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Quantifying regional variations in components of acute stroke unit (ASU) care in the international HeadPoST study

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ABSTRACT

Objective: Access to acute stroke unit (ASU) care is known to vary worldwide. We aimed to quantify regional variations in the various components of ASU care.

Method: Secondary analysis of the Head Positioning in acute Stroke Trial (HeadPoST), an international, multicentre, cluster crossover trial of head-up versus head-down positioning in 11,093 acute stroke patients at 114 hospitals in 9 countries. Patients characteristics and 11 standard components of processes of care were described according to ASU admission within and across four economically-defined regional groups (Australia/UK, China [includes Taiwan], India/Sri Lanka, and South America [Brazil/Chile/Colombia]). Variations in process of ASU care estimates were obtained in hierarchical mixed models, with adjustment for study design and potential patient- and hospital-level confounders.

Results: Of 11,086 patients included in analyses, 59.7% (n = 6620) had an ASU admission. In China, India/Sri Lanka and South America, ASU patients were older, had greater neurological severity and more premorbid conditions than non-ASU patients. ASU patients were more likely to receive reperfusion therapy and multidisciplinary care within regions, but the components of care varied across regions. With Australia/UK as reference, patients in other regions had a lower probability of receiving reperfusion therapy, especially in India/Sri Lanka (adjusted odds ratio [aOR] 0.27, 95% confidence interval [CI] 0.12–0.63) and multidisciplinary care (mainly in formal dysphagia assessment, physiotherapy and occupational therapy).

Conclusion: There is significant variation in the components of stroke care across economically-defined regions of the world. Ongoing efforts are required to reduce disparities and optimise health outcomes, especially in resource poor areas.

Clinical trial registration: HeadPoST is registered at ClinicalTrials.gov (NCT02162017).

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1. Introduction

National guidelines universally recommend well-organised, interdisciplinary, acute stroke unit (ASU) care [1–4], based upon consistent evidence from systematic reviews and individual trials showing improved survival and functional recovery [5,6], with the treatment effect being consistent across a range of patient characteristics within all age groups and different stroke subtypes [7–10]. However, such care is absence or only partially established in many hospitals around world [11]. While ASU care is relatively well-defined in high resource settings, less attention has been given to its availability and appropriateness in low- and middle- income countries (LMICs), where most of the global burden of stroke occurs [12,13]. Previous studies have shown large variations in the organisation of stroke care across hospitals which may compromise effective ourcomes, as significant associations between receipt of evidence-based care and clinical outcomes were reported in our international, multicentre, Head Positioning in acute Stroke Trial (HeadPoST) [7,14]. Despite acknowledging variations in stroke care pathways, access to ASU, and other aspects of stroke care [14,15], few studies have systematically quantified how the specific components of ASU care may differ across regions of the world [16]. Herein, we quantify the components of ASU care, within and across hospitals, in four participating income-grouped geographical regions for patients who participated in the HeadPoST. This study included a large and broad range of relatively unselected patients with acute stroke with systematic assessment of their management and outcome.

2. Methods

2.1. Study design and population

This descriptive study is a secondary analysis using data prospectively collected from 114 hospitals in nine countries in the HeadPoST study. In brief, HeadPoST was an international, multicentre, cluster crossover, randomised trial that involved 11,093 adults (≥18 years) with acute stroke who were randomly allocated to lying flat (head down) or sitting up (head up) positioning between March 2015 and November 2016 [17]. Patients were excluded if they had early resolution of their neurological symptoms consistent with a transient ischaemic attack; a clear contraindication to either head position; any medical condition that would compromise adherence to the protocol or assigned head position; or refused participation. A cluster guardian consent process was used to implement the randomised intervention as a policy of usual service delivery to a pre-defined patient cluster; patients provided consent for use of their medical record data and centralised telephone follow-up. HeadPoST study is registered at ClinicalTrials.gov (NCT02162017).

2.2. Procedures

ASU admission and processes of care were derived from hospital management data collected at Day 7 post-randomisation (or at hospital separation, if earlier). Eleven in-hospital processes of care data of evidence-based guideline recommendations and/or clinical quality of care indicators were assessed [18–20], including reperfusion treatment (thrombolysis or endovascular clot retrieval), antiplatelet therapy for acute ischaemic stroke (AIS), anticoagulant for atrial fibrillation (AF), blood pressure (BP) lowering, dysphagia screening, formal dysphagia assessment for those failed screening, feeding assistance in those with dysphagia, and components of multidisciplinary care including physiotherapy, occupational therapy and psychological therapy (Supplemental Table S1). Baseline data collection included demography, medical history and clinical information, including severity of neurological impairment on the National Institutes of Health Stroke Scale [21] (NIHSS). Patients were re-grouped into four principle geographical regions and world bank country income levels: [22] Australia/UK, China (includes Taiwan), India/Sri Lanka, and South America (including Brazil/Chile/Colombia). Outcomes were time to hospital discharge, death, and functional outcomes on the modified Rankin scale [23] (mRS), as determined by trained staff, blind to treatment allocation, through telephone interviews at 90-days of follow-up.

2.3. Statistical analysis

Randomised patients with no record of ASU care were excluded from analyses. Differences in baseline characteristics and processes of care were compared according to ASU admission within and between grouped regions; where there were limited data, standardised differences (SD) were used to describe any imbalances. For outcomes by ASU admission, univariate analyses were reported with Chi-square and Wilcoxon rank-sum tests. To estimate regional variations in the processes of ASU care, logistic regression hierarchical mixed models were used with adjustment for the study design (with fixed effects of head position and crossover period, and random effects of cluster and interaction between cluster and crossover period) and potential baseline confounders related to patient (age, sex, neurological severity [NIHSS score], and pathological stroke subtype) and hospital (academic status, size, and location) factors. Data are reported with odds ratios (OR) and 95% confidence intervals (CI), and a standard level of significance ($P < 0.05$) was used. All analyses were performed with SAS Enterprise 7.1 (SAS Institute, Cary, NC), and R Studio 3.6.3 was used for data visualisation.

2.4. Data sharing

Individual participant data used in these analyses can be shared by formal request and protocol from any qualified investigator to the Research Office of The George Institute for Global Health, Australia.

3. Results

A total of 11,086 patients were included in these analyses: their average age was 68.0 (±13.8) years, 39.9% were female, 85.6% had AIS, and 59.7% received ASU care (Supplementary Table S2). Table 1 shows that ASU admission varied from 98.2% in Australia/UK, 84.0% in India/Sri Lanka, 41.3% in South America, and 20.0% in China, with associated regional variations in the distribution of patient characteristics and processes of care. In Australia/UK, care processes were generally balanced, except for ASU patients being less likely to have dysphagia assessment and more likely to receive physiotherapy and occupational therapy, compared to non-ASU patients. In China, ASU patients were older, more often had AIS and greater neurological impairment but fewer pre-morbid health problems, compared to other patients. Moreover, ASU patients were more likely to receive reperfusion therapy, antihypertensive treatment, dysphagia screening and formal assessment, assisted feeding, and input from an occupational therapist than patients on other wards in China (Fig. 1). Although ASU patients in India/Sri Lanka had less severe neurological impairment and greater pre-morbid health problems, they received more multidisciplinary care than patients on other wards (Fig. 1). Finally, in South America, ASU patients were older, had more history of hypertension (Table 1) and greater use of reperfusion therapy, intensive BP lowering, and physiotherapy, occupational and psychological therapy but less screening or assessment for dysphagia (Fig. 1).

There were significant variations in a range of processes of ASU care, except early use of antiplatelets and psychological therapy, in adjusted analyses with Australia/UK as the reference group (Fig. 2). ASU patients in India/Sri Lanka had the lowest probability of receiving reperfusion therapy (adjusted odds ratio [aOR] 0.27, 95%CI 0.12–0.63) but highest probability of receiving anticoagulation for AF, whereas Chinese ASU patients were more likely to receive early BP lowering (aOR 2.50, 95% CI 1.10–5.68) and less likely to receive oral BP lowering treatment for secondary prevention (aOR 0.49, 95% CI 0.36–0.67). ASU patients in

South America were the least likely to have dysphagia screening (aOR 0.07, 95% CI 0.01–0.37) but together with those in India/Sri Lanka, were more likely to receive feeding assistance (aOR 5.83, 95% CI 2.47–13.74, and aOR 2.41, 95% CI 1.15–5.00, respectively). The probability of receiving allied health care (formal dysphagia assessment, physiotherapy and occupational therapy) was much lower in all regions compared to Australia/UK (Fig. 2).

Time from hospital arrival to discharge was longest in China and shortest in Australia/UK (median 11.0 [IQR 8.0–15.0] days vs. 4.0 [IQR 2.0–10.]; Supplementary Table S3). Within regions, there were no significant differences in time to discharge in Australia/UK and South America by ASU admission, but this was prolonged for patients without ASU care in China and ASU patients in India/Sri Lanka (Supplementary Table S3). Death and functional outcomes also varied across regions (Supplementary Fig. 1): case fatality was greatest in India/Sri Lanka (12.3%) and lowest in China (3.5%) (Supplementary Table S3), whilst death and dependence (mRS scores 3–6) in patients admitted ASU was significantly lower in India/Sri Lanka compared to those without ASU care (Supplementary Table S3).

4. Discussion

In these post-hoc analyses of the large international HeadPoST study, we have shown considerable regional variations in patient characteristics, processes of care, and outcomes according to the receipt of ASU care, where admission was highest in Australia/UK and lowest in China. Except for patients in Australia/UK, those admitted to ASU differed in age, neurological severity and comorbid risk factors, and were generally more likely to receive reperfusion therapy and multidisciplinary team care.

Our study confirms findings elsewhere, that ASU is more accessible and available in high-income countries compared to LMIC [24]. The fragmentation of care and absence of standardised healthy policies also undermine access to ASU care [25]. However, some of this variation may reflect differences in definitions, concepts and approaches to monitoring; for example, use of neuro-intensive care and neurosurgery for stroke patients is high in China [26,27], and interdisciplinary vascular units, which combine stroke with cardiac care, are popular in Brazil [28,29]. As shown in various national registries in China and India [30–32], the patients who are more likely to receive ASU care are those who are old, have AIS, greater neurological severity and more vascular risk factors.

Our finding of lower thrombolysis treatment rates for AIS patients in China and India/Sri Lanka, compared to Australian/UK patients, is consistent with Asian registries [32,33]. Underlying barriers for thrombolysis in Asia include delayed presentation from the onset of symptoms, concerns over harm, inexperience, and high cost of thrombolysis treatment when there is no health insurance coverage [31,34,35]. Although ASU care is defined as multidisciplinary and a Level I guideline recommendation, early rehabilitation is less common in China and India/Sri Lanka, and many other resource settings in LMICs, in part due to limited availability of allied healthcare professionals and ethnic/cultural differences in the understanding of 'passive' and 'active' rehabilitation [11,33,36,37]. Additionally, compared to AU/UK, the recommendation for assessment by a speech pathologist and assisted feeding is explicit stroke management guidelines in China and India [38,39], which also influences their implementation into practice [40]. The consistent high use of antiplatelet therapy across

Table 1
Patient baseline characteristics according to acute stroke unit (ASU) admission by region.

Variable	AU/UK			China (includes Taiwan)			India/Sri Lanka			South America[b]		
	ASU care			ASU care			ASU care			ASU care		
	Yes	No	SD[a]	Yes	No	SD[a]	Yes	No	SD[a]	Yes	No	SD[a]
Number of patients	4669 (98.2)	88 (1.9)		931 (20.0)	3721 (80.0)		647 (84.0)	123 (16.0)		373 (41.3)	534 (58.7)	
Age, yr	72.5 (±13.9)	71.7 (±14.1)	0.05	66.5 (±12.0)	63.9 (±12.0)	0.22	61.3 (±13.1)	60.0 (±14.0)	0.09	70.4 (±13.8)	67.4 (±14.2)	0.21
Female	2122 (45.4)	37 (42.0)	0.07	350 (37.6)	1253 (33.7)	0.08	239 (36.9)	34 (27.6)	0.20	173 (46.4)	218 (40.8)	0.11
Pre-morbid disability[c]	1036 (22.2)	22 (26.5)	0.10	150 (16.1)	807 (21.7)	0.14	112 (17.3)	11 (8.9)	0.25	84 (22.6)	114 (21.4)	0.03
Stroke subtype												
AIS	3767 (81.1)	65 (73.9)	0.17	855 (91.8)	3323 (89.3)	0.11	560 (86.6)	98 (79.7)	0.26	336 (90.1)	463 (86.7)	0.30
ICH	355 (7.6)	9 (10.2)		64 (6.9)	338 (9.1)		83 (12.8)	25 (20.3)		28 (7.5)	28 (5.2)	
Uncertain	522 (11.2)	14 (15.9)		12 (1.3)	59 (1.6)		4 (0.6)	0 (0.0)		9 (2.4)	43 (8.1)	
NIHSS score	4.0 (2.0–10.0)	5.0 (2.0–13.0)	0.13	4.0 (2.0–8.0)	3.0 (2.0–6.0)	0.25	7.0 (4.0–12.0)	12.0 (8.0–18.0)	0.66	6.0 (3.0–11.0)	5.0 (3.0–11.0)	0.02
Severe, score ≥ 15	674 (14.8)	18 (20.9)	0.13	56 (6.0)	142 (3.9)	0.21	106 (16.4)	47 (38.2)	0.55	64 (17.3)	97 (18.2)	0.13
Coronary heart disease	730 (15.8)	9 (10.2)	0.17	114 (12.3)	506 (13.6)	0.04	76 (11.8)	16 (13.0)	0.04	38 (10.3)	50 (9.6)	0.02
Atrial fibrillation	837 (18.3)	23 (26.4)	0.20	66 (7.1)	151 (4.1)	0.13	20 (3.1)	3 (2.4)	0.04	36 (9.8)	41 (7.9)	0.07
Heart failure	250 (5.4)	3 (3.4)	0.10	17 (1.8)	74 (2.0)	0.01	11 (1.7)	1 (0.8)	0.08	20 (5.4)	37 (7.1)	0.07
Diabetes mellitus	986 (21.2)	11 (12.5)	0.23	226 (24.4)	848 (22.8)	0.04	265 (41.0)	41 (33.3)	0.16	112 (30.0)	163 (30.7)	0.01
Prior stroke	895 (19.3)	10 (11.4)	0.22	252 (27.1)	1124 (30.2)	0.07	93 (14.4)	11 (8.9)	0.17	96 (25.8)	125 (23.5)	0.05
Hypertension	2940 (63.3)	47 (53.4)	0.20	610 (65.5)	2438 (65.5)	<0.01	375 (58.0)	62 (50.4)	0.15	264 (71.0)	411 (77.7)	0.15
COPD	269 (5.8)	5 (5.7)	<0.01	19 (2.0)	58 (1.6)	0.04	11 (1.7)	3 (2.4)	0.05	21 (5.8)	20 (3.8)	0.09
Current smoker	633 (13.8)	7 (8.0)	0.19	253 (27.3)	959 (25.8)	0.03	90 (14.0)	22 (17.9)	0.11	57 (15.4)	104 (19.7)	0.11
Dysphagia	1069 (23.2)	30 (34.1)	0.24	102 (11.0)	413 (11.2)	0.01	131 (20.2)	49 (39.8)	0.44	98 (26.3)	151 (28.4)	0.05

Data are N (%), mean (±standard deviation) or median (interquartile range). AF donates atrial fibrillation, AIS acute ischaemic stroke, ASU acute stroke unit, AU Australia, BP blood pressure, COPD chronic obstructive pulmonary disease, ICH intracerebral haemorrhage, mRS modified Rankin scale, NIHSS National Institute of Health Stroke Scale, SD standardised difference, UK United Kingdom.

[a] Standardised difference = absolute difference in means or proportions divided by standard error; imbalance defined as value greater than 0.20.

[b] South America including Brazil, Chile and Colombia.

[c] Defined by scores 2–5 on the mRS.

regions reflects its simplicity, safety and low cost [24,41], whilst the similarly infrequent use of psychological therapy reflects its limited availability and high cost; even in the UK, only one-third of ASUs have access to clinical psychology services [42].

It is well recognised that the length of time stroke patients spend in hospital varies across regions, and tends to be longer in China with some variations by the level of hospitals (teaching/tertiary vs. rural/secondary) [43]. It is important to note that the variations in functional outcomes between patients in China and India does not appear to be explained entirely by the severity of stroke deficit [31], when the benefits of ASU care have been shown to apply equally across grades of neurological severity [44].

Some strengths of our study include the large number of patients with wide ranging characteristics who were managed in contrasting health care settings, where the pragmatic cluster crossover design minimised selection bias and facilitated recruitment and efficient application of the intervention as part of routine care. However, as these data were derived from a clinical trial, only a limited range of management variables were collected; and they lacked standardised definitions across hospitals. Since hospitals were purposefully selected to participate in the trial, these results might be more favourable than compared to other, less research active hospitals in these regions. Finally, our approach to clustering hospitals within regions was rather arbitrary, while post-hoc analyses and multiple testing introduces potential bias and chance findings. Further data on variation in ASU care would help design multinational research studies and strengthen the external validity of these findings [45].

In summary, further analysis of our large international study has shown considerable variation in the characteristics of patients, and the types of care and management they receive under the umbrella of ASU care, within and across different health care systems. The extent to which this is driven by policy, costs, skills, beliefs, and expectations, requires further investigation.

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Author contributions

CSA and MO contributed to the concept and rationale for the study. MO undertook statistical analyses with assistance from LB and XW. MO wrote the first draft of manuscript with input from LS, XW, YZ and CSA. All authors commented upon and approved the final version of the manuscript for publication.

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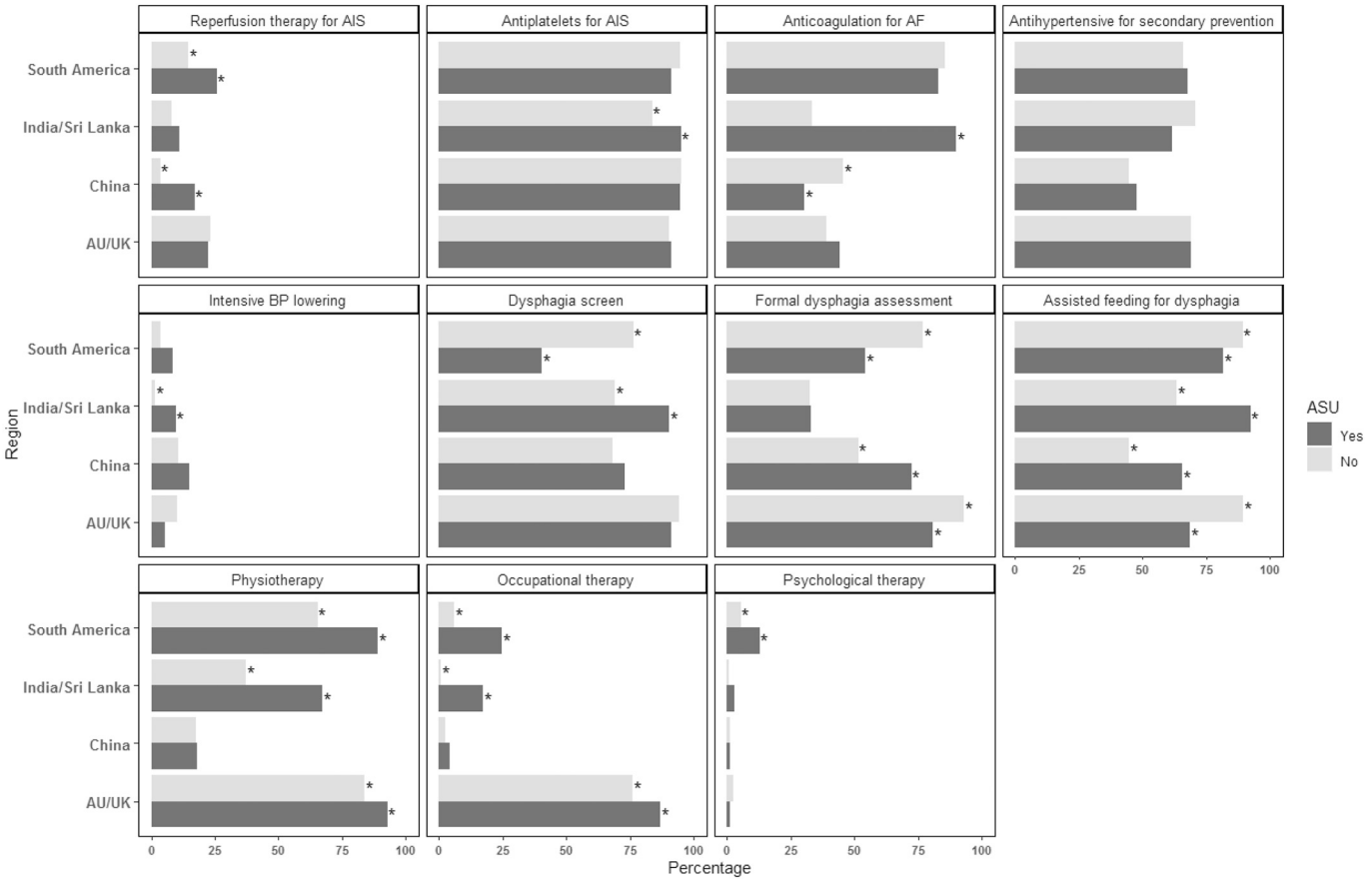

Fig. 1. Process of care according to acute stroke unit (ASU) admission by region.
AF denotes atrial fibrillation, AIS acute ischaemic stroke, ASU acute stroke unit, AU Australia, BP blood pressure, UK United Kingdom.
*Standardised difference (absolute difference between two groups in proportions divided by standard error) greater than 0.20.

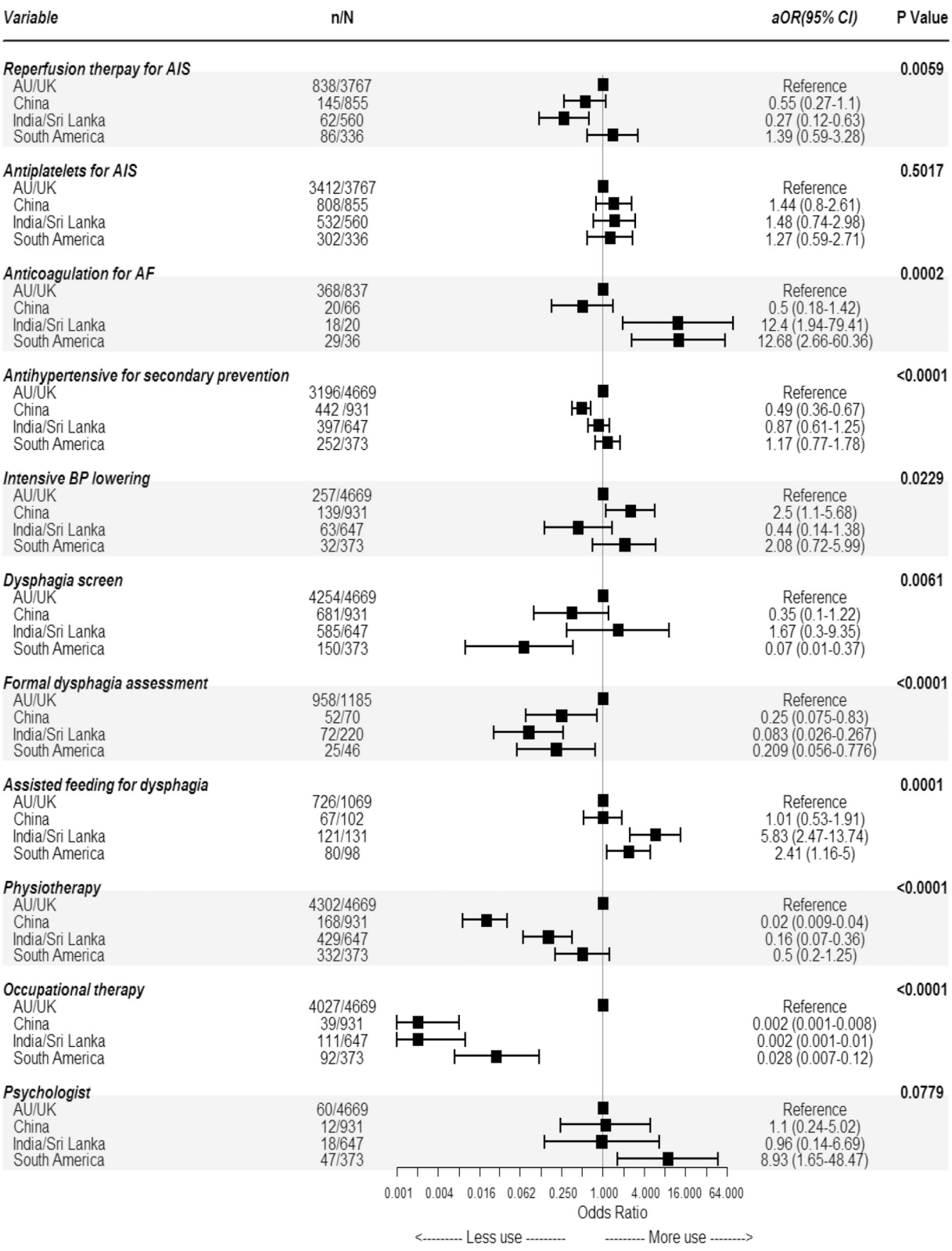

Fig. 2. Variations of acute stroke unit (ASU) process of care by region.

AF denotes atrial fibrillation, AIS acute ischaemic stroke, aOR adjusted odds ratio, ASU acute stroke unit, AU Australia, BP blood pressure, CI confidence interval, UK United Kingdom.

Square indicates point estimate and error bar indicates 95% CI.

Hierarchical mixed models adjusted study design (fixed effects of head position [lying-flat vs. sitting-up] and crossover period, and random effects of cluster and interaction between cluster and crossover period) and baseline variables related to the patients (age, sex, neurological severity [National Institutes of Health Stroke Scale score] and pathological stroke subtype) and hospital (academic status, size and geographical region).

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jns.2020.117187.

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