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1 **Variations in practice patterns and outcomes after stroke across countries**  
2 **at different economic levels: the INTERSTROKE study**

3  
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120 **Cover title:** Practice variations and outcomes after stroke

121 **List:**

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

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

126 Table 3. Association of treatments available with patient outcomes at one month; univariate  
127 and multivariate analyses

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

130 Figure 1. The association between admission to a hospital with a stroke unit and patient  
131 outcomes at one month; subgroup analysis by patient and service characteristics

132 Figure 2. The association between use of antiplatelet therapy in hospital and patient  
133 outcomes at one month; subgroup analysis by patient and service characteristics

134

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150

151 **Abstract**

152 Background

153 Stroke disproportionately affects people in low and middle-income countries (LMICs).  
154 Although improvements in stroke care and outcomes have been reported in high income  
155 countries (HICs), little is known about practice and outcomes in LMICs. We aimed to compare  
156 patterns of care available and their association with patient outcomes across countries at  
157 different economic levels.

158 Methods

159 We studied the patterns and impact of practice variations (treatments used and access to  
160 services) among stroke participants in the INTERSTROKE study, an international  
161 observational study that enrolled 13,447 stroke patients from 142 clinical sites in 32 countries  
162 between January 11, 2007 and August 8, 2015. We supplemented patient data with a  
163 questionnaire about healthcare and stroke service facilities at each participating hospital. Using  
164 univariate and multivariate regression analyses to account for patient case-mix and service  
165 clustering, we estimated the association between services available, treatments given, and  
166 patient outcomes (death or dependency) at one month.

167 Findings

168 We obtained full information for 12,342 (92%) of 13,447 INTERSTROKE patients, from 108  
169 hospitals in 28 countries; 2576 from 38 hospitals in 10 HICs and 9766 from 70 hospitals in 18  
170 LMICs. Patients in LMICs more often ( $P<0.0001$ ) had severe strokes, intracerebral  
171 haemorrhage, poorer access to services, and lower use of investigations and treatments,  
172 although only differences in patient characteristics explained the poorer clinical outcomes in  
173 LMICs. However across all countries, access to a stroke unit was associated ( $P<0.0001$ ) with  
174 improved use of investigations and treatments, access to other rehabilitation services, and  
175 improved survival without severe dependency (1.29; 1.14-1.44) which was independent of

176 patient case-mix characteristics and other measures of care. Use of acute antiplatelet therapy  
177 was associated with improved survival (1.39; 1.12-1.72) irrespective of other patient and  
178 service characteristics.

#### 179 Interpretation

180 Evidence based treatments, diagnostics, and availability of stroke units were less commonly  
181 available or used in LMICs. Access to stroke units and appropriate use of antiplatelet therapy  
182 were associated with improved recovery. Improved care and facilities in LMICs are essential  
183 to improve outcomes.

#### 184 Funding

185 This analysis was supported by Chest, Heart and Stroke Scotland. INTERSTROKE was  
186 supported by range of funders.

187

188

## 189 **Introduction**

190 Stroke is the second commonest cause of death worldwide and one of the leading causes of  
191 disability.<sup>1-3</sup> Although prevention strategies can reduce this burden of disease<sup>4,5</sup> effective and  
192 affordable treatments are essential for reducing mortality and morbidity in those who have  
193 already suffered a stroke. Aspirin<sup>4,5</sup>, intravenous thrombolysis<sup>4,5</sup> and mechanical  
194 thrombectomy<sup>6</sup> for acute ischaemic stroke, and plus stroke unit care and early rehabilitation  
195 services for all stroke patients<sup>4,5</sup> can reduce mortality and morbidity.

196 The PURE study<sup>7</sup> recently demonstrated that after stroke clinical outcomes were substantially  
197 poorer in low- and middle-income countries (LMIC) than in high income countries (HICs). It  
198 is not clear if this reflects differences in the patient population, services available, or  
199 treatments received. In many HICs, clinical practice guidelines and national strategies now  
200 recommend the establishment of stroke units in all hospitals that care for patients with acute  
201 stroke<sup>9-13</sup>. This has been linked to an increased provision of evidence-based care<sup>14-19</sup> and  
202 improved patient outcomes<sup>17-20</sup>. However the greatest adoption of these practices has been in  
203 HICs where most clinical trials of stroke units have been carried out. It is not known how  
204 common stroke units are in LMICs or whether they are associated with improved  
205 outcomes.<sup>4,5,8</sup> Such information could inform the establishment of stroke units in LMICs.

206 INTERSTROKE is an international observational stroke study conducted in 32 countries at  
207 different economic levels.<sup>21</sup> Individuals who had had a stroke were selected using  
208 standardised criteria and were characterised in detail. This allowed us to compare the  
209 patterns of care available, and their association with patient outcomes, across a much broader  
210 range of healthcare settings than has previously been possible.

211

## 212 **Methods**



213 INTERSTROKE is an international case-control study of risk factors for first stroke<sup>21</sup>, which  
214 enrolled 13,447 stroke patients from 142 clinical sites in 32 countries between January 11, 2007  
215 and August 8, 2015.

216 For this analysis of practice patterns, our hypotheses were that, across all countries studied,  
217 there would be variations in access to stroke treatments and services and that, after adjusting  
218 for variations in patient case-mix, patient outcomes will be influenced by the treatments and  
219 services they can access. We proposed that outcomes would be better where; i) healthcare  
220 resources are greater, ii) guideline investigations and treatments are provided, and iii) guideline  
221 services (especially stroke units) are available at the hospital.

222 Data collection operated at two levels;

223 a) Individual stroke patient data included the following; demographic features (age, sex, level  
224 of education), risk factors, pre-stroke disability (using the modified Rankin Score<sup>22</sup>),  
225 comorbidity (based on the Charleston Comorbidity Index<sup>23</sup>), stroke characteristics (including  
226 haemorrhage or infarct classified with the Oxfordshire Community Stroke Project (OCSP)  
227 classification<sup>24</sup>, modified Rankin Score<sup>22</sup> at baseline, level of consciousness at baseline) and  
228 acute management received at enrolment in the study (brain imaging, antiplatelet therapy,  
229 thrombolysis, lipid lowering therapy and blood pressure lowering therapy).

230 b) Data collected at the level of the service; Using a short questionnaire (see Appendix), we  
231 collected information on service features at each participating hospital: i) local and national  
232 healthcare characteristics (e.g. source of health funding, items for payment), ii) hospital  
233 characteristics and resources (e.g. tertiary or secondary level hospital, departments and beds  
234 available), iii) stroke service characteristics (presence of stroke unit, stroke unit  
235 characteristics and resources), iv) additional features (other aspects of patient care such as  
236 post-discharge rehabilitation). The survey was first circulated electronically in June 2011

237 with a reminder sent in early 2012. If no there was no reply by early 2012, the electronic  
238 message was resubmitted via national leads.

239

## 240 **Outcomes**

241 Patient outcomes were recorded at one month follow up<sup>21</sup> and included; death, discharge  
242 disposition after hospital (home, rehabilitation centre or nursing home), dependency using the  
243 modified Rankin score<sup>22</sup>, and length of hospital stay. Patient details were collected from the  
244 participants or from a proxy respondent<sup>21</sup>.

## 245 **Analysis**

246 We carried out the following analyses:

247 1) Description of the patient characteristics and clinical practice (investigations,  
248 treatments and services provided) at recruiting hospitals grouped by the 2011 World  
249 Bank Country Income Categories (CIC), using Chi-squared and t-tests,

250 We carried out statistical analyses using SPSS V.23 and SAS V.9.4. using multivariate  
251 analyses to calculate case-mix adjusted outcomes (see below) and a 2-level multivariable  
252 model using random intercepts to take into account potential clustering of clinical practice by  
253 centre. We used multivariable logistic regression models to adjust for case-mix covariates  
254 that are known to influence patient outcomes<sup>25</sup>; age, sex, level of education, pre-stroke  
255 disability, number of comorbidities, stroke type and classification and initial stroke severity.  
256 No significant multi-collinearity was identified. Adjustment was subsequently also made for  
257 country wealth (ranked by GDP) and clustering by centre. We then used binary logistic  
258 regression to identify variables that had the closest association with patient outcomes.

259 Subgroup analyses stratified results by key patient and service characteristics. Availability of  
260 a stroke unit was clustered in regions and correlated with patient age, level of consciousness

261 and stroke severity. Therefore we also sought to confirm our findings in a propensity-  
262 matching analysis accounting for these variables. Finally we conducted exploratory  
263 sensitivity analyses of the association between patient outcomes and access to stroke units  
264 (with or without particular characteristics). These comparisons were based on;  
265 a) Stroke unit quality criteria<sup>26</sup> in terms of whether six key features were present; (i) discrete  
266 ward, ii) multidisciplinary care, iii) staff specialist interest in stroke, iv) programmes of staff  
267 education and v) patient management protocols and vi) information for patients and families,  
268 b) Staffing levels that meet basic benchmark levels for nursing, medical and therapy staff<sup>26</sup>,  
269 c) Stroke unit capacity (ability to manage >50% of the stroke patients in the hospital), and  
270 d) Access to post-discharge rehabilitation.

## 271 **Ethics**

272 The study was approved by the ethics committees in all participating centres.<sup>21</sup> Participants,  
273 or their proxy, provided written informed consent. None of the authors reported major  
274 conflicts of interest.

275

## 276 **Role of the funding source**

277 The current analysis was supported by a grant from Chest, Heart and Stroke Scotland. The  
278 main INTERSTROKE study was supported by several funders (see Appendix). None of the  
279 funders had a role in the study design, data collection, data analysis, data interpretation, or  
280 writing of the report. The corresponding author had full access to all the data and final  
281 responsibility for the decision to submit for publication.

282

## 283 **Results**

284 Between January 11, 2007 and August 8, 2015, the INTERSTROKE study<sup>21</sup> enrolled 13,447  
285 acute stroke patients from 142 centres; 34 centres (1105 participants) did not provide  
286 information on the service survey. We therefore had complete individual patient data and  
287 service information from 12,342 participants from 108 hospitals in 28 countries covering  
288 Western Europe, East and Central Europe, the Middle East, Africa, South Asia, China, South  
289 East Asia, Latin America, North America and Australia.

290 Table 1 outlines the characteristics of patients, investigations and treatments provided and  
291 services available. These are categorised by the 2011 World Bank Country Income Category.  
292 A total of 38 hospitals (2576 participants) were in HICs (Australia, Canada, Croatia,  
293 Denmark, Germany, Ireland, Poland, Sweden, United Arab Emirates, UK) and 70 hospitals  
294 (9766 participants) in LMICs. The latter consisted of 50 hospitals (5859 participants) in  
295 upper-middle income countries (Argentina, Brazil, Chile, China, Columbia, Ecuador,  
296 Malaysia, Peru, Russia, South Africa, Turkey), 17 hospitals (3361 participants) in lower-  
297 middle income countries (India, Nigeria, Pakistan, Philippines, Sudan), and 3 hospitals (546  
298 participants) in low income countries (Mozambique, Uganda). LMIC hospitals (Table 1)  
299 recruited patients who were on average younger, less well educated, had fewer comorbidities,  
300 more severe strokes and more intracerebral haemorrhage (all  $P < 0.0001$ ). Although CT  
301 scanning was mandated for all INTERSTROKE patients, those from HICs were more likely  
302 to get imaging done on the day of admission. Other investigations were also more readily  
303 available (Table 1). HIC patients were more likely to receive antiplatelet therapy, intravenous  
304 thrombolysis or a carotid intervention following an ischaemic stroke, but any variations in BP  
305 lowering treatments and lipid lowering therapy were not clearly linked to World Bank CIC.  
306 Data reporting was almost complete (12266; 99.4%) for all reported variables with the

307 exception of thrombolysis and carotid interventions for which non-reporting was assumed to  
308 indicate that the treatment was not given.

309

310 Table 1 also summarises the services available in each site categorised by World Bank CIC.  
311 A total of 6055 patients (49%) were admitted to hospitals reporting that they had some form  
312 of stroke unit available; (95% of centres and 92% of patients in HIC; 30% of centres and 38%  
313 of patients in LMICs). However there was no clear gradient by World Bank CIC with fewest  
314 stroke units being available in upper-middle income countries. When present, stroke units in  
315 LMICs were less likely to meet all of the six key quality characteristics<sup>26</sup> or to report having  
316 sufficient capacity to accommodate most hospitalised stroke patients (Table 1). This was  
317 corroborated by information that, for the same number of admissions (a median of 50 stroke  
318 patient admissions per month), HIC stroke units reported having a median of 18 beds  
319 available compared with 8 beds in LMIC units.

320 Stroke patients from wealthier countries had better outcomes at one month. When grouped as  
321 HICs versus LMICs, the number (%) surviving and surviving without major dependency  
322 (mRS 0-3) were 2501 (98%) and 2308 (90%) respectively in HICs compared with 8580  
323 (88%) and 7536 (78%) in LMICs. This was confirmed when outcomes were regressed against  
324 country wealth; ranked from lowest to highest country GDP (Table 2). Differences in patient  
325 characteristics appeared to explain much, but not all, of the variation by country wealth. After  
326 adjusting for baseline patient case-mix variables (age, sex, education, pre-stroke disability,  
327 stroke type, number of comorbidities, level of consciousness, and modified Rankin score at  
328 baseline) the relationship between country income and recovery was reduced but not  
329 abolished (Table 2). There was no further attenuation of the relationship after including  
330 common medications given (antiplatelet, lipid lowering and BP lowering therapy plus  
331 thrombolysis), and access to services (medical stroke specialist, stroke unit and rehabilitation

332 post-discharge). These results indicate that the incrementally better patient outcomes  
333 observed in wealthier countries were partly explained by patient case-mix.

334 We then explored the relationships between treatments given, services available and patient  
335 outcomes across all World Bank CIC settings (Table 3). For these analyses we included all  
336 treatments and services that were less common in LMIC centres (Table 1). We did not  
337 include carotid interventions as this applied to only 97 patients overall. After adjustment for  
338 patient case-mix and country wealth (GDP ranking), the appropriate provision of antiplatelet  
339 therapy (prescribed for those with cerebral infarction), and the availability of stroke unit care  
340 and post-discharge rehabilitation were each associated with a greater chance of survival  
341 without severe dependency (Table 3). The appropriate provision of antiplatelet therapy, and  
342 availability of stroke unit care and post-discharge rehabilitation were also associated with a  
343 higher odds of survival at one month (Table 3). When the analysis also took into account  
344 clustering by centre (Table 3), the availability of stroke unit care and post-discharge  
345 rehabilitation were each associated with a greater chance of survival without severe  
346 dependency (Table 3). The appropriate provision of antiplatelet therapy, and availability of  
347 post-discharge rehabilitation were associated with a higher odds of survival at one month  
348 when taking into account clustering by centre.

349 Using a forward binary logistic regression, including all variables listed in Table 3, we found  
350 that survival without severe dependency (mRS 0-3) was greater with access to stroke unit  
351 care and appropriate antiplatelet therapy. Significant covariates were pre-stroke disability  
352 plus the five patient variables (age, comorbidities, baseline mRS, level of consciousness and  
353 stroke classification). Survival at one month was best explained by appropriate antiplatelet  
354 therapy, access to stroke unit care, and access to post-discharge rehabilitation. Significant  
355 covariates were country GDP ranking, patient education and the five patient variables above.

356 Table 4 highlights the univariate and multivariate analyses exploring the association of access  
357 to a stroke unit with the provision of other stroke treatments and with patient outcomes.  
358 Admission to a hospital with a stroke unit was associated with increased odds of receiving all  
359 the other process measures plus an increased odds of survival and survival without severe  
360 dependency. However after adjusting for clustering by centre, access to a stroke unit was only  
361 associated with increased access to CT scanning and post-discharge rehabilitation and with  
362 survival without severe dependency (1.29; 1.14-1.44).

363 As stroke unit availability was unevenly distributed between regions we used a matched  
364 propensity analysis that excluded the five regions where availability was either universal  
365 (Western Europe, Eastern Europe, North America, Australia) or absent (Middle East).  
366 Variables that were related to patient outcomes and also closely associated with stroke unit  
367 availability were patient age and stroke severity. Therefore we compared two groups of 3,466  
368 stroke participants with or without access to a stroke unit who were matched on; age (mean of  
369 60 versus 60 years); reduced level of consciousness (45% versus 45%); baseline modified  
370 Rankin Scale, (mean of 3.40 versus 3.40). Admission to a hospital with a stroke unit was  
371 again associated with increased odds of survival (1.15; 1.01-1.31) and of survival without  
372 major disability (1.30; 1.17-1.44).

373

374 In view of the imbalance between HIC and LMIC in the numbers of patients with  
375 intracerebral haemorrhage, we repeated the analyses with the exclusion of intracerebral  
376 haemorrhages (supplemental Tables 1-2). On multivariate analyses patients with ischaemic  
377 stroke had an increased odds of survival without severe dependency (1.42; 1.23-1.64;  
378  $p < 0.0001$ ) if admitted to a hospital with a stroke unit. Results were directionally consistent  
379 but non-significant for survival (1.15; 0.96-1.39;  $p = 0.14$ ).

380 Further subgroup analyses found a consistent association of access to stroke unit services  
381 with patient outcomes across a range of patient and service subgroups (Figure 1). The  
382 association of improved outcomes with antiplatelet drug use was seen across all subgroups  
383 (Figure 2) except for stroke type where no benefit was seen for the very small number of  
384 haemorrhage patients treated with aspirin.

385

386 Finally in sensitivity analyses we repeated the analysis in Table 4 for the outcome of survival  
387 without severe dependency (mRS 0-3) but compared stroke units with and without specific  
388 quality characteristics (as described in Table 1). The association with improved outcomes  
389 was greater in the presence (compared to absence) of quality features; the stroke unit was  
390 described as having the six key characteristics (1.32; 1.11-1.56); stroke unit staffing met basic  
391 benchmark levels (1.34; 1.11-1.62); and the stroke unit had the capacity to house at least 50%  
392 of stroke patient admissions (1.20; 1.00-1.45). The availability of post-discharge  
393 rehabilitation was not associated with additional benefit in this analysis (1.08; 0.67-1.33).

## 394 **Discussion**

395 We had anticipated that INTERSTROKE patients enrolled in LMIC hospitals would have  
396 poorer access to investigations, treatments and services than those from HIC hospitals.

397 However, LMIC patients also had poorer clinical outcomes (survival 88% compared with  
398 98% in HICs; survival without severe disability 78% versus 90%) which could only be partly  
399 explained by the inclusion of more severe stroke patients. Across all countries studied, the  
400 practice variables most consistently associated with improved patient outcomes were access  
401 to stroke unit care and post-discharge rehabilitation plus receiving appropriate antiplatelet  
402 therapy. This may reflect more limited access to state or insurance funded healthcare  
403 services.



404 The poorer stroke prognosis in LMICs has been described previously.<sup>2,3,7</sup> We have confirmed  
405 that stroke in poorer countries appears to be either a more severe disease (more intracerebral  
406 haemorrhage) and/or has different referral patterns (patients admitted to hospital more likely  
407 to have severe stroke). The potential role of stroke units and antiplatelet therapy in LMIC  
408 settings has not been described before but is potentially complex. Access to drugs or services  
409 could not explain differences between patient outcomes in wealthy versus less wealthy  
410 countries but they did appear to explain associations across all countries. This may reflect the  
411 observation that access to a stroke unit varied greatly within as well as between wealth  
412 categories (World Bank CICs).

413 Several observational studies<sup>16,18,20,28</sup> have reported on the association of appropriate  
414 antiplatelet therapy (early use in acute cerebral ischaemia) with improved survival and  
415 reduced disability. Also a recent meta-analysis of aspirin trials<sup>29</sup> confirms an important short  
416 term benefit of aspirin therapy to prevent recurrent cerebral ischaemia. However, these  
417 studies have almost all been in higher income settings<sup>28</sup>. Earlier access to brain imaging may  
418 serve to facilitate earlier antiplatelet use.

419 In the INTERSTROKE study, the apparent benefit of stroke units is comparable to that  
420 reported in RCTs<sup>4</sup> and appears to be due to a combination of an “intrinsic” stroke unit effect  
421 as well as stroke unit patients having better access to antiplatelet therapy, risk factor  
422 modification, and post-discharge rehabilitation. The apparent benefits were seen across a  
423 range of stroke patient groups and tended to be greater if the stroke unit was reported to be  
424 well staffed, to meet recognised service standards, and to have sufficient capacity to provide  
425 care for most stroke patients admitted to hospital. Our findings suggest that, stroke units can  
426 have a similar benefit in LMICs as has been observed in HICs.

427 At present few hospitals in LMICs have stroke units. Even in our study, which is likely to  
428 have included a higher proportion of better-resourced tertiary care centres (with better access  
429 to imaging and drug therapies) than in average LMIC hospitals, only 38% had stroke units.  
430 Our study suggests that establishment of simple stroke units could enhance the level and  
431 organisation of care and improve stroke outcomes in LMICs. The World Health Organisation  
432 has targeted a 25% reduction in premature mortality from cardiovascular disease globally by  
433 2025. This is unlikely to be achieved by risk factor reduction alone but also requires  
434 investment in medical treatments and organisation of better systems of care. Investment in  
435 specialised stroke units is likely to be cost effective and should be a priority worldwide.

436 Limitations of this study include the observational design which cannot completely exclude  
437 the possibility of residual confounding. We carried out a large number of analyses which  
438 raises the possibility of chance findings. However, use of the 99% confidence threshold  
439 would not alter our main conclusions. Service features were described at the level of the  
440 hospital so we cannot be certain which specific patients were actually admitted to a stroke  
441 unit. Although this introduces some uncertainty it also reduces any potential bias resulting  
442 from selective admission of better prognosis patients within a hospital to the stroke unit; it is  
443 testing the impact of the stroke unit on all patients at that hospital. Interestingly the sensitivity  
444 analyses suggest improved outcomes where stroke units had greater capacity to accept most  
445 stroke patients. As only a proportion of patients were enrolled in INTERSTROKE it is  
446 possible (but unlikely) that stroke unit sites enrolled patients with a better prognosis. An  
447 additional challenge was that service characteristics tended to cluster together in hospitals,  
448 countries and regions making it difficult to separate the impact of different aspects of service  
449 delivery. In particular, the availability of post-discharge rehabilitation services was closely  
450 related to stroke units. Finally, several regions had no variation in the provision of stroke  
451 units, although exclusion of these regions from the analysis did not alter our conclusions.

452 The strengths of our study are that we collected standardised information from over 12,000  
453 well-characterised acute stroke patients including an independent assessment of outcome at  
454 one month. We recruited from a large number of hospitals in diverse settings with variations  
455 in care. This was facilitated by national co-ordinators and investigators who were trained in  
456 collecting data in a standardised manner. The study investigators had a research interest in  
457 stroke epidemiology, but there was not usually a special interest in service delivery.

458 Although we recognise that the hospitals participating in INTERSTROKE are likely to have  
459 had a higher level of resources and support than is typical of poorer resourced areas, we know  
460 of no other study that has obtained such a broad range and quality of data using such  
461 standardised and prospective methods. If the centres participating in INTERSTROKE were  
462 better equipped than the average centres in each country ( especially in LMICs), the gaps  
463 between HIC and LMIC in facilities , organized care , treatments and outcomes for stroke  
464 patients may be even greater than what we report.

465 Several previous studies have explored the potential impact of indicators of service quality in  
466 routine hospital settings,<sup>27,28</sup> however, almost all have been carried out in HIC settings. The  
467 most recent review of LMICs<sup>8</sup> could only identify limited observational information that  
468 could not adjust for confounders. Individual case studies in India, Thailand, South Africa and  
469 Mauritania<sup>8</sup> suggested that stroke unit care could have a beneficial impact in those settings.

470 Only two studies have explored the impact of antiplatelet agents in LMICs and their results  
471 were inconclusive<sup>28</sup>.

472 We believe that this analysis supports the widespread provision of appropriate early  
473 antiplatelet therapy and stroke unit care within hospitals in LMIC settings. It also indicates  
474 that a certain basic standard of care and supporting resources are likely to be needed to fully  
475 realise these benefits. These include adequate staffing and the capacity to accept the majority

476 of stroke patients. Further research needs to develop and test methods of effectively  
477 implementing lower-cost, regionally appropriate models of stroke unit care.

478

### **Research in context**

#### **Evidence before this study**

We searched Medline, EMBASE and PubMed from January 1, 2000 to May 24, 2017, for large stroke register studies using Medical Subject Headings including stroke OR cerebral hemorrhage OR cerebral infarction AND quality indicator OR performance indicator OR quality improvement OR quality of care OR quality of health care OR registry OR register OR audit AND outcome OR mortality OR case fatality OR survival OR disability OR function OR recovery OR discharge OR discharge destination OR return home OR complications.. We identified 20 studies but none had been done in low or middle-income country settings.

#### **Added value of this study**

This is the first large study to use standardised, prospective data collection across a range of CIC levels in over 12,000 carefully characterised acute stroke patients from 108 hospitals in 28 countries. We have found that evidence-based treatments, diagnostics, and availability of stroke units were less common in LMICs. Access to stroke units and appropriate antiplatelet therapy were consistently associated with improved recovery.

#### **Implications of all the available evidence**

This analysis supports the widespread provision of appropriate early antiplatelet therapy and stroke unit care within hospitals in LMIC settings. A certain basic standard of care and supporting resources are likely to be needed to fully achieve these benefits. Further

research needs to develop and test methods of effectively implementing lower-cost, regionally appropriate models of stroke unit care.

480 **Contributors**

481

482 This sub-project of INTERSTROKE was conceived and jointly led by PL and MJO'D in  
483 conjunction with the study secretariat comprising the key national coordinators and members  
484 of the coordinating team at PHRI. PL and MJO'D designed the study, planned analyses, and  
485 wrote the first draft of the report. PL, MT and MJM did statistical analyses. All authors  
486 contributed to the collection of data, discussion and interpretation of the data, and to the  
487 writing of the report. All authors had full access to data and reviewed and approved the drafts  
488 of the report. MJO'D and SY jointly designed and led the overall INTERSTROKE study.

489

490 **Declaration of interests**

491 GJH reports personal fees from Bayer and Medscape, outside of the submitted work. H-CD  
492 has received honoraria for participation in clinical trials, contribution to advisory boards, or  
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501 *Arzneimitteltherapie*, *Kopfschmerznews*, *Stroke News*, and the Treatment Guidelines of the  
502 German Neurological Society within the past year; and served as co-editor of *Cephalalgia*,  
503 and on the editorial board of *Lancet Neurology*, *Stroke*, *European Neurology*, and  
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506 OSO, AO, HKI, GM, ZR, DM, YN, AR, SO, SY declare no competing interests.

507

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