

# The Independent Association of Prestroke Psychiatric Symptoms and Acute Phase Delirium with Poststroke Mortality at One Year in Nigeria

Akin Ojagbemi, MD, PhD, MSc,\*† Toyin Bello, MSc,\*  
Mayowa Owolabi, MD, DrM,† and Olusegun Baiyewu, MD‡

---

*Background:* Undetected acute phase delirium contributes to high poststroke mortality in sub-Saharan Africa (SSA). The present study adds to existing literature by examining the association of prestroke psychiatric symptoms with poststroke mortality at 3 and 12 months in Nigeria. *Methods:* A prospective observational study with repeated delirium assessments conducted using the Confusion Assessment Method (CAM). Delirium was characterised in participants meeting criteria in the Fifth edition of the Diagnostic and Statistical Manual of mental disorders (DSM-V) as well as in those with  $\geq$ two core delirium features. Prestroke psychiatric symptoms were ascertained using the Neuropsychiatric Inventory Questionnaire (NPI-Q). Information on mortality was obtained by research supervisors during medical follow-up. Associations were investigated using multivariate logistic regression analyses and presented as odds ratios (O.R) within 95% confidence intervals (C.I). *Results:* Forty-five (30%) of 150 participants who provided data in the first week of stroke died by one-year follow-up. Those who died were more likely to have had a prestroke psychiatric symptom (64.4%,  $p=0.005$ ) and delirium in the acute phase (60.0%,  $p=0.002$ ). In analyses adjusting for the effect of age, education, tobacco smoking and stroke severity, prestroke psychiatric symptoms (O.R=3.3, 95% C.I=1.3,8.2; O.R=2.2, 95% C.I=1.0,4.6) and acute phase delirium (O.R=3.1, 95% C.I= 1.2,7.6; O.R=3.4, 95% C.I=1.5, 7.6) predicted mortality at 3 and 12 months post-stroke, respectively. *Conclusion:* This study found that prestroke psychiatric symptoms and acute phase delirium independently predicted post-stroke mortality at 3- and 12 months. Detection and treatment of mental health conditions in the population at increased risk of stroke may help reduce poststroke mortality in SSA.

**Key Words:** Stroke burden—Neurocognitive disorders—Mental health complications—Prestroke symptoms—Sub-Saharan Africa

© 2021 Elsevier Inc. All rights reserved.

---

From the \*World Health Organization (WHO) Collaborating centre for Research and Training in Mental health, Neuroscience, and Substance abuse, Department of Psychiatry, College of Medicine, University of Ibadan, P.M.B 5017 (G.P.O), Ibadan, Nigeria; †Division of Neurology, Department of Medicine, College of Medicine University of Ibadan, Nigeria; and ‡Department of Psychiatry, College of Medicine University of Ibadan, Nigeria.

Received December 2, 2020; revision received January 11, 2021; accepted January 15, 2021.

Attribution: Department of Psychiatry, College of Medicine University of Ibadan, Nigeria.

Grant support: Medical Education Partnership Initiative- Junior Faculty Research Training Program [under Fogarty International grant number D43TW010140].

Address correspondence to Akin Ojagbemi MD, PhD, MSc, World Health Organization (WHO) Collaborating centre for Research and Training in Mental health, Neuroscience, and Substance abuse, Department of Psychiatry, College of Medicine, University of Ibadan, P.M.B 5017 (G.P.O), Ibadan, Nigeria. E-mail: [aa.ojagbemi@ui.edu.ng](mailto:aa.ojagbemi@ui.edu.ng).

1052-3057/\$ - see front matter

© 2021 Elsevier Inc. All rights reserved.

<https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.105622>

## Introduction

Studies in non-stroke populations suggest that persistently unresolved delirium is more likely in the context of premorbid psychiatric symptoms.<sup>1</sup> The stroke literature also identifies key roles for pre-existing psychiatric symptoms in, not only onset<sup>2</sup> and severity<sup>3</sup> of stroke, but also in poststroke disability outcomes.<sup>4</sup> The impact of pre-stroke psychiatric symptoms on poststroke mortality is yet to be carefully examined.

Analyses of National health registers in Taiwan and the Netherlands found no direct statistical link between prior non-specialist-diagnosed mental health conditions and poststroke mortality within a median of 11<sup>5</sup> and 90 days.<sup>6</sup> It is yet unclear whether the effect of prestroke psychiatric symptoms on poststroke mortality accumulates up to a threshold in the period beyond 90 days poststroke. Examination of the relationship between prestroke psychiatric symptoms and mortality in the medium to longer term period after stroke is important as such investigation could provide evidence that may enhance primary prevention strategies against poststroke mortality.

Presumably, the risk of mortality is likely to be increased in stroke survivors living in sub-Saharan Africa (SSA) and other low/middle-income countries (LMICs) where stroke burden is high and acute phase management is often inefficient.<sup>7</sup> In the present study, which is based on Nigerian survivors of a first ever stroke, we aimed to examine the association of prestroke psychiatric symptoms as well as delirium occurring in the acute phase of stroke with mortality at one-year poststroke. We relied on evidence from our previous studies<sup>8,9</sup> and others in the literature<sup>10,11</sup> to group delirium in a spectrum that includes, not only stroke survivors meeting full criteria in the fifth edition of diagnostic and statistical manual of mental disorder (DSM V), but also those with attenuated sub-types.<sup>12</sup> Though cited<sup>12</sup> but not fully espoused in the DSM V, attenuated delirium is characterised by the presence of one,<sup>13</sup> but most precisely two,<sup>11</sup> core features of delirium in persons not meeting DSM V criteria for the full syndrome.<sup>12</sup> Full and attenuated spectrums of delirium share similar risk factors, severity and outcomes in the stroke population.<sup>8,10</sup>

## Methods

The study is a longitudinal observation of the evolution of prestroke psychiatric symptoms as well as delirium occurring in the first week of surviving a stroke among adults Nigerians. Participants were residents of Ibadan as well as surrounding communities and were admitted for acute stroke care at the University College Hospital (UCH) Ibadan, South-Western Nigeria. Ibadan is inhabited by about 3 million people, who are mostly Yoruba speaking. The UCH is the main referral hospital serving Ibadan and surrounding communities. Ethical approval

was obtained from the University of Ibadan/UCH ethics committee.

### Subjects

Consecutive adult ischaemic or haemorrhagic stroke survivors were recruited between May, 2017 and March 2019 after they had been seen by a consultant neurologist (MO) primarily responsible for their care. The diagnosis of stroke was confirmed based on neuro-imaging and clinical examination criteria (Sacco et al., 2013). Written consent was obtained from all eligible stroke survivors and/or their spouses or adult children after the procedure of the study was explained to them either in English or the local Yoruba languages. We excluded patients who were unable to communicate reliably (N=16) or aphasia (N=20) and those with severe conditions that could limit participation in follow-up assessment (N=44). These included those with severe cognitive impairment [(Mini-Mental State Examination (MMSE)<15)]<sup>14</sup> or significant comorbid medical illnesses (e.g., chronic kidney disease requiring dialyses). Stroke survivors with mild or moderate cognitive impairment (MMSE  $\geq$ 15)<sup>14</sup> were included only after full assessment for capacity to consent.

### Measures

#### Confusion assessment method (CAM)<sup>15</sup>

The CAM consists of nine delirium criteria and takes about 5 minutes to complete. In the present study, the CAM was administered by a research assistant with experience in epidemiologic research in the older population of south-Western Nigeria. She was trained using the CAM training manual. Inter-rater reliability on a subgroup of 29 stroke survivors independently assessed by the research assistant and a consultant in old age psychiatry (AO) produced Kappa values of between 0.51-0.76 for each CAM item, and 0.63 overall.

The presence of CAM symptoms was ascertained after observations of patients' behaviour and responses during an initial cognitive screening test using the MMSE.<sup>16</sup> Additional information was also requested from nursing staff assigned to the patient. We conducted two (maximum of 72 hours apart) evening-time (usually between 4pm and 7pm) assessments for delirium symptoms in one week.

*Definition of delirium syndrome:* Full delirium was diagnosed according to DSM V criteria.<sup>12</sup> The diagnosis was made following a standard algorithm which is part of the CAM instrument. According to the scoring convention, a diagnosis of delirium is warranted when a patient displays core features of delirium: acute onset and fluctuating course of, inattention, and either disorganised thinking or altered levels of consciousness.<sup>15</sup> To determine the presence of DSM V delirium, a clinician psychiatrist (AO) reviewed information from the CAM, interviewer's

observations and reports from the responsible nursing staff and primary caregivers. Stroke survivors meeting full DSM V criteria for delirium as well as those with two or three core features of delirium who, nevertheless, did not meet DSM V criteria for the full delirium<sup>9,11</sup> were categorized as having delirium syndrome.

*Definition of course of delirium symptoms:* All study participants were included in defining the course of delirium symptoms. Stroke survivors with no core feature of delirium after two repeated CAM assessments were considered as normal (i.e., no delirium detected). Those with one or more core features of delirium were categorized as follows: Improving, if a lower delirium symptoms count was demonstrated on second CAM assessment; Persistent, if delirium symptoms count on first and second CAM assessments were the same; Worsening, if a higher delirium symptoms count was demonstrated on second CAM assessment.

### Prestroke psychiatric symptoms

Information on psychiatric symptoms occurring in the four weeks prior to stroke symptoms was obtained using the proxy-reported version of the Neuropsychiatric Inventory (NPI-Q).<sup>17</sup> The neuropsychiatric symptoms assessed by the NPI-Q include delusions, hallucinations, agitation/aggression, depression, anxiety, elation, apathy, disinhibition, irritability, aberrant motor behaviour, night time/sleep disturbance and appetite change. The measure has been previously validated in stroke patients: 'sensitivity of 74.1%, specificity of 79.5%, Cronbach's alpha=0.76'.<sup>18</sup>

### Ascertainment of mortality

Information on poststroke mortality was collected after the completion of baseline assessment, and at 3- and 12-months follow-up. The research assistant and her supervisor (AO) continuously monitored the study population. When they have been reliably informed, usually by a member of the household, about the death of a participant who was not available or could not be traced, they recorded this information in a case record.

### Other data collection

The following information was obtained from all participants using a standardized questionnaire: demographic data, marital status, years of formal education, personal history of smoking, alcohol consumption, medical history of hypertension, diabetes, other comorbid medical conditions. We ascertained economic status using asset based measures relevant to developing countries.<sup>19</sup>

Judgements about global cognitive functioning was made using results from the mini-mental state examination (MMSE).<sup>16</sup> The informant questionnaire for cognitive decline in the elderly (IQ-CODE)<sup>20</sup> was used to screen

participants for the possibility of cognitive deterioration in the years up to one month before the stroke event. The severity of stroke was ascertained using the stroke levity scale (SLS).<sup>21</sup> The average of two blood pressure (B.P) measurements was recorded. Records of other relevant risk factors for stroke were also made. These include fasting blood glucose, serum urea and creatinine profiles.

### Statistical analyses

We summarized delirium syndrome, courses of delirium symptoms, socio-demographic, prestroke and immediate poststroke risk factor variables using frequency and percentage, while mean and standard deviation (SD) were calculated for age and other continuous variables. Participants were considered to have reached an endpoint if they were available for outcome assessments at 3- and 12-months follow-up, or when the research assistant or supervisor have been reliably informed of their death.

We examined in separate analyses the association of delirium syndrome, as well as courses of delirium symptoms, with demographic, prestroke and immediate poststroke risk factor variables. These associations were conducted by first comparing stroke survivors who developed delirium syndrome (by having two or more core delirium features) with those not meeting study threshold for delirium syndrome. Next, we compared stroke survivors with a persistent or worsening course of symptoms with those who were normal or improving. We estimated odds ratios (O.R) with 95% confidence intervals (CI) of these associations using regression analyses. We first conducted unadjusted analyses. Next, we adjusted for variables with p-values <0.1 in multivariable analyses.

The same methods were used in the investigation of the association of prestroke psychiatric symptoms and acute phase delirium syndrome with mortality at 3 and 12 months poststroke. The results of the associations are presented O.R with 95% CI. Analyses were conducted using Stata version 13.0 (22). A level of significance of p<0.05 was set for all analyses.

## Results

### Participants characteristics

The prestroke and immediate poststroke characteristics of the study sample as well as the course of delirium symptoms in the first week of stroke are presented in Table 1. Course of delirium symptoms was not associated with prestroke demographic, lifestyle and immediate poststroke factors investigated in the study (Supplementary Table 1).

Sixty-one (40.7%) participants met study threshold for delirium syndrome by having two or more core delirium features. They comprised 32 (21.3%) with attenuated delirium and 29 (19.3%) who met full DSM V criteria.

**Table 1.** Baseline characteristics and course of delirium symptoms in the first week of stroke.

	All, N=150 n(%)	Normal, N=14 n(%)	Improving, N=59 n(%)	Persistent, N=50 n(%)	Worsening, N=27 n(%)
<i>Prestroke demographic factors</i>					
<i>Age, years</i>					
≥60	82 (54.7)	7 (50.0)	33 (55.9)	30 (60.0)	12 (44.4)
Mean (SD)	60.2 (12.8)	57.4 (14.8)	61.2 (12.1)	60.8 (13.4)	58.6 (12.2)
<i>Formal education, years</i>					
≥1	124 (82.7)	13 (92.9)	49 (83.1)	40 (80.0)	22 (81.5)
Mean (SD)	9.1 (6.4)	8.6 (6.0)	9.1 (6.2)	8.6 (6.6)	10.0 (6.7)
<i>Male gender</i>					
Unmarried status <sup>a</sup>	35 (23.3)	5 (35.7)	14 (23.7)	9 (18.0)	7 (25.9)
Low economic status	76 (50.7)	7 (50.0)	26 (44.1)	30 (60.0)	13 (48.1)
<i>Prestroke health and lifestyle factors</i>					
Ever used alcohol	71 (47.3)	8 (57.1)	27 (45.8)	20 (40.0)	16 (59.3)
Ever smoked tobacco	24 (16.0)	1 (7.1)	7 (11.9)	8 (16.0)	8 (29.6)
Systemic hypertension	123 (82.0)	11 (78.6)	48 (81.4)	43 (86.0)	21 (77.8)
Diabetes mellitus	35 (23.3)	2 (14.3)	18 (30.5)	9 (18.0)	6 (22.2)
Multimorbidity	46 (32.4)	2 (15.4)	20 (36.4)	15 (31.9)	9 (33.3)
Poor social support	57 (38.0)	8 (57.1)	20 (33.9)	17 (34.0)	12 (44.4)
Prestroke neuropsychiatric symptoms	78 (52.0)	5 (35.7)	32 (54.2)	28 (56.0)	13 (48.1)
<i>Pre-stroke cognitive decline</i>					
Mean (SD) IQCODE	3.1 (0.2)	3.1 (0.1)	3.2 (0.3)	3.2 (0.3)	3.1 (0.2)
<i>Immediate post-acute stroke factors</i>					
<i>Severe stroke</i>					
Mean (SD) SLS scores	8.1 (3.4)	9.0 (3.2)	8.0 (3.9)	8.3 (3.3)	7.1 (2.7)
<i>Lesion types</i>					
Infarcts	82 (54.7)	7 (50.0)	33 (55.9)	26 (52.0)	16 (59.3)
Haemorrhage	58 (38.7)	6 (42.9)	24 (40.7)	19 (38.0)	9 (33.3)
Haemorrhagic infarcts	10 (6.7)	1 (7.1)	2 (3.4)	5 (10.0)	2 (7.4)
<i>Urea≥20 mg/dl</i>					
Mean (SD)	78 (75.7)	7 (87.5)	26 (66.7)	28 (80.0)	17 (81.0)
<i>Glucose≥6.9 mmol/L</i>					
Mean (SD)	37.2 (29.4)	39.5 (23.6)	35.7 (32.6)	33.8 (23.5)	44.7 (34.4)
<i>Creatinine≥1.2mg/dl</i>					
Mean (SD)	13 (14.8)	0 (0)	5 (13.9)	4 (11.8)	4 (26.7)
<i>MMSE scores, mean (SD)</i>					
Mean (SD)	3.3 (4.9)	3.4 (2.7)	3.1 (4.7)	3.0 (4.9)	4.7 (5.9)
<i>Modified Rankin scores, mean (SD)</i>					
Mean (SD)	41 (39.8)	4 (50.0)	14 (34.1)	14 (41.2)	9 (45.0)
Mean (SD)	1.3 (1.2)	1.2 (0.4)	1.5 (1.6)	1.2 (1.0)	1.2 (0.6)
Mean (SD)	17.4 (8.2)	20.8 (7.1)	16.7 (8.6)	17.8 (8.7)	16.2 (6.9)
Mean (SD)	3.4 (1.4)	2.4 (1.9)	3.7 (1.2)	3.3 (1.5)	3.8 (1.0)

<sup>a</sup>Death or divorce, Normal=No core features of delirium; Improving=Lower delirium symptoms count on second CAM assessment; Persistent= Same delirium symptoms count on first and second CAM assessments; Worsening=Higher delirium symptoms count on second CAM assessment; CAM=Confusion Assessment Method; SLS= Stroke Levity Scale; IQCODE= Informant Questionnaire for Cognitive Decline in the Elderly, MMSE=Mini-mental state examination.

#### *Prestroke and immediate poststroke correlates of delirium*

In Table 2, prestroke educational attainment (O.R=2.8, 95% C.I=1.1-7.1), tobacco smoking (O.R=3.6, 95% C.I=1.3-9.6), stroke severity (O.R=2.4, 95% C.I=1.1-5.2), and immediate poststroke cognitive (O.R=0.9, 95% C.I=0.8-0.9) and motor functioning scores (O.R=1.5, 95% C.I=1.0-2.1) were independently associated with acute phase delirium syndrome. Conversely, prestroke psychiatric symptoms were not associated with delirium syndrome. The frequency distribution of the various psychiatric symptoms is presented in Supplementary Fig. 1. Factors associated with full DSM V delirium are presented in supplementary Table 2.

#### *Delirium and poststroke mortality*

Details of participant flow across the study is presented in Fig. 1. Thirty-four participants who provided data in the first week of stroke were lost to follow-up at one year for reasons such as relocation from study catchment area (N=26) and refusal of further participation (N=8). The mean age of the follow-up sample 59.0 ±13.4 years.

Forty-five deaths were recorded at one-year follow-up, and 27 (60.0%, p=0.002) of these participants who died had delirium syndrome in the acute phase of stroke. Those who died were also more likely to have a prestroke psychiatric symptoms (64.4%, p=0.005). In multivariate logistic regression analyses, prestroke psychiatric

**Table 2.** Cross-sectional association of prestroke and immediate poststroke factors with delirium syndromes.

	Attenuated/full delirium, N=61			
	Unadjusted O.R(95% C.I)	p-value	Adjusted O.R(95% C.I) <sup>a</sup>	p-value
<i>Prestroke demographic factors</i>				
Age ≥60 years	2.1 (1.1, 4.2)	<b>0.027</b>	1.9 (0.9, 3.9)	0.071
No Formal education	3.4 (1.4, 8.3)	<b>0.006</b>	2.8 (1.1, 7.1)	<b>0.027</b>
Male gender	1.1 (0.6, 2.1)	0.785	1.8 (0.8, 3.8)	0.141
Unmarried <sup>b</sup>	2.1 (0.9, 4.4)	0.064	1.4 (0.6, 3.2)	0.466
Loweconomic status	1.6 (0.8, 3.0)	0.175	1.3 (0.7, 2.7)	0.417
<i>Prestroke health and lifestyle</i>				
Ever drank alcohol	1.0 (0.5, 2.0)	0.966	1.3 (0.6,2.6)	0.474
Ever smoked tobacco	2.4 (0.9, 5.7)	0.059	3.6 (1.3, 9.6)	<b>0.012</b>
Systemic hypertension	1.5 (0.6,3.5)	0.393	2.1 (0.8, 5.4)	0.145
Diabetes mellitus	0.9 (0.5, 2.1)	0.927	0.9 (0.4, 2.0)	0.726
Multimorbidity	1.1 (0.6, 2.3)	0.747	1.1 (0.5, 2.3)	0.878
Poor social support	2.0 (1.0,3.9)	<b>0.048</b>	1.4 (0.7, 2.9)	0.367
Prestroke neuropsychiatric symptoms	1.2 (0.6, 2.2)	0.670	1.1 (0.5, 2.2)	0.825
<i>Immediate poststroke factors</i>				
Severe stroke	2.6(1.2,5.4)	<b>0.013</b>	2.4 (1.1, 5.2)	<b>0.025</b>
Haemorrhagic lesions	0.9 (0.5, 1.8)	0.976	1.0 (0.5,2.1)	0.969
IQ-CODE scores	1.3 (0.4, 4.6)	0.724	0.8 (0.2, 3.4)	0.780
MMSE scores	0.9 (0.8, 0.9)	<b>&lt;0.001</b>	0.9 (0.8, 0.9)	<b>&lt;0.001</b>
Modified Rankin scale scores	1.6 (1.1, 2.1)	<b>0.006</b>	1.5 (1.0, 2.1)	<b>0.028</b>
Urea (mg/dl)	1.0 (0.9, 1.0)	0.372	1.0 (0.9,1.0)	0.874
Glucose(mmol/L)	0.9 (0.9,1.1)	0.368	0.9 (0.8,1.0)	0.185
Creatinine(mg/dl)	0.8 (0.6,1.2)	0.343	0.8 (0.5,1.2)	0.301

<sup>a</sup>Adjusted for age, education, smoking status, social support, stroke severity, cognitive and motor functioning.

<sup>b</sup>Death or divorce, MMSE=Mini-mental state examination.

symptoms (Adjusted O.R=2.1, 95% C.I=1.0-4.6) and acute poststroke delirium syndrome (Adjusted O.R=3.4, 95% C.I=1.5-7.6) predicted mortality at one year poststroke.

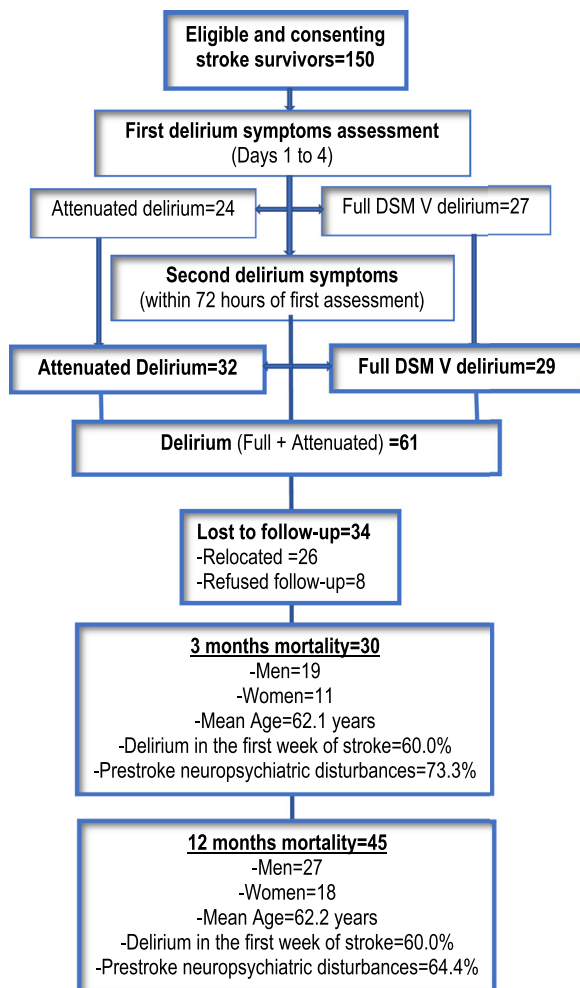
## Discussion

We found in the present study that 52% of stroke survivors had a prestroke psychiatric symptom while 40.7% had delirium syndrome in the first week of surviving a stroke. Contrary to findings in critical care populations, delirium as well as persistent course of delirium symptoms were not associated with prestroke psychiatric symptoms. A total of 45 (30%) deaths were recorded at one year. Prestroke psychiatric symptoms and acute phase delirium syndrome independently predicted poststroke mortality.

Our results are in keeping with those of many previous studies of the link between acute phase delirium and poststroke mortality.<sup>23-25</sup> The present study adds to existing literature by demonstrating that similar to acute phase delirium, prestroke psychiatric symptoms are predictive of short and medium-term mortality. These results are important as, partly due to limited published literature investigating the link between prestroke psychiatric conditions and poststroke mortality,<sup>5</sup> prestroke mental health conditions are rarely listed among the modifiable risk factors for poststroke mortality.<sup>26</sup> In a previous Dutch study<sup>5</sup>

where general practice (GP) database was used to identify stroke survivors with a lifetime history prestroke mental health conditions, psychiatric diagnoses were not associated with an increased risk of dying within a median of 11 days of in-hospital observation. Notably, mental health conditions are substantially underdiagnosed in GP settings globally.<sup>27</sup> In the present study, we ascertained the presence of psychiatric symptoms in the four weeks prior to stroke onset using the well validated NPI-Q, and investigated their association with mortality at 3 and 12 months poststroke.

We could not replicate findings in critical care populations<sup>1</sup> suggesting that delirium, especially when persistent, is more likely in the context of prior psychiatric conditions. Such findings have led to debates<sup>28</sup> about the prognostic value of premorbid psychiatric symptoms since some, especially hallucination and agitation, may reflect underlying delirium. Viewed from this perspective, the question may arise as to whether in the present study, some of the reported prestroke psychiatric symptoms were not, in fact, the behavioural component of a pre-existing delirium. While our assessment of prestroke psychiatric symptoms did not exclude core features of delirium, caregivers-observed neuropsychiatric disturbances in the weeks before stroke onset was not statistically associated with directly assessed delirium after the stroke. We are thus reasonably confident that prestroke psychiatric



**Fig. 1.** Flow chart of the study of association prestroke psychiatric symptoms and acute phase delirium with poststroke mortality at one year.

symptoms in the present study are independent of delirium ascertained in the acute phase of stroke. Whereas both prestroke psychiatric symptoms and acute phase

delirium independently predicted short to medium term mortality after stroke.

In keeping with findings in the general population,<sup>29</sup> the most common prestroke psychiatric symptoms in the present study were depression, anxiety and sleep difficulties. Notably, these conditions are interrelated and respond to treatment with selective serotonin reuptake inhibitors (SSRI).<sup>30</sup> Recent evidence suggests that identification and SSRI treatment of depression in persons at risk of stroke provide protection around the time of stroke onset and reduce poststroke disability.<sup>30</sup> It is reasonable to hypothesise from our results that the strategy to identify and treat prestroke psychiatric disturbances (especially depression, anxiety and sleep symptoms) with SSRI may also be applicable to reduce poststroke mortality. Future studies may wish to investigate this hypothesis.

#### Limitations

Findings of the present study must be interpreted within several caveats. First is that the NPI-Q identified symptoms one month before stroke and some of the psychiatric symptoms identified may also be related to dementia. Information about the presence of psychiatric symptoms several months or years before stroke could give a better understanding about patient's psychopathology. Second, many psychiatric symptoms are subjectively experienced. In this way, proxy reported symptoms as required by the NPI-Q may be influenced by factors unrelated to the stroke survivor. For example, caregivers' rating of patients' symptoms may be influenced by the rater's own state of burden.<sup>31</sup> While burden was not directly measured in the present study, we note that over 90% of caregivers rated their general health as good. Third is the possibility that, due to the fluctuant nature of delirium symptoms, some participants with core delirium features may have been misclassified as normal, and vice versa.

**Table 3.** Multivariate association of prestroke psychiatric symptoms and delirium syndromes with mortality at three and twelve months poststroke.

Delirium syndromes	O.R (95% C. I) <sup>a</sup>	
	At three months poststroke	At twelve months poststroke
Normal	Reference	Reference
Attenuated/full delirium	Unadjusted: 2.7 (1.2,6.1), p= <b>0.018</b> Adjusted: 3.1 (1.2,7.6), p= <b>0.015</b>	Unadjusted: 3.1 (1.5,6.5), p= <b>0.002</b> Adjusted: 3.4 (1.5,7.6), p= <b>0.003</b>
<i>Covariates in adjusted model</i>		
Prestroke neuropsychiatric symptoms	3.3 (1.3,8.2), p= <b>0.011</b>	2.2 (1.0,4.6), p= <b>0.048</b>
Age ≥60years	1.7 (0.7,4.2), p=0.241	1.8 (0.8,3.9), p=0.156
No formal education	0.5 (0.2,1.8), 0.295	0.4 (0.1,1.1), p=0.072
Tobacco smoking	0.5 (0.4,5.3), 0.538	1.7 (0.3,1.9), p=0.504
Severe stroke	0.9 (0.3,2.4), 0.836	0.9 (0.4,2.3), p=0.913
<i>Interaction terms</i>		
Delirium syndromes* Prestroke neuropsychiatric symptoms	0.4 (0.1,2.5), p=0.292	1.1 (0.1,13.0), p=0.933

<sup>a</sup>Based on logistic regression analyses.

In conclusion, prestroke psychiatric symptoms and acute phase delirium predicted mortality at 3 and 12 months poststroke in Nigeria. Findings are important as prior studies relying on GP diagnosed mental health conditions in the lifetime of stroke survivors found no association between prestroke psychiatric disorders and short-term in-hospital mortality. As such, prestroke neuropsychiatric conditions are rarely listed among the modifiable risk factors for poststroke mortality in current literature and practice. This is despite evidence of treatability of common neuropsychiatric conditions in the stroke population. The findings of the present study may suggest that treatment of common neuropsychiatric conditions such as depression in the population at high risk of stroke may constitute a primary prevention strategy for poststroke mortality. Onset of delirium is also preventable through multicomponent non-pharmacological strategies including education of health care providers, medical workup for possible causes of delirium, and avoiding high-risk medications such as anticholinergics, sedative hypnotics, low potency antipsychotics, corticosteroids, and H2 receptor blockers.<sup>32</sup> Future studies pursuing a similar line of research may wish to investigate whether, as it is with poststroke disability, treatment of psychiatric conditions in the population at increased risk of stroke reduces mortality in the event of a stroke.

### Declaration of Competing Interest

The authors declare that there is no conflicts of interest.

**Acknowledgement:** Medical Education Partnership Initiative- Junior Faculty Research Training Program [under grant number D43TW010140].

### Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:[10.1016/j.jstrokecerebrovasdis.2021.105622](https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.105622).

### References

- van der Kuur A, Bethlehem C, Bruins N, de Jager C, van Alst C, Haagsma OG, et al. Impact of a premorbid psychiatric disorder on the incidence of delirium during ICU stay, morbidity, and long-term mortality. *Crit Care Res Pract* 2019;2019:6402097.
- Barlinn K, Kepplinger J, Puetz V, Illigens BM, Bodechtel U, Siepmann T. Exploring the risk-factor association between depression and incident stroke: a systematic review and meta-analysis. *Neuropsychiatr Dis Treat* 2015;11:1-14.
- Aron AW, Staff I, Fortunato G, McCullough LD. Pre-stroke living situation and depression contribute to initial stroke severity and stroke recovery. *J Stroke Cerebrovasc Dis* 2015;24(2):492-499.
- Sharrief AZ, Sanchez BN, Lisabeth LD, Skolarus LE, Zahuranec DB, Baek J, et al. The impact of pre-stroke depressive symptoms, fatalism, and social support on disability after stroke. *J Stroke Cerebrovasc Dis* 2017;26(11):2686-2691.
- Nuyen J, Spreeuwenberg PM, Groenewegen PP, van den Bos GA, Schellevis FG. Impact of preexisting depression on length of stay and discharge destination among patients hospitalized for acute stroke: linked register-based study. *Stroke* 2008;39(1):132-138.
- Kang JH, Xirasagar S, Lin HC. Lower mortality among stroke patients with schizophrenia: a nationwide population-based study. *Psychosom Med* 2011;73(1):106-111.
- Owolabi MO, Akarolo-Anthony S, Akinyemi R, Arnett D, Gebregziabher M, Jenkins C, et al. The burden of stroke in Africa: a glance at the present and a glimpse into the future. *Cardiovasc J Afr* 2015;26(2 Suppl 1):S27-S38.
- Ojagbemi A, Bello T, Elugbadebo O, Owolabi M, Baiyewu O. Different cognitive and functional outcomes in attenuated and full delirium syndromes among recent stroke survivors. *J Stroke Cerebrovasc Dis* 2020;29(11):105251.
- Ojagbemi A, Bello T, Owolabi M, Baiyewu O. Cognitive, functional, and mortality outcomes of attenuated delirium syndrome in stroke survivors. *J Geriatr Psychiatry Neurol* 2020;891988720944234.
- Klimiec-Moskal E, Lis A, Pera J, Slowik A, Dziedzic T. Subsyndromal delirium is associated with poor functional outcome after ischaemic stroke. *Eur J Neurol* 2019;26(6):927-934.
- Cole MG, Ciampi A, Belzile E, Dubuc-Sarrasin M. Subsyndromal delirium in older people: a systematic review of frequency, risk factors, course and outcomes. *Int J Geriatr Psychiatry* 2013;28(8):771-780.
- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders 5ed*. Arlington, VA: American Psychiatric Publishing; 2013.
- Azuma K, Mishima S, Shimoyama K, Ishii Y, Ueda Y, Sakurai M, et al. Validation of the prediction of delirium for intensive care model to predict subsyndromal delirium. *Acute Med Surg* 2019;6(1):54-59.
- Guruje O, Unverzagt FW, Osuntokun BO, Hendrie HC, Baiyewu O, Ogunniyi A, et al. The CERAD Neuropsychological test battery: norms from a Yoruba-speaking Nigerian sample. *West Afr J Med* 1995;14(1):29-33.
- Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegel AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med* 1990;113(12):941-948.
- Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12(3):189-198.
- Kaufner DI, Cummings JL, Ketchel P, Smith V, MacMillan A, Shelley T, et al. Validation of the NPI-Q, a brief clinical form of the neuropsychiatric inventory. *J Neuropsychiatry Clin Neurosci* 2000;12(2):233-239.
- Wong A, Cheng ST, Lo ES, Kwan PW, Law LS, Chan AY, et al. Validity and reliability of the neuropsychiatric inventory questionnaire version in patients with stroke or transient ischemic attack having cognitive impairment. *J Geriatr Psychiatry Neurol* 2014;27(4):247-252.
- Ferguson B, Tandon A, Gakidou E, Murray C, Evans D. Estimating permanent income using indicator variables. *Health systems Performance Assessment: diabetes, methods and empiricism*. Geneva: World Health Organisation; 2003. p. 747-760.
- Jorm AF. A short form of the informant questionnaire on cognitive decline in the elderly (IQCODE): development and cross-validation. *Psychol Med* 1994;24(1):145-153.

21. Owolabi MO, Platz T. Proposing the stroke levity scale: a valid, reliable, simple, and time-saving measure of stroke severity. *Eur J Neurol* 2008;15(6):627-633.
22. Stata Corp. *Stata Statistical Software*. College Station, TX: StataCorp LP; 2013.
23. Shi Q, Presutti R, Selchen D, Saposnik G. Delirium in acute stroke: a systematic review and meta-analysis. *Stroke* 2012;43(3):645-649.
24. Ojagbemi A, Owolabi M, Bello T, Baiyewu O. Stroke severity predicts poststroke delirium and its association with dementia: Longitudinal observation from a low income setting. *J Neurol Sci* 2017;375:376-381.
25. Vahidy FS, Bambhroliya AB, Meeks JR, Rahman O, Ely EW, Slooter AJC, et al. In-hospital outcomes and 30-day readmission rates among ischemic and hemorrhagic stroke patients with delirium. *PLoS One* 2019;14(11): e0225204.
26. Bell CL, LaCroix A, Masaki K, Hade EM, Manini T, Mysiw WJ, et al. Prestroke factors associated with post-stroke mortality and recovery in older women in the Women's Health Initiative. *J Am Geriatr Soc* 2013;61(8):1324-1330.
27. Sinnema H, Terluin B, Volker D, Wensing M, van Balkom A. Factors contributing to the recognition of anxiety and depression in general practice. *BMC Fam Pract* 2018;19(1):99.
28. Holttä E, Laakkonen ML, Laurila JV, Strandberg TE, Tilvis R, Kautiainen H, et al. The overlap of delirium with neuropsychiatric symptoms among patients with dementia. *Am J Geriatr Psychiatry* 2011;19(12):1034-1041.
29. Kessler RC, Sampson NA, Berglund P, Gruber MJ, Al-Hamzawi A, Andrade L, et al. Anxious and non-anxious major depressive disorder in the world health organization world mental health surveys. *Epidemiol Psychiatr Sci* 2015;24(3):210-226.
30. Stulberg EL, Dong L, Zheutlin AR, Kim S, Claflin ES, Skolarus LE, et al. Associations of self-reported history of depression and antidepressant use before stroke onset with poststroke post-acute rehabilitation care-an exploratory study: the BASIC (Brain Attack Surveillance in Corpus Christi) Project. *J Am Heart Assoc* 2019;8(16): e013382.
31. Ojagbemi A, Owolabi M. Do occupational therapy interventions improve quality of life in persons with dementia? A meta-analysis with implications for future directions. *Psychogeriatrics* 2017;17(2):133-141.
32. American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults. American geriatrics society abstracted clinical practice guideline for postoperative delirium in older adults. *J Am Geriatric Soc* 2015;63(1):142-150.