

Preferences and values for treatment goals in patients with acute ischemic stroke: Medical staff perspectives in China

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Abstract

Individual values and beliefs vary according to cultural and social factors. To better understand clinical decision-making and inform future research, we undertook a survey of preferences in treatment goals for managing patients with acute ischemic stroke among medical professionals in China. We designed a web-based survey through literature search, face-to-face interviews, pilot questionnaire development, and focus group meetings. Key outcomes explored were death, disability, quality of life, neurological impairments, cognitive dysfunction, and hemorrhagic transformation. Participants were asked to rate the importance of each outcome on a 5-point Likert scale to allow calculation of a weighted score of importance: higher scores indicating greater importance. A total of 1,189 participants completed the survey. For established therapies with bleeding risk (e.g. thrombolysis and thrombectomy), death was the most important outcome (weighted score 4.60), followed by disability (4.45), quality of life (4.45), neurological impairments (4.34), cognitive dysfunction (4.03), and hemorrhagic transformation (3.99). For other acute therapies without bleeding risk, quality of life ranked first (4.08), followed by disability (4.03), neurological impairment (3.92), death (3.79), cognitive dysfunction (3.78), and hemorrhagic transformation (3.51). From the perspective of Chinese medical staff, death is the most important outcome measure for patients with acute ischemic stroke. When reduction of death or disability were less likely to be achievable, the improvement in quality of life is an acceptable outcome measure. In contrast to the previously perceived high fear of bleeding in practice, hemorrhagic transformation was the least concerned even for therapies with a potential bleeding risk.

Keywords: Survey, opinions, outcome measures, ischemic stroke, China

INTRODUCTION

While death and disability are the primary outcome measures used to assess the effects of therapies for acute ischemic stroke (AIS) in randomized controlled trials (RCTs)¹⁻³, the action of clinicians in interpreting such results depends upon many factors, such as the size, consistency and scope of net benefit over risks, and affordability of treatment. Guidelines recommend thrombolysis and thrombectomy for AIS based on a large body of evidence from RCTs.^{4,5} However, these therapies are only available to a small proportion (<20%) of AIS patients worldwide,

and even fewer (<10%) in China and other parts of Asia⁶⁻¹¹, where neuroprotective agents, herbal products, and other therapies are more widely available and popular^{6,12,13} despite insufficient supporting evidence. Reasons for the discrepancy between scientific evidence and clinical practice are complex.

The choice of treatment therapies is a joint decision between physicians and nurses, and patients and/or their families, where values and preferences over the importance of different outcomes from AIS vary across cultures, experiences and roles. The importance of patient-centered outcomes is now well accepted^{14,15}, but

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few studies have been undertaken on the issue in China. The aim of our study was to determine the preferences and values of Chinese medical staff place upon key clinical outcomes used across treatments for AIS.

METHODS

We conducted a staged study (Figure 1), with approval from the Biomedical Research Ethics Committee of West China Hospital, Sichuan University [No. 2018(100)], and informed consent from all participants.

Stage 1: Face-to-face interviews

Two researchers (YW, SW) independently undertook a literature search and identified 33 common outcome measures used in stroke RCTs (see Supplementary). Next, 31 stroke physicians from the West China Hospital, Sichuan University, participated in 1:1 face-to-face interviews, where they were asked to answer an open question: “which outcome measures do you think are important to assess the treatment effect for AIS during the acute phase” among the list of 33 outcome measures. Participants were required to provide at least 1 and no more than 10 responses, in rank order of clinical importance. A total of

306 responses were collected and these were categorized down to 20 outcome measures.

Stage 2: Pilot questionnaire development

A paper-based questionnaire was developed from the 20 outcome measures (Supplementary Table S1) for testing among 71 neurologists from 17 hospitals. In a round-table discussion, they had to choose 10 key outcome measures and provide feedback on design of the questionnaire.

Stage 3: Focus group meetings

A focus group of 4 stroke neurologists (ML, BW, SZ, and SW) finalized the survey content based upon the clinical importance of each outcome measure in sections: (i) baseline information; (ii) ranking importance of outcome measures in relation to established acute therapies with bleeding risk (thrombolysis, thrombectomy and antithrombotic agents) and other common therapies of neuroprotective agents, rehabilitation, acupuncture, Chinese patent medicine, and traditional Chinese medicine; (iii) three questions on “If an acute therapy may not reduce death or disability at 3 months but improves neurological deficits in short-term, do you think it is worth trying for stroke patients during the acute phase?”

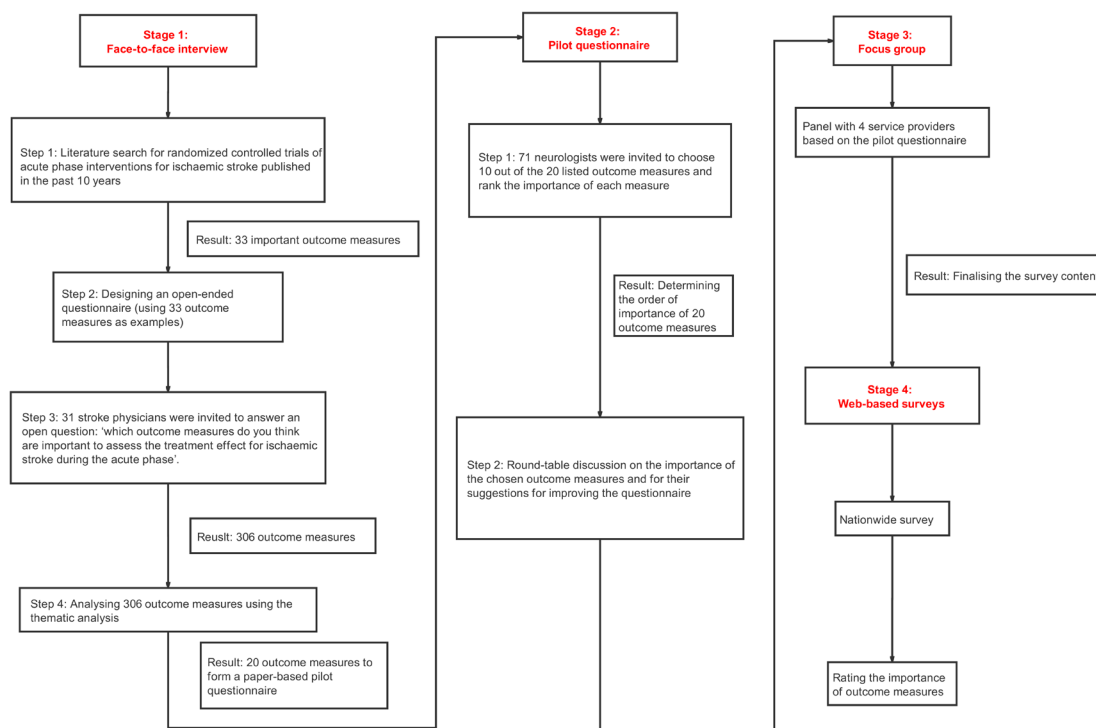


Figure 1. Key stages/steps of study

and if ‘Yes’, “which therapies would you like to use?” and “Please specify the outcome measures that you expect to improve with the chosen therapies”.

Stage 4: Web-based surveys

An online questionnaire developed by SurveyStar (Changsha, China) was delivered at 1 national and 6 regional academic, neurology conferences in China from April 2018 to September 2018. A two-dimensional code linked to the questionnaire was promoted in lecture slide presentations and on postcards at the conference venues. Delegates were invited to scan the code and complete the questionnaire via mobile phones.

Statistical analysis

Two researchers (YW, SW) independently coded all interview data and performed thematic analysis of the pilot questionnaire.¹⁶ The web questionnaire was then finalized after comparisons of the included categories with disagreements agreed through consensus. Quantitative data are

presented as means and standard deviations for continuous variables, and percentage frequencies for categorical variables. To quantify the importance of each outcome measure ranked by participants, a 5-point Likert scale¹⁷ was used: not important at all = 1, not important = 2, neutral = 3, important = 4, very important = 5. A weighted score was calculated using the following equation: $(1*a+2*b + 3*c + 4*d + 5*e) / (a + b + c + d + e)$, where a, b, c, d, and e represent participants’ numbers for ranked each outcome measure. A higher weighted score equated to greater clinical importance. All statistical analyses were performed in SPSS 25.0 (IBM, Chicago, IL, USA).

RESULTS

Among 2,700 delegates across seven conferences, 1,895 accessed the web questionnaire and 1,189 completed the survey. Of 1,189 participants, the mean age was 40 ± 10 years and 53% participants were females. More than half had over 10 years clinical experience and 43% had more than 5 years of research experience in stroke (Table 1).

Table 1: Baseline characteristics of 1189 participants from 30 provinces in China

Characteristics	
Age (years)	40±10
Female	631 (53)
Highest academic degree	
Junior college degree or below	21 (2)
Bachelor’s degree	540 (45)
Master’s degree	471 (40)
Doctor’s degree	157 (13)
Occupation	
Clinician	1141 (96)
Nurse	48 (4)
Clinical experience in stroke (years)	
None	62 (5)
≤5	253 (21)
6-10	245 (21)
11-19	280 (24)
≥20	349 (29)
Research experience in stroke (years)	
None	319 (27)
≤5	357 (30)
6-10	203 (17)
11-19	159 (13)
≥20	151 (13)
Teaching hospital	914(77)
Tertiary level hospital	946 (80)

Data are n (%) or mean (SD)

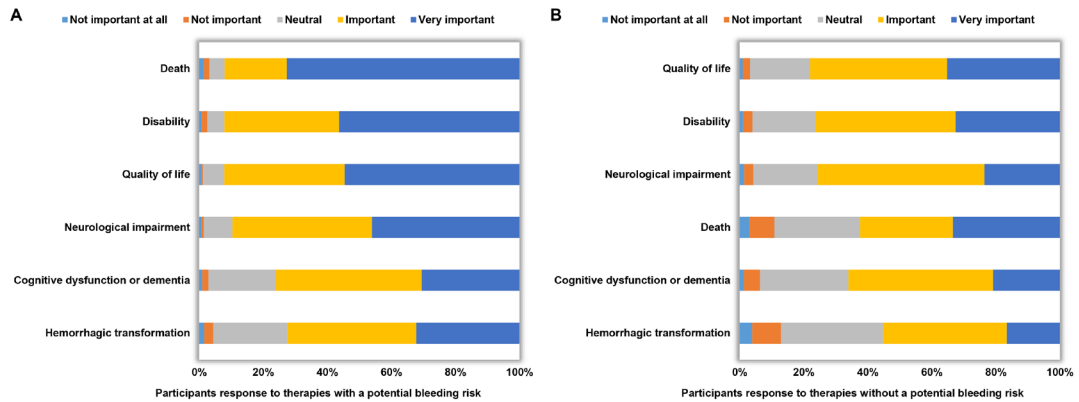


Figure 2. Participant rating importance of outcome measures for therapies with potential bleeding risk (A) and without potential bleeding risk (B).

Of the established acute therapies in AIS with potential bleeding risk, death was rated as the most important outcome measure (weighted score 4.60, 72.7% of participants ranked as ‘very important’), followed by disability (weighted score 4.45, 56.4%) and quality of life (weighted score 4.45, 54.6%), neurological impairment (weighted score 4.34, 46.1%), cognitive dysfunction/dementia (weighted score 4.03, 30.1%), and hemorrhagic transformation (weighted score 3.99, 32.1%) (Figure 2A). For other low-risk therapies, quality of life was ranked as most important outcome measure (weighted score 4.08, 35.2%), followed by disability (weighted score 4.03, 32.6%), neurological impairment (weighted score 3.92, 23.6%), death (weighted score 3.79, 33.4%), cognitive dysfunction/dementia (weighted score 3.78, 20.9%), and hemorrhagic transformation (weighted score 3.51, 16.6%) (Figure 2B).

Similar results were found in sensitivity analysis with the exclusion of responses from nurses (Supplementary appendix).

There were 845 (71%) participants who answered ‘Yes’ to the question on treatments with potential to improve neurological impairment but without a benefit on death or disability, with neuroprotective agents (57%), acupuncture (39%), Chinese patent medicine (24%), and traditional Chinese medicine (12%) being the most commonly chosen therapies. The key outcome measure targeted in the use of these therapies were limb function (77%), medical complication (defined as pneumonia, deep venous thrombosis or urinary tract infection) (65%), level of consciousness (64%), and pathological changes on brain imaging (defined as infarction volume expansion, reduction of hemorrhagic transformation, brain edema or middle shift) (56%) (Figure 3).

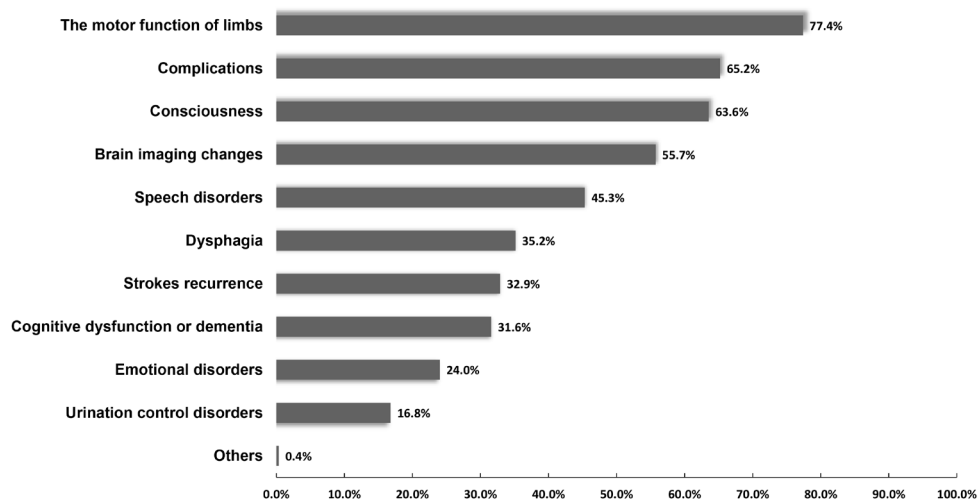


Figure 3. Participant responses for choosing outcome measures in regard to complications (pneumonia, deep venous thrombosis or urinary tract infection), and brain imaging changes on CT/MRI (infarction volume expansion, hemorrhagic transformation, brain oedema or middle shift), speech capability (aphasia or dysarthria) and emotional disorder (anxiety and depression)

DISCUSSION

In our study of the preferences and values of health professionals involved in the management of AIS in China, we have shown that death is the outcome of most importance in the use of reperfusion therapies which are proven to reduce death and disability, whilst quality of life is also important. Hemorrhagic transformation had a low priority for these therapies which have a bleeding risk.

The finding that death had a higher priority than disability supports the old adage in Asian cultures that 'better to live than to die', whilst the ability to maintain functional independence in everyday life seems more important in Western culture. For example, as a life-saving intervention for malignant cerebral infarction, decompressive craniectomy was only acceptable to 7% of the general population in Germany, because the potential downside was the chance to continue living with severe disability.¹⁸ However, recognition that people can change their views when affected is reflected in other studies in other countries showing higher rates of acceptance of decompressive hemicraniectomy: 28% in AIS patients, 47% in relatives¹⁹, 16% in nurses²⁰, and 39% in physicians.²¹ With regard to low-risk therapies, neuroprotection, rehabilitation, acupuncture, Chinese patent medicine, and traditional Chinese medicine, are all widely used alongside Western medicines in China⁶, despite their limited evidence from RCTs. Our study shows these therapies are primarily used with the intent to improve quality of life.

Due to concerns over treatment-related hemorrhagic transformation, many Asian clinicians prefer to use lower doses of intravenous alteplase for thrombolysis treatment of AIS patients.²²⁻²⁴ However, our study suggests this adverse event is regarded as less important than the other clinical outcome measures, which is consistent with findings of dichotomized positive outcomes outweighing the risks of these treatments in RCTs. Education of doctors and patients over hemorrhagic transformation being an acceptable complication in the context of the poor prognosis of AIS may improve the uptake of reperfusion therapies.

Our web-based survey was able to gather opinions from a large number of health professionals at a relatively low cost; it was able to overcome the selection bias from those who were highly skilled and experienced, mainly clinicians, who had the opportunity to attend certain neurology conferences.

In summary, our survey of Chinese medical staff shows they rank death as the outcome of most importance for the use of proven reperfusion therapies, and contrary to current perceptions, the risk of hemorrhagic transformation had a low priority. When a therapy is unlikely to reduce the chances of death or disability, quality of life is more meaningful and acceptable outcome to target. These results may help improve the design of stroke RCTs and counselling of patients and families.

DISCLOSURE

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Conflicts of interest: None

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Supplementary materials

Search strategy and inclusion criteria in Stage 1

Two researchers (YW and SW) independently performed an electronic search of literature in PubMed, Ovid EMBASE and the Cochrane Library databases and Chinese Science and Technology Journals Database between January 2008 and April 2018, using the follow keywords: 'acute ischaemic stroke', 'outcome measure', 'endpoint', 'randomised controlled trials'. We also manually screened specialized journals in neurology and stroke in April 2018, to identify randomised controlled trials of acute phase interventions for ischaemic stroke. These journals include: *The Lancet Neurology*, *JAMA Neurology*, *Neurology*, *Stroke*, *International Journal of Stroke and Cerebrovascular Diseases*.

Subgroup analysis and multivariable regression for different ratings

To explore possible reasons underlying different weighted scores of the listed outcome measures, we performed subgroup analyses and ordinal multi-categorical regression analysis to assess the effect of age (dichotomized by the mean age), sex (male versus female), academic degree (Bachelor or below versus Master or above), occupation (physicians versus nurses), years of clinical practice (dichotomized by the median category of years), years of research practice (dichotomized by the median category of years), whether working in the teaching hospital (yes versus no) or tertiary hospital (yes versus no). We conducted Pearson Chi-square test to assess the association between the distribution of the above subgroup characteristics and the participant's response to the importance of each listed outcome measures. If significant association was found, the Cramer's V value (range: 0 – 1; the value closer to 1 indicates the stronger association) was calculated for showing strengths of the association.[1] For each outcome measure, we further calculated adjusted standardized residual (ASR) to identify the between-subgroup difference in each of the five rating categories. The absolute value of ASR > 2 indicated a significant discrepancy and ASR -2 to +2 represented a non-significant difference.[2] A 2-sided P <0.05 was considered statistically significant.

Sensitivity analysis after removing the nurse' results

For the established acute therapies with a potential bleeding risk, the rated importance was different for the six listed outcome measures (Supplementary Fig. 2A). Death was most commonly ranked as the very important outcome measure (73%, 833/1141 of the physicians, weighted score 4.6), followed by disability (55.8%, 637/1141, weighted score 4.44), quality of life (53.9%, 615/1141, weighted score 4.45), neurological impairment (46.3%, 528/1141, weighted score 4.34), cognitive dysfunction or dementia (29.7%, 339/1141, weighted score 4.01), and haemorrhagic transformation (31.1%, 355/1141, weighted score 3.96).

For the other type of therapies (Supplementary Fig. 2B), quality of life was the most commonly ranked important outcome measure (by 34.5%, 394/1141 of physicians, weighted score 4.07), followed by disability (32%, 365/1141, weighted score 4.02), neurological impairment (23.3%, 266/1141, weighted score 3.91), death (33%, 376/1141, weighted score 3.77), cognitive dysfunction or dementia (20.2%, 230/1141, weighted score 3.76), and haemorrhagic transformation (16%, 182/1141, weighted score 3.48).

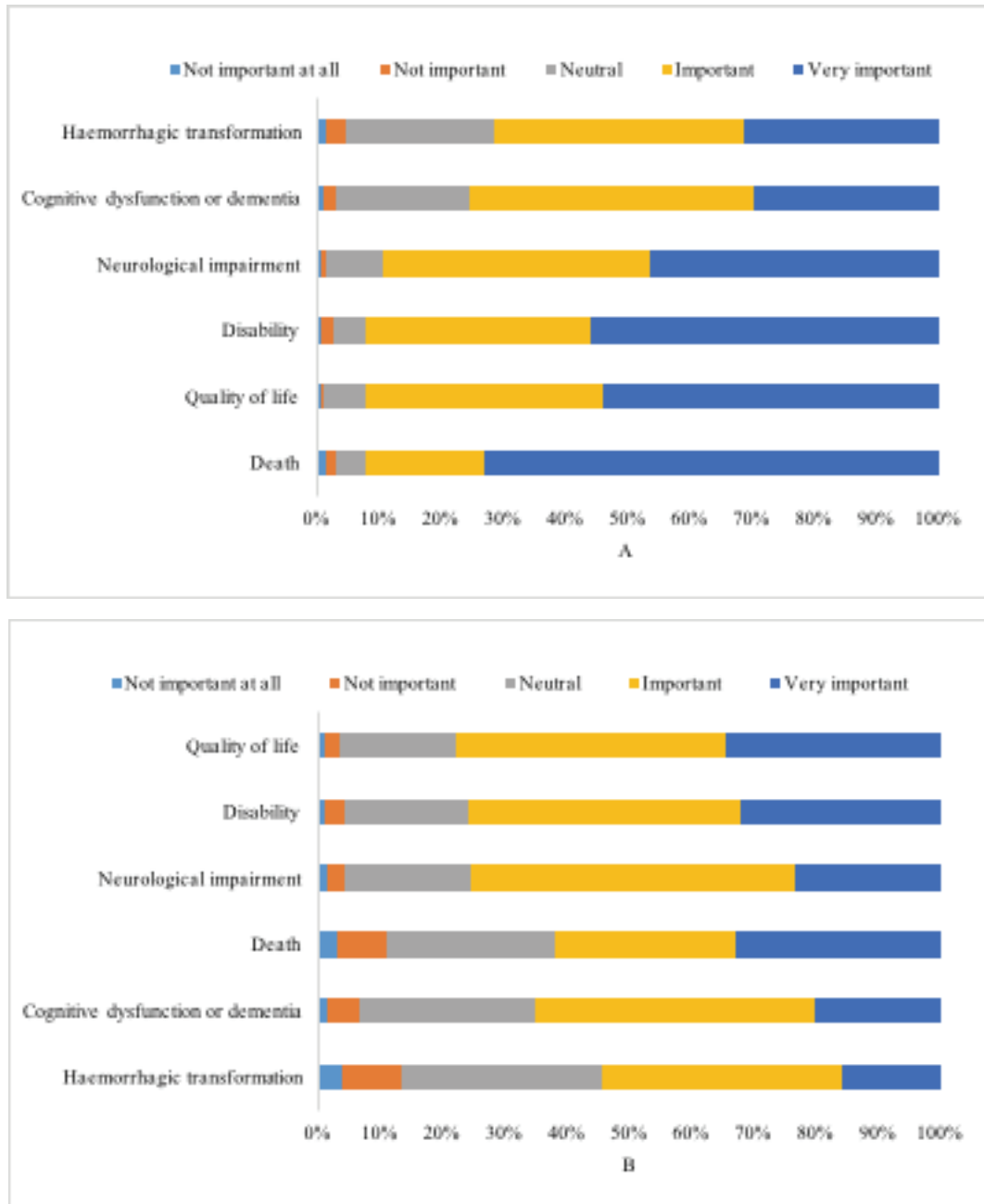
Ordinal multi-categorical regression analysis

For the established acute stroke therapies with a potential bleeding risk, we found females were more likely to rate disability (OR 0.75 95%CI 0.59 - 0.95, P=0.017) and cognitive function (OR 0.64 95%CI 0.51 - 0.80, P<0.001) as very important; nurses were more likely to rate haemorrhagic transformation (OR 0.34 95%CI 0.18 - 0.64, P=0.001) and cognitive function (OR 0.47 95%CI 0.25 - 0.86, P=0.014); Participants with less than 10 years of clinical experience (OR 1.42 95%CI 1.01 - 2.01, P=0.045) were more likely to rate cognitive function as very important; participants with less than 5 years research experience in stroke (OR 1.35 95%CI 1.02 - 1.78, P=0.033); and participants who were working in teaching hospitals (OR 1.40 95%CI 1.01 - 1.94, P=0.047) were more likely to rate death as very important (Supplementary Table 4).

For the other type of therapies that are commonly used in practice and without a potential bleeding risk, we found females were more likely to rate death (OR 0.81 95%CI 0.65 - 1, P=0.048), disability (OR 0.66 95%CI 0.53 - 0.83, P<0.001), neurological impairment (OR 0.7 95%CI 0.56 - 0.88, P=0.002),

cognitive function (OR 0.68 95%CI 0.54 - 0.85, P=0.001) and quality of life (OR 0.64 95%CI 0.51 - 0.80, P<0.001) as very important; and nurses were more likely to rate haemorrhagic transformation (OR 0.41 95%CI 0.23 - 0.73, P=0.003) and cognitive function (OR 0.47 95%CI 0.26 - 0.84, P=0.011) as very important (Supplementary Table 4).

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Supplementary Figure 2. Physicians rating the importance of outcome measures for therapies with a potential bleeding risk (A) versus therapies without a potential bleeding risk (B)

Supplementary Table 1: The results of preliminary survey

Rank	Preliminary survey (n=71)	
	Outcomes selected ≥ 5 times	Frequency
1	Basic activities of daily living	60
2	Death	59
3	Brain imaging changes on CT/MRI	56
4	Cognitive function	52
5	Complications	47
6	Disability	45
7	Overall quality of life	44
8	Psychological health	43
9	Consciousness	41
10	Aphasia	39
11	The motor function of limb	39
12	Strokes recurrence	35
13	Dysphagia	27
14	Urination control disorder	24
15	Vital signs	19
16	Social Activities	16
17	Degree of vascular stenosis	16
18	Instrumental Activities of Daily Living	15
19	Blood routine and biochemical examination	6
20	Vision disorder	5

CT: computed tomography; MRI: magnetic resonance imaging

Supplementary Table 2: Subgroup analyses for the established acute stroke therapies with a potential bleeding risk (n=1,189)

	Age	Not important at all	Not important	Neutral	Important	Very important	P-values
	≤ 40, n (%)	5 (0.4%)	9 (0.8%)	28 (2.4%)	114 (9.9%)	469 (40.5%)	0.109
Death	ASR	-2.1	-1.0	0.1	-1.3	1.9	
	> 40, n (%)	12 (1.0%)	12 (1%)	23 (2.0%)	113 (9.8%)	372 (32.2%)	
	ASR	2.1	1.0	-0.1	1.3	-1.9	
	≤ 40, n (%)	2 (0.2%)	8 (0.7%)	25 (2.2%)	238 (20.6%)	352 (30.4)	0.010
Disability	ASR	-1.9	-1.5	-2.2	2.0	-0.2	
	÷ 40, n (%)	7 (0.6)	13 (1.1%)	37 (3.2%)	172 (14.9%)	303 (26.2%)	
	ASR	1.9	1.5	2.2	-2.0	0.2	
	≤ 40, n (%)	4 (0.3%)	2 (0.2%)	50 (4.3%)	285 (24.6%)	284 (24.5%)	0.234
Neurological impairment	ASR	-0.6	-1.4	-1.4	1.6	-0.5	
	> 40, n (%)	5 (0.4%)	5 (0.4%)	55 (4.8%)	217 (18.8%)	250 (21.6%)	
	ASR	0.6	1.4	1.4	-1.6	0.5	
	≤ 40, n (%)	3 (0.3%)	14 (1.2%)	130 (11.2)	259 (22.4%)	219 (18.9%)	0.001
Haemorrhagic transformation	ASR	-3.2	-1.5	-2.1	1.1	2.1	
	> 40, n (%)	15 (1.3%)	20 (1.7%)	138 (11.9%)	204 (17.6%)	155 (13.4%)	
	ASR	3.2	1.5	2.1	-1.1	-2.1	
	≤ 40, n (%)	5 (0.4%)	7 (0.6%)	129 (11.1%)	289 (25%)	195 (16.9%)	0.296
Cognitive dysfunction or dementia	ASR	-0.6	-2.1	-0.1	0.3	0.5	
	> 40, n (%)	6 (0.5%)	15 (1.3%)	111 (9.6%)	241 (20.8%)	159 (13.7%)	
	ASR	0.6	2.1	0.1	-0.3	-0.5	
	≤ 40, n (%)	3 (0.3%)	3 (0.3%)	33 (2.9%)	240 (20.7%)	346 (29.9%)	0.230
Quality of life	ASR	-0.6	-0.2	-2.3	0.7	0.6	
	> 40, n (%)	4 (0.3%)	3 (0.3%)	46 (4%)	194 (16.8%)	285 (24.6%)	
	ASR	0.6	0.2	2.3	-0.7	-0.6	

	Sex	Not important at all	Not important	Neutral	Important	Very important	P-values
Death	Male, n (%)	9 (0.8%)	13 (1.1%)	23 (1.9%)	104 (8.7%)	409 (34.4%)	0.508
	ASR	0.5	1.4	-0.9	-0.6	0.5	
	Female, n (%)	8 (0.7%)	8 (0.7%)	33 (2.8%)	127 (10.7%)	455 (38.3%)	
	ASR	-0.5	-1.4	0.9	0.6	-0.5	
Disability	Male, n (%)	6 (0.5%)	17 (1.4%)	36 (0.9%)	205 (0.6%)	294 (0.5%)	0.002
	ASR	1.2	3.2	1.7	0.6	-2.4	
	Female, n (%)	3 (0.3%)	4 (0.3%)	27 (2.3%)	221 (18.0%)	376 (31.0%)	
	ASR	-1.2	-3.2	-1.7	-0.6	2.4	
Neurological impairment	Male, n (%)	4 (0.3%)	7 (0.3%)	56 (2.3%)	243 (18.0%)	248 (31.0%)	0.044
	ASR	-0.1	2.8	1.2	0.0	-1.1	
	Female, n (%)	5 (0.4%)	0 (0%)	51 (4.3%)	275 (23.0%)	300 (25.0%)	
	ASR	0.1	-2.8	-1.2	0.0	1.1	
Haemorrhagic transformation	Male, n (%)	7 (0.6%)	21 (1.8%)	133 (11.0%)	216 (18.0%)	181 (15.0%)	0.374
	ASR	-0.7	1.8	0.5	-1.0	0.2	
	Female, n (%)	11 (0.9%)	13 (1.13%)	143 (1.23%)	262 (8.104%)	202 (34.409%)	
	ASR	0.7	-1.8	-0.5	1.0	-0.2	
Cognitive dysfunction or dementia	Male, n (%)	7 (0.6%)	15 (1.6%)	147 (1.6%)	243 (8.6%)	146 (34.6%)	<0.001
	ASR	1.1	1.8	4.2	-1.3	-3.1	
	Female, n (%)	4 (0.3%)	8 (0.3%)	103 (2.3%)	299 (18.0%)	217 (31.0%)	
	ASR	-1.1	-1.8	-4.2	1.3	3.1	
Quality of life	Male, n (%)	4 (0.3%)	6 (0.5%)	54 (4.5%)	221 (18.6%)	273 (23.0%)	<0.001
	ASR	0.5	2.6	3.8	1.3	-3.7	
	Female, n (%)	3 (0.3%)	0 (0%)	26 (2.2%)	226 (19%)	376 (31.6%)	
	ASR	-0.5	-2.6	-3.8	-1.3	3.7	

	Academic degree	Not important at all	Not important	Neutral	Important	Very important	P-values
Death	Bachelor or below, n (%)	9 (0.8%)	14 (1.2%)	29 (2.4%)	114 (9.6%)	395 (33.2%)	0.279
	ASR	0.5	1.8	0.7	0.7	-1.6	
	Master or above, n (%)	8 (0.7%)	7 (0.6%)	27 (2.3%)	117 (9.8%)	469 (39.4%)	
	ASR	-0.5	-1.8	-0.7	-0.7	1.6	
Disability	Bachelor or below, n (%)	4 (0.3%)	16 (1.3%)	34 (2.9%)	204 (17.2%)	303 (25.5%)	0.052
	ASR	-0.2	2.7	1.1	0.4	-1.5	
	Master or above, n (%)	5 (0.4%)	5 (0.4%)	29 (2.4%)	222 (18.7%)	367 (30.9%)	
	ASR	0.2	-2.7	-1.1	-0.4	1.5	
Neurological impairment	Bachelor or below, n (%)	3 (0.3%)	6 (1.3%)	52 (2.9%)	245 (17%)	255 (25.5%)	0.283
	ASR	-0.8	2.0	0.3	0.1	-0.4	
	Master or above, n (%)	6 (0.5%)	1 (0.1%)	55 (4.6%)	273 (23.0%)	293 (24.6%)	
	ASR	0.8	-2.0	-0.3	-0.1	0.4	
Haemorrhagic transformation	Bachelor or below, n (%)	9 (0.8%)	18 (1.2%)	120 (2.4%)	229 (9.6%)	185 (33.2%)	0.677
	ASR	0.2	0.7	-1.4	0.4	0.5	
	Master or above, n (%)	9 (0.8%)	16 (1.2%)	156 (2.4%)	249 (9.6%)	198 (33.2%)	
	ASR	-0.2	-0.7	1.4	-0.4	-0.5	
Cognitive dysfunction or dementia	Bachelor or below, n (%)	5 (0.4%)	12 (0.4%)	120 (2.4%)	244 (18.7%)	180 (30.9%)	0.704
	ASR	-0.1	0.5	0.3	-1.4	1.1	
	Master or above, n (%)	6 (0.5%)	11 (0.1%)	130 (4.6%)	298 (23.0%)	183 (24.6%)	
	ASR	0.1	-0.5	-0.3	1.4	-1.1	
Quality of life	Bachelor or below, n (%)	2 (0.2%)	5 (0.4%)	56 (4.7%)	197 (16.6%)	301 (25.3%)	<0.001
	ASR	-1.0	1.8	4.2	-1.7	-0.6	
	Master or above, n (%)	5 (0.4%)	1 (0.4%)	24 (2.4%)	250 (18.7%)	348 (30.9%)	
	ASR	1.0	-1.8	-4.2	1.7	0.6	

	Occupation	Not important at all	Not important	Neutral	Important	Very important	P-values
Death	Physicians, n (%)	17 (1.4%)	20 (1.7%)	52 (4.4%)	219 (18.4%)	833 (70.1%)	0.495
	ASR	0.9	-0.2	-1.2	-1.0	1.3	
	Nurses, n (%)	0 (0%)	1 (0.1%)	4 (0.3%)	12 (1.0%)	31 (2.6%)	
	ASR	-0.9	0.2	1.2	1.0	-1.3	
Disability	Physicians, n (%)	9 (0.8%)	21 (1.8%)	62 (5.2%)	412 (34.7%)	637 (53.6%)	0.377
	ASR	0.6	0.9	1.0	1.0	-1.8	
	Nurses, n (%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	14 (1.2%)	33 (2.8%)	
	ASR	-0.6	-0.9	-1.0	-1.0	1.8	
Neurological impairment	Physicians, n (%)	9 (0.8%)	7 (0.8%)	104 (3.2%)	493 (25.7%)	528 (20.6%)	0.71
	ASR	0.6	0.5	0.7	-1.2	0.6	
	Nurses, n (%)	0 (0.0%)	0 (0.0%)	3 (0.3%)	25 (2.1%)	20 (1.7%)	
	ASR	-0.6	-0.5	-0.7	1.2	-0.6	
Haemorrhagic transformation	Physicians, n (%)	18 (1.5%)	34 (2.9%)	273 (23.0%)	461 (38.8%)	355 (29.9%)	0.001
	ASR	0.9	1.2	2.8	0.7	-4.0	
	Nurses, n (%)	0 (0.0%)	0 (0.0%)	3 (0.3%)	17 (1.4%)	28 (2.4%)	
	ASR	-0.9	-1.2	-2.8	-0.7	4.0	
Cognitive dysfunction or dementia	Physicians, n (%)	11 (0.9%)	23 (1.9%)	248 (20.9%)	520 (43.7%)	339 (28.5%)	0.006
	ASR	0.7	1.0	2.9	0.0	-3.0	
	Nurses, n (%)	0 (0.0%)	0 (0.0%)	2 (0.2%)	22 (1.9%)	24 (2.0%)	
	ASR	-0.7	-1.0	-2.9	0.0	3.0	
Quality of life	Physicians, n (%)	7 (0.6%)	6 (0.5%)	78 (2.6%)	435 (12.6%)	615 (34.7%)	0.234
	ASR	0.5	0.5	0.7	1.8	-2.3	
	Nurses, n (%)	0 (0.0%)	0 (0.0%)	2 (0.2%)	12 (1.0%)	34 (2.9%)	
	ASR	-0.5	-0.5	-0.7	-1.8	2.3	

Clinical practice (years%)	Not important at all	Not important	Neutral	Important	Very important	P-values
Death						
≤10, n (%)	6 (0.5%)	7 (0.6%)	27 (2.3%)	104 (8.7%)	416 (35.0%)	0.500
ASR	-1.0	-1.3	0.2	-0.7	1.2	
>10, n (%)	11 (0.9%)	14 (1.2%)	29 (2.4%)	127 (10.7%)	448 (37.7%)	
ASR	1.0	1.3	-0.2	0.7	-1.2	
Disability						
≤10, n (%)	2 (0.2%)	5 (0.4%)	24 (2.0%)	208 (17.5%)	321 (27.0%)	0.049
ASR	-1.5	-2.2	-1.5	0.9	0.6	
>10, n (%)	7 (0.6%)	16 (1.3%)	39 (3.3%)	218 (18.3%)	349 (29.4%)	
ASR	1.5	2.2	1.5	-0.9	-0.6	
Neurological impairment						
≤10, n (%)	4 (0.3%)	1 (0.1%)	49 (4.1%)	247 (20.8%)	259 (21.8%)	0.053
ASR	-0.2	-1.7	-0.3	0.4	0.1	
>10, n (%)	5 (0.4%)	6 (0.5%)	58 (4.9%)	271 (22.8%)	289 (24.3%)	
ASR	0.2	1.7	0.3	-0.4	-0.1	
Haemorrhagic transformation						
≤10, n (%)	4 (0.3%)	10 (0.8%)	107 (9.0%)	232 (19.5%)	207 (17.4%)	<0.001
ASR	-2.1	-2.1	-3.2	0.8	3.3	
>10, n (%)	14 (1.2%)	24 (2.0%)	169 (14.2%)	246 (20.7%)	176 (14.8%)	
ASR	2.1	2.1	3.2	-0.8	-3.3	
Cognitive dysfunction or dementia						
≤10, n (%)	4 (0.3%)	6 (0.5%)	110 (9.3%)	251 (21.1%)	189 (15.9%)	0.055
ASR	-0.7	-2.0	-1.1	-0.5	2.3	
>10, n (%)	7 (0.6%)	17 (1.4%)	140 (11.8%)	291 (24.5%)	174 (14.6%)	
ASR	0.7	2.0	1.1	0.5	-2.3	
Quality of life						
≤10, n (%)	3 (0.3%)	1 (0.1%)	29 (2.4%)	211 (17.7%)	316 (26.6%)	0.151
ASR	-0.2	-1.5	-2.0	0.1	1.2	
>10, n (%)	4 (0.3%)	5 (0.4%)	51 (4.3%)	236 (19.8%)	333 (28.0%)	
ASR	0.2	1.5	2.0	-0.1	-1.2	

	Research practice (years%)					P-values	
	Not important at all	Not important	Neutral	Important	Very important		
Death	≤5, n (%)	7 (0.6%)	8 (0.7%)	37 (3.1%)	127 (10.7%)	497 (41.8%)	0.128
	ASR	-1.3	-1.8	1.4	-0.6	0.8	
	>5, n (%)	10 (0.8%)	13 (1.1%)	19 (1.6%)	104 (8.7%)	367 (30.9%)	
Disability	ASR	1.3	1.8	-1.4	0.6	-0.8	0.096
	≤5, n (%)	1 (0.1%)	14 (1.2%)	30 (2.5%)	248 (20.9%)	383 (32.2%)	
	ASR	-2.8	0.9	-1.5	0.7	0.2	
Neurological impairment	>5, n (%)	8 (0.7%)	7 (0.6%)	33 (2.8%)	178 (15.0%)	287 (24.1%)	0.333
	ASR	2.8	-0.9	1.5	-0.7	-0.2	
	≤5, n (%)	3 (0.3%)	2 (0.2%)	59 (5.0%)	297 (25.0%)	315 (26.5%)	
Haemorrhagic transformation	ASR	-1.4	-1.5	-0.4	0.3	0.4	<0.001
	>5, n (%)	6 (0.5%)	5 (0.4%)	48 (4.0%)	221 (18.6%)	233 (19.6%)	
	ASR	1.4	1.5	0.4	-0.3	-0.4	
Cognitive dysfunction or dementia	≤5, n (%)	6 (0.5%)	16 (0.4%)	131 (4.0%)	278 (18.6%)	245 (19.6%)	0.141
	ASR	-2.0	-1.2	-3.6	0.7	3.4	
	>5, n (%)	12 (1.0%)	18 (1.5%)	145 (12.2%)	200 (16.8%)	138 (11.6%)	
Quality of life	ASR	2.0	1.2	3.6	-0.7	-3.4	0.368
	≤5, n (%)	4 (0.3%)	9 (0.8%)	142 (11.9%)	302 (25.4%)	219 (18.4%)	
	ASR	-1.4	-1.7	0.0	-0.7	1.6	
Quality of life	>5, n (%)	7 (0.6%)	14 (1.2%)	108 (9.1%)	240 (20.2%)	144 (12.1%)	0.141
	ASR	1.4	1.7	0.0	0.7	-1.6	
	≤5, n (%)	2 (0.2%)	2 (0.2%)	46 (3.9%)	249 (20.9%)	377 (31.7%)	
Quality of life	ASR	-1.5	-1.2	0.1	-0.6	0.9	0.368
	>5, n (%)	5 (0.4%)	4 (0.3%)	34 (2.9%)	198 (16.7%)	272 (22.9%)	
	ASR	1.5	1.2	-0.1	0.6	-0.9	

	Teaching hospital	Not important at all	Not important	Neutral	Important	Very important	P-values
Death	Yes, n (%)	8 (0.7%)	10 (0.8%)	38 (3.2%)	179 (15.1%)	679 (57.1%)	<0.001
	ASR	-2.9	-3.2	-1.6	0.2	2.3	
	No, n (%)	9 (0.8%)	11 (0.9%)	18 (1.5%)	52 (4.4%)	185 (15.6%)	
	ASR	2.9	3.2	1.6	-0.2	-2.3	
Disability	Yes, n (%)	6 (0.5%)	11 (0.9%)	47 (4.0%)	316 (26.6%)	534 (44.9%)	0.014
	ASR	-0.7	-2.7	-0.4	-1.6	2.6	
	No, n (%)	3 (0.3%)	10 (0.8%)	16 (1.3%)	110 (9.3%)	136 (11.4%)	
	ASR	0.7	2.7	0.4	1.6	-2.6	
Neurological impairment	Yes, n (%)	6 (0.5%)	5 (0.4%)	83 (7.0%)	388 (32.6%)	432 (36.3%)	0.560
	ASR	-0.7	-0.3	0.2	-1.4	1.5	
	No, n (%)	3 (0.3%)	2 (0.2%)	24 (2.0%)	130 (10.9%)	116 (9.8%)	
	ASR	0.7	0.3	-0.2	1.4	-1.5	
Haemorrhagic transformation	Yes, n (%)	13 (1.1%)	25 (2.1%)	219 (18.4%)	357 (30.0%)	300 (25.2%)	0.537
	ASR	-0.5	-0.5	1.1	-1.5	0.8	
	No, n (%)	5 (0.4%)	9 (0.8%)	57 (4.8%)	121 (10.2%)	83 (7.0%)	
	ASR	0.5	0.5	-1.1	1.5	-0.8	
Cognitive dysfunction or dementia	Yes, n (%)	6 (0.5%)	18 (1.5%)	196 (16.5%)	407 (34.2%)	287 (24.1%)	0.250
	ASR	-1.8	0.2	0.6	-1.3	1.2	
	No, n (%)	5 (0.4%)	5 (0.4%)	54 (4.5%)	135 (11.4%)	76 (6.4%)	
	ASR	1.8	-0.2	-0.6	1.3	-1.2	
Quality of life	Yes, n (%)	4 (0.3%)	4 (0.3%)	58 (4.9%)	342 (28.8%)	506 (42.6%)	0.523
	ASR	-1.2	-0.6	-1.0	-0.2	1.0	
	No, n (%)	3 (0.3%)	2 (0.2%)	22 (1.9%)	105 (8.8%)	143 (12.0%)	
	ASR	1.2	0.6	1.0	0.2	-1.0	

	Tertiary hospital	Not important at all	Not important	Neutral	Important	Very important	P-values
Death	Yes, n (%)	9 (0.8%)	14 (1.2%)	41 (3.4%)	177 (14.9%)	705 (59.3%)	0.006
	ASR	-2.7	-1.5	-1.2	-1.2	2.8	
	No, n (%)	8 (0.7%)	7 (0.6%)	15 (1.3%)	54 (4.5%)	159 (13.4%)	
Disability	ASR	2.7	1.5	1.2	1.2	-2.8	
	Yes, n (%)	5 (0.4%)	11 (0.9%)	52 (4.4%)	325 (27.3%)	553 (46.5%)	0.001
	ASR	-1.8	-3.1	0.6	-2.1	2.9	
Neurological impairment	No, n (%)	4 (0.3%)	10 (0.8%)	11 (0.9%)	101 (8.5%)	117 (9.8%)	
	ASR	1.8	3.1	-0.6	2.1	-2.9	
	Yes, n (%)	7 (0.6%)	5 (0.4%)	83 (7.0%)	409 (34.4%)	442 (37.2%)	0.897
Haemorrhagic transformation	ASR	-0.1	-0.5	-0.5	-0.5	0.9	
	No, n (%)	2 (0.2%)	2 (0.2%)	24 (2.0%)	109 (9.2%)	106 (8.9%)	
	ASR	0.1	0.5	0.5	0.5	-0.9	
Cognitive dysfunction or dementia	Yes, n (%)	13 (1.1%)	26 (2.2%)	220 (18.5%)	381 (32.0%)	306 (25.7%)	0.934
	ASR	-0.8	-0.5	0.1	0.1	0.2	
	No, n (%)	5 (0.4%)	8 (0.7%)	56 (4.7%)	97 (8.2%)	77 (6.5%)	
Quality of life	ASR	0.8	0.5	-0.1	-0.1	-0.2	
	Yes, n (%)	6 (0.5%)	17 (1.4%)	201 (16.9%)	438 (36.8%)	284 (23.9%)	0.222
	ASR	-2.1	-0.7	0.4	1.0	-0.8	
Quality of life	No, n (%)	5 (0.4%)	6 (0.5%)	49 (4.1%)	104 (8.7%)	79 (6.6%)	
	ASR	2.1	0.7	-0.4	-1	0.8	
	Yes, n (%)	4 (0.3%)	3 (0.3%)	60 (5.0%)	355 (29.9%)	524 (44.1%)	0.137
Quality of life	ASR	-1.5	-1.8	-1.0	-0.1	1.1	
	No, n (%)	3 (0.3%)	3 (0.3%)	20 (1.7%)	92 (7.7%)	125 (10.5%)	
	ASR	1.5	1.8	1.0	0.1	-1.1	

Supplementary Table 3: Subgroup analyses for the other type of therapies that are commonly used in practice and without a potential bleeding risk (n=1,189)

	Age	Not important at all	Not important	Neutral	Important	Very important	P-values
Death	≤40, n (%)	18 (1.6%)	47 (4.1%)	153 (13.20)	176 (15.2%)	231 (2%)	0.092
	ASR	-0.7	-0.2	-1.9	-0.6	2.7	
	>40, n (%)	19 (1.6%)	42 (3.6%)	156 (13.5%)	158 (13.7%)	157 (13.6%)	
Disability	ASR	0.7	0.2	1.9	0.6	-2.7	
	≤40, n (%)	6 (0.5%)	18 (1.6%)	113 (9.8%)	292 (25.2%)	196 (16.9%)	0.17
	ASR	-0.3	-0.5	-1.5	2.5	-1.1	
Neurological impairment	>40, n (%)	6 (0.5%)	18 (1.6%)	115 (9.9%)	210 (18.2%)	183 (15.8%)	
	ASR	0.3	0.5	1.5	-2.5	1.1	
	≤40, n (%)	6 (0.5%)	18 (1.6%)	119 (10.3%)	344 (29.7%)	138 (11.9%)	0.155
Haemorrhagic transformation	ASR	-1.6	-0.1	-0.9	2.2	-1.2	
	>40, n (%)	11 (1%)	16 (1.4%)	113 (9.8%)	258 (22.3%)	134 (11.6%)	
	ASR	1.6	0.1	0.9	-2.2	1.2	
Cognitive dysfunction or dementia	≤40, n (%)	20 (1.7%)	58 (5%)	181 (15.6%)	255 (22%)	111 (9.6%)	0.087
	ASR	-1.6	0.3	-2.1	1.5	1.2	
	>40, n (%)	27 (2.3%)	47 (4.1%)	184 (15.9%)	194 (16.8%)	80 (6.9%)	
Quality of life	ASR	1.6	-0.3	2.1	-1.5	-1.2	
	≤40, n (%)	9 (0.8%)	29 (2.5%)	163 (14.1%)	296 (25.6%)	128 (11.1%)	0.588
	ASR	0.2	-0.8	-1.1	1.5	-0.3	
Quality of life	>40, n (%)	7 (0.6%)	30 (2.6%)	154 (13.3%)	228 (19.7%)	113 (9.8%)	
	ASR	-0.2	0.8	1.1	-1.5	0.3	
	≤40, n (%)	6 (0.5%)	14 (1.2%)	109 (9.4%)	277 (23.9%)	219 (18.9%)	0.75
Quality of life	ASR	0.0	-0.2	-1.2	1.1	-0.2	
	>40, n (%)	5 (0.4%)	13 (1.1%)	107 (9.2%)	218 (18.8%)	189 (16.3%)	
	ASR	0.0	0.2	1.2	-1.1	0.2	

	Sex	Not important at all	Not important	Neutral	Important	Very important	P-values
Death	Male, n (%)	17 (1.4%)	54 (4.5%)	157 (13.2%)	160 (13.5%)	170 (14.3%)	0.071
	ASR	-0.1	2.4	1.0	-0.2	-2.0	
	Female, n (%)	20 (1.7%)	38 (3.2%)	161 (13.5%)	185 (15.6%)	227 (19.1%)	
	ASR	0.1	-2.4	-1.0	0.2	2.0	
	Male, n (%)	8 (0.7%)	26 (2.2%)	118 (9.9%)	253 (21.3%)	153 (12.9%)	<0.001
	ASR	1.4	3.1	1.3	1.0	-3.5	
Disability	Female, n (%)	4 (0.3%)	10 (0.8%)	115 (9.7%)	268 (22.5%)	234 (19.7%)	
	ASR	-1.4	-3.1	-1.3	-1.0	3.5	
	Male, n (%)	11 (0.9%)	21 (1.8%)	125 (10.5%)	284 (23.9%)	117 (9.8%)	0.025
	ASR	1.5	1.8	1.9	-0.8	-2.0	
	Female, n (%)	6 (0.5%)	13 (1.1%)	114 (9.6%)	335 (28.2%)	163 (13.7%)	
	ASR	-1.5	-1.8	-1.9	0.8	2.0	
Haemorrhagic transformation	Male, n (%)	26 (2.2%)	58 (4.9%)	180 (15.1%)	204 (17.2%)	90 (7.6%)	0.267
	ASR	1.2	1.7	0.2	-1.4	-0.4	
	Female, n (%)	21 (1.8%)	48 (4.0%)	200 (16.8%)	255 (21.4%)	107 (9.0%)	
	ASR	-1.2	-1.7	-0.2	1.4	0.4	
	Male, n (%)	10 (0.8%)	40 (3.4%)	175 (14.7%)	233 (19.6%)	100 (8.4%)	<0.001
	ASR	1.3	3.1	2.7	-2.2	-2.3	
Cognitive dysfunction or dementia	Female, n (%)	6 (0.5%)	20 (1.1%)	153 (9.6%)	304 (28.2%)	148 (13.7%)	
	ASR	-1.3	-3.1	-2.7	2.2	2.3	
	Male, n (%)	7 (0.6%)	18 (1.5%)	125 (10.5%)	241 (20.3%)	167 (14.0%)	<0.001
	ASR	1.1	1.9	3.1	0.2	-3.6	
	Female, n (%)	4 (0.3%)	10 (0.8%)	97 (9.7%)	268 (22.5%)	252 (19.7%)	
	ASR	-1.1	-1.9	-3.1	-0.2	3.6	

	Academic degree	Not important at all	Not important	Neutral	Important	Very important	P-values
Death	Bachelor or above, n (%)	16 (1.3%)	45 (3.8%)	155 (13.0%)	156 (13.1%)	189 (15.9%)	0.876
	ASR	-0.5	0.3	0.7	-0.9	0.2	
	Master or above, n (%)	21 (1.8%)	47 (4.0%)	163 (13.7%)	189 (15.9%)	208 (17.5%)	
Disability	ASR	0.5	-0.3	-0.7	0.9	-0.2	
	Bachelor or above, n (%)	2 (0.2%)	15 (1.3%)	110 (9.3%)	248 (20.9%)	186 (15.6%)	0.279
	ASR	-2.1	-0.7	0.0	0.3	0.4	
Neurological impairment	Master or above, n (%)	10 (0.8%)	21 (1.8%)	123 (10.3%)	273 (23.0%)	201 (16.9%)	
	ASR	2.1	0.7	0.0	-0.3	-0.4	
	Bachelor or above, n (%)	4 (0.3%)	13 (1.1%)	118 (9.9%)	282 (23.7%)	144 (12.1%)	0.09
Haemorrhagic transformation	ASR	-2.0	-1.1	0.8	-1.2	1.6	
	Master or above, n (%)	13 (1.1%)	21 (1.80%)	121 (10.20%)	337 (28.30%)	136 (11.40%)	
	ASR	2.0	1.1	-0.8	1.2	-1.6	
Cognitive dysfunction or dementia	Bachelor or above, n (%)	20 (1.7%)	49 (4.1%)	175 (14.7%)	215 (18.1%)	102 (8.6%)	0.676
	ASR	-0.6	-0.2	-0.5	-0.2	1.4	
	Master or above, n (%)	27 (2.3%)	57 (4.8%)	205 (17.2%)	244 (20.5%)	95 (8.0%)	
Quality of life	ASR	0.6	0.2	0.5	0.2	-1.4	
	Bachelor or above, n (%)	5 (0.4%)	33 (2.8%)	156 (13.1%)	235 (19.8%)	132 (11.1%)	0.055
	ASR	-1.3	1.2	0.2	-2.1	2.1	
Quality of life	Master or above, n (%)	11 (0.9%)	27 (2.3%)	172 (14.5%)	302 (25.4%)	116 (9.8%)	
	ASR	1.3	-1.2	-0.2	2.1	-2.1	
	Bachelor or above, n (%)	1 (0.1%)	16 (1.21%)	111 (10.123%)	226 (23.273%)	207 (16.201%)	0.031
Quality of life	ASR	-2.5	1.1	0.9	-1.7	1.1	
	Master or above, n (%)	10 (0.8%)	12 (1.8%)	111 (10.3%)	283 (23.0%)	212 (16.9%)	
	ASR	2.5	-1.1	-0.9	1.7	-1.1	

	Occupation	Not important at all	Not important	Neutral	Important	Very important	P-values
Death	Physicians, n (%)	37 (3.1%)	90 (7.6%)	306 (25.7%)	332 (27.9%)	376 (31.6%)	0.391
	ASR	1.3	0.9	0.3	0.3	-1.6	
	Nurses, n (%)	0 (0.0%)	2 (0.2%)	12 (1.0%)	13 (1.1%)	21 (1.8%)	
	ASR	-1.3	-0.9	-0.3	-0.3	1.6	
Disability	Physicians, n (%)	12 (1.0%)	36 (3.0%)	227 (19.1%)	501 (42.1%)	365 (30.7%)	0.194
	ASR	0.7	1.2	1.3	0.3	-2.0	
	Nurses, n (%)	0 (0.0%)	0 (0.0%)	6 (0.5%)	20 (1.7%)	22 (1.9%)	
	ASR	-0.7	-1.2	-1.3	-0.3	2.0	
Neurological impairment	Physicians, n (%)	17 (1.4%)	34 (2.9%)	231 (19.4%)	593 (49.9%)	266 (22.4%)	0.533
	ASR	0.9	1.2	0.6	-0.3	-0.9	
	Nurses, n (%)	0 (0.0%)	0 (0.0%)	8 (0.7%)	26 (2.2%)	14 (1.2%)	
	ASR	-0.9	-1.2	-0.6	0.3	0.9	
Haemorrhagic transformation	Physicians, n (%)	47 (4.0%)	106 (8.9%)	370 (31.1%)	436 (36.7%)	182 (15.3%)	0.003
	ASR	1.4	2.2	1.7	-1.4	-2.8	
	Nurses, n (%)	0 (0.0%)	0 (0.0%)	10 (0.8%)	23 (1.9%)	15 (1.3%)	
	ASR	-1.4	-2.2	-1.7	1.4	2.8	
Cognitive dysfunction or dementia	Physicians, n (%)	16 (1.3%)	60 (5.0%)	323 (27.2%)	512 (43.1%)	230 (19.3%)	0.003
	ASR	0.8	1.6	2.7	-1.0	-2.9	
	Nurses, n (%)	0 (0.0%)	0 (0.0%)	5 (0.4%)	25 (2.1%)	18 (1.5%)	
	ASR	-0.8	-1.6	-2.7	1.0	2.9	
Quality of life	Physicians, n (%)	11 (0.9%)	28 (2.4%)	213 (17.9%)	495 (41.6%)	394 (33.1%)	0.098
	ASR	0.7	1.1	0.0	1.9	-2.5	
	Nurses, n (%)	0 (0.0%)	0 (0.0%)	9 (0.8%)	14 (1.2%)	25 (2.1%)	
	ASR	-0.7	-1.1	0.0	-1.9	2.5	

	Clinical practice (years%)					Not important at all					P-values					
	≤10, n (%)	ASR	>10, n (%)	ASR	≤10, n (%)	ASR	>10, n (%)	ASR	≤10, n (%)	ASR	>10, n (%)	ASR	≤10, n (%)	ASR	>10, n (%)	ASR
Death	18 (1.5%)	0.2	19 (1.6%)	-0.2	40 (3.4%)	-0.7	52 (4.4%)	0.7	143 (12.0%)	-0.9	161 (13.5%)	-0.2	174 (14.6%)	-1.4	198 (16.7%)	1.4
Disability	7 (0.6%)	-0.2	7 (0.6%)	-0.2	12 (1.0%)	0.7	12 (1.0%)	0.9	112 (9.4%)	0.3	255 (21.4%)	0.2	174 (14.6%)	-1.4	199 (16.7%)	-1.0
Neurological impairment	7 (0.6%)	-0.8	7 (0.6%)	-0.8	12 (1.0%)	1.7	12 (1.0%)	-0.3	113 (9.4%)	-0.3	302 (21.4%)	-1.1	126 (14.6%)	1.0	126 (14.6%)	0.8
Haemorrhagic transformation	18 (1.5%)	-1.2	18 (1.5%)	-1.2	49 (3.4%)	-0.2	29 (2.4%)	-0.2	159 (12.0%)	-2.5	231 (13.5%)	1.8	103 (16.7%)	1.6	94 (7.9%)	-1.6
Cognitive dysfunction or dementia	7 (0.6%)	0.3	7 (0.6%)	0.3	24 (1.0%)	-1.1	9 (0.8%)	-1.1	143 (9.4%)	-1.5	265 (21.4%)	1.4	121 (14.6%)	0.6	127 (10.7%)	-0.6
Quality of life	6 (0.5%)	0.5	6 (0.5%)	0.5	10 (0.8%)	-1.2	5 (0.4%)	-1.2	103 (8.7%)	-0.2	247 (20.8%)	0.9	194 (16.3%)	-0.4	225 (18.9%)	0.4

	Research practice (years%)						P-values
	Not important at all	Not important	Neutral	Important	Very important		
Death	≤5, n (%)	20 (1.7%)	56 (4.7%)	165 (13.9%)	200 (16.8%)	235 (19.8%)	0.289
	ASR	-0.3	0.8	-2.1	0.5	1.2	
	>5, n (%)	17 (1.4%)	36 (3.0%)	153 (12.9%)	145 (12.2%)	162 (13.6%)	
	ASR	0.3	-0.8	2.1	-0.5	-1.2	
Disability	≤5, n (%)	5 (0.4%)	20 (1.7%)	120 (10.1%)	317 (26.7%)	214 (18.0%)	0.106
	ASR	-1.1	-0.2	-1.8	2.5	-0.8	
	>5, n (%)	7 (0.6%)	16 (1.3%)	113 (9.5%)	204 (17.2%)	173 (14.6%)	
	ASR	1.1	0.2	1.8	-2.5	0.8	
Neurological impairment	≤5, n (%)	6 (0.5%)	20 (1.7%)	128 (10.8%)	363 (30.5%)	159 (13.4%)	0.273
	ASR	-1.8	0.2	-1.2	1.3	0.0	
	>5, n (%)	11 (0.9%)	14 (1.2%)	111 (9.3%)	256 (21.5%)	121 (10.2%)	
	ASR	1.8	-0.2	1.2	-1.3	0.0	
Haemorrhagic transformation	≤5, n (%)	22 (1.9%)	64 (5.4%)	189 (15.9%)	279 (23.5%)	122 (10.3%)	0.004
	ASR	-1.4	0.8	-3.4	2.2	1.6	
	>5, n (%)	25 (2.1%)	42 (3.5%)	191 (16.1%)	180 (15.1%)	75 (6.3%)	
	ASR	1.4	-0.8	3.4	-2.2	-1.6	
Cognitive dysfunction or dementia	≤5, n (%)	5 (0.4%)	35 (2.9%)	177 (14.9%)	312 (26.2%)	147 (12.4%)	0.173
	ASR	-2.1	0.2	-1.2	0.8	0.9	
	>5, n (%)	11 (0.9%)	25 (2.1%)	151 (12.7%)	225 (18.9%)	101 (8.5%)	
	ASR	2.1	-0.2	1.2	-0.8	-0.9	
Quality of life	≤ 5, n (%)	4 (0.3%)	19 (1.6%)	120 (10.1%)	292 (24.6%)	241 (20.3%)	0.392
	ASR	-1.4	1.2	-0.9	0.3	0.3	
	>5, n (%)	7 (0.6%)	9 (0.8%)	102 (8.6%)	217 (18.3%)	178 (15.0%)	
	ASR	1.4	-1.2	0.9	-0.3	-0.3	

	Teaching hospital		Not important at all			Neutral	Important	Very important	P-values
	Yes, n (%)	Not important at all	Not important	Neutral	Important	Very important	P-values		
Death	Yes, n (%)	28 (2.4%)	65 (5.5%)	244 (20.5%)	269 (22.6%)	308 (25.9%)	0.666		
	ASR	-0.2	-1.5	-0.1	0.6	0.4			
	No, n (%)	9 (0.8%)	27 (2.3%)	74 (6.2%)	76 (6.4%)	89 (7.5%)			
	ASR	0.2	1.5	0.1	-0.6	-0.4			
Disability	Yes, n (%)	8 (0.7%)	26 (2.2%)	177 (14.9%)	401 (33.7%)	302 (25.4%)	0.818		
	ASR	-0.8	-0.7	-0.4	0.1	0.7			
	No, n (%)	4 (0.3%)	10 (0.8%)	56 (4.7%)	120 (10.1%)	85 (7.1%)			
	ASR	0.8	0.7	0.4	-0.1	-0.7			
Neurological impairment	Yes, n (%)	13 (1.1%)	27 (2.30%)	181 (15.20%)	481 (40.50%)	212 (17.80%)	0.945		
	ASR	0.0	0.4	-0.5	0.7	-0.5			
	No, n (%)	4 (0.3%)	7 (0.6%)	58 (4.9%)	138 (11.6%)	68 (5.7%)			
	ASR	0.0	-0.4	0.5	-0.7	0.5			
Haemorrhagic transformation	Yes, n (%)	39 (3.3%)	77 (6.50%)	298 (25.10%)	356 (29.90%)	144 (12.10%)	0.371		
	ASR	1.0	-1.1	0.9	0.4	-1.4			
	No, n (%)	8 (0.7%)	29 (2.4%)	82 (6.9%)	103 (6.7%)	53 (7.5%)			
	ASR	-1.0	1.1	-0.9	-0.4	1.4			
Cognitive dysfunction or dementia	Yes, n (%)	12 (1.0%)	39 (3.3%)	254 (21.4%)	422 (35.5%)	187 (15.7%)	0.197		
	ASR	-0.2	-2.2	0.3	1.3	-0.6			
	No, n (%)	4 (0.3%)	21 (1.8%)	74 (6.2%)	115 (9.7%)	61 (5.1%)			
	ASR	0.2	2.2	-0.3	-1.3	0.6			
Quality of life	Yes, n (%)	8 (0.7%)	22 (1.9%)	163 (13.7%)	406 (34.1%)	315 (26.5%)	0.319		
	ASR	-0.3	0.2	-1.4	2.0	-1.0			
	No, n (%)	3 (0.3%)	6 (0.5%)	59 (5.0%)	103 (8.7%)	104 (8.7%)			
	ASR	0.3	-0.2	1.4	-2.0	1.0			

	Tertiary hospital		Not important at all		Neutral	Important	Very important	P-values
	Yes, n (%)	32 (2.7%)	67 (5.6%)	251 (21.1%)	276 (23.2%)	320 (26.9%)	0.400	
Death	ASR	1.1	-1.7	-0.3	0.2	0.6		
	No, n (%)	5 (0.4%)	25 (2.1%)	67 (5.6%)	69 (5.8%)	77 (6.5%)		
	ASR	-1.1	1.7	0.3	-0.2	-0.6		
Disability	Yes, n (%)	9 (0.8%)	27 (2.3%)	189 (15.9%)	415 (34.9%)	306 (25.7%)	0.907	
	ASR	-0.4	-0.7	0.7	0.1	-0.3		
	No, n (%)	3 (0.3%)	9 (0.8%)	44 (3.7%)	106 (8.9%)	81 (6.8%)		
Neurological impairment	ASR	0.4	0.7	-0.7	-0.1	0.3		
	Yes, n (%)	15 (1.3%)	27 (2.3%)	191 (16.1%)	500 (42.1%)	213 (17.9%)	0.483	
	ASR	0.9	0.0	0.2	1.1	-1.7		
Haemorrhagic transformation	No, n (%)	2 (0.2%)	7 (0.6%)	48 (4.0%)	119 (10.0%)	67 (5.6%)		
	ASR	-0.9	0.0	-0.2	-1.1	1.7		
	Yes, n (%)	41 (3.4%)	75 (6.3%)	313 (26.3%)	374 (31.5%)	143 (12.0%)	0.004	
Cognitive dysfunction or dementia	ASR	1.3	-2.4	1.6	1.3	-2.7		
	No, n (%)	6 (0.5%)	31 (2.6%)	67 (5.6%)	85 (7.1%)	54 (4.5%)		
	ASR	-1.3	2.4	-1.6	-1.3	2.7		
Quality of life	Yes, n (%)	14 (1.2%)	44 (3.7%)	262 (22.0%)	438 (36.8%)	188 (15.8%)	0.236	
	ASR	0.8	-1.2	0.2	1.6	-1.6		
	No, n (%)	2 (0.2%)	16 (1.3%)	66 (5.6%)	99 (8.3%)	60 (5.0%)		
Quality of life	ASR	-0.8	1.2	-0.2	-1.6	1.6		
	Yes, n (%)	9 (0.8%)	22 (1.9%)	179 (15.1%)	413 (34.7%)	323 (27.2%)	0.063	
	ASR	0.2	-0.1	0.4	1.2	-1.6		
Quality of life	No, n (%)	2 (0.2%)	6 (0.5%)	43 (3.6%)	96 (8.1%)	96 (8.1%)		
	ASR	-0.2	0.1	-0.4	-1.2	1.6		

Supplementary Table 4: Ordinal multi-categorical regression analysis (n=1189)

The established acute stroke therapies with a potential bleeding risk												
	Death		Disability		Neurological impairment		Haemorrhagic transformation		Cognitive dysfunction or dementia		Quality of life	
	OR (95%CI)	P-values	OR (95%CI)	P-values	OR (95%CI)	P-values	OR (95%CI)	P-values	OR (95%CI)	P-values	OR (95%CI)	P-values
Age												
≤ 40 years	1.20 (0.82 - 1.77)	0.349	0.82 (0.58 - 1.15)	0.255	0.95 (0.68 - 1.33)	0.77	0.97 (0.71 - 1.34)	0.863	0.80 (0.58 - 1.10)	0.168	0.93 (0.66 - 1.30)	0.666
>40 years	Reference											
Sex												
Male	1.08 (0.83 - 1.41)	0.579	0.75 (0.59 - 0.95)	0.017	0.81 (0.65 - 1.02)	0.077	1.09 (0.88 - 1.36)	0.441	0.64 (0.51 - 0.80)	<0.001	0.64 (0.51 - 0.81)	<0.001
Female	Reference											
Academic degree												
Bachelor or below	0.92 (0.68 - 1.24)	0.563	0.82 (0.63 - 1.07)	0.136	0.95 (0.73 - 1.23)	0.677	0.98 (0.77 - 1.26)	0.898	1.02 (0.79 - 1.31)	0.881	0.87 (0.67 - 1.13)	0.297
Master or above	Reference											
Occupation												
Physicians	1.55 (0.80 - 2.99)	0.196	0.56 (0.28 - 1.11)	0.098	1.20 (0.66 - 2.18)	0.561	0.34 (0.18 - 0.64)	0.001	0.47 (0.25 - 0.86)	0.014	0.57 (0.29 - 1.13)	0.109
Nurses	Reference											
Clinical practice												
≤ 10 years	1.00 (0.66 - 1.51)	0.982	1.11 (0.77 - 1.59)	0.574	0.97 (0.68 - 1.37)	0.844	1.39 (0.99 - 1.96)	0.056	1.42 (1.01 - 2.01)	0.045	1.05 (0.73 - 1.50)	0.806
> 10 years	Reference											
Research practice												
≤ 5 years	1.18 (0.85 - 1.64)	0.322	1.17 (0.87 - 1.57)	0.289	1.16 (0.87 - 1.55)	0.307	1.35 (1.02 - 1.78)	0.033	1.00 (0.76 - 1.33)	0.985	1.13 (0.85 - 1.52)	0.404
> 5 years	Reference											
Teaching hospital												
Yes	1.40 (1.01 - 1.94)	0.047	1.31 (0.97 - 1.76)	0.079	1.24 (0.92 - 1.66)	0.155	1.09 (0.82 - 1.45)	0.537	1.09 (0.82 - 1.45)	0.568	1.00 (0.75 - 1.35)	0.977
No	Reference											

Tertiary hospital		Reference		Disability		Neurological impairment		Haemorrhagic transformation		Cognitive dysfunction or dementia		Quality of life	
	OR (95% CI)	P-values	OR (95% CI)	P-values	OR (95% CI)	P-values	OR (95% CI)	P-values	OR (95% CI)	P-values	OR (95% CI)	P-values	
Yes	0.90 (0.66 - 1.23)	0.496	0.87 (0.66 - 1.15)	0.317	1.09 (0.83 - 1.44)	0.529	1.09 (0.84 - 1.41)	0.535	0.99 (0.76 - 1.30)	0.96	0.81 (0.61 - 1.07)	0.136	
No													
The other type of therapies that are commonly used in practice and without a potential bleeding risk													
Death		Disability		Neurological impairment		Haemorrhagic transformation		Cognitive dysfunction or dementia		Quality of life			
	OR (95% CI)	P-values	OR (95% CI)	P-values	OR (95% CI)	P-values	OR (95% CI)	P-values	OR (95% CI)	P-values			
Age													
≤ 40 years	1.33 (0.97 - 1.82)	0.074	1.07 (0.78 - 1.47)	0.682	0.99 (0.71 - 1.37)	0.928	1.01 (0.74 - 1.39)	0.944	0.87 (0.63 - 1.19)	0.374	1.05 (0.76 - 1.45)	0.763	
> 40 years													
Sex													
Male	0.81 (0.65 - 1.00)	0.048	0.66 (0.53 - 0.83)	<0.001	0.70 (0.56 - 0.88)	0.002	0.91 (0.73 - 1.13)	0.385	0.68 (0.54 - 0.85)	0.001	0.64 (0.51 - 0.80)	<0.001	
Female													
Academic degree													
Bachelor or below	1.05 (0.82 - 1.34)	0.713	1.05 (0.82 - 1.35)	0.711	1.11 (0.86 - 1.43)	0.422	1.04 (0.81 - 1.33)	0.756	1.05 (0.82 - 1.35)	0.695	1.02 (0.79 - 1.31)	0.898	
Master or above													
Occupation													
Physicians	0.80 (0.45 - 1.43)	0.456	0.61 (0.34 - 1.11)	0.108	0.83 (0.46 - 1.50)	0.529	0.41 (0.23 - 0.73)	0.003	0.47 (0.26 - 0.84)	0.011	0.68 (0.38 - 1.23)	0.204	
Nurses													
Clinical practice													
≤ 10 years	0.92 (0.66 - 1.28)	0.613	0.79 (0.56 - 1.11)	0.168	0.96 (0.67 - 1.35)	0.794	1.24 (0.89 - 1.73)	0.212	1.20 (0.85 - 1.68)	0.307	0.86 (0.61 - 1.22)	0.396	
> 10 years													
Research practice													
≤ 5 years	1.05 (0.80 - 1.37)	0.733	1.17 (0.89 - 1.54)	0.274	1.11 (0.84 - 1.47)	0.466	1.12 (0.85 - 1.47)	0.427	1.08 (0.82 - 1.42)	0.606	1.11 (0.84 - 1.46)	0.471	
> 5 years													
Teaching hospital													
Yes	1.07 (0.81 - 1.41)	0.644	1.15 (0.86 - 1.52)	0.347	1.06 (0.79 - 1.41)	0.711	0.95 (0.72 - 1.25)	0.693	1.05 (0.79 - 1.39)	0.76	0.96 (0.73 - 1.28)	0.8	
No													
Tertiary hospital													
Yes	0.93 (0.72 - 1.20)	0.574	0.99 (0.76 - 1.30)	0.964	1.07 (0.82 - 1.41)	0.604	1.12 (0.87 - 1.46)	0.383	0.94 (0.72 - 1.22)	0.618	0.95 (0.73 - 1.24)	0.705	
No													