Supplemental Material

Prognostic significance of urinary catheterization after acute stroke: secondary analyses of the HeadPoST trial

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Mutiple imputation method

Multiple imputation was used to impute missing outcome data, using PROC MI and PROC MIANALYZE in SAS version 9.2 (or later) software. Multiple imputation is generally considered the least biased method since it incorporates uncertainty to the imputed value, and a non-monotone missing pattern is assumed modified Rankin Scale (mRS) score at 90 days for urianry tract infection (UTI). A distribution for the outcome will be derived from a regression model that accounts for covariates (listed in the hierarchical mixed model) and a random sample from this distribution will be used to impute values for missing outcomes. Ten multiple sample data sets with complete outcome data will be generated through PROC MI, and the results (regression parameter and covariance matrix estimates) for each sample combined and analysed with PROC MIANALYZE to derive a valid statistical inference about the association with outcomes.

Table S1. Characteristics of patients by modified Rankin scale (mRS) score at 90 days

Characteristic	Poor outcome (mRS 3-6) N=3826	Favourable outcome (mRS 0-2) N=5922	P value‡
Age (years)	72.8±13.2	65.1±13.0	<0.0001
Male	2023 (52.9)	3866 (65.3)	<0.0001
Region			<0.0001
Australia and UK	1687 (44.1)	2165 (36.6)	
China and Taiwan	1284 (33.6)	3063 (51.7)	
India and Sri Lanka	411 (10.7)	283 (4.8)	
South America	444 (11.6)	411 (6.9)	
Hypertension	2119 (55.4)	2876 (48.6)	0.0008
Previous stroke	619 (16.2)	728 (12.3)	<0.0001
Coronary artery disease	595 (15.6)	416 (7.0)	<0.0001
Atrial fibrillation	234 (6.1)	120 (2.0)	<0.0001
Heart failure	1123 (29.4)	1185 (20.0)	<0.0001
Diabetes mellitus	870 (22.7)	1110 (18.7)	0.842
Stroke category			<0.0001
AIS	3266 (85.6)	5103 (86.4)	
ICH	404 (10.6)	414 (7.0)	
Uncertain	146 (3.8)	387 (6.6)	
NIHSS at admission	8.0 (4.0, 14.0)	3.0 (2.0, 5.0)	<0.0001
GCS score at admission	15.0 (12.0, 15.0)	15.0 (15.0, 15.0)	<0.0001
Pre-morbid mRS 0-1*	2578 (67.3)	5131 (86.6)	<0.0001
NIHSS at 7 days/before discharge	6.0 (2.0, 12.0)	1.0 (0.0, 3.0)	<0.0001
mRS at 7 days/before discharge	4.0 (2.0, 4.0)	1.0 (1.0, 2.0)	<0.0001
ICU admission	2467 (64.6)	3136 (53.0)	<0.0001
ASU admission	2467 (64.6)	3136 (53.0)	<0.0001
Antibiotic treatment	1041 (27.4)	447 (7.6)	<0.0001
Underwent surgery†	26 (0.7)	9 (0.2)	<0.0001

Data are n (%), mean(SD) and median (IQR)

AIS donates acute ischemic stroke, ASU acute stroke unit, GCS Glasgow coma scale, ICH intracerebral hemorrhage, ICU intensive care unit, mRS modified Rankin scale, NIHSS National Institutes of Health Stroke Scale, UK United Kingdom

*Estimated functional grade score 0-1 on the mRS

†Includes decompressive hemicranectomy, open craniotomy, minimally invasive surgery and intraventricular drainage of ICH

‡P value from Chi-squared test, T-test or Wilcoxon test as appropriate

Table S2. Characteristics of patients according to urinary tract infection (UTI) within 90 days

	UTI		
Characteristics	Yes N=76	No N=11017	P value§
Age (years)	77.6±11.6	67.9±13.8	<0.0001
Male	32 (42.1)	6632 (60.2)	0.001
Region			
Australia and UK	56 (73.7)	4705 (42.7)	<0.0001
China and Taiwan	5 (6.6)	4647 (42.2)	
India and Sri Lanka	5 (6.6)	765 (6.9)	
South America	10 (13.2)	900 (8.2)	
Hypertension	50 (65.8)	5567 (50.5)	0.061
Previous stroke	15 (20.0)	2591 (23.6)	0.464
Coronary artery disease	9 (11.8)	1530 (14.0)	0.591
Atrial fibrillation	17 (22.4)	1159 (10.5)	0.001
Heart failure	5 (6.6)	407 (3.7)	0.206
Diabetes mellitus	18 (23.7)	2203 (20.0)	0.757
Stroke category			
AIS	63 (82.9)	9404 (85.6)	0.772
ICH	8 (10.5)	922 (8.4)	
Uncertain	5 (6.6)	658 (6.0)	
NIHSS at admission	6.0 (4.0, 12.0)	4.0 (2.0, 8.0)	<0.0001
GCS score at admission	15.0 (13.0, 15.0)	15.0 (14.0, 15.0)	0.003
Pre-morbid mRS 0-1*	48 (63.2)	8681 (78.8)	<0.0001
NIHSS at 7 days or before discharge	5.0 (2.0, 15.0)	2.0 (1.0, 6.0)	<0.0001
mRS at 7 days/before discharge	4.0 (3.0, 5.0)	2.0 (1.0, 3.0)	<0.0001
ICU admission	2 (2.7)	515 (4.7)	0.585
ASU admission	67 (88.2)	6553 (59.5)	<0.0001
Antibiotic treatment	49 (65.3)	1633 (14.9)	<0.0001
Underwent surgery†	0 (0.0)	36 (0.3)	0.781
Poor outcome‡	46 (71.9)	3780 (39.0)	<0.0001

Data are n (%), mean (SD) and median (IQR)

AIS donates acute ischemic stroke, ASU acute stroke unit, GCS Glasgow coma scale, ICH intracerebral hemorrhage, ICU intensive care unit, mRS modified Rankin scale, NIHSS National Institutes of Health Stroke Scale, UK United Kingdom

*Estimated functional grade score 0-1 on the mRS

†Includes decompressive hemicranectomy, open craniotomy, minimally invasive surgery and intraventricular drainage of ICH

‡Poor outcome defined as modified Rankin scale scores 3-6

§P value from Chi-squared test, T-test or Wilcoxon test as appropriate

Table S3: Urine catheter use by region

Urinary catheter use	Australia + UK	China + Taiwan	India + Sri Lanka	South America	Overall	P value*
Yes	535 (11.4)	266 (5.7)	259 (33.8)	107 (11.8)	1167 (11.6)	<0.0001
No	4154 (88.6)	4371 (94.3)	507 (66.2)	797 (88.2)	9829 (88.6)	
Length of insertion						<0.0001
Median	6.0 (3.0, 7.0)	6.0 (3.0, 7.0)	4.0 (3.0, 5.0)	5.0 (3.0, 7.0)	5.0 (3.0, 7.0)	

Data are n (%) and median (IQR)

*P value from chi-squared test or Wilcoxon rank sum test as appropriate

Table S4. Length of indwelling urinary catheter (IUC) use by outcomes

Outcomes	Length of IUC insertion Median (IQR)	P value*
Urinary tract infections		0.167
Yes	4.0 (3.0-6.0)	
No	5.0 (3.0-7.0)	
modified Rankin scale score at 90 days		0.013
0-2 (favourable)	5.0 (3.0-7.0)	
3-6 (poor)	6.0 (3.0-7.0)	

Data are median (IQR)

*Wilcoxon rank sum test for P value

Table S5. Clinical outcomes by use of urine catheter

	Urinary catheter use		
Outcomes	Yes	No	P value*
Urinary tract infection	18/1167 (1.5)	58/9829 (0.6)	0.0002
Poor outcome†	793/1167 (76.6)	2991/9829 (34.7)	<0.0001
Any SAE	431/1167 (36.9)	1087/9829 (11.1)	<0.0001
Any infection‡	43/1167 (3.7)	113/9829 (1.2)	<0.0001
Death	292/1167 (25.6)	490/9829 (5.1)	<0.0001
Death by any SAE	268/292 (91.8)	420/490 (85.7)	0.0116
Death by any infection‡	16/268 (6.0)	24/420 (5.7)	0.889
Death by UTI	3/268 (1.1)	9/420 (2.1)	0.317

Data are n (%)

UTI denotes urinary tract infection, SAE serious adverse event

*Chi-squared test for P value

†Defined as modified Rankin scale score 3 to 6

‡Any infection includes urinary tract infection, septicaemia or other type of infection in body or septic shock (except pneumonia).

Table S6. Duration of urinary catheterization and outcome in patients with catheterization.

Outcomes	OR* (95% CI)	P value	aOR† (95% CI)	P value
Poor outcome	1.14 (1.05-1.23)	0.002	1.03 (0.93-1.14)	0.534
UTI	0.86 (0.66-1.12)	0.252	Did not converge	

aOR denotes adjusted odds ratio, CI confidence interval, UTI urinary tract infection

*Unadjusted binomial logistic regression with adjustment for the fixed effects of head position (lying-flat versus sitting-up) and crossover period, and random effects of cluster, and random interaction effects between cluster and crossover period.

† Adjusted region as groups (Australia/UK, China and Taiwan, India/Sri Lanka, South America), baseline age as continuous, sex, premorbid grade according to modified Rankin scale (mRS) at admission, National Institutes of Health Stroke Scale (NIHSS) at baseline as continuous, past medical history of heart disease, diabetes or previous stroke and stroke type, intensive care unit admission, acute stroke unit admission, antibiotic treatment, NIHSS at Day 7/before discharge as continuous.

Table S7. Predictors of death or dependency (mRS 3-6) at 90 days (n=9155)

Covariate	aOR (95% CI)	P value
Indwelling urine catheter	1.41 (1.13-1.75)	0.002
Region (vs. South America)		<0.0001
China + Taiwan	0.52 (0.35-0.75)	
Australia + United Kingdom	0.76 (0.51-1.12)	
India + Sri Lanka	1.52 (0.91-2.53)	
Age, per 5 years	1.22 (1.19-1.25)	<0.0001
Female	1.29 (1.15-1.44)	<0.0001
NIHSS at admission, per unit	1.03 (1.02-1.05)	<0.0001
AIS (vs. ICH)	0.84 (0.68-1.04)	0.262
Pre-morbid mRS (vs. no symptoms)*		<0.0001
No significant disability	1.41 (1.20-1.65)	
History of heart disease, stroke or diabetes	1.42 (1.27-1.59)	<0.0001
ICU admission	1.25 (0.90-1.74)	0.192
ASU admission	0.98 (0.77-1.24)	0.861
Antibiotic treatment	1.44 (1.21-1.70)	<0.0001
NIHSS at day 7, per unit	1.27 (1.25-1.30)	<0.0001
Urinary Tract Infection	1.46 (0.70-3.04)	0.319

AIS denotes acute ischemic stroke, aOR adjusted odds ratio, ASU acute stroke unit, CI confidence interval, GCS Glasgow coma scale, ICH intracerebral hemorrhage, ICU intensive care unit, mRS modified Rankin scale, NIHSS National Institutes of Health Stroke Scale

*Premorbid functional grade according to the full range of scores on the mRS assessed at admission: slight disability vs. no symptoms (aOR 2.09, 95% CI 1.73-2.51); moderate disability vs. no symptoms (aOR 3.81, 95% CI 3.01-4.82); moderate/severe disability vs. no symptoms (aOR 4.44, 95% CI 3.06-6.44); and severe disability vs. no symptoms (aOR 5.88, 95% CI 2.33-14.87)

Table S8. Stratified analysis of indwelling urinary catheterization and death or dependency in patients without reported urinary tract infection (UTI)

Stratification	No UTI (N=11017)	
	aOR (95% CI)	P value
Unadjusted*	5.44 (4.63-6.39)	<0.0001
Model 1†	5.27 (4.49-6.18)	<0.0001
Model 2‡	2.34 (1.93-2.83)	<0.0001
Model 3§	1.43 (1.15-1.78)	0.001

aOR denotes adjusted odds ratio, CI confidence interval, UTI urinary tract infection

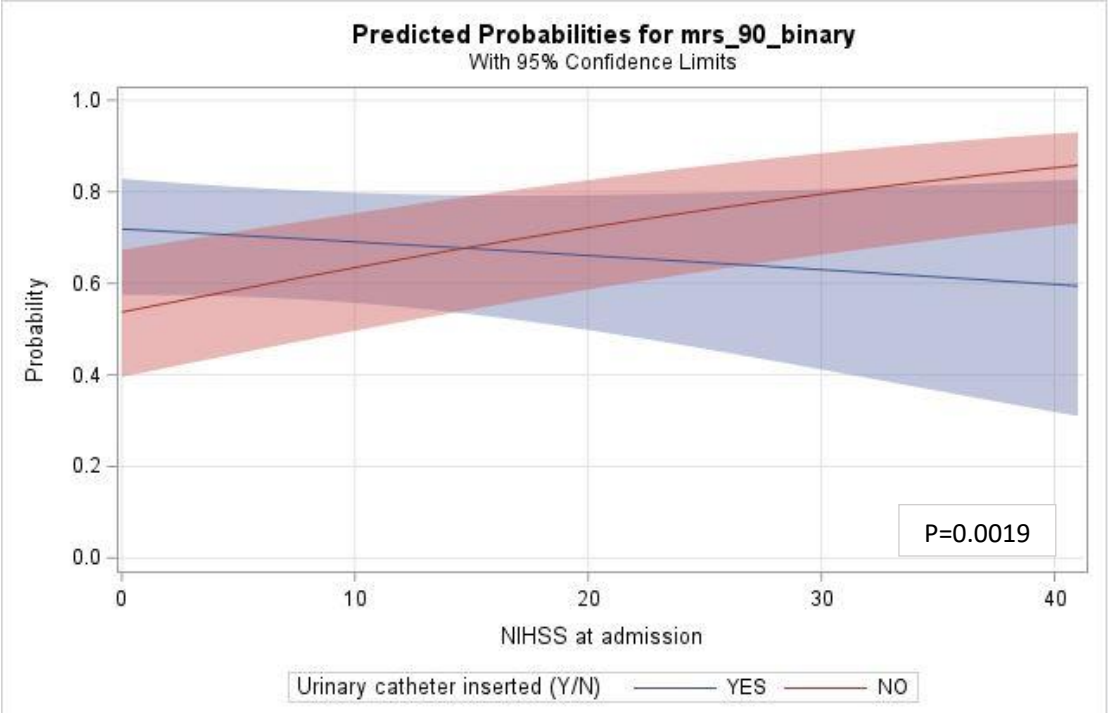
*Unadjusted binomial logistic regression with adjustment for the fixed effects of head position (lying-flat versus sitting-up) and crossover period, and random effects of cluster, and random interaction effects between cluster and crossover period.

†Model I: adjusted region as groups (Australia/UK, China and Taiwan, India/Sri Lanka, South America)

‡Model II: further adjusted baseline covariates, include age as continuous, sex, premorbid grade according to modified Rankin scale (mRS) at admission, National Institutes of Health Stroke Scale (NIHSS) at baseline as continuous, past medical history of heart disease, diabetes or previous stroke and stroke type.

§Model III: further adjusted individual characteristics at discharge, include intensive care unit admission, acute stroke unit admission, antibiotic treatment, NIHSS at Day 7/before discharge as continuous.

Figure S1. Plot of interaction between urinary catheter use and NIHSS at admission on death or dependency at 90 days



mrs_90_binary donates death or dependency at 90 days according to scores 3-6 on the modified Rankin scale

NIHSS denotes National Institutes of Health Stroke Scale

Hierarchical mixed models used in analyses

Figure S2. Distribution of time to urinary tract infection (UTI) events from stroke onset

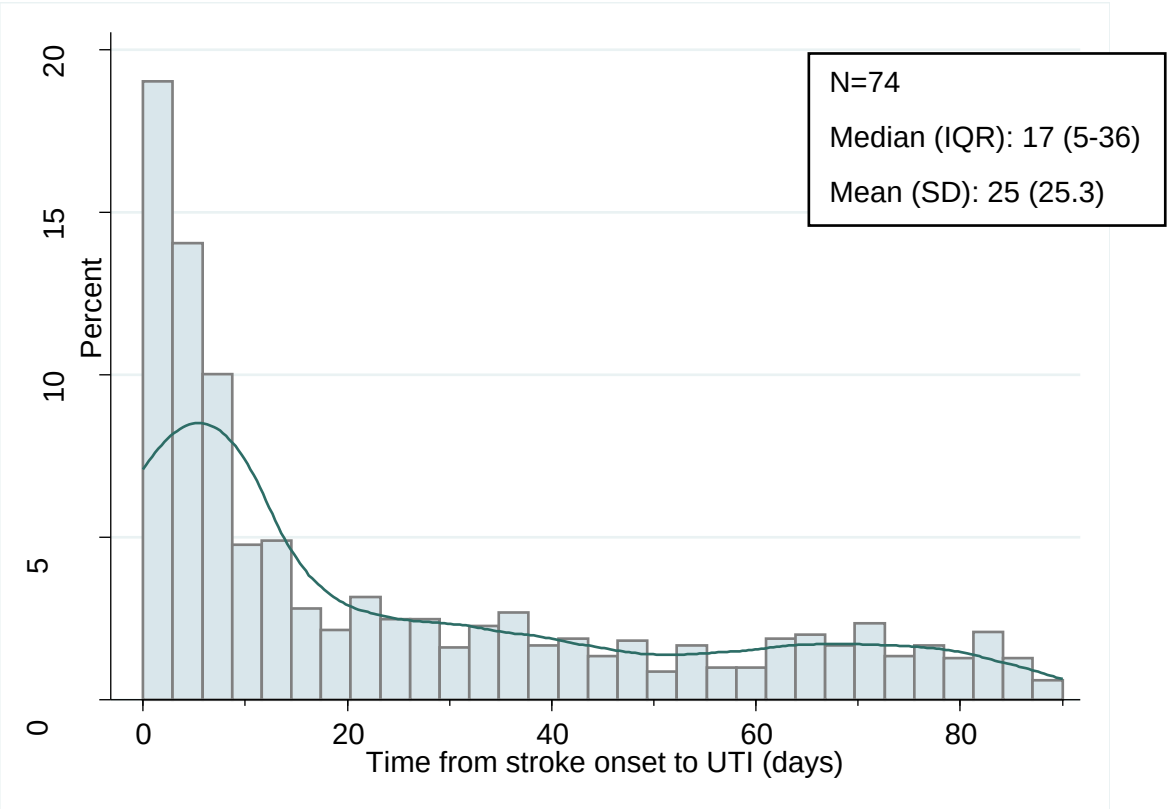
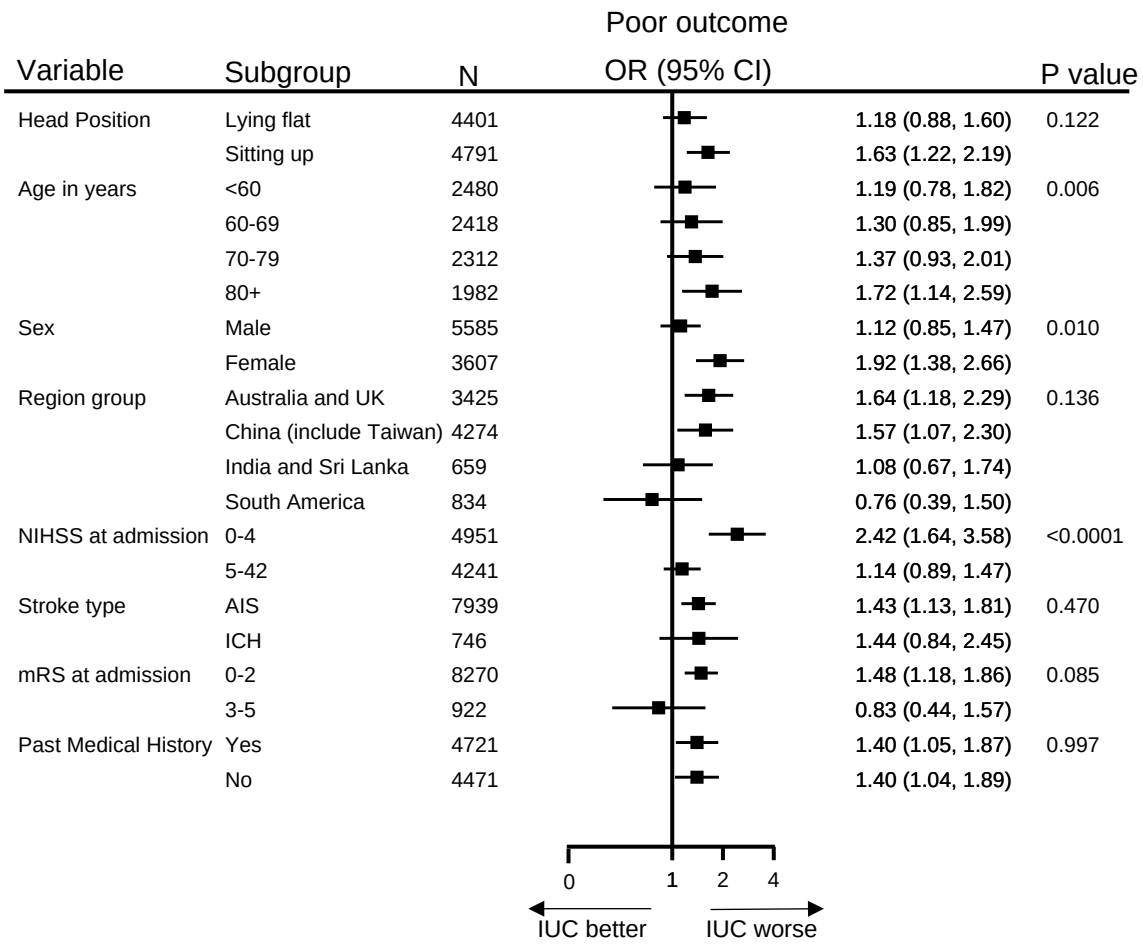


Figure S3. Subgroup analysis for death or dependency outcome (mRS 3-6)

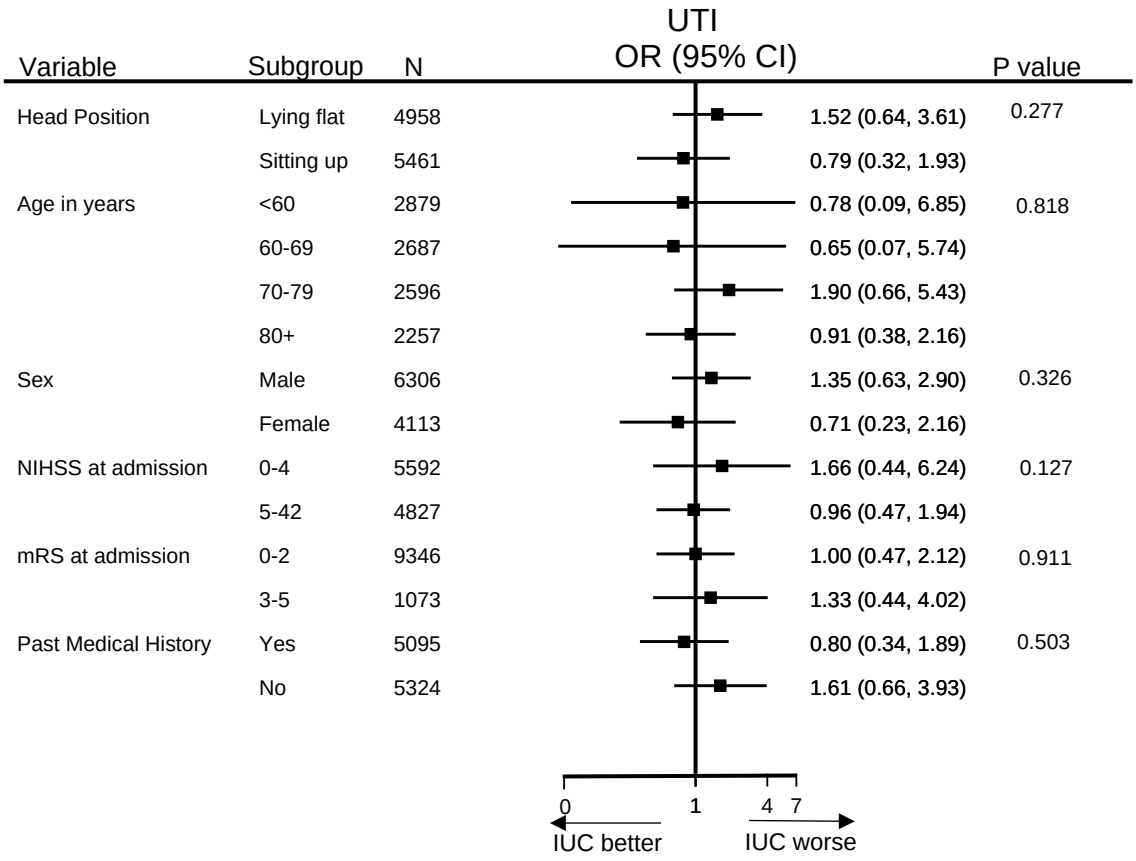


AIS donates acute ischemic stroke, ICH intracerebral hemorrhage, mRS modified Rankin scale, N number of patients in each subgroup, NIHSS National Institutes of Health Stroke Scale

Poor outcome is death or dependency at 90 day according to mRS scores 3-6

Hierarchical mixed models used in analyses

Figure S4. Subgroup analysis for urinary tract infection (UTI) within 90 days



AIS donates acute ischemic stroke, ICH intracerebral hemorrhage, mRS modified Rankin scale, N number of patients in each subgroup, NIHSS National Institutes of Health Stroke Scale

Hierarchical mixed models used in analyses