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Significant variation in mortality and functional outcome after acute ischaemic stroke between western countries: data from the 'Tinzaparin in Acute Ischaemic Stroke Trial' (TAIST)

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ABSTRACT

Background The medical care of patients with acute stroke varies considerably between countries which could lead to measurable differences in mortality and functional outcome.
Methods All 1,484 patients from 11 countries who were enrolled into the 'Tinzaparin in Acute Ischaemic Stroke Trial' (TAIST) were included in this sub-study. Prospectively collected information on demographics, risk factors, clinical features, measures of service quality (e.g. admission to stroke unit), and outcome were assessed. Outcomes were adjusted for treatment assignment, case mix and service relative to the British Isles.
Results Differences in case mix (mostly minor in magnitude) and clinical service (many of prognostic relevance) were present between the countries. Significant differences in outcome were present between the countries. When assessed by geographical region, death or dependency were lower in North America (odds ratio adjusted for treatment group only, OR 0.52, 95% confidence intervals, 95% CI 0.39-0.71) and North West Europe (OR 0.54, 95% CI 0.37-0.78) relative to the British Isles; similar reductions were seen when adjustments were made for 11 case mix variables and 5 service quality measures. Similarly, case fatality rates were lower in North America (OR 0.44, 95% CI 0.30-0.66) and Scandinavia (OR 0.50, 95% CI 0.33-0.74) relative to the British Isles whether crude or adjusted for case mix and service quality.
Conclusions Both functional outcome and case fatality vary considerably between countries, even when adjusted for prognostic case mix variables and measures of good stroke care. Differing health care systems, and the management of patients with acute stroke, may contribute to these findings.

INTRODUCTION

Outcome and the incidence of stroke vary between different countries,[1-3] variations in case mix, including demographics (age, gender) and the prevalence of vascular risk factors explain some of these differences.[4-6] Disparities in outcome may also result from variations in medical practice, e.g. the use of stroke units which are known to reduce death and disability,[7] and the treatment of acute stroke.[8] Finally, different processes of care may also be important, e.g. hospitalisation rates for stroke differ across various countries.[9]

Within the western world it might be expected that functional outcome, corrected for case mix and service provision, would be similar. However, evidence suggests that this may not be the case. In a study comparing outcome in 12 centres (22 hospitals) in 7 European countries, outcome varied twofold when adjusted for case mix and use of health service resources.[8] Analysis of functional outcome in the 'International Stroke Trial' revealed similar findings.[10] In both studies, outcome was worst in the UK.[8, 10] In contrast, functional outcome was not significantly different between countries when corrected for case mix and health care resource use in the GAIN trial, despite significant variations in unadjusted case fatality.[11]

We compared case mix, clinical management and functional outcome between eleven countries to further assess this question using data from the 'Tinzaparin in Acute Ischaemic Stroke Trial' (TAIST).[12]

METHODS

TAIST
The 'Tinzaparin in Acute Ischaemic Stroke Trial' (TAIST) compared the safety and efficacy of tinzaparin (low molecular weight heparin) given at high dose (175 anti-Xa IU/kg/day), tinzaparin at medium dose (100 anti-Xa IU/kg/day), and aspirin (300 mg od) in patients with acute ischaemic stroke.[12] The principal investigators from the 100 centres participating in TAIST were experienced in taking part in acute stroke trials. All information was collected prospectively as part of the trial protocol.

Case mix/prognostic factors
Case mix variables included demographic - age, gender, race; vascular risk factors - smoking, history of hypertension, diabetes mellitus, stroke, myocardial infarction; pre-morbid dependency (mRS); stroke syndrome; severity – Scandinavian Neurological Stroke Scale (SNSS); systolic blood pressure; investigations - atrial fibrillation on ECG, visible infarct on CT; time to randomisation; and pre-stroke prevention - aspirin, anticoagulation, anti-hypertensive therapy, lipid-lowering therapy.

Clinical management
The use of evidence-based interventions in hospital was recorded: admission to an Acute Stroke Unit (ASU) and/or Stroke Rehabilitation Unit (SRU), application of venous compression stockings, treatment by a physiotherapist and/or speech and language therapist, and secondary prevention (aspirin, anticoagulation, anti-hypertensive therapy, lipid-lowering therapy).

Outcomes
Outcome was determined as combined death or dependency - modified Rankin Scale (mRS) greater than two, measured at day 180 and recorded by face-to-face interview, length of stay in hospital, and discharge disposition.

Country and geographical region
Outcome was assessed by the 11 participating countries and aggregates of these defined by geographical region and similarity of health care system: British Isles (Ireland, UK), Franco (Belgium, France); North America (Canada), North-West Europe (Germany, Netherlands), and Scandinavia (Denmark, Finland, Norway, Sweden).

Definitions
TAIST used the following definitions for stroke units: an Acute Stroke Unit (ASU) - 'high-dependency nursing unit (or area) caring only/mainly for patients with acute stroke and providing close monitoring of neurological and vascular signs';[12] Stroke Rehabilitation Unit (SRU) - 'dedicated rehabilitation unit (or area) caring only/mainly for patients with recent stroke and providing multi-disciplinary therapy (e.g. physiotherapy, occupational therapy, speech & language therapy)'.[12]

Statistical analysis
Prognostic case mix factors, clinical management factors, and outcomes were compared by country and geographical region, using chi square tests in the case of categorical data and Kruskal-Wallis tests for continuous data. Models utilising logistic regression and Cox proportional hazard approaches were developed using variables known to be of prognostic significance.[13] The likelihood test was used for assessing homogeneity. All analyses were performed using SAS (SAS Inst., USA). Significance was taken at $p<0.05$ and 95% confidence intervals are given.

RESULTS

Subjects

1,499 patients were randomised, however emerging exclusion criteria prevented treatment in 15 patients. Analyses were performed on the 1,484 patients with acute ischaemic stroke who received at least one randomised treatment with tinzaparin or aspirin.[12] The number of patients enrolled by country varied between 27 (Finland) and 388 (Canada, table 1). Significant statistical differences in the demographic and clinical characteristics of enrolled patients (except gender and the incidence of previous stroke) existed between the countries (table 1), including: pre-morbid independence (mRS=0, Denmark 57.3%, France 88.5%), previous hypertension (Norway 32.9%, Belgium 67.5%), atrial fibrillation (Finland 0.0%, Ireland 26.2%), and total anterior circulation infarct (Germany 2.8%, Finland 63.0%). Similarly, the prevalence of pre-stroke vascular prophylaxis varied between countries (table 2), e.g. lipid lowering therapy (Finland 0.0%, Belgium 22.5%%).

TABLE 1

Baseline demographics, risk factors and clinical measures by country. Mean (SD) or frequency (%); comparison by Chi Square test or Kruskal-Wallis test.

Country	Belgium	Canada	Denmark	Finland	France	Germany	Ireland	Netherlands	Norway	Sweden	UK	Total	p
Subjects	40	388	110	27	191	36	61	143	82	123	283	1484	
Centres	4	27	6	4	18	4	4	6	5	7	15	100	
Age (yr)	72.8 (8.8)	70.8 (11.2)	72.4 (11.7)	69.6 (10.6)	70.1 (12.4)	70.7 (10.3)	70.3 (12.1)	71.8 (10.8)	75.3 (7.9)	74.8 (8.1)	71.1 (11.0)	71.6 (11.0)	0.0012
Gender (male, %)	22 (55.0)	218 (56.2)	58 52.7)	16 (59.3)	113 (59.2)	19 (52.8)	33 (54.1)	67 (46.9)	48 (58.5)	68 (55.3)	145 (51.2)	807 (54.4)	0.66
Race, white (%)	40 (100)	356 (91.8)	110 (100)	27 (100)	186 (97.4)	36 (100)	61 (100)	139 (97.2)	82 (100)	123 (100)	269 (95.1)	1429 (96.3)	0.0002
Current smoking (%)	11 (27.5)	116 (29.9)	50 (45.5)	4 (14.8)	27 (14.1)	6 (16.7)	18 (29.5)	35 (24.5)	20 (24.4)	20 (16.3)	75 (26.5)	382 (25.7)	<0.001
Previous HT (%)	27 (67.5)	225 (58.0)	38 (34.5)	14 (51.9)	100 (52.4)	22 (61.1)	33 (54.1)	68 (47.6)	27 (32.9)	54 (43.9)	119 (42.0)	727 (49.0)	<0.001
Previous DM (%)	7 (17.5)	97 (25.0)	17 (15.5)	6 (22.2)	35 (18.3)	5 (13.9)	6 (9.8)	20 (14.0)	7 (8.5)	18 (14.6)	32 (11.3)	250 (16.8)	0.0002
Previous MI (%)	5 (12.5)	90 (23.2)	12 (10.9)	6 (22.2)	12 (6.3)	2 (5.6)	8 (13.1)	15 (10.5)	14 (17.1)	22 (17.9)	46 (16.3)	232 (15.6)	<0.001
Previous stroke (%)	5 (12.5)	58 (15.9)	11 (10.0)	2 (7.4)	10 (5.2)	5 (13.9)	7 (11.5)	18 (12.6)	12 (14.6)	17 (13.8)	48 (17.0)	193 (13.0)	0.06
Premorbid mRS (=0, %)	24 (60.0)	295 (76.0)	63 (57.3)	22 (81.5)	169 (88.5)	26 (72.2)	39 (63.9)	104 (72.7)	55 (67.1)	76 (61.8)	179 (63.3)	1052 (70.9)	<0.001
OCSP type (TACI, %)	25 (62.5)	97 (25.0)	21 (19.1)	17 (63.0)	65 (34.0)	1 (2.8)	34 (55.7)	66 (46.2)	25 (30.5)	52 (42.3)	119 (42.0)	522 (35.2)	<0.001
SSS	30.3	34.8	36	31.9	29.4	36.1	28.6	30.4	35.5	32.5	30.0	32.3	<0.0

	(12.8)	(12.4)	(11.8)	(13.1)	(13.7)	(11.6)	(11.8)	(12.3)	(10.0)	(13.1)	(13.1)	(12.8)	001
SBP (mmHg)	152.2 (19.6)	153.8 (21.9)	162.8 (24.2)	154.7 (18.6)	157.0 (23.5)	159.2 (19.0)	155.2 (20.0)	157.8 (23.7)	157.2 (19.9)	163.3 (21.0)	153.0 (23.0)	156.2 (22.4)	0.000 1
AF on ECG (%)	1 (2.5)	26 (6.7)	10 (9.1)	0 (0)	18 (9.4)	3 (8.3)	16 (26.2)	16 (11.2)	8 (9.8)	31 (25.2)	52 (18.4)	181 (12.2)	<0.0 001
Infarct on CT (%)	14 (35.0)	230 (59.3)	76 (69.1)	21 (77.8)	91 (47.6)	26 (72.2)	38 (62.3)	78 (54.5)	41 (50.0)	81 (65.9)	201 (71.0)	897 (60.4)	<0.0 001
Time to randomisation (hr)	24.2 (13.0)	25.8 (13.1)	28.6 (12.9)	28.9 (13.4)	21.7 (12.9)	16.1 (9.8)	31.1 (11.4)	22.3 (11.9)	28.7 (11.9)	24.4 (11.7)	30.6 (13.6)	26.1 (13.2)	<0.0 001

AF: atrial fibrillation; DM: diabetes mellitus; HT: hypertension; MI: myocardial infarction; OCSP: Oxford Community Stroke Project; SBP: systolic blood pressure; SSS: Scandinavian Stroke Scale (range 0-58)

Clinical practice

In-hospital care varied considerably between countries, including (table 2): admission to a SRU (Finland 0.0%, Netherlands 67.1%), use of venous compression stockings (Sweden 13.0%, Netherlands 94.4%), and management by a speech and language therapist (Sweden 13.8%, Ireland 62.3%). Similarly, secondary prevention rates differed significantly between countries (table 2): anticoagulation in patients with presumed cardio-embolic stroke (Netherlands 3.6%, Finland 100.0%), and anti-platelet treatment in non-cardioembolic stroke (Belgium 57.1%, Norway 84.9%).

TABLE 2

Clinical management prior to, during and after acute ischaemic stroke by country. Number (%); comparison by Chi-square test or Kruskal-Wallis test.

Country	Belgium	Canada	Denmark	Finland	France	Germany	Ireland	Netherlands	Norway	Sweden	UK	Total	p
Subjects	40	388	110	27	191	36	61	143	82	123	283	1484	
Pre-stroke													
Antiplatelet (%)	2 (5.0)	1 (0.3)	0 (0)	2 (7.4)	1 (0.5)	2 (5.6)	0 (0)	8 (5.6)	0 (0)	5 (4.1)	3 (1.1)	24 (1.6)	<0.0001
Anticoagulation (%)	0 (0)	1 (0.3)	2 (1.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.8)	0 (0)	4 (0.3)	0.28
Antithrombotic (%)	2 (5.0)	2 (0.5)	2 (1.8)	2 (7.4)	1 (0.5)	2 (5.6)	0 (0)	8 (5.6)	0 (0)	6 (4.9)	3 (1.1)	28 (1.9)	0.0001
Anti hypertensive (%)	28 (70)	186 (47.9)	45 (40.9)	12 (44.4)	97 (50.8)	17 (47.2)	31 (50.8)	70 (48.9)	35 (42.7)	63 (51.2)	98 (34.6)	682 (46.0)	0.0008
Lipid lowering (%)	9 (22.5)	32 (8.3)	1 (0.9)	0 (0)	20 (10.5)	1 (2.8)	2 (3.3)	18 (12.6)	2 (2.4)	8 (6.5)	7 (2.5)	100 (6.7)	<0.0001
In-hospital													
Acute Stroke Unit (%)	5 (12.5)	60 (15.5)	42 (38.2)	4 (14.8)	45 (23.6)	13 (36.1)	1 (1.6)	68 (47.8)	53 (64.6)	56 (45.5)	225 (79.5)	572 (38.5)	<0.0001
Stroke Rehabilitation Unit (%)	16 (40.0)	84 (21.6)	63 (57.3)	0 (0)	1 (0.5)	24 (66.7)	3 (4.9)	96 (67.1)	32 (39.0)	55 (44.7)	80 (28.3)	454 (30.6)	<0.0001
Stroke Unit (%)	17 (42.5)	141 (36.3)	90 (81.8)	4 (14.8)	45 (23.6)	29 (80.6)	4 (6.6)	113 (79.0)	82 (100)	96 (78.0)	234 (82.7)	855 (57.6)	<0.0001
Compression stockings (%)	35 (87.5)	149 (38.4)	15 (13.6)	6 (22.2)	118 (61.8)	29 (80.6)	41 (67.2)	135 (94.4)	13 (15.9)	16 (13.0)	246 (86.9)	803 (54.1)	<0.0001
Physiotherapy (%)	34 (85.0)	326 (84.0)	98 (89.1)	23 (85.2)	168 (88.0)	34 (94.4)	52 (85.2)	127 (88.8)	78 (95.1)	102 (82.9)	249 (88.0)	1291 (87.0)	0.0009
Speech therapy (%)	17 (42.5)	171 (44.1)	28 (25.5)	9 (33.3)	32 (16.8)	19 (52.8)	38 (62.3)	50 (35.0)	18 (22.0)	17 (13.8)	138 (48.8)	537 (36.2)	<0.0001

Post-stroke													
Antiplatelet* (%)	16 (57.1)	207 (64.7)	70 (76.1)	19 (76.0)	91 (64.5)	20 (80.0)	22 (73.3)	89 (78.8)	56 (84.9)	67 (84.8)	141 (77.5)	798 (72.5)	0.0001
Anti coagulation† (%)	3 (25.0)	23 (35.4)	3 (20.0)	2 (100.0)	4 (8.2)	2 (18.2)	9 (29.0)	1 (3.6)	7 (53.9)	7 (15.9)	22 (22.5)	83 (22.6)	0.0002
Anti thrombotic (%)	19 (47.5)	230 (59.7)	73 (68.2)	21 (77.8)	95 (50.0)	22 (61.1)	31 (50.8)	90 (63.8)	63 (79.8)	74 (60.2)	163 (58.2)	881 (60.0)	0.0002
Anti hypertensive (%)	22 (55.0)	216 (55.7)	46 (41.8)	11 (40.7)	97 (50.8)	21 (58.3)	24 (39.3)	53 (37.1)	39 (47.6)	66 (53.7)	108 (38.2)	703 (47.4)	0.0001
Lipid lowering (%)	8 (20.0)	63 (16.2)	4 (2.8)	0 (0)	25 (13.1)	1 (2.8)	10 (16.4)	22 (15.4)	5 (6.1)	15 (12.2)	34 (12.0)	187 (12.6)	0.0028

*% anticoagulation = number on anticoagulant / number with presumed cardioembolic ischaemic stroke
†% antiplatelet = number on antiplatelet / number with presumed non-cardioembolic ischaemic stroke

Functional outcome
The eleven countries differed in each measure of outcome (table 3), including combined death and dependency at day 180 (mRS>2, Germany 44.4%, Ireland 67.2%), length of stay in hospital (Denmark/Finland 11 days, Ireland 39 days), and discharge to an institution.

The following case mix variables were associated with a poor outcome in univariate analyses: increasing age, female gender, pre-morbid disability (mRS 1,2), non-smoker, history of previous stroke, diabetes mellitus, high blood pressure, atrial fibrillation, increasing stroke severity (SSS), and visible infarction on the baseline CT scan (data not shown). Measures of clinical care were also associated with a poor outcome: non-admission to a SRU, care by a physiotherapist and/or speech therapist, and use of compression stockings. Functional outcome was not related to race, time to treatment, admission to an ASU, or treatment with tinzaparin versus aspirin (data not shown). When assessing the effect of treatment on functional outcome by country, comparisons of tinzaparin versus aspirin did not differ apart from for German patients where tinzaparin was inferior to aspirin.

The odds of being dead or dependent (mRS >2) at 6 months were significantly lower in Canada, Germany and the Netherlands as compared with the UK (figure 1). When analysed by geographical region, death or dependency was 50% lower in North America and North West Europe as compared with the British Isles ($p<0.0001$) (figure 2). The significant difference in outcome between North America and the British Isles remained following adjustment for case mix variables alone (model A), and case mix with indicators of clinical care (model B) (figure 2).

TABLE 3

Outcome measured as death, death or dependency (mRS>2), length of stay in hospital, and institutionalisation, by country. Number (%) or median (interquartile range); comparison by Chi-square test or Kruskal-Wallis test.

Country	Belgium	Canada	Denmark	Finland	France	Germany	Ireland	Netherlands	Norway	Sweden	UK	Total	p
Subjects	40	388	110	27	191	36	61	143	82	123	283	1484	
Dead													
Day 10	1 (2.5)	7 (1.8)	2 (1.8)	1 (3.7)	9 (4.7)	0 (0)	2 (3.3)	11 (7.7)	3 (3.7)	8 (6.5)	19 (6.7)	63 (4.2)	0.035
Day 180 (%)	6 (15.0)	38 (9.8)	12 (10.9)	1 (3.7)	32 (16.8)	0 (0)	13 (21.3)	31 (21.7)	8 (9.8)	16 (13.0)	58 (20.5)	215 (14.5)	0.0002
mRS>2													
Day 180 (%)	23 (57.5)	185 (47.7)	55 (50.0)	16 (59.3)	119 (62.3)	16 (44.4)	41 (67.2)	73 (51.0)	46 (56.1)	77 (62.6)	179 (63.3)	830 (55.9)	0.0040
Length of stay (days)	23 (14-47)	14 (8-27)	11 (8-25)	11 (9-17)	16 (12-22)	21 (15-39)	39 (16-78)	19 (12-35)	14 (10-20)	17 (10-35)	27 (10-79)	16 (10-34)	<0.0001
Institution (%)	18 (47.4)	212 (56.4)	62 (57.9)	21 (80.8)	125 (69.4)	23 (63.9)	30 (51.7)	66 (52.0)	55 (69.6)	60 (52.6)	97 (37.0)	769 (54.8)	<0.0001

mRS: modified Rankin Scale;

Death
The eleven countries differed in death rates by days 10 (end of treatment) and 180 (Germany 0.0%, Netherlands 21.7%). The following case mix variables were associated with an increased risk of death in univariate analyses: increasing age, pre-morbid disability, non-smoking, atrial fibrillation, prior stroke, diabetes mellitus, increasing stroke severity, and visible infarction on the CT scan. Measures of care were also associated with case fatality: use of compression stockings, lack of physiotherapy (all $p<0.05$, data not shown). Gender, race, blood pressure, admission to an ASU or SRU, speech therapy, and treatment with tinzaparin were not related to death. When assessing the effect of treatment on death by country no statistically significant effects were seen (data not shown).

The hazard of death at 6 months differed significantly by country ($p<0.0001$); in comparison with the UK, death rates were lower in Canada, Denmark, Germany and Norway (figure 1). When grouped by geographical region, death rates were 40-50% lower in North America and Scandinavia than in the British Isles ($p=0.0001$) (figures 3 and 4). The significant difference in case fatality remained after adjustment for case mix variables alone, and with service indicators ($p<0.0001$).

DISCUSSION

The important finding in this study is that functional outcome and death after stroke differed significantly between the eleven countries, and geographical aggregates of these countries. In univariate analyses, both functional outcome and case fatality varied by a factor of two, a magnitude which is more powerful than treatment effects associated with stroke units and thrombolysis.[7, 14] Differences between countries have been observed in previous studies for both functional outcome [8, 10] and case fatality [2, 8, 10, 11] after stroke.

Since case mix is well known to influence clinical outcome, variations in outcome will, at least in part, reflect differences in case mix.[15] Hence, studies comparing populations need to adjust for case mix [16, 17] although this is not without methodological problems and demands rigorous analysis.[15] In TAIST, differences in most baseline variables were present with some likely to be of significant clinical relevance, e.g. pre-morbid status, previous hypertension, atrial fibrillation and clinical stroke syndrome. Nevertheless, adjustment for up to 13 prognostic factors did not remove differences in outcome between the countries. Similar adjustment for case mix, but using fewer prognostic variables, did not remove outcome differences in other studies.[8, 10]

It is now realised that adjustment for prognostic clinical factors alone is insufficient; process of care (equating to quality of care) also needs to be included since these factors can have powerful effects on outcome.[18, 19] We included some such measures, including admission to a stroke unit, care by therapists and use of compression stockings. Again, adjustment for both case mix and these clinical process measures did not explain the differences in outcome seen in TAIST, a finding that was also seen in BIOMED and IST (although based on fewer variables).[8, 10]

Explaining the residual differences between the countries after adjustment for case mix and process of care is difficult. The TAIST investigators were, in general, experienced in managing stroke and taking part in acute stroke trials, and cared for patients within the context of a stroke service. Furthermore, all patients had a CT scan prior to enrolment. A number of potential explanations exist relating to chance, systematic bias and confounding, as for any observational study that does not include consecutively admitted patients.

First, the study was relatively large, and the differences profound and consistent both within (internal validity) and outwith (external validity) [2, 8, 10] the study so chance alone is unlikely. It maybe possible that the care received by patients in a clinical trial is different from routine stroke management. It is also possible that some centres may not be representative of their countries. However in analysing outcome by geographical regions with similar health services statistical power was increased thereby reducing the chance that unrepresentative centres may have affected the results.[11] We did not analyse outcome by centre since most recruited few patients thereby limiting the power of analyses.

Second, the interpretation of definitions for case mix variables, quality markers and outcome might vary between countries leading to systematic bias. Our data came from an industry sponsored trial with a detailed protocol, and it is unlikely that interpretations in the definitions of clinical variables would differ significantly. There is some evidence that the interpretation of functional status may vary between countries.[20-22] If relevant, a systematic bias in the recording of both pre-morbid

and post-stroke mRS would be present and their relationship would be very strong, which was not the case in TAIST. Even if a bias in functional outcome was present, the between-country differences in case fatality, which were of comparable magnitude to those seen for functional outcome, cannot be explained in this manner.

Third, unmeasured variation in case mix and/or processes of care may explain the observed differences.[23] IST, GAIN and BIOMED each reported limited numbers of case mix variables,[8, 10, 24] in contrast to our study which adjusted for pre-morbid function, co-morbid conditions, clinical process and brain imaging. However, the inclusion of these factors in the prognostic models was not helpful in explaining between-country differences in outcome. Whilst other case mix variables might explain some of the observed differences in outcome, it is unlikely that they would exert such a powerful effect individually.

Finally, the differences seen in this study may relate to the quality of hyperacute and acute care, i.e. management within 48 hours post stroke. Patients who are monitored for, and maintain, physiological homeostasis (e.g. blood pressure, temperature, glucose) following acute stroke have an improved outcome.[25, 26] Some acute stroke patients may also benefit from interventions such as thrombolysis or neurosurgery [27] although these treatments were not given in TAIST. Health care models focussing on the hyperacute phase exist variably within countries but are less common in the British Isles than in North America and much of Western Europe. For example, interventions to alter abnormal physiological parameters occur less frequently in the UK.[8] Nevertheless, this explanation for the differences in outcome seen in TAIST are largely hypothetical and randomised controlled trials examining the roles of intensive monitoring and physiological intervention are required.[28] Further evidence could also be obtained from observational studies on consecutively admitted patients with data on basic physiological interventions in the acute phase.

In summary, we have shown that outcome from stroke varies significantly between countries using prospective data from a large multicentre international acute stroke trial. Correction for case mix and markers of service provision did not explain these differences.

Completing interests: There are no completing interests for all authors in terms of the analysis presented here, but all authors, apart from LJG and NS, were involved in the original TAIST trial. PMWB, PS, GB, PDD, PF, DL, RM, JEO, DO, BR, JJVDS, AGGT were on the trial steering committee for TAIST and EL works for Leo Pharma A/S.

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is Stroke Association Professor of Stroke Medicine. This study was presented, in part, at the 10th European Stroke Conference, Lisbon 2001.[29]

FIGURE 1

Hazard ratio (HR) of death, and odds ratio (OR) of a poor functional outcome (dead or dependent, modified Rankin Score 3-6), with 95% confidence intervals, at 180 days by country, relative to UK (adjusted for treatment group, tinzaparin, aspirin)

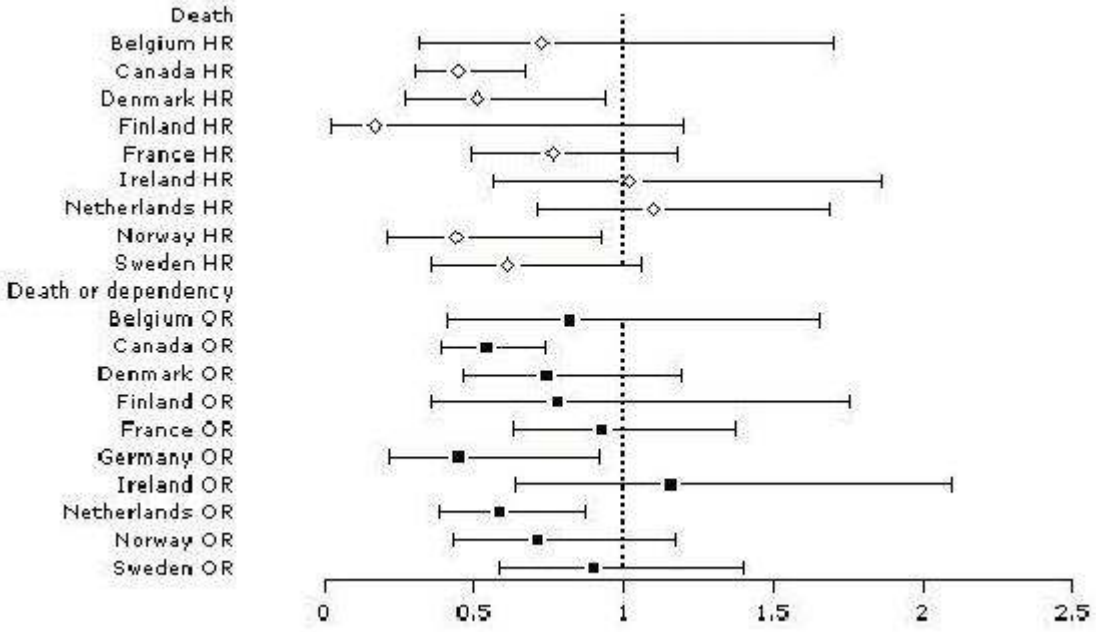


FIGURE 2

Odds ratio (95% confidence intervals) of a poor outcome (dead or dependent, modified Rankin Score 3-6) at day 180 by geographical region, relative to British Isles. Crude and adjusted rates given.

All models include adjustment for TAIST treatment group
Model A, case mix: age, gender, race, current smoking, diabetes mellitus, previous stroke, systolic blood pressure, atrial fibrillation, severity (SSS), infarct on baseline CT scan, prior modified Rankin Scale, time to treatment
Model B, case mix and clinical care: model A, plus care in an Acute Stroke Unit, care in a Stroke Rehabilitation Unit, physiotherapy, speech therapy, stockings

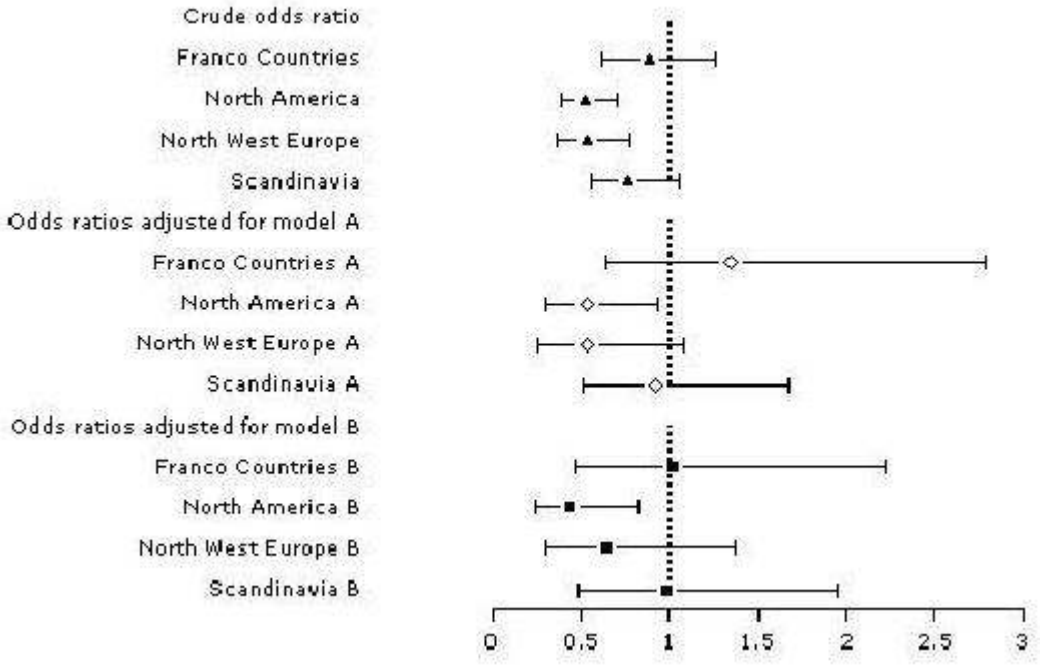


FIGURE 3

Hazard ratio (95% confidence intervals) of death at 6 months by geographical region, relative to British Isles. Crude and adjusted rates given.

All models include adjustment for TAIST treatment group
Model A, case mix: age, gender, race, current smoking, diabetes mellitus, previous stroke, systolic blood pressure, atrial fibrillation, severity (SSS), infarct on baseline CT scan, prior modified Rankin Scale, time to treatment
Model B, case mix and clinical care: model A, plus care in an Acute Stroke Unit, care in a Stroke Rehabilitation Unit, physiotherapy, speech therapy, stockings

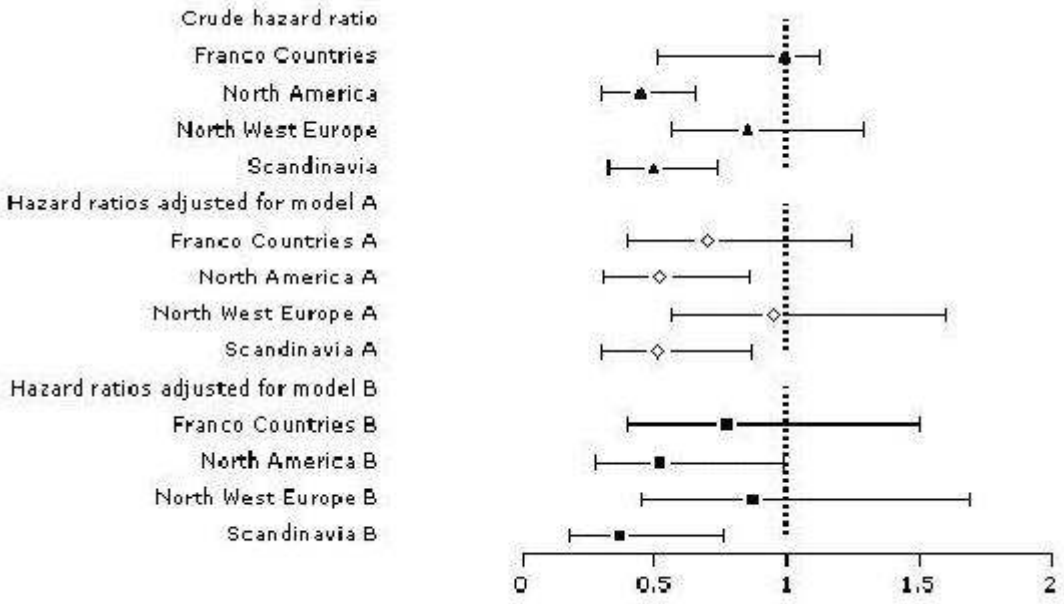
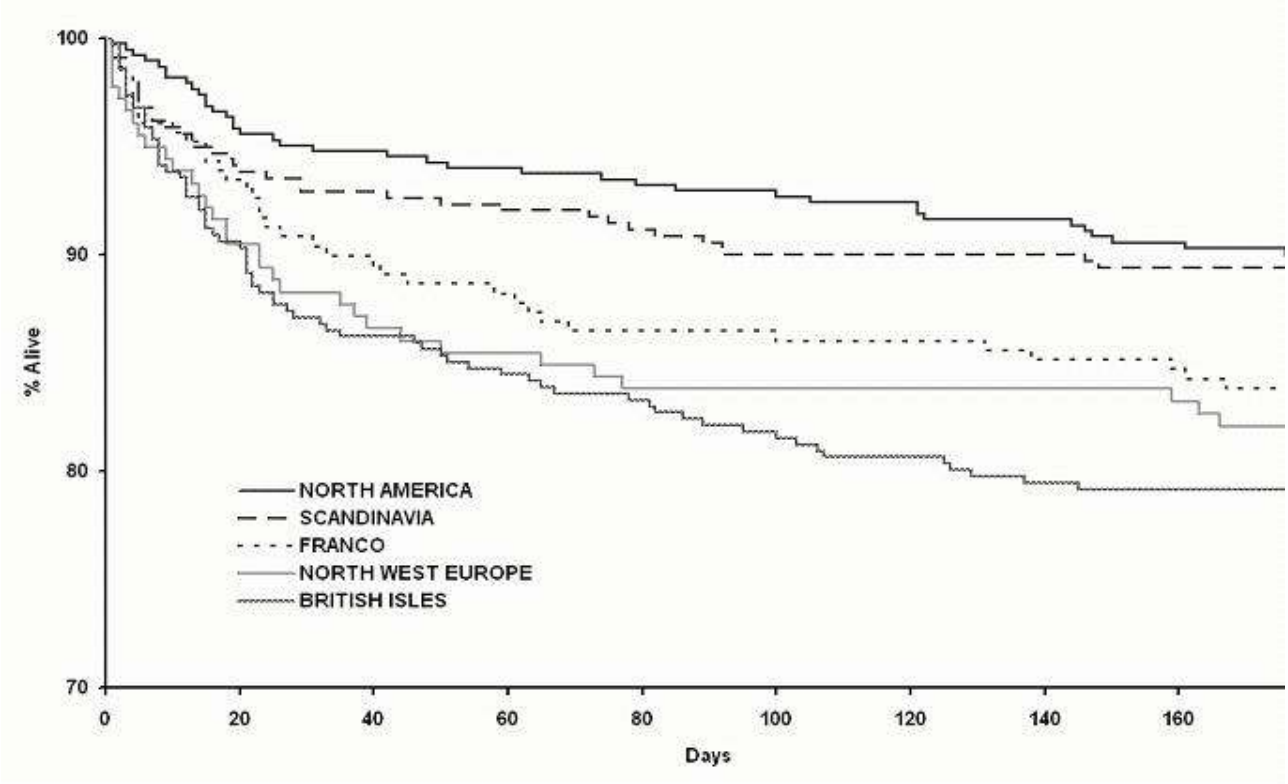


FIGURE 4

Kaplan-Meier survival plot for the five geographical regions.



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