Patient-reported outcomes after stroke in young adults: UCL Young Stroke Systematic Evaluation Study (ULYSSES)

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AUTHOR CONTRIBUTIONS

RM, HO, RS, AC, DJW: study concept and design; RM, HO, JM: data acquisition; RM, GA: data analysis; RM, GA, HO, JM, GB, APL, SML, RJP, RS, AC, DJW: data interpretation; RM, GA, HO, JM, GB, APL, SML, RJP, RS, AC, DJW: drafting and/or revising the manuscript for important intellectual content. All authors approved the final version of the manuscript. DJW is the guarantor of this work.

DECLARATION OF CONFLICTING INTEREST

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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DATA AVAILABILITY

Requests for derived data supporting the findings of this study will be considered by the corresponding author.

ETHICAL APPROVAL AND INFORMED CONSENT

The UCL Young Stroke Systematic Evaluation Study (ULYSSES) is a sub-study within the Stroke Investigation Group in North And central London (SIGNAL) registry. SIGNAL was approved by the University College London Hospitals (UCLH) NHS Foundation Trust Governance Review Board as a continuous service evaluation of a comprehensive clinical care programme (5-

201920-SE). It was also approved by the London South-East Research Ethics Committee (REC) (24/LO/0368). Written informed consent was waived for the 6-month follow-up collected as part of this study as all procedures were part of standard patient care.

ABSTRACT

Background Few studies have investigated patient-reported non-motor outcomes after stroke in young adults. We aimed to assess their prevalence and patterns in this population to identify unmet needs.

Methods This prospective cohort study included consecutive patients (aged <55) admitted to University College London Hospitals Hyperacute Stroke Unit with ischaemic stroke or intracerebral haemorrhage (ICH) between 2017-2020. At 6 months, we collected data on eight non-motor domains (anxiety, depression, fatigue, sleep disturbance, pain interference, reduced social participation, bowel and bladder dysfunction). We assessed outcome co-occurrence, compared prevalence by modified Rankin Scale (mRS) score (favourable: 0-1 vs unfavourable: 2-5), and performed multivariable logistic regression to identify predictors of each adverse outcome and high non-motor outcome burden (≥3 adverse outcomes).

Results We included 493/527 (94%) eligible patients (median age 48, IQR 41-52; 33% female; 82% ischaemic stroke). Fatigue (55%) reduced social participation (47%), and sleep disturbance (46%) were most common. Prevalence rates did not differ significantly by mRS score. 91% reported ≥1 adverse outcome; 27% reported ≥4. Anxiety was predicted by ICH (OR 1.92; 95%CI 1.11-3.33; p=0.019) and higher education levels (per decile increase in education deprivation, OR 1.12; 95%CI 1.03-1.22; p=0.012). Pain interference was predicted by admission stroke severity (per NIHSS 10-point increase, OR 1.54; 95%CI 1.05–2.25; p=0.025).

Conclusions Adverse non-motor outcomes are common in young adults 6-months post-stroke, even in those with an mRS score of 0-1 (indicating a favourable functional recovery). Furthermore, non-motor outcomes rarely occur in isolation, highlighting the need for early and comprehensive screening, recognition, and management.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Adverse patient-reported non-motor outcomes are common after stroke, yet their prevalence and patterns in young adults (<55 years old) remain understudied. Often, studies in this population assess only one or two outcomes in isolation, with limited exploration of the full range of non-motor outcomes or their co-occurrence. Additionally, the extent to which the modified Rankin Scale (mRS) captures these outcomes in young patients is unclear.

WHAT THIS STUDY ADDS

This prospective hospital-based cohort study showed that adverse patient-reported non-motor outcomes are common and rarely occur in isolation in young stroke patients. Fatigue, reduced ability to participate in social roles and activities, and sleep disturbance were most prevalent. Similar prevalence rates between patients with favourable (0-1) vs unfavourable (2-5) mRS scores suggested that good functional recovery (as defined by the mRS) does not necessarily equate to a good outcome in non-motor domains.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

These findings highlight the need for early recognition and management of adverse non-motor outcomes, which traditional measures, such as the mRS, fail to capture. Larger population-based studies are needed to identify predictors and the progression of these outcomes, alongside high-quality intervention studies to address the current evidence gap in how best to manage them. Together, this research could inform effective interventions and rehabilitation pathways, thereby improving functional independence, the likelihood of returning to work, and overall quality of life for young stroke patients.

INTRODUCTION

Patient-reported non-motor outcomes are increasingly recognised as a common post-stroke consequence and a priority area for research.[1] The 10-year prevalence rates of depression and anxiety in UK stroke populations are reportedly as high as 29%[2] and 38%[3] respectively, compared with a 22% background level of mild-to-moderate depression or anxiety in the general population.[4] Fatigue, which has a 48%[5] prevalence rate among post-stroke populations, is associated with a reduced ability to return to paid work[6,7] – an outcome that is particularly important to younger adults with stroke, who are often in their most economically productive and demanding years of employment. This diminished ability to return to the workforce further contributes to substantial productivity-related economic losses, with premature death and lost working days due to stroke estimated to cost approximately €12 billion annually across Europe.[8]

The current literature on patient-reported non-motor outcomes in young stroke populations is limited, as most studies primarily focus on older adults (mean age over 70) and often exclude patients with intracerebral haemorrhage (ICH).[3,9–13] Furthermore, studies in young patients mainly focus on one or two outcomes in isolation, rarely assessing the broader spectrum of non-motor outcomes or their co-occurrence.[6,14–17] This gap highlights the need for a comprehensive assessment of patient-reported non-motor outcomes in a young stroke population.

The modified Rankin Scale (mRS) is widely used as the sole outcome measure after stroke; however, it primarily assesses disability and functional independence, and may lack sufficient detail to capture changes in non-motor health domains, which are an important determinant

of quality of life.[18] For example, one small study found that over half of stroke patients with favourable mRS scores (i.e., 0-1) experience reintegration restrictions and one-third have depression.[19] This suggests that relying solely on the mRS as a post-stroke outcome measure may underestimate the impact of stroke.

To address these gaps, we aimed to: (1) assess the prevalence and patterns (i.e., overall burden and co-occurrence) of adverse non-motor outcomes (anxiety, depression, fatigue, sleep disturbance, pain interference, reduced social participation, and bowel and bladder dysfunction) in young adults with stroke to identify unmet needs in this population; (2) evaluate the extent to which these outcomes are captured by the mRS; and (3) identify predictors of each adverse outcome and high non-motor outcome burden (≥3 adverse outcomes).

METHODS

Study design and population

This study is part of the UCL Young Stroke Systematic Evaluation Study (ULYSSES); a prospective hospital-based cohort study investigating the causes and consequences of stroke in young adults. The ULYSSES study included consecutive young adults (<55 years old) who were admitted to the University College London Hospitals Hyperacute Stroke Unit (UCLH HASU) between 1st January 2017 and 1st January 2020 and clinically diagnosed with acute ischaemic stroke or ICH (confirmed on CT or MRI by a consultant neuroradiologist). The UCLH HASU provides specialised stroke care to an ethnically diverse population of approximately 1.6 million people from five North Central London boroughs (i.e., Barnet, Camden, Enfield, Haringey, Islington).

Data collection and follow-up

Study practitioners had full access to the hospital electronic health record system and were able to extract routine clinical data including patient demographics, medical history, admission stroke severity (measured by the National Institutes of Health Stroke Scale, NIHSS), and functional independence at both hospital admission and discharge (assessed using the modified Rankin Scale, mRS) (see Table S1 for risk factor definitions). Ischaemic stroke was classified using the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification.[20] ICH was classified as probable cerebral small vessel disease (cSVD); macrovascular; other secondary cause; and undetermined aetiology, using a modified CLAS-ICH classification.[21,22] Extracted data were checked for completeness and consistency. This study is reported in accordance with the RECORD (REporting of studies Conducted using Observational Routinely-collected Data) statement.[23]

Socioeconomic deprivation was calculated using the Index of Multiple Deprivation (IMD), a multi-domain measure of relative deprivation.[24] The IMD ranks 32,844 small areas in England (Lower-layer Super Output Areas (LSOA) each comprising approximately 1500 residents) from most deprived to least deprived, then divides them into 10 deciles. Deciles range from 1 (the most deprived 10%) to 10 (the least deprived 10%) of neighbourhoods nationally. We identified whether a patient was living in an area of socioeconomic deprivation by matching their postcode to the corresponding LSOA, and thereafter, obtained their IMD decile and decile for each sub-domain (see Table 1 for definitions).

All patients were invited to participate in a follow-up assessment 6-months after hospital discharge. Follow-up assessments were conducted as part of routine clinical care by trained

practitioners, primarily through outpatient clinic visits and telephone appointments. 6-month mRS scores were also collected during follow-up, with favourable scores defined as mRS 0-1.[25–28] To accommodate patients with moderate-to-severe impairments, such as communication difficulties or significant functional disability (mRS 4-5), additional support measures including home visits and postal questionnaires, were provided to reduce patient burden. In cases of language barriers, next of kin assisted with translating documents.

Patient-reported non-motor outcome measures

We assessed a range of patient-reported non-motor outcomes at 6-month follow-up using the Patient-Reported Outcome Measurement Information System-29 (PROMIS-29)[29] and Barthel Index.

PROMIS-29 evaluates seven health domains: anxiety, depression, fatigue, sleep disturbance, pain interference, ability to participate in social roles and activities, and physical function. Because of our focus on non-motor outcomes, we included all domains apart from physical function. PROMIS-29 was chosen over individual domain-specific instruments as it allows for the comprehensive assessment of multiple non-motor domains within a single standardised tool, reducing patient burden at follow-up. It has also demonstrated strong psychometric performance in chronic disease populations.[30] Anxiety, depression, fatigue, sleep disturbance, and pain interference are assessed based on the patient's experiences over the past seven days, while the ability to participate in social roles and activities domain reflects their present condition. The sleep disturbance domain asks patients to reflect on their sleep quality and whether they have difficulty falling asleep, while pain interference measures the extent to which pain disrupts daily activities, rather than the intensity of pain itself.

PROMIS-29 domain scores were standardised on a T scale with a mean of 50 and a standard deviation of 10, where higher scores indicate worse health. An adverse non-motor outcome was defined as a standardised domain score of ≥55, representing at least half a standard deviation above the general population average, which is considered indicative of mild symptoms.[11,31–33]

The Barthel Index assesses 10 activities of daily living including feeding, bathing, grooming, dressing, bowel control, bladder control, toileting, chair transfer, mobility, and stair-climbing. We focused on non-motor symptoms, including only the bowel and bladder control domains, which were assessed via patient self-report. For bowel control, patients reported being: (1) fully continent; (2) occasionally incontinent (i.e., occasional accidents); or (3) incontinent or requiring enemas. For bladder control, patients reported being: (1) fully continent; (2) occasionally incontinent; or (3) incontinent or catheterised and unable to manage alone. Only patients who reported being incontinent, requiring enemas, or catheterisation and unable to manage alone, were classified as having bowel or bladder dysfunction.

Statistical analysis

Data were analysed using STATA version 18. Patients from the ULYSSES cohort were included in the current analyses if they completed the PROMIS-29 and/or the Barthel Index at 6-month follow-up. Patient demographics and clinical characteristics were summarised using descriptive statistics. According to visual histogram and Q-Q plots, all continuous variables were non-normally distributed and were therefore, reported as median (interquartile range, IQR). Missing data were handled using pairwise deletion. For each non-motor outcome

domain, only patients with available data for that specific outcome measure were included in the analysis, and appropriate denominators were used.

Prevalence rates of each non-motor outcome domain were described using descriptive statistics. Differences in prevalence between patients with favourable (0-1) and unfavourable (2-5) mRS scores were compared using Pearson's chi-squared test or Fisher's exact test as appropriate. Co-occurrence of adverse outcomes was assessed by calculating the number of outcome domains reported per patient. For each of the eight non-motor outcome domains, the proportion of patients experiencing the domain alone or in combination with one or more additional domains was determined. To further explore patterns of co-occurrence, a co-occurrence matrix was constructed to quantify the percentage of patients experiencing each pair of outcome domains together.

To identify patient demographics and clinical characteristics associated with high non-motor outcome burden (≥3 adverse outcomes), categorical variables were compared using the Pearson chi-squared test or Fisher's exact test, and continuous variables using the Wilcoxon rank-sum test. Variables with p-values <0.2 in univariable analysis were entered into a multivariable logistic regression model. For each adverse non-motor outcome, unadjusted logistic regression analyses were performed to explore associations with baseline characteristics and variables significant at $p<0.2$ were included in an adjusted logistic regression model for each outcome. We considered variables that were significant at $p<0.05$ to be predictors of the outcome.

Data source and ethics statement

ULYSSES is a sub-study of the Stroke Investigation Group in North And central London (SIGNAL) registry. SIGNAL was approved by the UCLH NHS Foundation Trust Governance Review Board as a continuous service evaluation of a comprehensive clinical care programme (5-201920-SE) and the London South-East Research Ethics Committee (24/LO/0368); for this reason, informed patient consent was not required.

RESULTS

Patient demographics and clinical characteristics

The ULYSSES cohort included 552 patients with confirmed acute ischaemic stroke or ICH. 25/552 (4.5%) patients died prior to the 6-month timepoint, leaving 527/552 (95%) patients eligible for follow-up assessment. 34/527 (6.5%) patients could not be reached and were lost to follow-up (n=30) or declined clinical follow-up (n=4). A total of 493/527 (94%) patients completed at least one patient-reported outcome measure (i.e., PROMIS-29 or Barthel Index) and were included in the analysis (median age 48, IQR 41-52; 34% female; 52% White) (see Figure 1 for patient selection flowchart). 403/493 (82%) patients had an ischaemic stroke and 90/493 (18%) had an ICH (see Table S2 for baseline characteristics of patients included in the analysis). At the end of the follow-up period, 461/493 (94%) had completed the PROMIS-29 questionnaire and 477/493 (97%) patients had completed the Barthel Index.

Prevalence of adverse non-motor outcomes

The most common adverse non-motor outcomes were fatigue in 254/461 (55%, 95%CI 50-60%), reduced ability to participate in social roles and activities in 216/461 (47%, 95%CI 42-52%), and sleep disturbance in 212/461 (46%, 95%CI 41-51%) (see Figure 2). 163/461 (35%,

95%CI 31-40%) had anxiety and 149/461 (32%, 95%CI 28-37%) had depression. Pain interference was reported by 82/461 (18%, 95%CI 14-22%) patients. Bowel dysfunction was reported by 122/477 (26%, 95%CI 22-30%) and bladder dysfunction by 72/477 (15%, 95%CI 12-19%). Notably, reported proportions for each adverse outcome did not differ significantly between patients with favourable (0-1) § unfavourable (2-5) mRS scores (see Table S3).

Co-occurrence of adverse non-motor outcomes

Most patients (91%) reported at least one adverse non-motor outcome. 27% reported ≥4 adverse outcomes, 24% reported 2, 22% reported 3, and 18% reported one adverse outcome (see Figure 3A).

We examined how frequently each adverse outcome occurred in combination with 1, 2, 3, or ≥4 additional non-motor outcome domains. Across all domains, adverse outcomes most commonly co-occurred with 2, 3, or ≥4 additional outcomes (see Figure 3B). Bowel and bladder dysfunction were associated with the highest burden of co-occurring outcomes, with 33% and 36% of patients respectively, reporting these symptoms alongside ≥4 other adverse non-motor outcomes.

Fatigue and reduced social participation were among the most frequently co-occurring outcomes, with 30% of patients reporting both symptoms (see Figure 4). Fatigue also commonly co-occurred with sleep disturbance (24%), depression (22%), and anxiety (21%). Another notable co-occurrence was observed between sleep disturbance and reduced social participation (21%).

Predictors of each adverse outcome and high non-motor outcome burden

We did not identify independent predictors of high non-motor outcome burden (i.e., ≥3 adverse outcomes) (see Tables 2-3) or for six of the eight non-motor outcome domains. IMD decile and deciles for each IMD sub-domain were included in the multivariable models where they met the inclusion threshold ($p<0.2$) in univariable analysis, but none were significantly associated with high non-motor outcome burden or with any individual non-motor outcome. Two specific non-motor outcomes had significant predictors. Anxiety at 6 months was predicted by baseline factors, including ICH (OR 1.92; 95%CI 1.11-3.33; p=0.019) and higher education levels (per decile increase in education deprivation, OR 1.12; 95%CI 1.03-1.22; p=0.012). Pain interference was predicted by admission stroke severity (per NIHSS 10-point increase, OR 1.54; 95%CI 1.05–2.25; p=0.025) (see Figure S1).

DISCUSSION

Our study shows that young patients who are free of disability, as measured by the mRS, are frequently dealing with a high burden of adverse patient-reported non-motor outcomes even 6 months after their stroke. Despite appearing to be fully recovered by their families, carers or clinical teams, this group may struggle with 'hidden' non-motor outcomes, which may have a major adverse impact on their quality of life. This finding highlights the limitations of the mRS in capturing the impact of stroke in young adults and indicates that mRS 0-1 might, therefore, not be appropriate to define a 'favourable' outcome. Instead, a comprehensive, domain-specific approach may be needed to accurately assess non-motor aspects of recovery.

Consistent with earlier studies, fatigue was the most commonly reported adverse outcome, affecting 55% of patients.[34–36] Reduced ability to participate in social roles and activities (47%)

and sleep disturbance (46%) were also frequently reported in this cohort. Our findings on sleep disturbance align with similar studies, which found that 36-41% of patients experienced sleep difficulties.[36,37] Notably, the prevalence of these outcomes is comparable to findings from an older UK stroke population (mean age 71), where fatigue, reduced social participation, and sleep disturbance were reported by 57%, 55%, and 54% respectively. This suggests that adverse non-motor outcomes are equally as prevalent in younger stroke patients.[11]

Anxiety and depression have been investigated in young adults post-stroke, but their reported prevalence rates vary widely with proportions for depression ranging from 17–46% and anxiety from 19–40%.[12,14,36–38] This variation may be due to differences in outcome measures, cut-off thresholds, and follow-up durations across studies. A recent meta-analysis identified pooled prevalence rates of 31% for depression and 39% for anxiety.[39] In line with these findings, 32% of patients in our cohort reported depression, while 35% reported anxiety.

Few studies have investigated the co-occurrence or overlap of adverse patient-reported non-motor outcomes post-stroke in young adults.[6,14–17] In our cohort, 91% reported at least one adverse non-motor outcome, and the co-occurrence of 2, 3, or ≥4 additional domains was typical. Bowel and bladder dysfunction were the most likely to co-occur with multiple other domains, with 33% and 36% of patients, respectively, reporting these symptoms alongside ≥4 additional adverse non-motor outcomes. These findings are in contrast with results from a similar study in an older UK stroke population (mean age 71), where patients were more likely to report an adverse outcome alongside only one additional domain.[11] Our results suggest that adverse non-motor outcomes rarely exist in isolation, particularly in younger patients.

Fatigue was the most common outcome to occur in combination with other symptoms, particularly reduced social participation, sleep disturbance, depression, and anxiety. In our study, 22% of patients experienced both fatigue and depression, a commonly reported symptom cluster after stroke.[14,34] Additionally, fatigue frequently co-occurred with a reduced ability to participate in social roles and activities (30%), which may contribute to difficulties in returning to work. Prior studies have shown that higher levels of post-stroke fatigue are associated with a lower likelihood of returning to work.[40] The cycle of fatigue, reduced work participation, and financial stress may amplify non-motor symptoms and hinder overall recovery. Young adults may have greater personal, societal, and financial responsibilities, and therefore, may be disproportionately affected by these symptoms, further emphasising the need for targeted interventions and tailored rehabilitation pathways. Furthermore, the persistence of these non-motor outcomes at 6 months could be linked to gaps in early recognition and treatment. For example, if fatigue is secondary to sleep disturbance or depression, it might be preventable through early intervention. Addressing these issues in the early stages of recovery is crucial, as delayed care may create additional barriers to reintegration into daily life and the community, including returning to work.[41]

We did not identify independent predictors for high non-motor outcome burden (≥3 adverse outcomes), which highlights the difficulty in identifying patients who would benefit most from targeted early interventions. However, anxiety was predicted by ICH and higher education levels (indicated by increasing education deprivation decile, where decile 1 represents the most education deprived areas and decile 10 the least deprived), while pain interference was predicted by severe stroke.

Large population-based studies have identified various predictors of post-stroke anxiety, though these studies did not specifically focus on young patients. In a South London cohort, predictors included female sex, smoking, inability to work, and severe stroke.[3] Another study found ICH and previous stroke or transient ischaemic attack to be additional predcitors.[11] ICH, as a more severe form of stroke, may be associated with anxiety due to challenges in recovery. Lesion location could also contribute to increased anxiety,[42] although we did not investigate this in our study. Additionally, our finding that higher education levels are associated with anxiety may indicate a greater awareness of stroke-related risks in these patients, potentially increasing concerns about recurrence or challenges with recovery.[43]

Consistent with our findings, several population-based studies found an association between pain and stroke severity.[44–46] We did not collect information on specific post-stroke pain syndromes, however, potential reasons for this association include lesions affecting the thalamus and increased sensory disturbances.[45]

~~A~~ strength of this study is the consecutive inclusion of all patients presenting to the UCLH HASU with ischaemic stroke or ICH , as well as the high follow-up rate (94%). UCLH HASU is one of eight centres in London that provides specialised stroke care to an ethnically diverse population of approximately 1.6 million people from five North Central London boroughs. Most patients in our cohort were resident within the North Central London catchment area, with smaller proportions coming from outside this region or overseas (see Table S2). This broad geographic distribution supports the generalisability of our findings to similar urban and multi-ethnic populations.

However, this study has several limitations. The small cohort size limited our ability to identify predictors for each adverse non-motor outcome. Additionally, we did not investigate associations with radiological characteristics such as lesion location and small vessel disease burden, which future studies should aim explore. Selection bias may have influenced our findings, as patients who declined clinical follow-up, were lost to follow-up, or had died before the 6-month follow-up assessment, might have experienced higher levels of adverse non-motor outcomes. Socioeconomic deprivation was measured at the geographical rather than individual level, limiting its accuracy. We used a conservative threshold on the PROMIS-29 to identify adverse non-motor outcomes, following guideline recommendations to classify patients based on symptom severity. While this approach allowed for the inclusion of patients with milder symptoms, more stringent cut-offs might have identified more severe cases. While the PROMIS-29 has demonstrated strong psychometric performance in chronic disease populations,[30] it has not been formally validated in stroke, limiting certainty in interpreting domain scores in this context. Additionally, we did not have data on pre-stroke non-motor symptoms, making it difficult to determine which symptoms were stroke-related or pre-existing. Similarly, we did not collect detailed information on clinical interventions, rehabilitation, or psychological support that patients may have received, which could have impacted the progression or improvement of adverse non-motor outcomes over time.

In conclusion, this study highlights the significant burden of patient-reported non-motor outcomes in young adults with stroke. These findings emphasise the need for early recognition, rehabilitation, and management of non-motor outcomes in clinical practice. Given the current low-quality evidence on the optimal management of non-motor symptoms, there is a critical need for high-quality intervention studies to guide effective rehabilitation

strategies. It is important to identify patients at highest risk, so they can be flagged for enhanced care plans and targeted for specific interventions or referral to community networks, thereby improving functional independence, the likelihood of returning to work, and overall quality of life.

The timing and long-term impact of non-motor symptom onset remain unclear. Some symptoms may appear immediately after stroke, post-discharge, or later in the recovery period (i.e., beyond 6 months). The 2023 National Institute for Health and Care Excellence (NICE) guidelines recommend a 6-month review for all stroke patients, providing a key opportunity for routine assessment of non-motor symptoms. Our findings support incorporating these evaluations into formal review. However, it remains unknown whether symptoms continue to progress beyond this time point or if additional assessments are needed. Further research is required to understand the predictors and long-term trajectory of these symptoms in this specific age group and the potential demand for increased support services.

Additionally, future research should investigate the broader psychosocial and functional consequences of stroke in young adults, particularly regarding their ability to return to work and maintain social roles. Young stroke patients are often in their most economically productive and demanding years of employment and may face additional unique challenges, such as caregiving responsibilities. Existing stroke rehabilitation resources are predominantly tailored toward older stroke patients and should be adapted to address the concerns of younger patients.[41] Developing targeted interventions and support systems will be essential

for improving long-term recovery and facilitating reintegration into daily life for young stroke patients.

TABLES

Table 1. Definitions of the Index of Multiple Deprivation (IMD) and its sub-domains[20]

Index of Multiple Deprivation (IMD):	Combines information from the seven domains to produce an overall relative measure of deprivation.
Income:	Measures the proportion of the population experiencing deprivation relating to low income. This includes people that are out-of-work and those that are in work but who have low earnings.
Employment:	Measures the proportion of the working age population in an area who are involuntarily excluded from the labour market. This includes people who would like to work but are unable to do so due to unemployment, sickness or disability, or caring responsibilities.
Education:	Measures the lack of attainment and skills in the local population.
Health disability:	Measures the risk of premature death and the impairment of quality of life through poor physical or mental health.
Crime:	Measures the risk of personal and material victimisation at the local level.
Barriers to housing and services:	Measures the physical and financial accessibility of housing and local services. This includes 'geographical barriers' (i.e., physical proximity of local services) and 'wider barriers' (i.e., affordability and homelessness).
Living environment:	Measures the quality of the local environment. This includes the 'indoors' living environment (i.e., quality of housing) and 'outdoors' living environment (i.e., air quality and road traffic accidents).

Table 2. Results of univariable analysis comparing patient characteristics in patients with 0-2 vs ≥3 adverse non-motor outcomes (high non-motor outcome burden) at 6 months (n=493)

	0-2 Adverse outcomes (n=249)	**≥3 Adverse outcomes (n=244)**	***p*-value**
Age (years), median (IQR)	48 (41-51)	47 (41-52)	0.904
Female, n (%)	82 (32.9)	83 (34.0)	0.799
Ethnicity, n (%)			0.060
White	119 (48.2)	134 (56.3)	
Black	26 (10.5)	32 (13.5)	
Asian	23 (9.3)	12 (5.0)	
Other	79 (32.0)	60 (25.2)	
Socioeconomic deprivation, median (IQR) *(n=471)	4 (2-6)	4 (3-6)	0.175
Socioeconomic deprivation per domain, median (IQR) *(n=471)			
Income	4 (2-6)	4 (3-6)	0.066
Employment	4 (3-7)	5 (3-7)	0.169
Education	6 (4-8)	7 (4-9)	*0.041
Health disability	6 (5-9)	6 (5-9)	0.822
Crime	4 (2-5)	4 (2-6)	0.806
Barriers to housing and services	2 (1-4)	3 (1-4)	0.156
Living environment	3 (2-4)	3 (2-4)	0.596
Medical history, n (%)			
Hypertension	109 (43.8)	88 (36.1)	0.081
Diabetes mellitus	39 (15.7)	34 (13.9)	0.589
Dyslipidaemia *(n=454)	134 (58.0)	128 (57.4)	0.895
Family history of TIA/stroke	33 (13.3)	31 (12.7)	0.856
Previous TIA/stroke	51 (20.5)	38 (15.6)	0.157
Heart failure	3 (1.2)	6 (2.5)	0.298
Ischaemic heart disease	20 (8.0)	17 (6.9)	0.654
Migraine	27 (10.8)	25 (10.3)	0.829
Cigarette smoking	94 (37.8)	78 (32.0)	0.178
Recreational drug use	21 (8.4)	25 (10.3)	0.489
Excess alcohol consumption	27 (10.8)	28 (11.5)	0.824
Stroke type, n (%)			0.899
Ischaemic stroke	203 (81.5)	200 (81.9)	
Intracerebral haemorrhage	46 (18.5)	44 (18.0)	
Inpatient treatment, n (%) *(n=403)			
Intravenous thrombolysis	41 (20.2)	43 (21.5)	0.747

Mechanical thrombectomy	14 (6.9)	11 (5.5)	0.561
Medication history, n (%)			
Antiplatelet	180 (72.3)	180 (73.8)	0.711
Anticoagulant	48 (19.3)	59 (24.2)	0.187
Antihypertensive	127 (51.0)	115 (47.1)	0.390
Statin	179 (71.9)	169 (69.3)	0.522
Admission NIHSS, median (IQR) *(n=462)	3 (2-7)	4 (2-8)	0.344
Length of stay (days), median (IQR)	2 (1-5)	3 (1-5)	0.145
Pre-morbid mRS, median (IQR)	0 (0-0)	0 (0-1)	0.506
Discharge mRS, median (IQR)	2 (1-4)	2 (1-4)	0.261
6-month mRS, median (IQR) *(n=478)	1 (1-2)	2 (1-3)	0.104

Values are presented as median (IQR) for continuous variables and n (%) for categorical variables, with % representing the proportion of column total. Categorical variables were compared using the Pearson chi-squared test or Fisher's exact test as appropriate, and continuous variables were compared using the Wilcoxon rank-sum test. * denotes statistically significant variables (p<0.05). For those variables with missing data, the number of records available and used to calculate the proportion is provided. mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; TIA, transient ischaemic attack; IQR, interquartile range.

Table 3. Results of multivariable analysis for predictors of ≥3 adverse non-motor outcomes (high non-motor outcome burden) at 6 months (n=433)

	OR	95%CI	*p*-value
Age (years)	1.010	0.984 – 1.036	0.451
Ethnicity			0.130
White	Ref	Ref	Ref
Black	0.998	0.523 – 1.903	
Asian	0.484	0.221 – 1.058	
Other	0.662	0.415 - 1.056	
Socioeconomic deprivation (per decile)	0.854	0.652 – 1.120	0.255
Socioeconomic deprivation per domain (per decile)			
Income	1.065	0.808 – 1.403	0.655
Employment	1.052	0.815 – 1.360	0.696
Education	1.104	0.983 – 1.240	0.094
Barriers to housing and services	1.076	0.952 - 1.217	0.242
Medical history			
Hypertension	0.805	0.514 – 1.259	0.341
Previous TIA/stroke	0.783	0.466 – 1.315	0.355
Cigarette smoking	0.740	0.483 - 1.133	0.166
Stroke type			
Ischaemic stroke	Ref	Ref	Ref
Intracerebral haemorrhage	0.940	0.537 – 1.646	0.829
Admission NIHSS (per point)	1.011	0.978 - 1.047	0.512
Length of stay (days)	1.016	0.982 - 1.051	0.354

Variables with p-values <0.2 in the univariable analysis (Table 2) were included in the multivariable model. Anticoagulant medication was excluded because it is not applicable to intracerebral haemorrhage patients in the cohort. The model was adjusted for age, stroke type and admission NIHSS. * denotes statistically significant variables (p<0.05). NIHSS, National Institute of Health Stroke Scale; TIA, transient ischaemic attack.

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FIGURE LEGENDS

Figure 1. Patient selection flowchart.

Figure 2. Prevalence of adverse patient-reported non-motor outcome domains in the total cohort and in patients with favourable (0-1) vs unfavourable (2-5) 6-month modified Rankin Scale (mRS) scores. mRS was available for 478/493 (97%) patients; PROMIS-29 (assessing anxiety, depression, fatigue, sleep disturbance, pain interference, and reduced social participation) was available for 461/493 (94%) patients; the Barthel Index (assessing bowel and bladder dysfunction) was available for 477/493 (97%) patients.

Figure 3. Co-occurrence of adverse patient-reported non-motor outcome domains displaying: (A) the percentage of patients reporting a specific number of adverse outcomes, and (B) the percentage of patients who reported each individual outcome alongside 1, 2, 3, or ≥4 additional co-occurring outcome domains.

Figure 4. Heat plot representing co-occurrence of adverse patient-reported non-motor outcome domains, with values indicating the percentage of patients experiencing each pair of outcomes together.

SUPPLEMENTARY MATERIAL

Patient-reported outcomes after stroke in young adults: UCL Young Stroke Systematic Evaluation Study (ULYSSES)

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Supplementary Tables

Supplementary Figures

Table S1. Definitions of risk factors

Hypertension:	Diagnosed during hospital admission or a history of hypertension according to the 2003 WHO criteria as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg.
Diabetes mellitus:	Diagnosed during hospital admission or a history of diabetes according to the 1999 WHO criteria as fasting plasma glucose ≥7.0 mmol/L (126 mg/dL).
Dyslipidaemia:	Fasting bloods at time of hospital admission show elevated total (≥5.0 mmol/L) or low-density lipoprotein (≥3.0 mmol/L) cholesterol levels, and/or a low high-density lipoprotein (<1.0 mmol/L) cholesterol level.
Family history of TIA/stroke:	History of TIA or stroke in a first-degree relative as reported by the patient.
Previous TIA/stroke:	History of previous TIA or stroke as reported by the patient.
Heart failure:	Left ventricular ejection fraction ≤40% as identified during hospital admission or reported in patients' medical history.
Ischaemic heart disease:	Recent history of ST-segment elevation myocardial infarction or non-ST-segment elevation myocardial infarction.
Migraine:	History of migraine as reported by the patient.
Cigarette smoking:	Currently or during the last 5 years, as disclosed by the patient.
Recreational drug use:	Current or previous use of cannabis, cocaine, heroin, amphetamines, methamphetamines, or other recreational drugs, as disclosed by the patient or toxicology testing at time of hospital admission.
Excess alcohol consumption:	More than clearly moderate drinking (estimated intake of >112g or 140ml) of pure alcohol per week, as disclosed by the patient or judged by treating clinical team.

TIA, transient ischaemic attack; WHO, World Health Organisation.

Table S2. Patient demographics and clinical characteristics for the whole cohort

	(n=493)
Age (years), median (IQR)	48 (41-52)
Female, n (%)	165 (33.5)
Ethnicity, n (%) *(n=485)	
White	253 (52.2)
Black	58 (12.0)
Asian	35 (7.2)
Other	139 (28.7)
Geographic distribution of patient residence, n (%)	
North Central London	310 (62.9)
Other UK regions	161 (32.7)
Overseas	22 (4.5)
Socioeconomic deprivation, median (IQR) *(n=471)	4 (3-6)
Socioeconomic deprivation per domain, median (IQR) *(n=471)	
Income	4 (2-6)
Employment	5 (3-7)
Education	7 (4-8)
Health disability	6 (5-9)
Crime	4 (2-6)
Barriers to housing and services	2 (1-4)
Living environment	3 (2-4)
Medical history, n (%)	
Hypertension	197 (40.0)
Diabetes mellitus	73 (14.8)
Dyslipidaemia *(n=454)	262 (57.7)
Family history of TIA/stroke	64 (13.0)
Previous TIA/stroke	89 (18.1)
Heart failure	9 (1.8)
Ischaemic heart disease	37 (7.5)
Migraine	52 (10.6)

Cigarette smoking	172 (34.9)
Recreational drug use	46 (9.3)
Excess alcohol consumption	55 (11.2)
Stroke type, n (%)	
Ischaemic stroke	403 (81.7)
Intracerebral haemorrhage	90 (18.3)
TOAST classification, n (%)	
Large artery atherosclerosis	36 (8.9)
Cardioembolism	91 (22.6)
Small-vessel occlusion	56 (13.9)
Other aetiology	82 (20.4)
Undetermined aetiology	138 (34.2)
ICH aetiology, n (%)	
Probable cerebral small vessel disease	64 (71.1)
Macrovascular	10 (11.1)
Other secondary cause	4 (4.4)
Undetermined aetiology	12 (13.3)
Inpatient treatment, n (%) *(n=403)	
Intravenous thrombolysis	84 (20.8)
Mechanical thrombectomy	25 (6.2)
Medication history, n (%)	
Antiplatelet	360 (73.0)
Anticoagulant	107 (21.7)
Antihypertensive	242 (49.1)
Statin	348 (70.6)
Admission NIHSS, median (IQR) *(n=462)	3 (2-8)
Length of stay (days), median (IQR)	2 (1-5)
Pre-morbid mRS, median (IQR)	0 (0-0)
Discharge mRS, median (IQR)	2 (1-4)
6-month mRS, median (IQR) *(n=478)	1 (1-3)

Values are presented as median (IQR) for continuous variables and n (%) for categorical variables, with % representing the proportion of column total. For those variables with missing data, the number of records

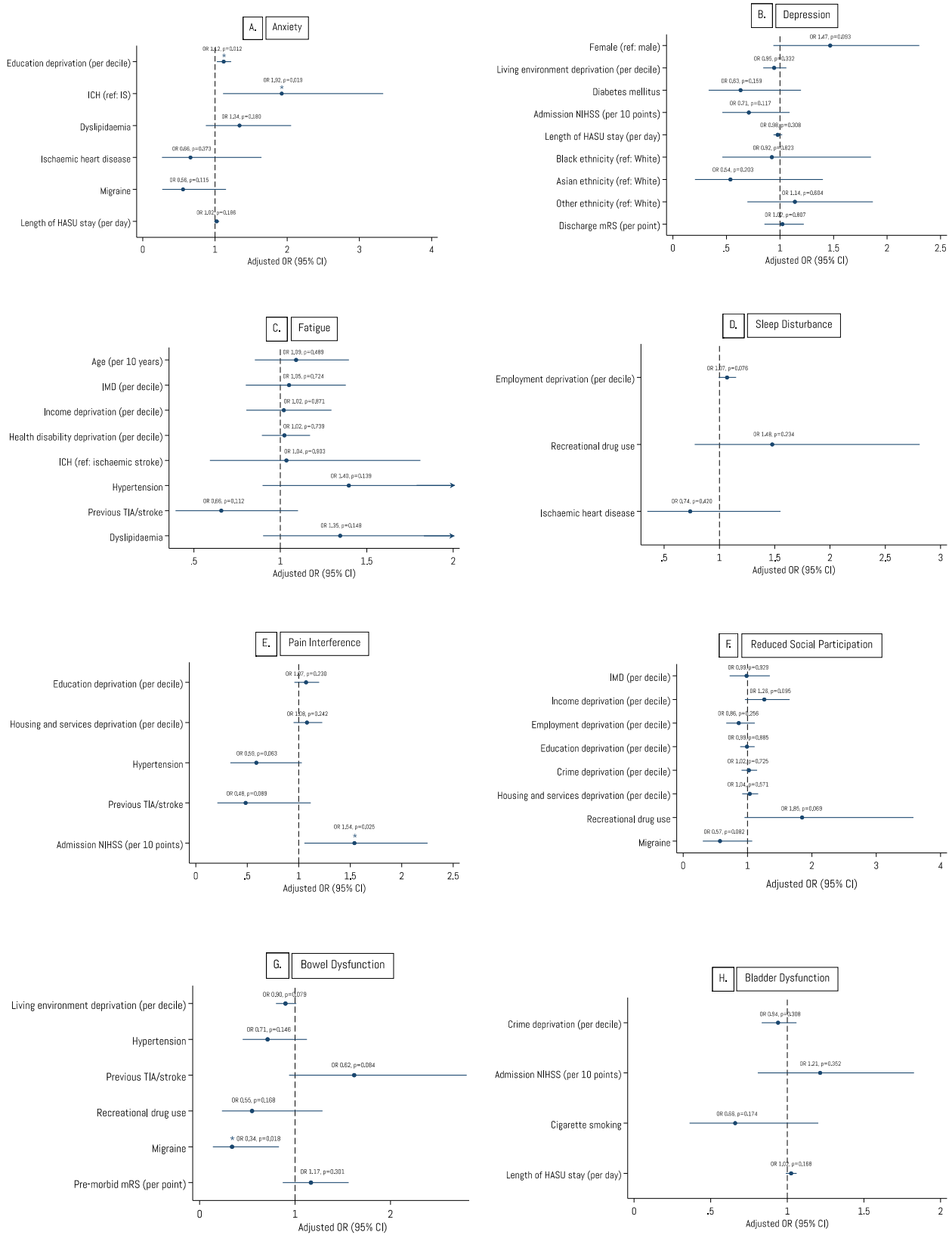
available and used to calculate the proportion is provided. North Central London boroughs include Barnet, Camden, Enfield, Haringey, Islington. mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; TIA, transient ischaemic attack; IQR, interquartile range; TOAST, Trial of Org 10172 in Acute Stroke Treatment; ICH, intracerebral haemorrhage.

Table S3. Results of univariable analysis comparing adverse patient-reported non-motor outcomes in patients with favourable (0-1) vs unfavourable (2-5) 6-month modified Rankin Scale (mRS) scores (n=478)

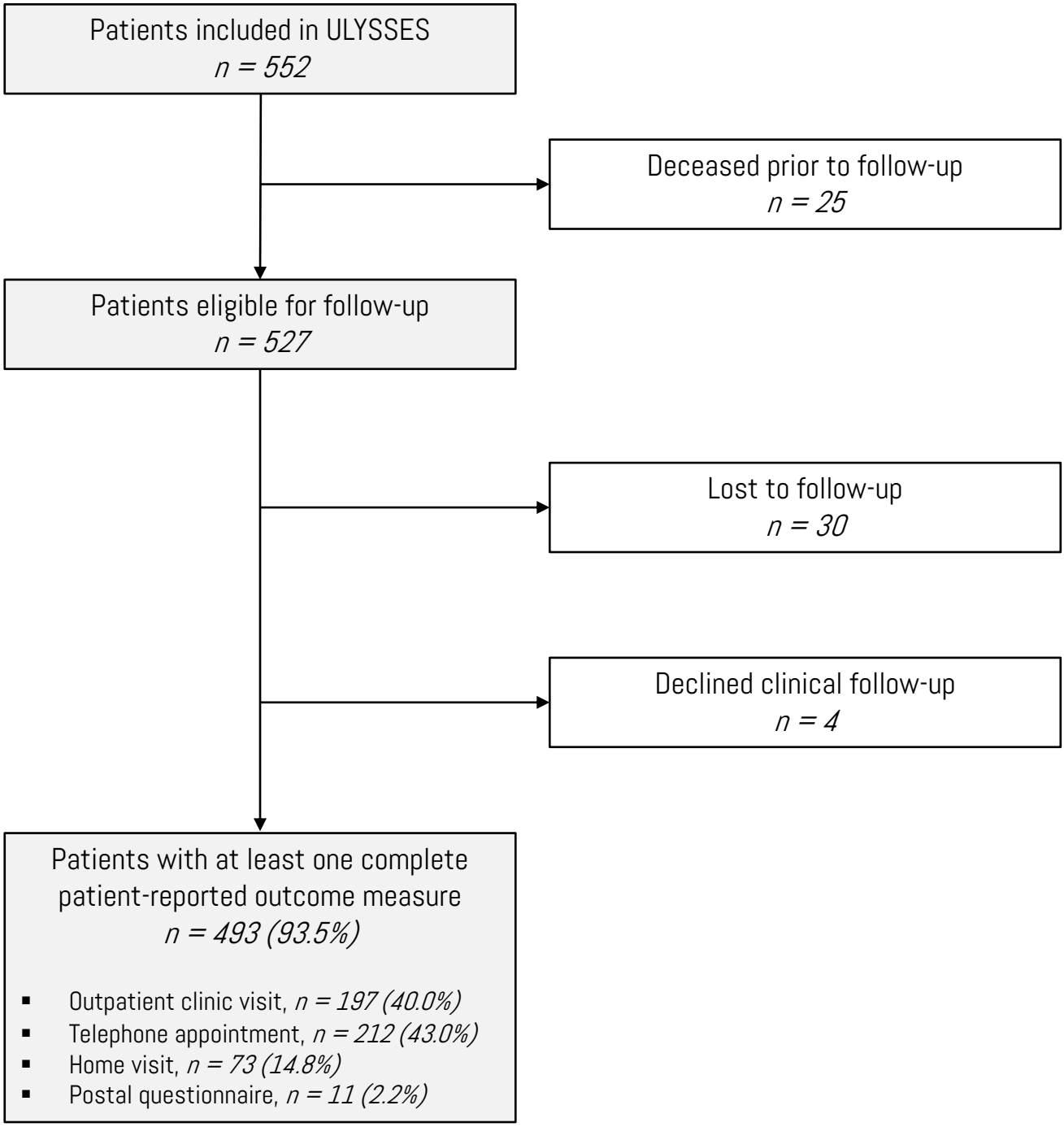
	mRS 0-1 (n=249)	**mRS 2-5 (n=229)**	***p*-value**
Anxiety, n (%) *(n=447)	75 (32.2)	82 (38.3)	0.175
Depression, n (%) *(n=447)	79 (33.9)	64 (29.9)	0.365
Fatigue, n (%)*(n=447)	132 (56.7)	115 (53.7)	0.536
Sleep disturbance, n (%)*(n=447)	109 (46.8)	96 (44.9)	0.684
Pain interference, n (%) *(n=447)	43 (18.5)	38 (17.8)	0.848
Reduced social participation, n (%) *(n=447)	107 (45.9)	102 (47.7)	0.713
Bowel dysfunction, n (%) *(n=463)	57 (23.9)	61 (27.2)	0.404
Bladder dysfunction, n (%) *(n=463)	33 (13.8)	36 (16.1)	0.494

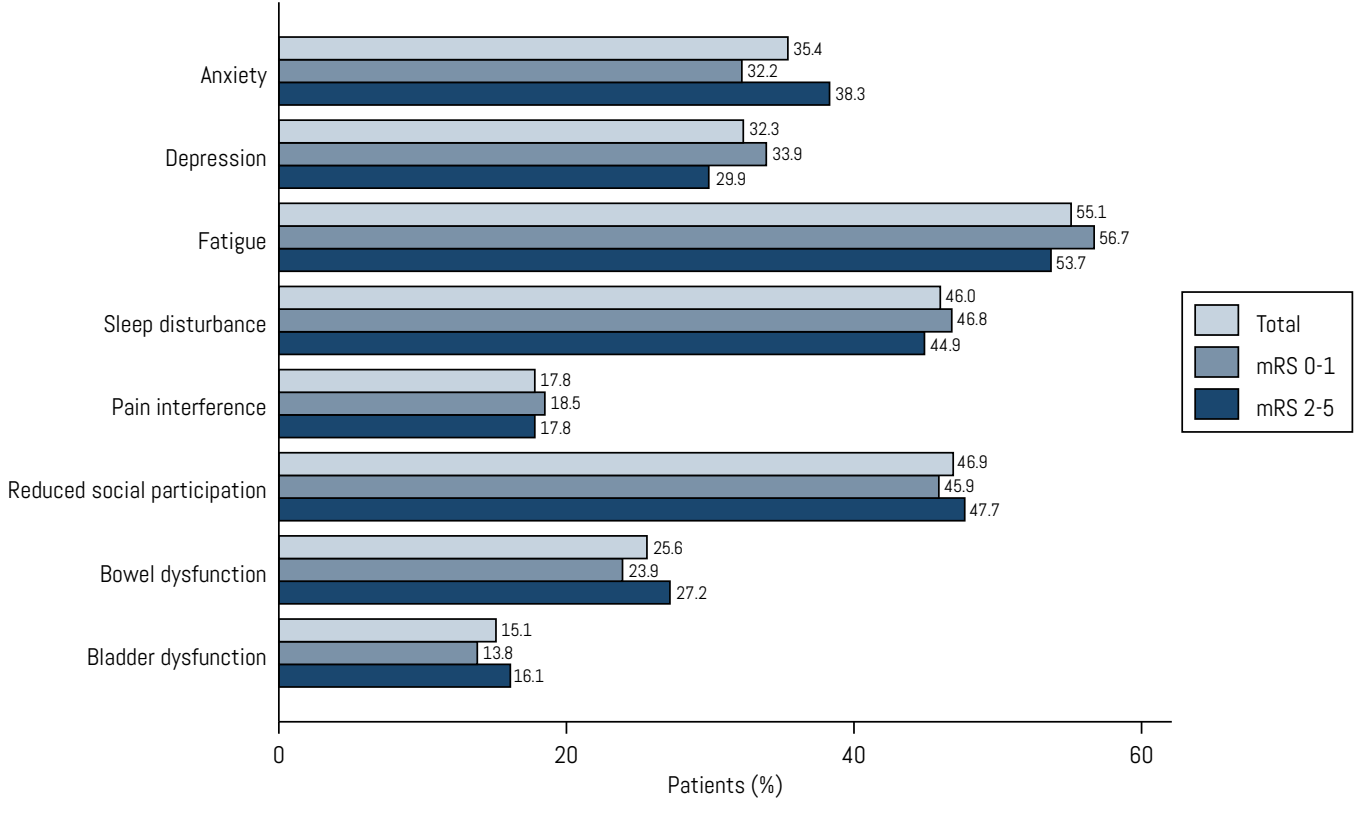
Values are presented as n (%), with % representing the proportion of column total. Variables were compared using the Pearson chi-squared test or Fisher's exact test as appropriate. * denotes statistically significant variables ($p<0.05$). For those variables with missing data, the number of records available and used to calculate the proportion is provided. mRS, modified Rankin Scale.

Figure S1. Adjusted analysis for each adverse patient-reported non-motor outcome after stroke

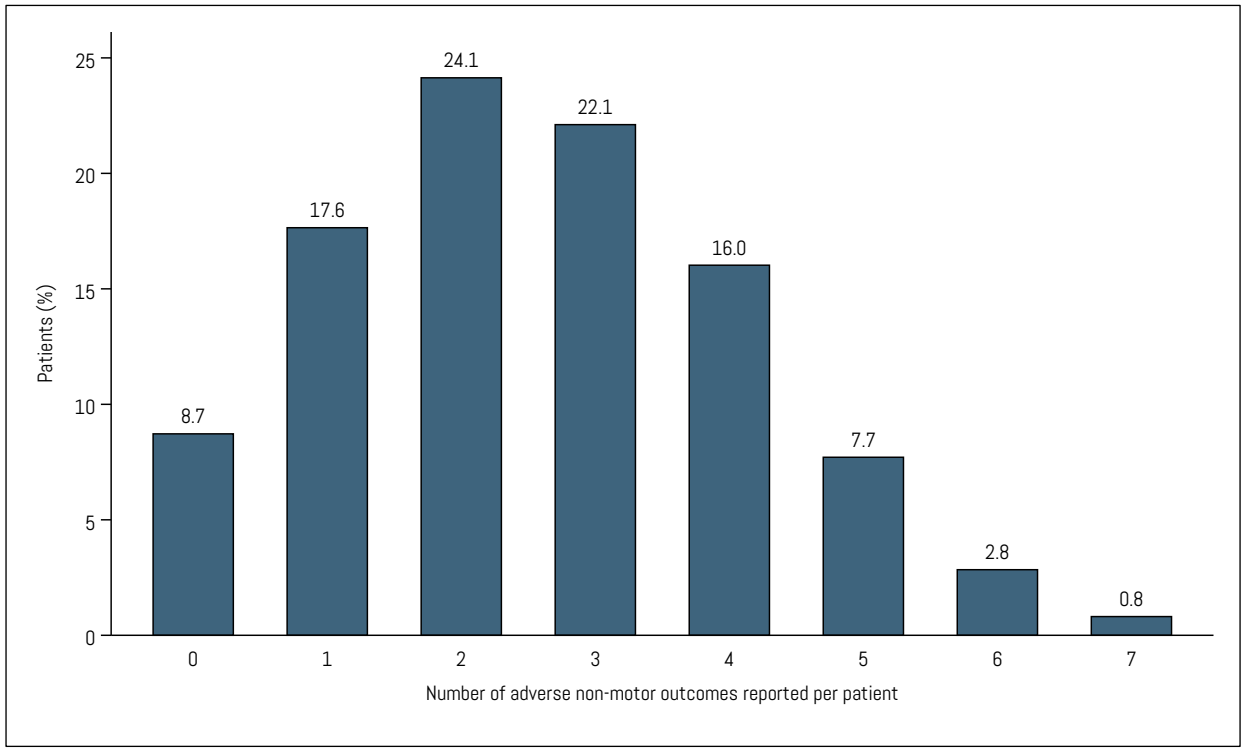


ICH, intracerebral haemorrhage; IS, ischaemic stroke; HASU, Hyperacute Stroke Unit; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; TIA, transient ischaemic attack; IMD, Index of Multiple Deprivation.

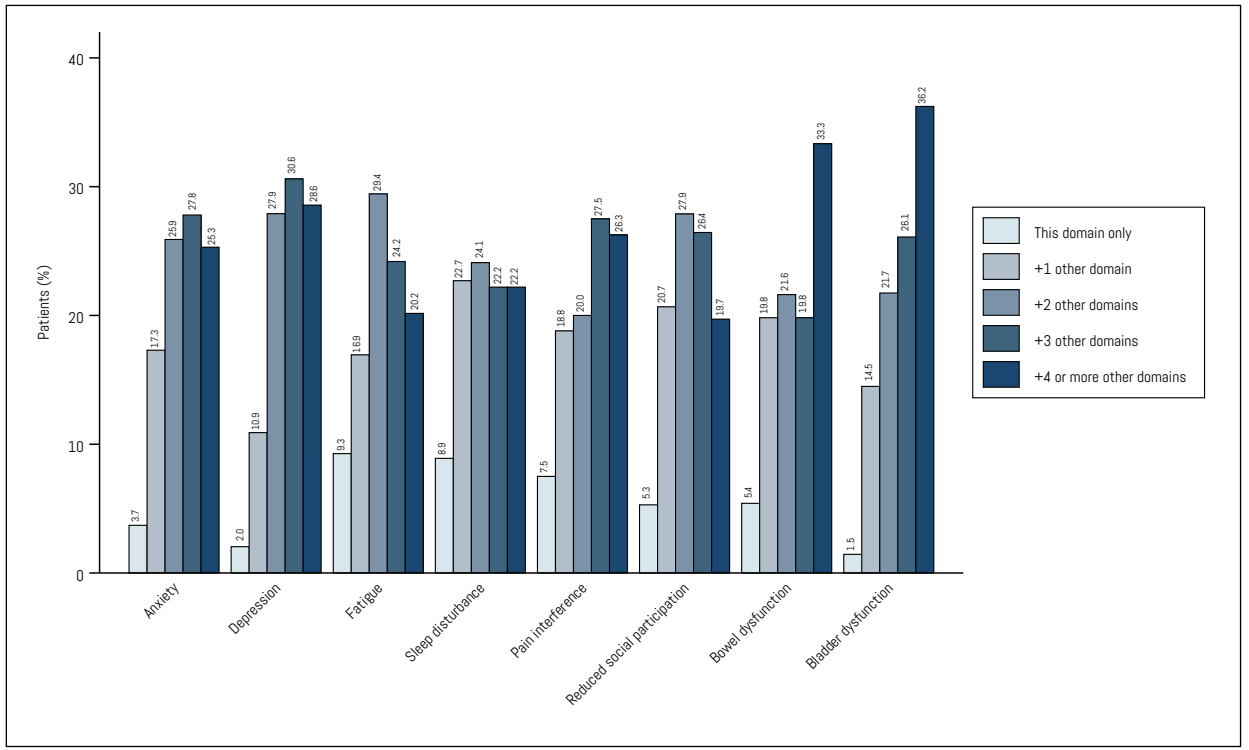

Patients included in ULYSSES
n = 552
Deceased prior to follow-up
n = 25
Patients eligible for follow-up
n = 527
Lost to follow-up
n = 30
Declined clinical follow-up
n = 4
Patients with at least one complete patient-reported outcome measure
n = 493 (93.5%)
Outpatient clinic visit, n = 197 (40.0%)
Telephone appointment, n = 212 (43.0%)
Home visit, n = 73 (14.8%)
Postal questionnaire, n = 11 (2.2%)

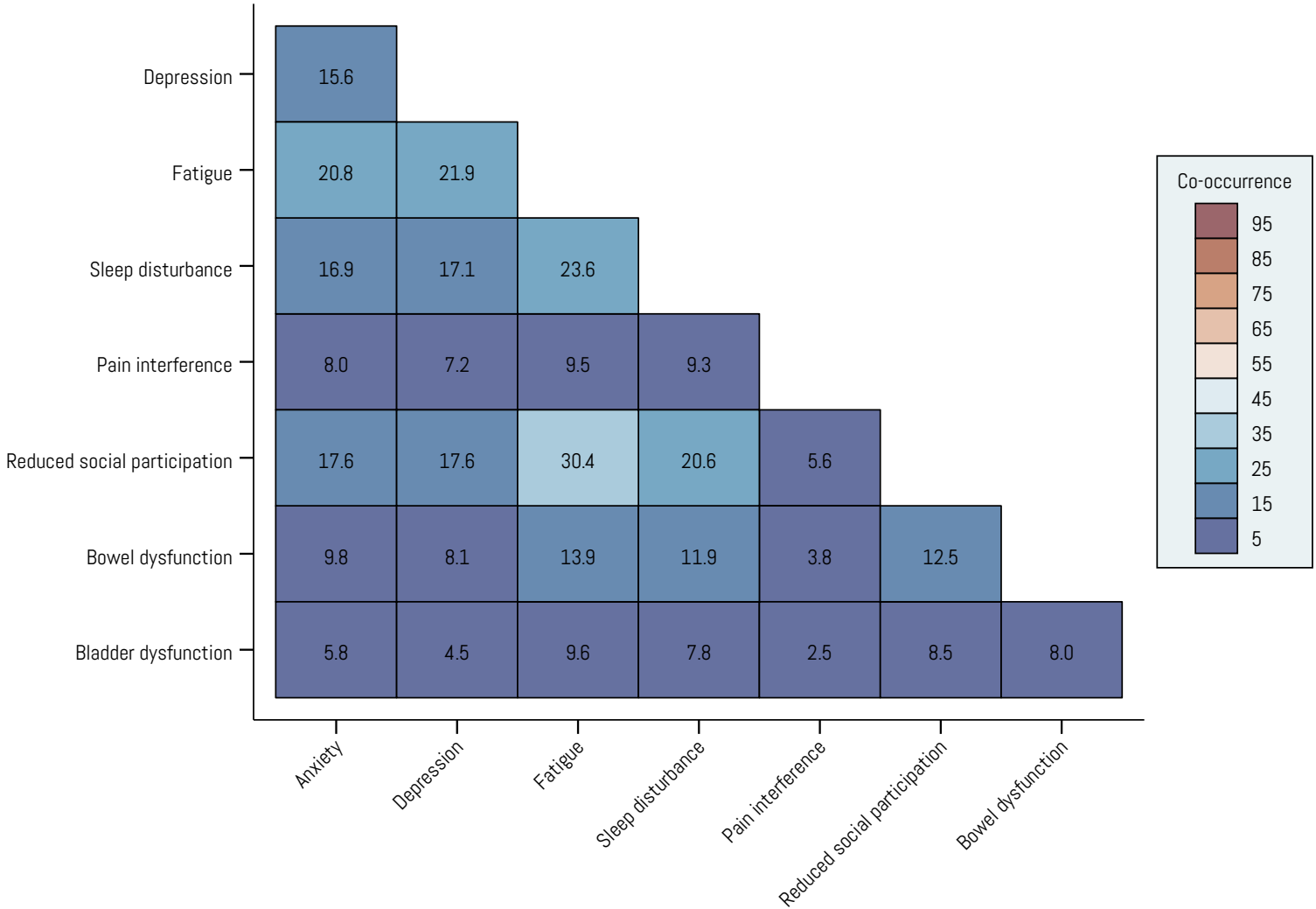

Anxiety
35.4
32.2
38.3
Depression
32.3
33.9
29.9
Fatigue
55.1
56.7
53.7
Sleep disturbance
46.0
46.8
44.9
Pain interference
17.8
18.5
17.8
Reduced social participation
46.9
45.9
47.7
Bowel dysfunction
25.6
23.9
27.2
Bladder dysfunction
15.1
13.8
16.1
0
20
40
60
Patients (%)
Total
mRS 0-1
mRS 2-5

A.


Patients (%)
25
20
15
10
5
0
24.1
22.1
17.6
16.0
8.7
7.7
2.8
0.8
0
1
2
3
4
5
6
7
Number of adverse non-motor outcomes reported per patient

B.


Patients (%)
40
30
20
10
0
3.7
17.3
25.9
27.8
25.3
2.0
10.9
27.9
30.6
28.6
9.3
16.9
29.4
24.2
20.2
8.9
22.7
24.1
22.2
22.2
7.5
18.8
20.0
27.5
26.3
5.3
20.7
27.9
26.4
19.7
5.4
19.8
21.6
19.8
33.3
1.5
14.5
21.7
26.1
36.2
Anxiety
Depression
Fatigue
Sleep disturbance
Pain interference
Reduced social participation
Bowel dysfunction
Bladder dysfunction
This domain only
+1 other domain
+2 other domains
+3 other domains
+4 or more other domains


Depression
Fatigue
Sleep disturbance
Pain interference
Reduced social participation
Bowel dysfunction
Bladder dysfunction
15.6
20.8 21.9
16.9 17.1 23.6
8.0 7.2 9.5 9.3
17.6 17.6 30.4 20.6 5.6
9.8 8.1 13.9 11.9 3.8 12.5
5.8 4.5 9.6 7.8 2.5 8.5 8.0
Anxiety
Depression
Fatigue
Sleep disturbance
Pain interference
Reduced social participation
Bowel dysfunction
Co-occurrence
95
85
75
65
55
45
35
25
15
5