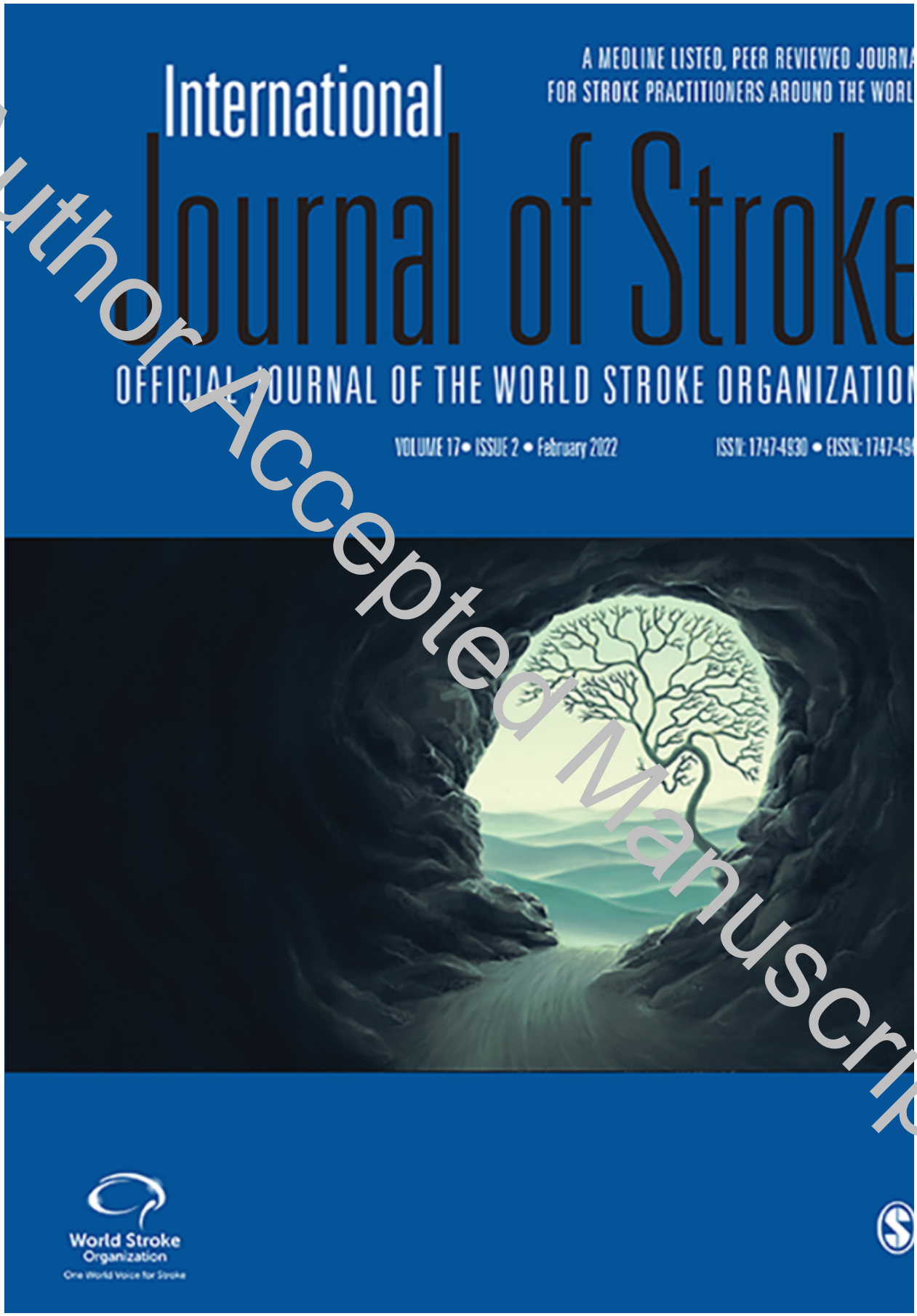

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Prevalence, patterns, and predictors of patient-reported non-motor outcomes at 30 days after acute stroke: prospective observational hospital cohort study

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Prevalence, patterns, and predictors of patient-reported non-motor outcomes at 30 days after acute stroke: prospective observational hospital cohort study

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ABSTRACT

Background Adverse non-motor outcomes are common after acute stroke and likely to substantially affect quality of life, yet few studies have comprehensively assessed their prevalence, patterns, and predictors across multiple health domains.

Aims We aim to identify the prevalence, patterns and the factors associated with non-motor outcomes 30 days after stroke.

Methods This prospective observational hospital cohort study (Stroke Investigation in North and Central London (SINGNAL) identified patients with acute ischaemic stroke or intracerebral haemorrhage (ICH) admitted to the Hyperacute Stroke Unit (HASU) University College Hospital (UCH), London, between August 1st 2018 and August 31st 2019. We assessed non-motor outcomes (anxiety, depression, fatigue, sleep, participation in social roles and activities, pain, bowel, and bladder function) at 30-day follow-up using the Patient Reported Outcome Measurement Information System-Version 29 (PROMIS-29) scale and Barthel Index scale.

Results We obtained follow-up data for 605/711 (84.1%) eligible patients (mean age 72.0 years; 48.3% female; 521 with ischaemic stroke, 84 with ICH). Anxiety (57.0%), fatigue (52.7%), bladder dysfunction (50.2%), reduced social participation (49.2%), and pain (47.9%) were the commonest adverse non-motor outcomes. The rates of adverse non-motor outcomes in ≥1, ≥2 and ≥3 domains were 89%, 66.3% and 45.8%, respectively; in adjusted analyses, stroke due to ICH (compared to ischaemic stroke) and admission stroke severity were the strongest and most consistent predictors. There were significant correlations between; bowel dysfunction and bladder dysfunction (κ= 0.908); reduced social participation and bladder dysfunction (κ= 0.844); and anxiety and fatigue (κ= 0.613). We did not identify correlation for other pairs of non-motor domains.

Conclusions Adverse non-motor outcomes are very common at one month after stroke, affecting nearly 90% of evaluated patients in at least one health domain, about two-thirds in two or more domains, and almost 50% in three or more domains. Stroke due to ICH and admission stroke severity were the strongest and most consistent predictors. Adverse outcomes occur in pairs of domains such as with anxiety and fatigue. Our findings emphasise the importance of a multi-domain approach to effectively identify adverse non-motor outcomes after stroke to inform the development of more holistic patient recovery programs.

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Introduction

Globally, stroke is the second most common cause of death and the third leading cause of disability-adjusted life years.[1] Outcome measurement in stroke is dominated by motor impairments, communication, and mobility, often assessed using the modified Rankin scale (mRS), which does not fully capture the impact of key non-motor outcome domains on health-related quality of life after stroke.[2-6,17] Furthermore, impairments not included in the mRS such as post-stroke anxiety, depression, and fatigue are associated with functional disability and premature death.[3-4]

Most previous studies investigated only individual non-motor domains, mainly in patients with ischaemic stroke.[8-16] We therefore aimed to: (1) assess a full range of patient-reported non-motor outcome domains at 30-days after acute stroke; (2) identify the burden of adverse outcomes in multiple domains; (3) investigate correlations between non-motor outcome domains; and (4) determine baseline independent predictors (including ischaemic stroke vs intracerebral haemorrhage, ICH) for each adverse non-motor outcome.

Methods

Study design and data source

The Stroke Investigation in North and Central London (SIGNAL) prospective hospital-based cohort study is based at the University College London Hospitals (UCLH) hyper-acute stroke unit (HASU) which serves an ethnically diverse population of 1.6 million adults resident within five North Central London boroughs (Camden, Islington, Enfield, Harringay, and Barnet).

Study Population

We assessed all patients admitted consecutively with acute stroke between 1st August 2018 to 31st August 2019, for eligibility. Patients were included if they were: aged ≥18 years old, resident in North Central London; had a clinical diagnosis of acute stroke (ischaemic or haemorrhagic) validated by a consultant stroke physician and confirmed on brain imaging (CT, MRI, or both) by a consultant neuroradiologist; and were able to provide complete data from two or more domains of the PROMIS 29 patient-reported health outcome scale at 30-day follow-up (further details below). Socio-demographic and clinical characteristics including age, sex, ethnic origin, admission stroke severity (defined using the NIH Stroke Scale, NIHSS), previous medical history, medication history, discharge destination and functional outcome at hospital discharge (mRS), were obtained from electronic health records.

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We made every effort to include all eligible participants by providing additional supporting measures. We reduced patient burden for individuals who reported moderate to severe communication problems, cognitive impairment, or language difficulties by providing options to be given extra time, complete a postal questionnaire or have the outcome measures translated or completed by a proxy responder. Proxy responders were eligible to assist individuals in completing the questionnaires if they were listed as a registered carer or next of kin (NOK) in the patients' health records.

Outcomes at 30-day follow-up

Patient-reported non-motor outcome scales were administered as part of routine care by clinically trained practitioners via telephone appointment. We used the PROMIS-29 v2.0 scale, which assesses seven health domains (physical function, anxiety, depression, fatigue, sleep disturbance, social participation, and pain, using four items per domain. Domains including anxiety, depression, fatigue, sleep disturbance, and pain capture individuals' status in real time, asking about their experiences in the past 7 days. By contrast, the physical function and social participation domains capture status at the time of the initial stroke. Each PROMIS-29 domain score is standardised to the US general population on the T scale, with a mean of 50 and a standard deviation of 10; higher mean scores indicate worse outcomes. We considered an adverse non-motor domain to be present if the standardised domain score was ≥55 (i.e., a score half a standard deviation worse than the general population).[11, 15]

We measured bowel and bladder function using the Barthel Index. We considered individuals to have bowel or bladder dysfunction if they scored between 0 – 1, or if they had a urinary catheter at 30-day follow-up.

Protocol Approvals, Registrations, and Patient Consent

The SIGNAL registry was approved by the UCL Hospitals NHS Foundation Trust Governance Review Board as a Service Evaluation (code: 5-201920-SE). Since the study data were collected as part of routine clinical care, the requirement for individual patient consent was waived.

Statistical analysis

We summarised patient demographics and clinical characteristics with descriptive statistics. We compared continuous data using the Wilcoxon rank sum test, and categorical data with Pearson's X^2 tests. We recorded the clinical and socio-demographic characteristics of those patients who did not meet the inclusion criteria (Supplementary Material, Table 1). We used histograms and q-q plots to

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understand the distribution of the data. We calculated the prevalence of adverse non-motor outcomes for each domain. We used the Pearson's X^2 test to compare the differences in prevalence of non-motor outcomes between ischaemic stroke and ICH. We used the Benjamin-Hochberg false discovery rate procedure to guard against potential false positive discoveries.[20] We performed multivariable logistic regression analysis for individual non-motor outcome domains controlling for clinically relevant variables (age, sex, previous history of stroke) and characteristics significantly ($p < 0.10$) associated with each non-motor outcome in univariable analysis; The statistical tests were two sided and statistical significance was set at $p < 0.05$.

The characteristics of those reporting more than two or three adverse outcomes were compared to the total study sample (see Supplementary Material, Table 3) using χ^2 test and *t* test or the Kruskal-Wallis test as appropriate. We calculated *Kappa* statistics to quantify co-occurrence of non-motor outcome pairs. All statistical analysis were performed using Stata statistical software version 16.1.

Results

Patient characteristics

We included 605/719 (84%) of potentially eligible survivors (mean age 72.0 years; 48.3% female; 521 with ischaemic stroke, 84 with ICH) (see Figure 1 and Table 1). The reasons for excluding 114 individuals were that they: declined follow-up; did not attend follow-up; were uncontactable; or were unable to provide non-motor data. Supplementary Material (Table 3) provides detailed baseline characteristics of individuals excluded from our analysis.

We provided additional supporting measures in 51/605 (8.4%). Of these 51 patients who needed additional support, 9 had a recorded dementia diagnosis, 17 had moderate-severe memory problems, and 13 had severe communication problems, while 12 were non-English speakers. Regarding the additional support provided, 27/51 (52.9%) needed direct proxy assistance (from a registered carer or next of kin) to complete outcomes, 4 (7.8%) required proxy assistance to translate, and 20 (39.2%) required extra time either during the assessment or by being sent a postal pack.

Prevalence of adverse non-motor outcomes

The most common adverse non-motor outcomes were anxiety (57.0%), fatigue (52.7%), impaired bladder function (50.2%), reduced participation in social roles and activities (49.3%), and pain (47.9%) (Figure 2). Compared to patients with ischaemic stroke, the following adverse non-motor outcomes were significantly more common in patients with ICH: anxiety (difference 15.3%, 95% CI 0.03% –

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27.4%); fatigue (difference 15.2%, 95% CI 0.02% – 19.3%); reduced participation in social roles and activities (difference 15.9, 95% CI 0.04% – 28.1%); pain (difference 14.2%, 95% CI 0.02% – 26.5%); and impaired bowel function (difference 16.4%, 95% CI 0.04% – 21.1%) (Figure 2; Supplementary Material, Table 2).

Data from the multivariable analysis are shown in Table 2. Compared with patients with ischaemic stroke, patients with ICH had significantly higher adjusted prevalence ratios for anxiety (adjusted odds ratio, OR, 1.83; 95% CI 1.01 – 3.12), fatigue (OR 1.80; 95% CI 1.00 – 3.24), reduced social participation (OR 1.72, 95% CI 1.02 – 3.19), pain (OR 1.93; 95% CI 1.14 – 3.41) and bowel dysfunction (OR 3.72; 95% CI 1.91 – 7.12). Other characteristics associated with adverse non-motor outcomes in multiple domains were: age >60 years; female sex; previous history of stroke or TIA; stroke severity on admission; ethnic origin; and discharge mRS score 4 – 5.

Prevalence of adverse non-motor outcomes in multiple domains

The prevalence of ≥1, ≥2 and ≥3 adverse non-motor outcomes were 88.4%, 66.3%, and 45.8%, respectively. Figure 3 shows how frequently each non-motor health domain outcome is associated with one, two or three co-occurring outcomes. All non-motor domains were frequently associated with other co-occurring adverse outcomes. Compared to the total study sample, those reporting multiple (>2) adverse non-motor outcomes had a higher stroke admission NIHSS (median= 7 *vs* 4, p= 0.0450) and hospital discharge mRS score (median 2 *vs* 1, p= 0.0230) (Supplementary Material, Table 4).

Correlations between each non-motor domain on PROMIS-29 and Barthel Index are summarised in figure 4. There was substantial correlation for anxiety with fatigue (κ= 0.613); reduced social participation with bladder dysfunction (κ= 0.844); and bowel dysfunction with bladder dysfunction (κ= 0.908).

Discussion

We found that adverse patient-reported non-motor outcomes were extremely common in people following acute stroke: 88.4% of the evaluated stroke survivors reported at least one adverse non-motor outcome, 66.3% two or more, and 45.8% 3 or more. The health domains most affected were anxiety (57.0%), fatigue (52.7%), impaired bladder function (50.2%), and reduced participation in social roles and activities (49.3%). Most health domains were more likely to be affected after ICH compared to ischaemic stroke, even after adjusting for confounding factors including stroke severity.

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We identified pairs of co-occurring domains such as bowel dysfunction and bladder dysfunction, reduced social participation and bladder dysfunction, and anxiety and. Our findings have potential clinical implications: first, they show high burden of patient-reported non-motor outcomes; second they underline a substantial unmet patient-reported healthcare need requiring the development of appropriate multidisciplinary specialist comprehensive multi-domain screening and care delivery pathways; third, they highlight those at highest risk, for example people with stroke due to ICH; fourth, the design of future care pathways to address adverse patient-reported non-motor outcomes may be informed by our findings of associations between these outcomes (e.g. anxiety and fatigue) .

Our findings are in line with other, predominantly single domain studies, [5-9, 12, 15, 17 - 25] including some which suggest that even after complete motor recovery, deficits in non-motor domains such as anxiety, depression, fatigue, pain, bowel and bladder dysfunction may prevent a return to independent living.[12,13,15] Our analysis extends these findings by providing new data for all key domains, and predictive factors in the same cohort; few previous studies investigated all these domains in the same population.[14, 15, 20, 25]

We found that anxiety affected 57% of patients and was associated with ICH (compared to ischaemic stroke), age <50 years, and worse admission stroke severity. A previous meta-analysis found persistent anxiety in 38–76% of patients but did not investigate predictive factors.[3,12] Small cohort studies suggest that ICH volume, lobar location, and MRI findings of cerebral amyloid angiopathy (CAA) predict anxiety after stroke,[33] but further larger studies are needed in ICH subgroups.

Our findings that fatigue and depression are common (affecting 52.7% and 36.5% of patients, respectively) are consistent with previous reports describing fatigue in 42 – 53% (between one month to 6 months after stroke) and depression in 24– 39% (between 3 months to 5 years).[3, 12, 21, 33] We found that fatigue is more prevalent after ICH than ischaemic stroke (65.8% *vs* 50% of patients, respectively), in line with a meta-analysis of small studies that found that ICH stroke survivors had nearly double the prevalence of fatigue compared to ischaemic stroke (66% *vs* 36%, respectively).[12,19,21,22]

Our findings of reduced social roles and participation after stroke are consistent with some,[23 – 26] but not all previous studies.[27,28] In agreement with previous studies,[23 –26] patients with previous stroke or TIA, and poor functional outcome at discharge, more often reported reduced social participation, but we additionally found associations with admission stroke severity and ICH which may be important to

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better target interventions such as training carers, improved social support, dedicated rehabilitation, and treatment of depression.[29]

Our findings confirm that pain is commonly reported after stroke (overall prevalence 47.9%), consistent with previous estimates of between 11- 55%.[30–33] We found that pain is more common after ICH than ischaemic stroke (60.3% *vs* 46%) consistent with a small cohort study which reported pain to be more frequent after thalamic ICH than ischaemic stroke.[34]

We identified sleep disturbance in 40.9% of patients at 30-day follow-up, in agreement with previous studies reporting prevalence of 20-67% at one month to 5 years after stroke;[35–40] black ethnic origin was associated with sleep disturbance, consistent with previous large cohort studies.[39,40]

We found that bladder dysfunction was more prevalent than bowel dysfunction and that bowel dysfunction was more prevalent after ICH than ischaemic stroke, in line with a previous meta-analysis.[41] We found a lower prevalence of bowel dysfunction than some previous reports, which could be attributed to not sub-classifying faecal incontinence and *s* constipation, under-reporting, the screening tool we used (Barthel Index), or selection or ascertainment bias in other studies.[41–44]

Few previous studies have investigated patterns of co-occurrence and correlations between adverse non-motor outcomes after stroke. We found a high burden of multiple adverse non-motor outcomes, with about two-thirds of participants reporting two or more, and nearly on-half reporting three or more. We also found that all adverse non-motor outcomes were associated with the co-occurrence of one, two, or three others (i.e., none occurred in isolation), but that some co-occurred more often than expected by chance (anxiety and fatigue, social participation and bladder function, and bladder and bowel function).

Our study has strengths. We included consecutive patients with acute stroke from a defined ethnically diverse large and defined North London population, and systematically assessed adverse non-motor outcomes in multiple health domains. Stroke diagnosis was confirmed by brain imaging ensuring accurate diagnosis and classification. We used false discovery rate analysis to avoid false-positive findings and were able to assess other independent baseline predictors (including ICH) while adjusting for potential confounding factors.

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We also acknowledge potential limitations including potential selection bias, though this was minimised by including sequential patients with a high rate of follow-up (84.1%). Compared to those included, there was a higher proportion of people of non-white ethnicity in those excluded, emphasising the importance for future studies including all ethnic groups. We also acknowledge that for anxiety and depression PROMIS-29 measures symptom burden over the 7 days and does not provide a formal diagnosis of these conditions. Our data describe the burden on non-motor outcomes at one month, but more data are needed at longer-term follow-up. Although 47.8% of participants were discharged to an Acute Stroke Unit (ASU), where they received rehabilitation input, including physiotherapy, speech and language, and occupational therapy, we do not have detailed data on the exact degree of rehabilitation input received for each participant. Furthermore, we did not have access to neuropsychological interventions provided after HASU discharge.

Our findings regarding the prevalence, patterns and predictors of adverse patient reported non-motor outcomes should help stroke services to plan pathways to first ascertain and then address these patient-reported adverse outcomes to improve post-stroke quality of life and provide patient-centred stroke care pathways. However, further long-term studies - including information on functional impact - are needed to fully establish the clinical relevance of these patient-reported non-motor outcomes.

Acknowledgements

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Disclosure

We declare no relevant conflicts of interest.

Sources of funding

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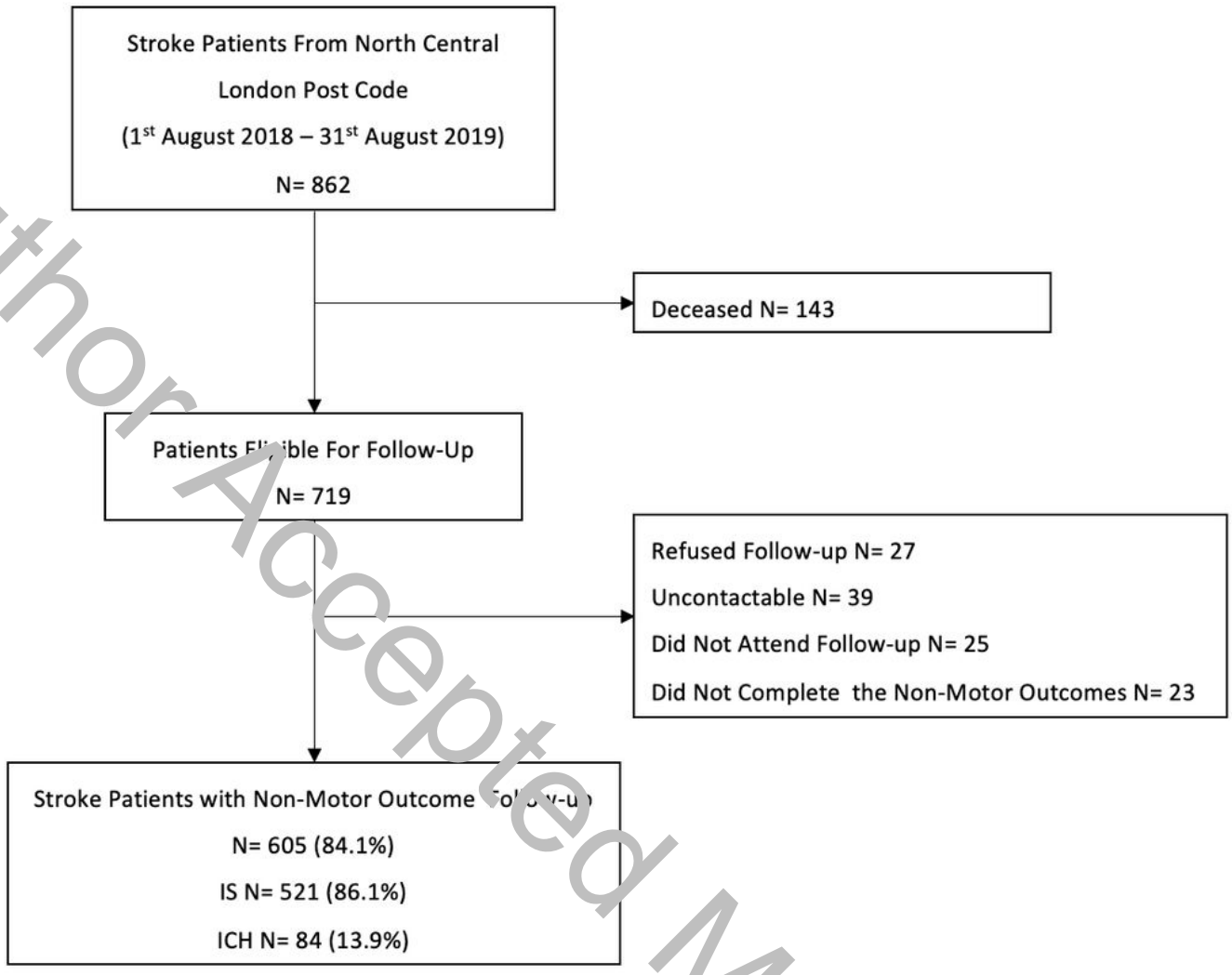
Figure 1 – Patient selection flow chart



IS= ischaemic stroke; ICH= intracerebral haemorrhage

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Table 1- Demographic and clinical characteristic data for all patients and according to stroke type (ischaemic stroke or ICH)

Characteristics	All stroke	IS	ICH	IS vs ICH P
	605	**521**	**84**	
Age range (IQR)	72.0 ± 14.9	72.2 ± 14.8	70.9 ± 15.8	0.4654
Female sex	292 (48.3%)	244 (46.8%)	48 (57.1%)	**0.103**
Ethnicity n (%) (n= 590)				
White	392 (66.4%)	328 (63.0%)	64 (76.1%)	**0.057**
Asian	48 (8.1%)	42 (8.1%)	6 (7.1%)	…
Black	28 (4.8%)	26 (5.0%)	2 (2.4%)	…
Other	122 (20.7%)	111 (21.9%)	11 (13.25%)	…
Medical history n (%)				
Previous stroke/TIA	208 (34.4%)	177 (33.9%)	31 (36.9%)	0.600
Hypertension	407 (67.9%)	337 (65.4%)	70 (83.3%)	**0.001**
Congestive Heart Failure	27 (4.5%)	22 (4.3%)	5 (5.9%)	0.489
Diabetes Miletus	166 (27.7%)	143 (27.8%)	23 (27.4%)	0.942
AF	132 (21.9%)	116 (22.3%)	16 (19.1%)	0.508
Dementia	9 (1.5%)	6 (1.2%)	3 (3.6%)	0.617
Smoking History (n= 558)	208 (37.3%)	180 (37.3%)	28 (36.8%)	0.933
Catheter	43 (7.1%)	37 (6.8%)	6 (6.7%)	0.539
Medication history n (%)				
Thrombectomy	32 (5.3%)	32 (5.3%)		…
Thrombolysis	124 (20.5%)	124 (20.5%)	0	…
Antiplatelet	340 (56.2%)	327 (62.8%)	13 (15.5%)	**<0.001**
Anticoagulant	142 (23.5%)	133 (25.5%)	9 (10.71%)	**0.003**
Antihypertensive	468 (77.7%)	393 (75.9%)	75 (89.3%)	**0.006**
Statin	260 (42.9%)	221 (42.4%)	39 (46.4%)	0.491
Antidepressants	23 (3.8%)	19 (3.6%)	4 (4.8%)	0.739
Clinical Outcomes Median (range)				
Pre-Morbid mRS	0 (0 – 1)	1 (0 – 1)	1 (0 – 2)	**0.0225**
Admission NIHSS	4 (2 – 8)	5.8 (2 – 9)	6.3 (4.5 – 12.5)	**0.0374**
Discharge mRS	3 (1 – 4)	1 (1 – 4)	3 (1 – 5)	**0.0428**
30-day mRS	2 (1 – 3)	1 (1 – 3)	2 (1 – 4)	**0.0235**
Time to Follow-up	32.4 (28 – 36)	31.8 (26 – 34)	32.1 (29 – 36.3)	0.5837
Discharge Location n (%) n= 579				
Home with ESD	141 (24.4%)	127 (25.6%)	14 (16.9%)	**<0.001**
ASU	277 (47.8%)	229 (46.2%)	48 (57.8%)	…

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Care Home	5 (0.9%)	1 (0.2%)	4 (4.8%)	…
Home No ESD	156 (26.9%)	139 (28.0%)	17 (20.5%)	…
Proxy Response (N, %)	31 (5.1%)	22 (4.2%)	9 (10.7%)	0.048

Significant differences in results are highlighted in bold. IS= ischaemic stroke; ICH= intracerebral haemorrhagic stroke; IQR= interquartile range; TIA= transient ischaemic attack; AF= arterial fibrillation; NIHSS= NIH stroke scale score; mRS= modified Rankin Scale; ESD= early supported discharge; ASU= acute stroke unit

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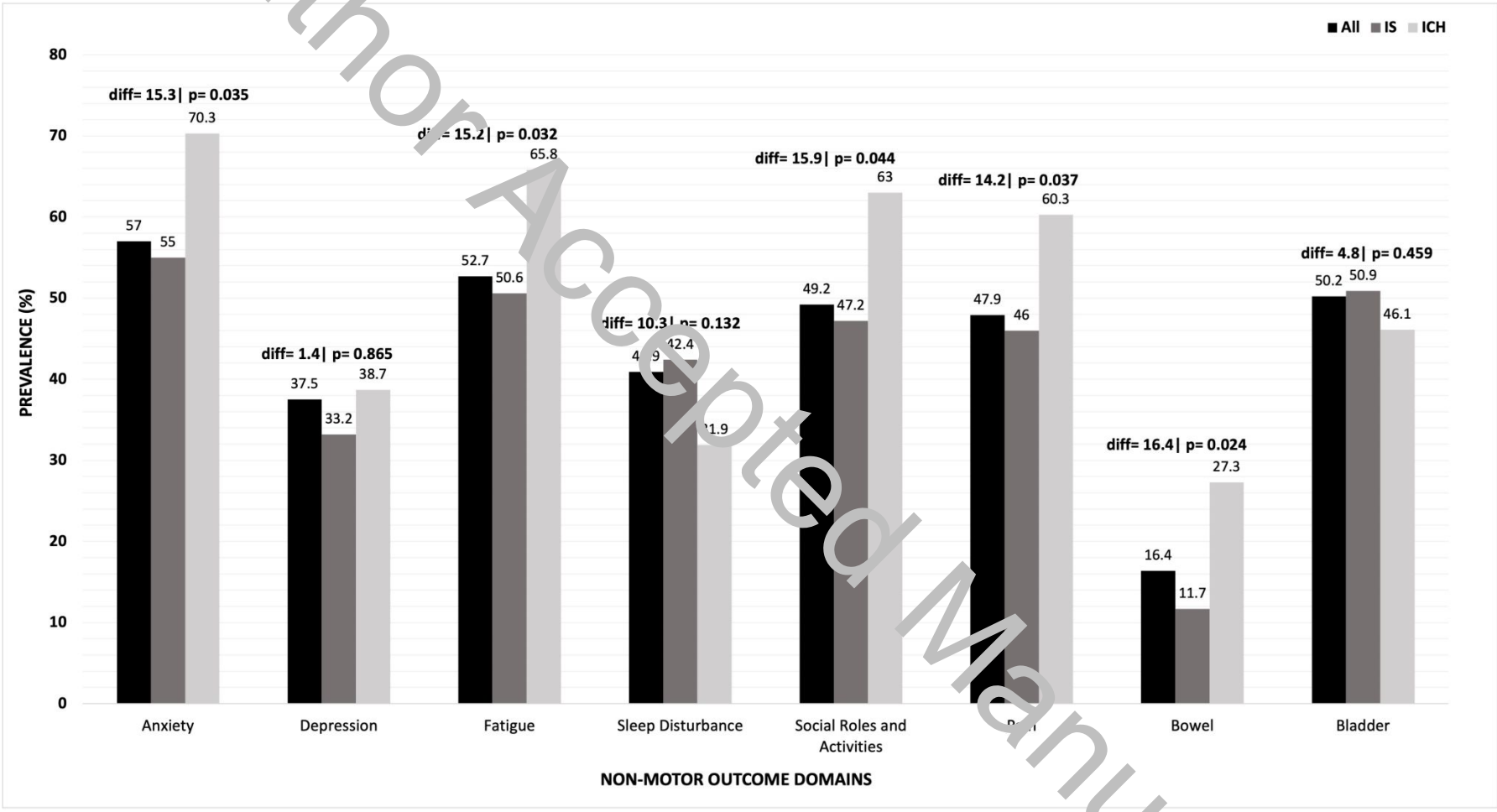
Figure 2. Prevalence of adverse non-motor outcomes at 30-day follow-up for all patients and according to stroke type (ischaemic stroke or ICH)



Adverse non-motor outcome prevalence at 30 day follow-up after acute stroke measured by 6 domains of the PROMIS-29 and the B subscales for bowel and bladder function. diff = absolute percentage difference in adverse non-motor outcome domain between IS and ICH (two independent sample t-test). IS= ischaemic stroke; ICH= intracerebral haemorrhage.

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Table 2. Multivariable analysis of baseline factors associated with adverse non-motor outcomes

		Adjusted OR [95% CI] *P* Value, IS *vs* ICH							
		Non-Motor Outcomes							
		Anxiety	**Depression**	**Fatigue**	**Sleep Disturbance**	**Social Roles and Activities**	**Pain**	**Bowel**	**Bladder**
Stroke Type (ICH vs IS)		**1.8 [1.0 – 3.1] 0.035**	0.9 [0.5 – 1.7] 0.8[illegible]	**1.8 [1.0 – 3.2] 0.042**	0.9 [0.5 – 1.6] 0.662	**1.7 [1.0 – 3.2] 0.046**	**1.9 [1.1 – 3.4] 0.030**	**3.7 [1.9 – 7.2] <0.001**	0.8 [0.5 – 1.3] 0.345
Age		**0.5 [0.3 – 0.8] 0.006**	1.0 [0.6 – 1.[illegible]] 0.991	1.1 [0.7 – 1.8] 0.596	1.1 [0.7 – 1.8] 0.701	**1.7 [1.0 – 2.8] 0.039**	**2.3 [1.4 – 2.0] 0.001**	1.5 [0.7 – 3.0] 0.255	**1.5 [1.0 – 2.4] 0.049**
Female sex		0.9 [0.6 – 1.3] 0.461	1.0 [0.7 – 1.4 0.951	**1.4 [1.0 – 1.9] 0.054**	1.3 [0.9 – 1.9] 0.168	1.1 [0.7 – 1.6] 0.678	**1.7 [1.2 – 2.5] 0.004**	1.3 [0.8 – 2.2] 0.296	**1.9 [1.3 – 2.7] 0.001**
Non-white tthnicity		0.9 [0.6 – 1.3] 0.431	**1.7 [1.1 – 2.4] 0.011**	1.1 [0.7 – 1.5] 0.77[illegible]	**1.7 [1.2 – 2.5] 0.006**	1.0 [0.7 – 1.5] 0.927	0.8 [0.5 – 1.1] 0.164	0.9 [0.5 – 1.6] 0.853	**0.3 [0.2 – 0.4] <0.001**
Previous Stroke/TIA		0.8 [0.5 – 1.1] 0.202	1.3 [0.9 – 1.9] 0.222	**1.5 [1.0 – 2.1] 0.0[illegible]9**	**1.6 [1.1 – 2.3] 0.021**	**4.2 [2.8 – 6.4] <0.001**	1.2 [0.8 – 1.7] 0.475	**3.0 [1.8 – 5.0] <0.001**	0.9 [0.6 – 1.4] 0.706
Hypertension		0.8 [0.6 – 1.2] 0.376	1.0 [0.6 – 1.4] 0.726	0.8 [0.5 – 1.1] 0.151	1.1 [0.7 – 1.6] 0.622	1.2 [0.8 – 1.8] 0.471	1.1 [0.8 – 1.7] 0.524	1.4 [0.8 – 2.6] 0.243	0.8 [0.5 – 1.2] 0.307
Admission NIHSS		**1.4 [1.0 – 2.1] 0.031**	**1.5 [1.0 – 2.3] 0.018**	0.9 [0.6 – 1.4] 0.715	1.[illegible] [0.8 – 1.8] 0.47[illegible]	**1.7 [1.1 – 2.7] 0.016**	1.2 [0.8 – 1.9] 0.398	**3.3 [1.9 – 6.1] <0.001**	**2.0 [1.3 – 3.0] 0.003**
Antiplatelet		0.9 [0.6 – 1.4] 0.741	0.8 [0.5 – 1.1] 0.200	0.8 [0.6 – 1.2] 0.253	1.4 [0.9 – 2.0] 0.177	0.9 [0.6 – 1.3] 0.429	1.2 [0.8 – 1.7] 0.418	0.6 [0.4 – 1.1] 0.101	1.3 [0.9 – 2.0] 0.140
Discharge mRS (0- 1 reference)	mRS 2 – 3	0.8 [0.5 – 1.3] 0.359	**0.3 [0.2 – 0.8] 0.013**	1.1 [0.7 – 1.8] 0.667	1.1 [0.7 – 1.[illegible]] 0.138	**2.5 [1.2 – 5.7] 0.018**	1.0 [0.6 – 1.7] 0.920	1.6 [0.8 – 1.9] 0.751	1.0 [0.7 – 2.1] 0.516
	mRS 4 -5	1.1 [0.6 – 2.0] 0.715	**0.6 [0.4 – 0.9] 0.010**	1.0 [0.5 – 1.7] 0.897	0.8 [0.5 – 1.4] 0.472	**4.4 [1.4 – 6.3] 0.0[illegible]9**	1.2 [0.4 – 2.1] 0.528	**1.3 [1.1 – 3.0] 0.016**	**1.5 [1.0 – 2.4] 0.048**
Discharge Location ASU		0.8 [0.4 – 1.3] 0.325	1.01 [0.6 – 1.8] 0.982	1.1 [0.6 – 1.6] 0.842	1.1 [0.7 – 1.9] 0.638	1.1 [0.[illegible] – 2.1 0.648	**1.4 [1.1 – 1.8] 0.040**	**1.9 [1.4 – 3.0] 0.051**	**1.7 [1.0 – 3.1] 0.015**
Care Home		0.9 [0.5 – 1.5] 0.633	0.7 [0.4 – 1.3] 0.293	0.9 [0.6 – 1.6] 0.833	1.2 [0.7 – 2.2] 0.495	**2.3 [1.2 – 4.[illegible]] 0.027**	0.9 [0.7 – 1.9] 0.685	1.0 [0.5 – 2.2] 0.900	1.5 [0.6 – 2.5] 0.516

Reference groups: age <60 years; male sex; white ethnic origin; discharge mRS 0 – 1; discharge destination home.

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Figure 3. Co-occurrence of non-motor outcome domains

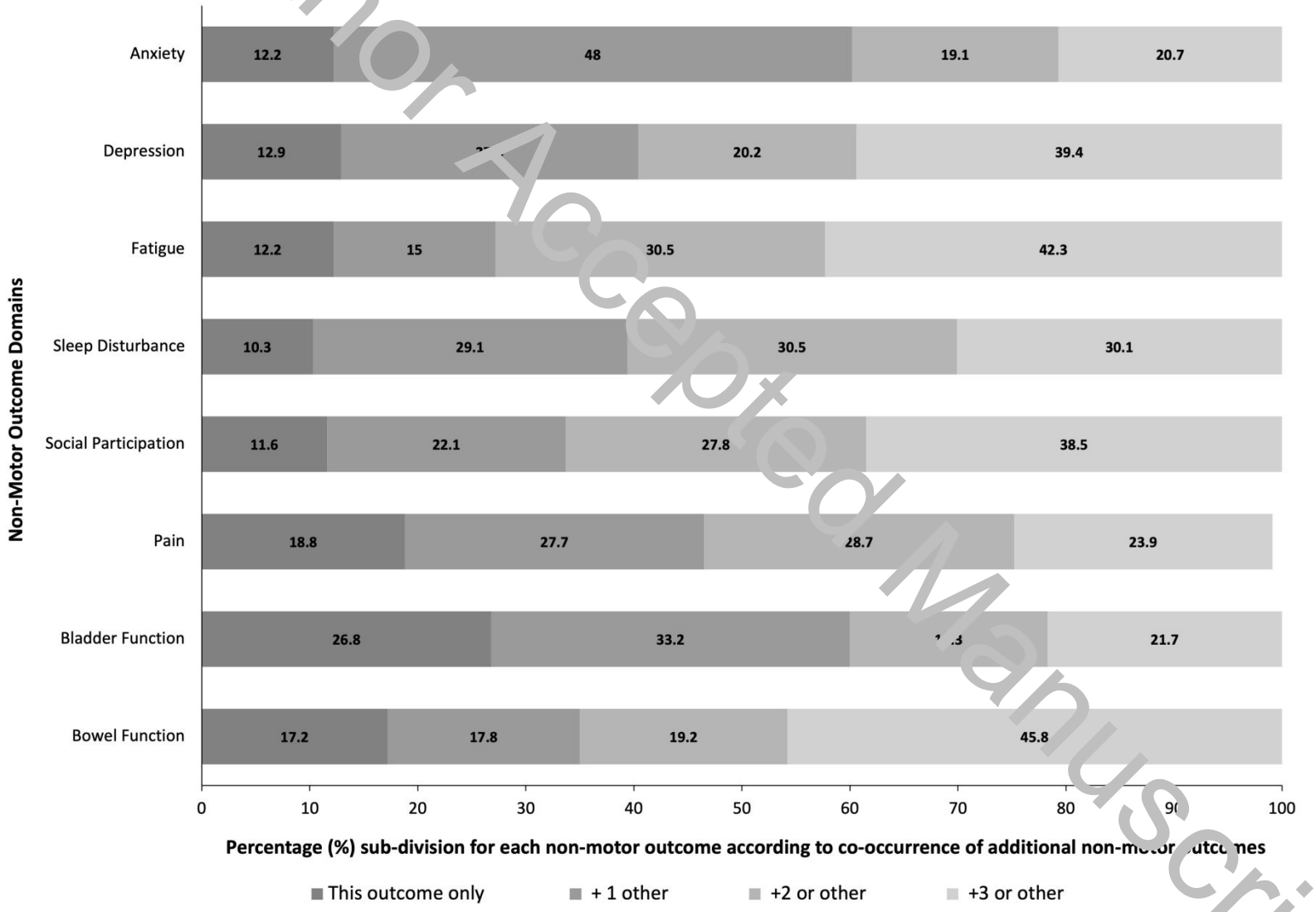

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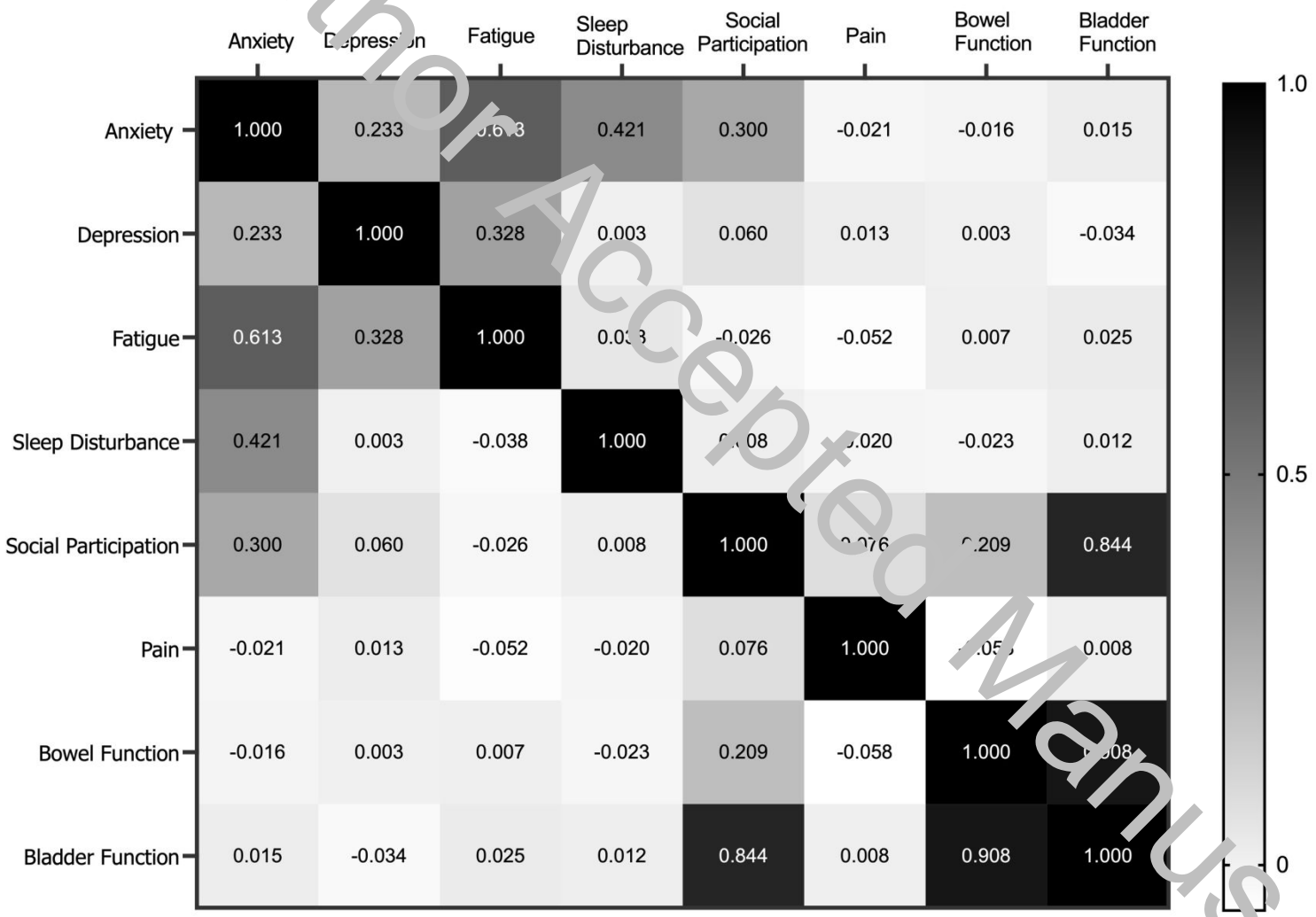
Figure 4. Correlations between pairs of non-motor outcome domains



**Kappa analysis to show proportion of agreement on outcome overlap beyond the observed prevalence identified by chance*

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Data availability

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

Contributors RJS obtained approvals from UCH. HO, RJS, and DJW designed the study. HO and GA conducted statistical analysis. SB helped in patient follow-up. HO, GA, GB, AJF, NSW, RJS, and DJW drafted wrote the paper.

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