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Research paper

# The natural history of depression and trajectories of symptoms long term after stroke: The prospective south London stroke register

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ABSTRACT

*Background:* The natural history of depression in stroke patients is complex and the mechanism of change in symptoms over time is not fully understood. We hypothesise that there are different trajectories of symptoms after stroke.
*Methods:* The primary analysis comprised 761 patients who completed 5 years follow up, obtained from the prospective South London Stroke Register (1998–2013). The Hospital Anxiety and Depression scale (HADs) was used to screen patients for depression symptoms at 3 months after stroke, then annually. Trajectories of depression symptoms were detected using group based trajectory modelling (GBTM).
*Results:* Four patterns of symptoms (Groups I–IV) were identified: 6.31% of patients had severe symptoms, improved slightly in early years then worsen (predicted mean HADs score, 15.74 (se=1.06)); 28.65% had moderate symptoms, a tendency to get worse over time, predicted mean score 7.36 (se=0.35); 49.54% had mild symptoms and a tendency of getting worse, predicted mean 3.89 (se=0.30), and 15.51% of the cohort, had no symptoms and remained so over time. The lowest rate of Selective serotonin reuptake inhibitors (SSRI) use, over 5 years after stroke was 1.1% for group (I) and highest was 35% for group (IV). Sensitivity analyses were used to assess the robustness of the findings using several inclusion criteria and findings agreed with the primary results.
*Limitations:* There is loss to follow up of around 20%.
*Conclusions:* The study identified 4 trajectories of depression symptoms, providing useful information for the long term management of stroke patients and for the implementation of cost effective personalized interventions.



## 1. Introduction

Systematic reviews and meta-analysis have recently estimated that depression prevalence at any time point up to 15 years after stroke is around 30%.(Ayerbe et al., 2013b; Hackett and Pickles, 2014) Depression is associated with disability, poor quality of life, increased mortality, and slow recovery (Lai et al., 2002; Robinson, 2003).

The pattern of depression development over time is not fully understood in stroke patients. Evidence is patchy and controversial, often suggesting decreasing incidence rates (Aben and Verhey, 2006), increasing (Lincoln et al., 2013) and or dynamic, with episodes of recovery and recurrence over time. (Ayerbe et al., 2013a; Farner et al., 2010; Wade et al., 1987) No study to our knowledge has either formally examined the heterogeneity of developmental patterns over time or used formal diagnostic criteria to estimate the prevalence rates of different severity levels of depression long term after stroke and the association of these with disability and socio-demographic factors.

The hypothesis that a single model or developmental pathway can explain everyone's risk of an outcome or disorder such as depression may be unrealistic. Conventional growth trajectory models use a rather simplified assumption that individuals belong to a single population and estimate a single average trajectory to describe development in the entire population (multilevel random

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effect models (Goldstein and Rasbash, 2003)). Group based trajectory models (GBTM)(Nagin and Odgers, 2010b), and Growth mixture modelling (GMM) (Muthen and Muthen, 2000), are up to date statistical procedures designed to identify clusters of individuals (trajectories) who have followed a similar developmental trajectory of an outcome of interest over time. The methods are increasingly being applied in clinical research and have helped to elucidate important associations, including relationships between different patterns of drug misuse (adolescent-limited versus life course persistent) and the development of antisocial behaviours; the identification of trajectories of prostate specific antigen (PSA) biomarker and the differential development of prostate cancer, have been used to estimate differences in the prevalence of psychiatric disorders among children with and without intellectual disabilities and to identify differential psychosocial exposures for each. (Emerson and Hatton, 2007; Kandel et al., 1992; Moffitt and Klaus-Grawe Think, 2013; Muthen, 2006; Pearson et al., 1994)

In this study we aim: (I) to establish the presence of different patterns of development (trajectories) in depression symptoms long term after stroke, (II) to estimate the prevalence of each, and to examine associations between different patterns and stroke severity, physical disability, and the uptake of antidepressants.

## 2. Methods

### 2.1. Design

Patients were recruited between 1998 and 2013 from the South London Stroke Register (SLSR), a prospective population-based cohort study, and were followed up to June 2014. The World Health Organization (WHO) definition of stroke was used (Hatano, 1976). To increase the completeness of notification sixteen overlapping referral sources were used (Heuschmann et al., 2008). The STROBE flowchart provides details (Fig. 1). Some of the patients who were lost to follow at 3 months were captured at a later time points. Data collected during the acute phase of stroke included socio-demographic factors, medication use, comorbidities and stroke severity, including Glasgow coma scale (GCS) scores (categorized as severe (3–8), moderate (9–12), and mild (13–15) levels of impairment), incontinence, and paresis. Patients were assessed at three months after stroke, one year after stroke and then annually. Follow up at 3 months after stroke was by postal questionnaire or interview. At follow up patients were screened for depression using the Hospital Anxiety and Depression scale (HADs) (Zigmond and Snaith, 1983). HADs comprised 14 items, 7 items screen for depression and 7for anxiety. The scale has been validated in stroke patients and has shown good performance both when it is used by an interviewer and when it is self-administered (Aben et al., 2002). Selective serotonin reuptake inhibitors (SSRI) use pre-stroke, at 3 months, and annually after stroke was reported. As a UK study, we have focused on the use of SSRI only, as these were the most commonly used, well defined as a group, and they cause fewer side effects, according to evidence from the NHS and the National Institute for Health and Care Excellence (NHS, 2015; NICE, 2015).

Patients with impaired communication were not assessed by HADs. Disability was assessed at the acute phase, and at follow up, using the Barthel Index (BI) (Mahoney and Barthel, 1965) categorised as severe disability (0–14); moderate (15–19) and independent (20). The scale was validated for use in stroke patients and was reported to have excellent reliability (Duffy et al., 2013; Wolfe et al., 1991). Primary and sensitivity analyses were performed using different inclusion criteria.

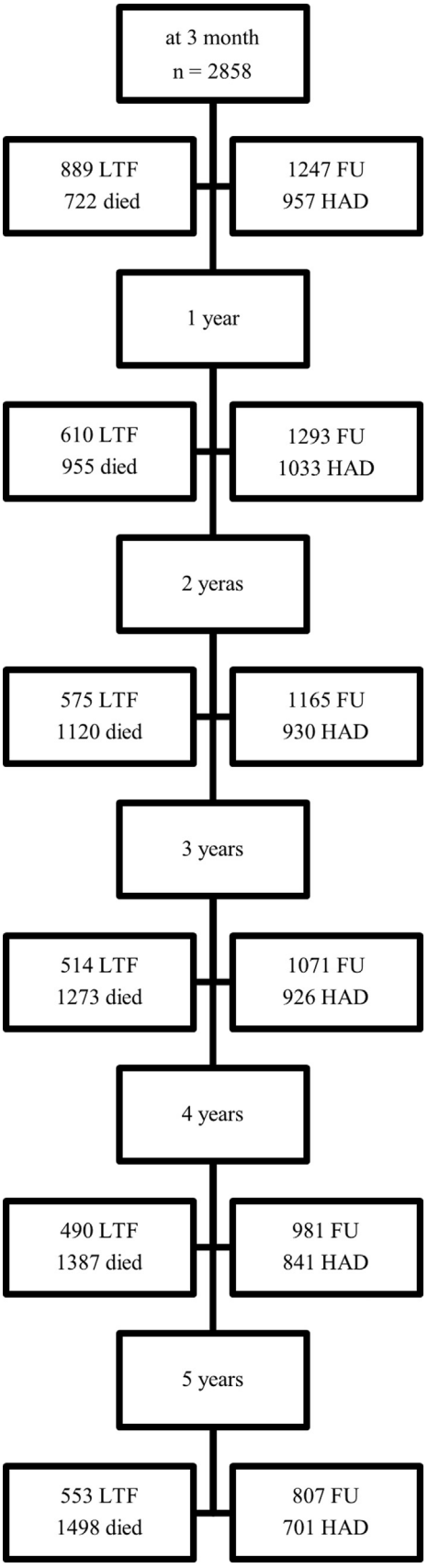


**Fig. 1.** Flow chart showing the number of stroke patients included at each follow-up (APA, 2000). [Legend: n=number of patients interviewed; LTF=Lost to follow up; FU=completed the follow up; HAD=HAD completed].