Table 1 Patient and practice characteristics categorised by World Bank country income category (CIC)

| Category                               | Detail                                   |             | World Bank Income | CIC                    | Significance |
|--|--|-------------|-------------------|------------------------|--------------|
|  |  | High        | Upper-middle      | Lower-middle or<br>low |              |
| Participant characteristics            | Number                                   | 2576        | 5859              | 3907                   | N/A          |
| Countries                              | Number                                   | 10          | 11                | 7                      | "            |
| Centres                                | Number                                   | 38          | 50                | 20                     | "            |
| Patient characteristics                |  |             |                   |                        |              |
| Age                                    | Mean (SD)                                | 65.8 (13.8) | 62.7 (13.3)       | 59-1 (13-5)            | P<0.0001     |
| Sex                                    | n (%) male                               | 1543 (60%)  | 3331 (57%)        | 2359 (60%)             | P=0.001      |
| Education                              | None/primary                             | 449 (17%)   | 3832 (66%)        | 2234 (58%)             | P<0.0001     |
|  | High school, trade college or university | 2127 (83%)  | 2025 (34%)        | 1673 (42%)             |              |
| Charleston Index Comorbidity           | None                                     | 730 (28%)   | 1886 (32%)        | 1430 (37%)             | P<0.0001     |
|  | One or more                              | 1845 (72%)  | 3972 (68%)        | 2477 (63%)             |              |
| Independent Pre-stroke                 | Modified Rankin Scale 0-2                | 2481 (96%)  | 5794 (99%)        | 3871 (99%)             | P=0.001      |
| Stroke classification                  | Intracerebral haemorrhage                | 258 (10%)   | 1666 (28%)        | 1275 (32%)             | P<0.0001     |
|  | Infarct – Total Anterior Circulation     | 111 (4%)    | 280 (5%)          | 208 (5%)               |              |
|  | Infarct – Partial Anterior Circulation   | 1022 (40%)  | 1927 (33%)        | 1319 (34%)             |              |
|  | Infarct – Posterior Circulation          | 406 (16%)   | 549 (9%)          | 311 (8%)               |              |
|  | Infarct – Lacunar                        | 706 (27%)   | 1149 (20%)        | 574 (15%)              |              |
|  | Unclassified                             | 70 (3%)     | 288 (5%)          | 219 (6%)               |              |
| Level of consciousness                 | Reduced                                  | 189 (7%)    | 1640 (28%)        | 2116 (54%)             | P<0.0001     |
| Baseline dependency                    | Mild (mRS 0-2)                           | 1605 (62%)  | 2180 (37%)        | 894 (23%)              | P<0.0001     |
| (modified Rankin score; mRS)           | Moderate (mRS 3)                         | 472 (18%)   | 1636 (28%)        | 994 (25%)              |              |
|  | Severe (mRS 4)                           | 373 (15%)   | 1391 (24%)        | 1076 (28%)             |              |
|  | Very severe (mRS 5)                      | 126 (5%)    | 651 (11%)         | 942 (24%)              |              |
| Length of stay in hospital             | Mean (days)                              | 9           | 16                | 6                      | P<0.0001     |
| Investigations performed in hospital   |  |             |                   |                        |              |
| Investigations                         | CT scan on day 1                         | 2460 (96%)  | 5567 (95%)        | 3455 (89%)             | P<0.0001     |
|  | MRI scanning                             | 503 (20%)   | 611 (10%)         | 43 (1%)                | P<0.0001     |
|  | Holter monitoring                        | 608 (24%)   | 94 (2%)           | 2 (1%)                 | P<0.0001     |
|  | Carotid Doppler                          | 1653 (64%)  | 1175 (20%)        | 76 (2%)                | P<0.0001     |
| Treatments given in hospital           |  |             |                   |                        |              |
| Treatments                             | Antiplatelet drugs for cerebral infarct  | 2344 (91%)  | 5121 (87%)        | 3116 (85%)             | P<0.0001     |
|  | Lipid lowering for cerebral infarct      | 1865 (72%)  | 4222 (72%)        | 3140 (80%)             | P<0.0001     |
|  | Thrombolysis (iv) for infarct (a)        | 463 (20%)   | 168 (4%)          | 73 (3%)                | P<0.0001     |
|  | Carotid intervention for infarct (a, b)  | 79 (3%)     | 16 (<1%)          | 2 (<1%)                | P<0.0001     |
|  | BP lowering for any stroke               | 1818 (71%)  | 3881 (66%)        | 2972 (76%)             | P<0.0001     |
| Services available at centre           |  | 1839 (72%)  |                   |                        |              |
| Hospital type                          |  |             | 3090 (53%)        | 2690 (69%)             | P<0.0001 *   |
| Medical stroke specialist availability | Any stroke specialist available          | 2397 (96%)  | 5155 (88%)        | 2410 (62%)             | P<0.0001 *   |
|  | Capacity to look after >50% of patients  | 2259 (90%)  | 4805 (82%)        | 1512 (39%)             | P<0.0001 **  |
| Stroke unit availability               | Any stroke unit available                | 2370 (92%)  | 1323 (23%)        | 2362 (61%)             | P<0.0001 **  |

|                                   | Capacity to look after >50% of patients | 2236 (89%) | 1297 (22%) | 1334 (34%) | P<0.0001 ** |
|-----------------------------------|---|------------|------------|------------|-------------|
|                                   | Unit meets all key characteristics (c)  | 1767 (71%) | 1088 (19%) | 783 (20%)  | P<0.0001 ** |
|                                   | Unit meets all staffing benchmarks (d)  | 475 (18%)  | 408 (7%)   | 723 (18%)  | P<0.0001 ** |
| Post-discharge rehabilitation     | Any service available                   | 2357 (92%) | 2170 (37%) | 1214 (31%) | P<0.0001 ** |
| Family training in rehabilitation | Any education of family reported        | 2169 (84%) | 4418 (75%) | 2509 (64%) | P<0.0001 *  |

The table summarises regional variations in the patient characteristics, services investigations and treatments available for stroke participants recruited to INTERSTROKE and grouped according to World Bank Income Category. Note all patients recruited were expected to have brain imaging (usually CT scan) and a 12 lead ECG.

Key: mRS = modified Rankin Scale; CT = Computerised Tomography; MRI = Magnetic Resonance Imaging; BP=blood pressure.

- a) Substantial missing data which were assumed to indicate non-treatment.
- b) Usually carotid endarterectomy (a small number had carotid stenting).
- c) The stroke unit characteristics included<sup>26</sup>; discrete ward, staff who specialise in stroke, regular multidisciplinary team (MDT) meetings, protocols for care in place, programmes of education and training for staff, information provided for patients and carers.
- d) Basic stroke unit staffing was benchmarked <sup>26</sup> at a staff complement (to cover all shifts) of 1.0 whole time equivalent of nursing staff per bed,
- 0.1 whole time equivalent of therapist, and 0.1 whole time equivalent of doctor.

All comparisons are at the level of the patient. As the services available were clustered at centres we also compared at the level of the centres: \* Proportions differ at P<0.001; \*\* at P<0.0001.

Table 2 Patient outcomes at one month by country wealth: univariate and multivariate analyses

| Outcome category at one month                     | Odds of a better outcome for each increase in ranking of country GDP |   |  |   |  |  |  |
|---|--|---|--|---|--|--|--|
|   | Univariate analysis<br>(OR and 95% CI)                               | Multivariate analysis <sup>i</sup><br>(OR and 95% CI) | Multivariate analysis <sup>ii</sup><br>(OR and 95% CI) | Multivariate analysis <sup>iii</sup><br>(OR and 95% CI) | Multivariate analysis <sup>iv</sup><br>Clustered by centre<br>(OR and 95%CI) |  |  |
| Full recovery (mRS 0-1) vs worse                  | 1·05 (1·04-1·05)   | 1·01 (0·99-1·01)                                      | 1·00 (0·99-1·01)                                       | 1·01 (0·99-1·00)  | 1·01 (0·99-1·00)   |  |  |
|   | P<0·0001   | P=0·72  | P=0·91   | P=0·07  | P=0·08   |  |  |
| Independent (mRS 0-2) vs worse                    | 1·05 (1·05-1·06)   | 1·00 (0·99-1·01)                                      | 1·00 (0·99-1·01)                                       | 1·00 (0·99-1·01)  | 1·01 (0·99-1·01)   |  |  |
|   | P<0·0001   | P=0.95  | P=0·99   | P=0·99  | P=0·43   |  |  |
| No major dependency (mRS 0-3) vs worse            | 1·06 (1·05-1·08)   | 1·00 (0·99-1·01)                                      | 1·00 (0·99-1·01)                                       | 0·99 (0·99-1·02)  | 1·00 (0·99-1·01)   |  |  |
|   | P<0·0001   | P=0·59  | P=0·47   | P=0·07  | P=0·70   |  |  |
| Without very severe dependency (mRS 0-4) vs worse | 1·10 (1·09·1·10)   | 1·02 (1·01·1·04)                                      | 1·03 (1·02-1·04)                                       | 1·02 (1·01-1·03)  | 1·03 (1·02-1·04)   |  |  |
|   | P<0·0001   | P<0·0001  | P<0·0001   | P=0·0005  | P<0·0001   |  |  |
| Alive (mRS 0-5) vs dead                           | 1·12 (1·11-1·14)   | 1·05 (1·04-1·06)                                      | 1·05 (1·04-1·06)                                       | 1·05 (1·03-1·06)  | 1·06 (1·04-1·07)   |  |  |
|   | P<0·0001   | P<0·0001  | P<0·0001   | P<0·0001  | P<0·0001   |  |  |

Data are Odds Ratio (95% CI); p value. Exploration of the association between country wealth and odds of patients having a better outcome (graded by the modified Rankin Scale; mRS) and the gross domestic product (GDP) ranked from lowest to highest income. The univariate analysis includes only country GDP ranked from the highest to lowest of the 28 included countries. i) Outcomes adjusted for country GDP ranking plus participant age, sex, education, pre-stroke disability, stroke type (haemorrhage or Oxfordshire Community Stroke Project category of infarct), number of comorbidities (Charleston comorbidity index), level of consciousness, and modified Rankin score at baseline (always recorded within 5 days of stroke onset). ii) Outcomes adjusted for all of the above plus accounting for services available (medical stroke specialist, stroke unit, and rehabilitation post discharge). iv) Outcomes adjusted for those in ‡ plus clustering by centre.

Table 3 Association of treatments available with patient outcomes at one month: univariate and multivariate analyses

| Outcome at one month | Treatment provided or service available at the | Univariate analysis<br>Odds Ratio (95% CI) | Multivariate analysis (i)<br>Odds Ratio (95% CI) | Multivariate analysis (ii)<br>Odds Ratio (95% CI) | Multivariate analysis (iii)<br>Odds ratio (95%CI) |
|----------------------|--|--|--|---|---|
|                      | recruiting centre                              | Odd3 Ratio (23 70 C1)                      | Outus Ratio (93 / 0 CI)                          | Odds Ratio (75 / 0 CI)                            | Odd3 1410 (22 70C1)                               |
| Alive without severe | Antiplatelet therapy for infarct               | 1.84 (1.61-2.10)                           | 1.28 (1.08-1.51)                                 | 1.29 (1.09-1.53)                                  | 1.12 (0.95-1.34)                                  |
| dependency (mRS 0-3) |  | P<0.0001                                   | P=0.0050   | P=0.0030  | P=0·19  |
|                      | Thrombolysis for infarct                       | 1.13 (0.91-1.41)                           | 1.09 (0.83-1.43)                                 | 1.06 (0.80-1.39)                                  | 0.90 (0.68-1.18)                                  |
|                      |  | P=0.28                                     | P=0.54   | P=0.69  | P=0·44  |
|                      | Medical stroke specialist                      | 1.79 (1.61-1.98)                           | 1.04 (0.91-1.18)                                 | 0.97 (0.82-1.14)                                  | 0.91 (0.77-1.08)                                  |
|                      | available *                                    | P<0.0001                                   | P=0.61   | P=0.69  | P=0.93  |
|                      | Stroke unit available *                        | 1.25 (1.14-1.36)                           | 1.42 (1.27-1.59)                                 | 1.42 (1.27-1.60)                                  | 1.29 (1.14-1.44)                                  |
|                      |  | P<0.0001                                   | P<0.0001   | P<0.0001  | P<0.0001  |
|                      | Post-discharge rehabilitation                  | 1.55 (1.43-1.70)                           | 1.20 (1.06-1.35)                                 | 1.37 (1.20-1.57)                                  | 1.18 (1.03-1.35)                                  |
|                      | available *                                    | P<0.0001                                   | P=0.0030   | P<0.0001  | P=0.0210  |
| Alive (mRS 0-5)      | Antiplatelet therapy for infarct               | 2.47 (2.07-2.96)                           | 1.65 (1.34-2.03)                                 | 1.62 (1.32-1.99)                                  | 1.39 (1.12-1.72)                                  |
|                      |  | P<0.0001                                   | P<0.0001   | P<0.0001  | P=0.0030  |
|                      | Thrombolysis for infarct                       | 1.67 (1.15-2.43)                           | 1.43 (0.94-2.17)                                 | 1.10 (0.72-1.69)                                  | 0.85 (0.55-1.31)                                  |
|                      |  | P=0.0070                                   | P=0·09   | P=0.66  | P=0·46  |
|                      | Medical stroke specialist                      | 1.62 (1.32-2.00)                           | 1.22 (0.97-1.54)                                 | 1.26 (0.99-1.59)                                  | 1.20 (0.94-1.52)                                  |
|                      | available *                                    | P<0.0001                                   | P=0·09   | P=0·05  | P=0·14  |
|                      | Stroke unit available *                        | 1.23 (1.09-1.39)                           | 1.17 (1.01-1.34)                                 | 1.18 (1.03-1.36)                                  | 1.00 (0.86-1.16)                                  |
|                      |  | P=0.0010                                   | P=0·0340   | P=0.0200  | P=0.99  |
|                      | Post-discharge rehabilitation                  | 3.79 (3.28-4.38)                           | 2.26 (1.91-2.66)                                 | 1.90 (1.58-2.28)                                  | 1.54 (1.28-1.85)                                  |
|                      | available *                                    | P<0.0001                                   | P<0.0001   | P<0.0001  | P>0.0001  |

Data are Odds Ratios (95% CI); p value. The multivariate analysis used multivariate regression to show case-mix adjusted outcomes. mRS=modified Rankin Scale. i) Outcomes adjusted for participant age, sex, education, pre-stroke disability, stroke type (haemorrhage or Oxfordshire Community Stroke Project category of infarct), number of comorbidities (Charleston comorbidity index), level of consciousness, and modified Rankin score at baseline (always recorded within 5 days of stroke onset). ii) Outcomes adjusted for all of the above plus country income (GDP ranking). iii) Outcomes adjusted for all those in iv) plus centre. §Service available at the recruiting centre but not necessarily received by every patient.

Table 4 Association of access to stroke unit care with processes of care and patient outcomes at one month: univariate and multivariate analyses

| Outcome category at one month             | Stroke unit available |             | Association with stroke unit availability |   |  |  |  |
|---|-----------------------|-------------|---|---|--|--|--|
|   | Yes No                |             | Univariate analysis<br>OR (95% CI)        | Multivariate analysis <sup>i</sup><br>OR (95% CI) | Multivariate analysis <sup>ii</sup><br>OR (95% CI) |  |  |
| Process measures                          |                       |             |   |   |  |  |  |
| CT scan conducted on day of admission     | 5727                  | 5754        | 1·69 (1·45-1·95)                          | 1·66 (1·43-1·94)                                  | 1·35 (1·10-1·66)                                   |  |  |
|   | (95%)                 | (92%)       | P<0·0001                                  | P<0·0001  | P=0·0040   |  |  |
| Antiplatelet for infarct                  | 4148                  | 3554        | 1·49 (1·31-1·63)                          | 1·40 (1·24-1·58)                                  | 1·16 (0·99-1·34)                                   |  |  |
|   | (86%)                 | (80%)       | P<0·0001                                  | P<0·0001  | P=0·06   |  |  |
| Lipid lowering for infarct                | 3366                  | 2772        | 1·35 (1·23-1·47)                          | 1·33 (1·21-1·47)                                  | 1·17 (0·76-1·81)                                   |  |  |
|   | (70%)                 | (63%)       | P<0·0001                                  | P<0·0001  | P=0·48   |  |  |
| Thrombolysis for infarct                  | 580<br>(12%)          | 123<br>(3%) | 4·74 (3·88-5·78)<br>P<0·0001              | 3·65 (2·96-4·50)<br>P<0·0001                      | Insufficient data                                  |  |  |
| BP lowering therapy given for any stroke  | 4357                  | 4313        | 1·17 (1·09-1·27)                          | 1·29 (1·18-1·41)                                  | 0.93 (0.73-1.17)                                   |  |  |
|   | (72%)                 | (69%)       | P<0·0001                                  | P<0·0001  | P=0.52   |  |  |
| Post-discharge rehabilitation provided    | 4564                  | 1198        | 13·0 (11·9-14·2)                          | 18·2 (16·4-20·3)                                  | 86·7 (66·4-1·13)                                   |  |  |
|   | (75%)                 | (19%)       | P<0·0001                                  | P<0·0001  | P<0·0001   |  |  |
| Clinical outcomes at one month            |                       |             |   |   |  |  |  |
| Alive without severe dependency (mRS 0-3) | 4936                  | 4907        | 1·25 (1·14-1·36)                          | 1·41 (1·26-1·58)                                  | 1·29 (1·14-1·44)                                   |  |  |
|   | (82%)                 | (79%)       | P<0·0001                                  | P<0·0001  | P<0·0001   |  |  |
| Alive (mRS 0-5)                           | 5492                  | 5588        | 1·23 (1·09-1·39)                          | 1·30 (1·12-1·49)                                  | 1·00 (0·86-1·16)                                   |  |  |
|   | (91%)                 | (89%)       | P=0·0010                                  | P<0·0001  | P=0·99   |  |  |

The table shows the number (percent) of patients in both service groups in each category of process measure (care received up to one month) and outcome measure (degree of recovery at one month post-stroke). Univariate analyses show the unadjusted odds ratio (OR) and 95% confidence interval (CI) for the association between access to stroke unit care and a better clinical outcome. The multivariate analysis used multivariate regression to show case-mix adjusted outcomes that were adjusted for; i) participant age, sex, education, pre-stroke disability, stroke type (haemorrhage or Oxfordshire community stroke project category of infarct), number of comorbidities (Charleston comorbidity index); level of consciousness, and modified Rankin score at baseline (always recorded within 5 days of stroke onset), plus country income (GDP ranking), ii) all of ii) plus centre.

Key: BP=blood pressure; mRS = modified Rankin Scale.