies that you have used to try and stop crying episodes, have any actually helped?

Looking away tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not
Hiding behind the newspaper tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not
Leaving the room tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not
Thinking of something else tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not
Controlling your breathing tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not

Relaxing tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not
Counting to ten tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not
Covering your face with hands tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not

Which other strategies, not mentioned above, have you found helpful to stop/limit crying episodes?

1.

2.

3.

(iv) Have other people used any of the following to try and stop/limit the crying episodes?

Ignoring you are crying	◯ Yes, others tried	◯ No, others not tried
Talking about something else	◯ Yes, others tried	◯ No, others not tried
Distracting you off the crying	◯ Yes, others tried	◯ No, others not tried
Comforting you	◯ Yes, others tried	◯ No, others not tried
Reassuring you	◯ Yes, others tried	◯ No, others not tried

(v) Which of these strategies tried by other people have helped?

Ignoring you are crying tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not
Talking about something else tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not
Distracting you off the crying tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not
Comforting you tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not
Reassuring you tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not

Which strategies used by others, not mentioned above, have been helpful to stop/limit the crying episodes?

1.

2.

3.

F. Post-Stroke Laughter: Screen Questions

It may seem unusual, because stroke is something people usually find upsetting, but some people find that they might laugh more than they did before the stroke, or switch suddenly between laughing and crying.

(i) Have you noticed difficulty controlling laughter outbursts **in the past two weeks**, more than before the stroke?

◯NO ◯YES**

(ii) Have you actually suddenly laughed out loud **in the past two weeks**, not just felt like it?

◯NO ◯YES**

***** If response is YES on <u>either</u> item (i) or item (ii), complete section G.***

If response is NO to both items (i) and (ii), go to section H.

G. Post-Stroke Laughter: Case Characteristics

I will now ask you more about your emotions since the stroke and about how you express those emotions in laughter - any changes to these, how this affects you and what you do.

OK, thinking again about the past two weeks:

has the laughing come on suddenly, with only a few seconds or no warning? ◯NO ◯YES

has the laughing occurred at times you were not expecting it? ◯NO ◯YES

has the laughing come on even if you did not feel amused at the time ◯NO ◯YES

Again thinking about the past two weeks:

when the laughing occurred, could you control yourself to stop it? ◯NO ◯YES

did the laughing come on in situations you would not have laughed in before the stroke?

◯NO ◯YES

Again thinking about the past two weeks:

(i) Exactly how often have you experienced laughter episodes?

◯ rare- less than once per week

◯ sometimes- at least once per week

◯ often- several times per week but less than every day

◯ very often- more than once per day

(ii) Approximately how long have the laughter episodes lasted?

◯ just a few seconds

◯ up to one minute

◯ several minutes

◯ ten minutes or more

(iii) How distressing have you found the laughter episodes?

◯ minimal/not distressing

◯ moderately distressing

◯ very distressing

◯ very severely distressing

◯ unsure

(iv) How embarrassing have you found the laughter episodes?

◯ minimally/not embarrassing

◯ moderately embarrassing

◯ very embarrassing

◯ very severely embarrassing

◯ unsure

(v) Again, thinking about the past two weeks, have any of the following events set off/triggered the laughter episodes:

Happy news item	◯NO ◯YES
Sad news item	◯NO ◯YES
Distressing news item	◯NO ◯YES
Emotional news item	◯NO ◯YES
Sentimental news item	◯NO ◯YES
Having happy memories in mind	◯NO ◯YES
Having sad memories in mind	◯NO ◯YES
Having distressing memories in mind	◯NO ◯YES
Having emotional memories in mind	◯NO ◯YES
Having sentimental memories in mind	◯NO ◯YES
Talking about the stroke	◯NO ◯YES
Talking about laughter since the stroke	◯NO ◯YES
A kind word from others	◯NO ◯YES

Have any factors not listed here set off the laughter episodes, please specify:

(vi) Again, thinking of the past two weeks, have the laughter episodes stopped you from doing anything?

◯YES ◯NO

If Yes, which three activities has the crying episodes most stopped you doing (e.g. meeting new people, meeting familiar people, going out, answering the telephone?)

Specify:

1.

2.

3.

(vi) Again, thinking of the past two weeks, have laughter episodes caused you to avoid people or situations?

◯NO
◯YES

If Yes, which three aspects have you most avoided because of the laughter episodes?

Specify:

1.

2.

Again thinking about any laughter episodes in the past two weeks:

(i) Have you used any of the following strategies to try and stop/limit the laughter episodes?

Looking away	◯NO	◯YES
Hiding behind a book or newspaper	◯NO	◯YES
Leaving a room	◯NO	◯YES
Trying to think of something else	◯NO	◯YES
Controlling your breathing	◯NO	◯YES
Trying to relax	◯NO	◯YES
Counting to ten	◯NO	◯YES
Covering your face with your hands	◯NO	◯YES

If Yes, can you describe which three main methods you use most:

1.

2.

3.

(iii) Of the strategies that you have used to try and stop crying episodes, have any actually helped?

Looking away tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not
Hiding behind the newspaper tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not
Leaving the room tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not
Thinking of something else tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not
Controlling your breathing tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not
Relaxing tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not
Counting to ten tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not
Covering your face with hands tried	◯ Yes, helpful	◯ No, unhelpful	◯ Not

I. Case Summary ** COMPLETED BY ASSESSOR **

(i) Considering the participants presentation and everything they have said **regarding the past two weeks**, how do they classify:

◯ No evidence of post-stroke emotionalism

◯ Evidence of post-stroke emotionalism, crying component only

◯ Evidence of post-stroke emotionalism, laughter component only

◯ Evidence of post-stroke emotionalism, crying and laughter components

Appendix G: Testing for Emotionalism After Recent Stroke Questionnaire (TEARS-Q)

Testing for Emotionalism After Recent Stroke-Questionnaire (TEARS-Q)

Stroke can cause changes to emotional expression (how we show our emotions), in particular through crying. The following statements relate to your pattern of crying since your stroke. Please indicate by circling one response how true each statement is for you, in **the past two weeks**.

1. I feel more tearful **in the past two weeks** than before the stroke

Strongly Agree Agree Unsure Disagree Strongly disagree

2. I have actually cried more **in the past two weeks** than before the stroke

Strongly Agree Agree Unsure Disagree Strongly disagree

***** If response is disagree or strongly disagree on both items 1 and 2, discontinue the test*****

3. My crying comes on suddenly, with only a few seconds or no warning

Strongly Agree Agree Unsure Disagree Strongly disagree

4. My crying comes on when I am not expecting it

Strongly Agree Agree Unsure Disagree Strongly disagree

5. My crying comes on even if I do not feel sad at the time

Strongly Agree Agree Unsure Disagree Strongly disagree

6. When my crying comes on, I cannot control or stop it

Strongly Agree Agree Unsure Disagree Strongly disagree

7. I cry in situations I would not have cried in before the stroke

Strongly Agree Agree Unsure Disagree Strongly disagree

8. I cry in this way at least once per week or more often

Strongly Agree Agree Unsure Disagree Strongly disagree

Appendix H: STROBE Checklist for Submission of Empirical Research Paper

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract ✓
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found ✓
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported ✓
Objectives	3	State specific objectives, including any prespecified hypotheses ✓
Methods		
Study design	4	Present key elements of study design early in the paper ✓
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection ✓
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up ✓ *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable ✓
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group ✓

Bias	9	Describe any efforts to address potential sources of bias ✓
Study size	10	Explain how the study size was arrived at ✓
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why ✓
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding ✓
		(*b*) Describe any methods used to examine subgroups and interactions ✓
		(*c*) Explain how missing data were addressed ✓
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed ✓ *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses ✓
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed ✓
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders ✓
		(b) Indicate number of participants with missing data for each variable of interest ✓
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) ✓
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time ✓
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included ✓
		(*b*) Report category boundaries when continuous variables were categorized ✓
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses ✓
Discussion		
Key results	18	Summarise key results with reference to study objectives ✓
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias ✓
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence ✓
Generalisability	21	Discuss the generalisability (external validity) of the study results ✓
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based ✓

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Appendix I: Ethical Approval Confirmation Letters (UEA Faculty of Medicine and Health Sciences Research Ethics Committee).

Faculty of Medicine and Health Sciences Research Ethics Committee

University of East Anglia

Emma Trigg
Norwich Medical School
Faculty of Medicine and Health Sciences
University of East Anglia
Norwich
NR4 7TJ

NORWICH MEDICAL SCHOOL

Bob Champion Research & Educational Building

James Watson Road

University of East Anglia

Norwich Research Park

5th January 2020

Dear Emma

Title: Post-Stroke Emotionalism: Examining the Trajectory of Psychological Maintaining Factors in the First Year After Stroke Reference: 2019/20-043

The submission of your research proposal was discussed at the Faculty Research Ethics Committee meeting on 19th December 2019. The Committee were happy to approve your application in principle but have the following concerns which they would like you to address and amend accordingly:

- Confidentiality: participants' initials are used in TEARS. The method for this study needs to say that participants' initials will be excluded from the dataset.
- As the original consent form was for a different study, the Committee would like to see a more detailed description of the consent processes, for example, the relevant sections of the study protocol or study SOPs or working instructions, and the PIS and/or consent and advice forms.

Please write to me once you have resolved/clarified the above issues. I require documentation confirming that you have complied with the Committee's requirements. The Committee have requested that you detail the changes below the relevant point on the text in this letter and also include your amendments as a tracked change within your application/proposal. The revisions to your application can be considered by Chair's action rather than go to a committee meeting, which means that the above documentation can be resubmitted at any time. Please could you send your revisions to me as an attachment in an email as this will speed up the decision making process.

As your project does not have ethics approval until the above issues have been resolved, I want to remind you that you should not be undertaking your research project until you have ethical approval by the Faculty Research Ethics Committee. Planning on the project or literature based elements can still take place but not the research involving the above ethical issues. This is to ensure that you and your research are insured by the University and that

your research is undertaken within the University's 'Guidelines on Good Practice in Research' approved by Senate in July 2015.

Yours sincerely

Prof Alastair Forbes

Chair, FMH Research Ethics Committee

Faculty of Medicine and Health Sciences Research Ethics Committee

University of East Anglia

NORWICH MEDICAL SCHOOL

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James Watson Road

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Emma Trigg
Norwich Medical School
Faculty of Medicine and Health Sciences
University of East Anglia
Norwich
NR4 7TJ

5th February 2020

Dear Emma

Title: Post-Stroke Emotionalism: Examining the Trajectory of Psychological Maintaining Factors in the First Year After Stroke Reference: 2019/20-043

Thank you for your email of 27th January 2020 notifying us of the amendments you would like to make to your above proposal. These have been considered and I can confirm that your amendments have been approved.

Please can you ensure that any further amendments to either the protocol or documents submitted are notified to us in advance, and that any adverse events which occur during your project are reported to the Committee.

Approval by the FMH Research Committee should not be taken as evidence that your study is compliant with GDPR and the Data Protection Act 2018. If you need guidance on how to make your study GDPR compliant, please contact your institution's Data Protection Officer.

Please can you arrange to send us a report once your project is completed.

Yours sincerely

Prof Alastair Forbes

Chair, FMH Research Ethics Committee