Methods of Implementation of Evidence-based Stroke Care in Europe: The EIS Collaboration

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Abstract

Background and Purpose—Differences in stroke care and outcomes reported in Europe may reflect different degrees of implementation of evidence-based interventions. We evaluated strategies for implementing research evidence into stroke care in ten European countries.

Methods—A questionnaire was developed and administered through face-to-face interviews with key informants. Implementation strategies were investigated considering three levels (macro, meso, and micro, e.g., policy, organisation, patients/professionals) identified by the framing analysis, and different settings (primary, hospital, specialist) of stroke care. Similarities and differences among countries were evaluated using the Categorical Principal Components Analysis (CATPCA).

Results—Implementation methods reported by seven or more countries included non-mandatory policies, public financial incentives, continuing professional education, distribution of educational material, educational meetings and campaigns, guidelines, opinion leaders’ and stroke patients associations’ activities. Audits were present in six countries at national level; national and regional regulations in four countries. Private financial incentives, reminders, and educational outreach visits were reported only in two countries. At national level, the first principal component of CATPCA separated England, France, Scotland, and Sweden, all with positive object scores, from the other countries. Belgium and Lithuania obtained the lowest scores. At regional level, England, France, Germany, Italy, and Sweden had positive scores in the first principal component, while Belgium, Lithuania, Poland, and Scotland showed negative scores. Spain was in an intermediate position.

Conclusions—We developed a novel method to assess different domains of implementation in stroke care. Clear variations were observed among European countries. The new tool may be used elsewhere for future contributions.
Introduction

Implementation Science is receiving increasing attention in medical literature, due to the perceived necessity to narrow the gap between research findings and everyday practice. Previous studies showed that about 30-40% of patients do not receive appropriate care according to available scientific evidence, leading to underuse of effective interventions. Methods of implementation influence program outcomes, and the implementation process is affected by variables related to communities, providers and innovations. The significant differences in incidence, mortality, and disability rates of stroke throughout European countries may reflect different degrees of implementation of evidence-based interventions in stroke prevention and care. Characteristics of evidence, barriers, and facilitators to changing practice, and effectiveness of implementation methods are factors affecting translation of research findings into practice. Both organisational and individual elements play a pivotal role in effective and sustainable uptake of innovation.

A number of strategies aimed at changing healthcare professional behavior, decision making processes, treatment and management, have been developed, including professional, financial, organizational, and regulatory interventions. The main objective of this work within the European Implementation Score (EIS) Collaboration, established in the EU 7th Framework Programme, was to evaluate different methods currently used to translate research findings into practice in stroke care in European countries at national and regional levels and in different settings of care.

Methods

Questionnaire development

A review of scientific literature on implementation strategies was performed, considering both the medical and social sciences. This provided the conceptual framework to develop a questionnaire designed to evaluate methods used to translate research findings into practice in
ten European countries in which either audits or population-based stroke registers agreed to participate in the EIS project: Belgium, England, France, Germany, Italy, Lithuania, Poland, Scotland, Spain, and Sweden.9

The questionnaire was developed after a series of meetings, audio conferences and email contacts among the work package board and other EIS collaborators. Adopting Goffman’s framing analysis models, as revised by Pope et al.,10 which consider modern healthcare as a complex, multilevel system, with multiple interacting actors and layers, implementation strategies were investigated at three levels: macro (e.g., national and regional policy), meso (organisational, e.g., audits, guidelines) and micro (e.g., patients, professionals), and in the different settings (primary, hospital and specialist) of stroke care.

The final version of the questionnaire consisted of 11 sections, covering the following different implementation strategies: national and regional policies (regulations having the force of law and non-mandatory policies); financial incentives; educational strategies, including continuing professional education, distribution of printed/electronic educational material, educational meetings and workshops, educational outreach visits, educational campaigns, and guidelines; audits; reminders; computerised decision support systems; opinion leaders; multiprofessional collaboration; multifaceted interventions; stroke patients’ associations; performance indicators.

A glossary including descriptions of implementation methods and aspects of stroke care was developed for guiding the interviews and clarifying potential variations in methods by healthcare system, together with a methodological guide. In addition, as accompanying material, forms defined “country overview” and “milestones” - designed to collect general information about the organization of stroke care in the respective country - were distributed. This provided a general framework of participating countries, reported in Table I in the online-only Data Supplement (please see http://stroke.ahajournals.org).
A pilot study was conducted to evaluate how the questionnaire worked, and what problems might be raised by respondents. Fourteen informants were interviewed, including health professionals, members of governmental organisations, scientific societies and stroke patients’ associations. The information obtained was discussed with the EIS collaborators, and the final version of the Questionnaire was released in February 2011 (online-only Data Supplement, please see http://stroke.ahajournals.org).

**Questionnaire administration and validation protocol**

After the pilot study, the questionnaire was administered through face-to-face interviews, performed by authors (A.D.C., F.R.P.) with experts in each country. A country coordinator was appointed from the EIS collaborators for each of the participating countries to identify respondents and collect all documents potentially useful to corroborate results. Respondents were asked to confirm questionnaire contents within four weeks of the interview, being allowed to change or add information if needed. In case of disagreement on single questions or parts of the questionnaire, a final decision was reached by consensus among respondents.

The content validity of the questionnaire was assessed by expert judgement, within the EIS Collaboration. The concurrent validity was assessed using the materials and documents delivered during the interviews, or independently collected by the coordinating team. Face-to-face interviews were conducted between March and July 2011, and involved researchers, health professionals, members of governmental organisations and regulatory bodies, members of scientific societies and stroke patients’ associations. In Spain, information on regional level is referred to the autonomous region of Catalonia. Catalonia has a Federal Government, a Federal Health Department and a specific stroke care organisation.

All interviews were conducted in English.

**Statistical analysis**

For each section of the questionnaire, data were categorized into three levels (low, medium,
high) using tertiles distribution. Similarities and differences among countries were evaluated using the Categorical Principal Components Analysis (CATPCA).\textsuperscript{12} This procedure simultaneously quantifies categorical variables, while reducing the dimensionality of the data into a smaller set of uncorrelated components retaining most of the information from original variables.

CATPCA finds the parameters of the Principal Component Analysis (PCA) model in an iterative process in which “Optimal Scaling” is incorporated. Optimal Scaling finds optimal quantifications for categorical variables, so that principal components account for a maximal percentage of variance of quantified variables.

CATPCA provides eigenvalues, component loadings, and object scores. Each principal component can be viewed as a composite variable summarizing the original variables. The first component is associated with the largest eigenvalue, and accounts for most of the variance, the second accounts for as much as possible of the remaining variance, and so on. The number of components, not correlated with each other, is kept small enough to make meaningful interpretations possible. Cronbach’s alpha is used as a measure of reliability.

Component loadings are a set of optimal weights, and are equal to a Pearson correlation between the principal component and a quantified variable. Object scores are the scores of the countries on the principal components obtained by CATPCA. Component loadings and object scores are obtained through an iterative process in which a least-squares loss function is minimized, reducing the loss of information due to representing the variables by a small number of components. Objects scores can be used to display the countries as points in the same space as the variables, revealing relationships between countries and variables. The objects scores, multiplied by the component loadings, approximate the original data as closely as possible. \textbf{The final objective is to summarize the data contained in numerous items, obtaining a “picture” that captures difference in countries performances at}
national and regional level, which may reflect the different level of implementation of stroke care. The joint plot of category points found by CATPCA can be inspected to see the location of the category points in relation to the other variables. If the countries are different for the aspects measured by the other variables, this is reflected in a considerable spread of the category points. The analysis was performed with the statistical software IBM SPSS (Statistical Package for the Social Sciences) for Windows, Version 20.0 (Armonk, NY: IBM Corp.).

Results

1. Implementation methods in EIS countries

Table 1 summarizes implementation methods used in EIS countries at national and regional levels, while detailed information by country and setting is reported in Tables II – XXXVIII in the online-only Data Supplement (please see http://stroke.ahajournals.org). Regulations having the force of law were present in just half of countries. Targeted processes included thrombolysis, networks of care, stroke units, prevention and care, quality certification and evaluation of performances. Non-mandatory policies were in place in almost all countries. At national level, more frequently targeted processes were prevention and care, guidelines and thrombolysis.

Public financial incentives were reported in the majority of countries, often as incentives to thrombolysis and stroke units implementation. Salary incentives were directed more often towards administrators than health professionals. Private financial incentives were reported only in two countries, mainly for educational purposes.

Among educational strategies, continuing professional education was mandatory in most countries. Printed or electronic educational materials were distributed in all countries, most often as guidelines. Material on counselling was only reported in half of countries.

Educational meetings and workshops were organised in all countries, aimed mainly at
primary prevention (primary care), or acute-phase management, guidelines, secondary prevention, and rehabilitation (hospital or specialist care). Educational outreach visits were reported in just two countries. Educational campaigns were reported in all countries. Major targets were risk factors, stroke as a medical emergency, and the need to call an ambulance. Guidelines for professionals were available in all countries, and were implemented using educational materials and meetings, opinion leaders’ actions, and interactive strategies. Audits were present in six countries at national level, and in eight at regional level. They focused mainly on referrals to stroke unit, acute and specialist care, compliance with guidelines, outcomes, and appropriate drug indications.

Electronic reminders were used at national level only in Scotland and England. Main targets were primary prevention and risk assessment, prescribing drugs, disease management, and secondary prevention.

The use of computerised decision support systems at both levels was limited to Scotland and England. Regional experiences were reported by Catalonia and Germany. Main targets were primary prevention, prescribing drugs and exams, administrative and clinical records, follow-up and secondary prevention, guidelines implementation.

Strategies involving opinion leaders were reported in all countries, and included educational campaigns, formal and informal education, distribution of educational material. Academics were those most acknowledged as opinion leaders in all countries, followed by health professionals, and celebrity stroke survivors.

Multiprofessional collaboration was quite diffuse, more in hospital and specialist settings than in primary care. Less frequently reported were pathways of care or protocols between general physicians and acute-phase care or rehabilitation services.

Multifaceted interventions on stroke care were in place in almost all countries, with different combinations of implementation strategies.
Stroke patients’ associations were widely represented, and acted mostly through campaigns aiming at increasing stroke awareness, but also to promote stroke units, rehabilitation, and secondary prevention. They also offered services for the often neglected psycho-social consequences of stroke, and, in some countries, provided advice, support and reablement of social inclusion. Less frequently stroke patients’ associations had a role in identifying priorities and designing research.

Performance indicators most frequently used were death during hospital period, brain imaging, stroke unit care, carotid vessels imaging, thrombolytic therapy, and anticoagulants in patients with atrial fibrillation.

2. CATPCA analysis. National & Regional levels

A 2-dimensional model explained 78% of the variance at national level, and 76% at regional level. The first principal component alone explained 55% of variance at both levels. This suggests that two principal components make the data interpretable with a reasonable approximation (Cronbach's alpha= 0.97 and 0.96, respectively). The models did not consider financial incentives, as all countries obtained a “low” score for this variable.

Table 2 shows that, on the first principal component, almost all variables had high (positive) component loadings. The second principal component was positively correlated mainly with reminders and computerised decision support systems (national and regional level), multifaceted interventions (national level), multiprofessional collaboration and performance indicators (regional level), while the correlation with audits (both levels), educational strategies and performance indicators (national level), and multifaceted interventions (regional level) was negative. Therefore, countries with high positive scores in the EIS variables will have a high value in the first principal component, while the value for the second principal component will be high or low depending on the direction and strength of the correlation.
Table 3 and Figures show object scores by country and a plot of countries by scores in the component analysis.

At the national level (Figure 1), the first principal component clearly separated England, France, Scotland, and Sweden, all with positive object scores, from the other countries, all with negative scores. England showed the highest positive values on the first principal component, due to the “high” scores obtained in all variables, especially in policy, where all other countries scored lower. Sweden and France had positive scores in the first principal component, and high negative values associated with the second principal component. This was explained by “high” scores obtained for educational strategies, audits, and performance indicators, negatively correlated with the second component. Scotland showed high positive value associated with the second principal component, due to the “medium” to “high” scores obtained in reminders, computerised decision support systems, and multifaceted interventions, variables with a strong and positive correlation with the second principal component.

Germany, Italy, Poland, and Spain had low scores in the first principal component, as “high” scores were obtained only in opinion leaders (Germany, Italy, and Poland), stroke patients’ associations (Italy), and multiprofessional collaboration (Spain). They were weakly correlated with variables characterizing the second principal component, positively (Italy), and negatively (Germany, Spain, and Poland).

Belgium and Lithuania obtained the lowest scores in the first principal component, and showed a weak positive correlation with the second principal component. This was confirmed by the lack of “high” scores in any of the considered variables.

At regional level (Figure 2), the first principal component clearly separated England, France, Germany, Italy, and Sweden, all with positive scores, from Belgium, Lithuania, Poland, and Scotland, all with negative scores. Spain was in an intermediate position, with score close to
zero. The first group obtained “high” scores for the variables policy (Italy), educational strategies (England, France, Italy, and Sweden), audits (France, Germany, Italy, and Sweden), computerised decision support systems (England), opinion leaders (England, France, Germany, and Italy), multiprofessional collaboration (England and France), multifaceted interventions (England, France, Germany, and Italy), stroke patients’ associations (England, France, and Italy), performance indicators (England, France, Italy, and Sweden).

As distribution was rather homogeneous, the second principal component characterized mainly countries with high or low object scores. Scotland scored from “medium” to “high” in variables showing the strongest positive association with the second principal component: reminders, computerised decision support systems, multiprofessional collaboration, and performance indicators. Conversely, Spain (Catalonia) obtained “high” scores in policy and multifaceted interventions, variables with a negative association with the second principal component, but also in multiprofessional collaboration, variable with a positive association, which reduced the negative value. Belgium and Lithuania showed “low” scores on almost all variables. In particular, they achieved “low” scores in multiprofessional collaboration and performance indicators, in which all the other countries obtained “medium” or “high” scores, explaining the high but negative correlation with the second principal component.

Discussion

We evaluated, with a newly developed questionnaire, implementation strategies in the field of stroke care in ten European countries, finding different levels and frameworks. Whether more effective implementation translates in better stroke services and outcomes is challenging, also because of difficulties arising when comparing quality measures across countries.⁹
England, Scotland and Sweden showed high levels of implementation. They all have long-lasting national programs monitoring stroke care: the Sentinel Stroke National Audit Programme,\textsuperscript{13} the Scottish Stroke Care Audit,\textsuperscript{14} and the Swedish Stroke Register (Riksstroke).\textsuperscript{15} In England, data referring to the period 2010-2014 indicate a significant increase, from 74\% to 90\%, of acute hospitals providing thrombolysis.\textsuperscript{13} After centralization, in 2010, of acute stroke services in Greater Manchester and in the metropolitan area of London, a significant reduction of hospital stay was observed in both areas, and of mortality in London.\textsuperscript{16} In Scotland, stroke care ‘bundles’ measure adherence to an evidence-based set of quality indicators. Between 2012 and 2013, patients receiving the appropriate bundle increased from 48\% to 58\%, and those admitted to a stroke unit within one day from 78\% to 82\%.\textsuperscript{14} Achieving a care bundle was associated with a significantly reduced mortality.\textsuperscript{17} In Sweden, 72 hospitals, all with dedicated stroke units, admit acute stroke patients. Thrombolysis is performed in 69. Continuous measurements of hospital performance and benchmarking indicate that survival and independence in daily living is similar for patients treated in university, specialized non-university, or community hospitals.\textsuperscript{15}

A National Stroke Plan was launched in France in 2010, focusing on prevention, educational campaigns, implementation of stroke units and stroke care networks.\textsuperscript{18} In 2010, about 20\% of French stroke patients were treated in 87 stroke units. The number of stroke units has increased to 120, but still less than 40\% of patients receive stroke unit care.\textsuperscript{19} In a study on barriers to effective implementation of stroke care, lack of resources was considered the chief obstacle, followed by coordination problems among facilities.\textsuperscript{20}

CATPCA analysis captured differences in countries performances at national or regional level, probably reflecting the different organization of healthcare systems. This was clear for
Germany and Italy, performing better at regional than national level. In Italy, the distribution of the stroke units and access to thrombolysis remain remarkably heterogeneous. Of 130 stroke units, 67% are located in Northern, 22% in Central and only 11% in Southern regions, which, however, include 34% of total Italian population. In a survey on adherence to quality process indicators, regional variability explained 25% of variance. The German Stroke Registers Study Group, including nine regional quality assurance projects, evaluated adherence to quality indicators in 2012. Relevant regional differences were found for intravenous thrombolysis, screening for dysphagia, and anticoagulation in patients with atrial fibrillation.

Spain also shows an unevenly distribution of stroke services, with a large concentration of stroke units and higher figures for thrombolysis in Madrid and Barcelona. The role of policy, multiprofessional collaboration, and multifaceted interventions is well evidenced in Catalonia, where a stroke code system has been operating since 2006, stroke care is provided by a network of Community Hospitals, Primary Stroke Centres and Comprehensive Stroke Centres, and where telestroke is effective between Community Hospitals and their respective Stroke Centres.

During the last decade, Poland witnessed a dynamic development of stroke services; stroke units increased from 105 to 150. A relevant role of opinion leaders was recognized, while current limits include unsatisfactory monitoring of services, scarce accessibility, in some areas, to comprehensive stroke centres, low numbers of thrombolysis and endovascular procedures. New policies and programs, organizational changes, education of medical staff and general population were proposed to improve stroke care.

Belgium and Lithuania reached low scores in our study. In Belgium, there is a large variability in the quality of stroke care. Stroke units exist, but without any formal
accreditation to assess compliance with official standards, although guidelines were developed in 2009. Numbers of hospitals providing thrombolysis, and its figures, are not reported. Identified limitations to an effective implementation include lack of knowledge of the benefits of stroke units, financial barriers, insufficient staffing, lack of protocols and of collaboration between professionals. Likewise, in Lithuania there is no formal requirement to have an organized stroke unit, or formal certification to provide stroke care. Compared with other European countries, Lithuania had higher incidence of stroke, higher prevalence of hypertension and atrial fibrillation, and a poor outcome after stroke. The adoption of more effective prevention strategies was recommended to reduce the stroke burden.

Some limitations of the study have to be acknowledged. Although our respondents were identified on their ability to evaluate stroke issues from a national/regional perspective, personal leadership, experience and knowledge of stroke policy, we cannot exclude different results from an alternative panel composition. Information collected is only a starting point, and the identification of missing measures and constructs, or incomplete information on existing measures is a challenge for future research.

Conclusions

In summary, we describe, for the first time in Europe, using a new dedicated questionnaire, strategies employed to translate research findings into practice in stroke care in ten countries. Both descriptive and CATPCA analyses found similarities and differences in frequency and type of implementation methods used, and our results seem to parallel development of stroke care in the real world. The new model we developed on assessing for the first time the different domains of stroke services and policies may be used elsewhere, as the relevance of implementation science in the field of stroke care become more apparent.
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Disclosure

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References


Figure 1. EIS countries’ score in Categorical Principal Components Analysis. National level.
Figure 2. EIS countries’ score in Categorical Principal Components Analysis. Regional level.
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</tr>
<tr>
<td>Performance indicators</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

CPE=Continuing professional education; na=not applicable; M=missing.
Table 2. Component loadings for different implementation methods in the field of stroke care at national and regional level. CATPCA analysis with two components.

<table>
<thead>
<tr>
<th>Implementation method</th>
<th>National level</th>
<th></th>
<th>Regional level</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Component 1</td>
<td>Component 2</td>
<td>Component 1</td>
<td>Component 2</td>
</tr>
<tr>
<td>Policy</td>
<td>0.883</td>
<td>0.022</td>
<td>0.897</td>
<td>-0.110</td>
</tr>
<tr>
<td>Educational strategies</td>
<td>0.752</td>
<td>-0.566</td>
<td>0.833</td>
<td>0.142</td>
</tr>
<tr>
<td>Audits</td>
<td>0.797</td>
<td>-0.531</td>
<td>0.776</td>
<td>-0.390</td>
</tr>
<tr>
<td>Reminders</td>
<td>0.756</td>
<td>0.641</td>
<td>-0.360</td>
<td>0.895</td>
</tr>
<tr>
<td>Computerised decision support systems</td>
<td>0.749</td>
<td>0.648</td>
<td>0.139</td>
<td>0.743</td>
</tr>
<tr>
<td>Opinion leaders</td>
<td>0.334</td>
<td>-0.247</td>
<td>0.714</td>
<td>-0.040</td>
</tr>
<tr>
<td>Multiprofessional collaboration</td>
<td>0.702</td>
<td>-0.330</td>
<td>0.780</td>
<td>0.469</td>
</tr>
<tr>
<td>Multifaceted interventions</td>
<td>0.759</td>
<td>0.639</td>
<td>0.834</td>
<td>-0.280</td>
</tr>
<tr>
<td>Stroke patients’ associations</td>
<td>0.724</td>
<td>0.177</td>
<td>0.892</td>
<td>-0.040</td>
</tr>
<tr>
<td>Performance indicators</td>
<td>0.808</td>
<td>-0.543</td>
<td>0.777</td>
<td>0.547</td>
</tr>
</tbody>
</table>
Table 3. Object scores for the 10 European countries at national and regional level. CATPCA analysis with two components.

<table>
<thead>
<tr>
<th>EIS country</th>
<th>National level</th>
<th>Regional level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Component 1 Object score</td>
<td>Component 2 Object score</td>
</tr>
<tr>
<td>England</td>
<td>2.283</td>
<td>0.431</td>
</tr>
<tr>
<td>France</td>
<td>0.828</td>
<td>-1.656</td>
</tr>
<tr>
<td>Scotland</td>
<td>0.714</td>
<td>2.162</td>
</tr>
<tr>
<td>Sweden</td>
<td>0.337</td>
<td>-1.371</td>
</tr>
<tr>
<td>Spain</td>
<td>-0.447</td>
<td>-0.268</td>
</tr>
<tr>
<td>Germany</td>
<td>-0.453</td>
<td>-0.095</td>
</tr>
<tr>
<td>Poland</td>
<td>-0.479</td>
<td>-0.256</td>
</tr>
<tr>
<td>Italy</td>
<td>-0.509</td>
<td>0.342</td>
</tr>
<tr>
<td>Lithuania</td>
<td>-1.128</td>
<td>0.372</td>
</tr>
<tr>
<td>Belgium</td>
<td>-1.145</td>
<td>0.339</td>
</tr>
</tbody>
</table>
Appendix

The European Implementation Score Collaboration Study Group Coinvestigators:

**Belgium**: Vincent Thijs, (Department of Neurology, University Hospitals Leuven, Belgium, Site Coordinator).

**England**: Charles DA Wolfe, (National Institute for Health Research Biomedical Research Centre at Guy's and St Thomas' NHS Foundation Trust and King's College, London, Principal Investigator); Chris McKevitt and Anthony Rudd (Division of Health and Social Care Research, King's College, London, Site Investigators); Annette Boaz, (Faculty of Health, Social Care and Education, St George’s, University of London and Kingston University, Site Investigator); Juan Baeza and Alec Fraser (Department of Management, School of Social Science and Public Policy, King’s College, London, Site Investigators).

**France**: Maurice Giroud and Yannick Bejot (Department of Neurology, University Hospital of Dijon, University of Burgundy, Site Coordinator and Site Investigator).

**Germany**: Peter Heuschmann and Silke Wiedmann (Institute of Clinical Epidemiology and Biometry, Comprehensive Heart Failure Center, Clinical Trial Center Würzburg, University of Würzburg, Site Coordinator and Site Investigator); Peter Hermanek (BAQ, Munich, Site Investigator); Markus Wagner (German Stroke Foundation, Gütersloh, Site Investigator).

**Italy**: Antonio Di Carlo and Marzia Baldereschi (Institute of Neuroscience, National Research Council, Florence, WP2 Coordinator and Site Investigator); Domenico Inzitari, MD (Department Neurofarba, Neurosciences Section, University of Florence, WP2 Leader, Site Coordinator); Francesca Bovis, Maria Lamassa, and Ilaria Romani (Department Neurofarba, Neurosciences Section, University of Florence, Site Investigators); Francesca Romana Pezzella (San Camillo-Forlanini Hospital, Rome, Site Investigator); Patrizia Nencini (Careggi University Hospital, Florence, Site Investigator).

**Lithuania**: Daiva Rastenyte (Institute of Cardiology, Kaunas University of Medicine, Site Coordinator).

**Poland**: Danuta Ryglewicz (1st Neurological Department, Institute of Psychiatry and Neurology, Warsaw, Site Coordinator); Anna Członkowska (2nd Neurological Department, Institute of Psychiatry and Neurology, Warsaw, Site Coordinator); Maciej Niewada (Dept. of Experimental and Clinical Pharmacology, Medical University of Warsaw, Site Investigator).

**Scotland**: Martin Dennis (Centre for Clinical Brain Sciences, University of Edinburgh, Site Coordinator).

**Spain**: Miquel Gallofré and Sonia Abilleira (Stroke Programme of Catalonia, Health Department of Catalonia, Barcelona, Site Coordinator and Site Investigator); Jaime Masjuan (Department of Neurology, Hospital Universitario Ramón y Cajal, Madrid, Site Investigator).

**Sweden**: Bo Norrving (Department of Clinical Neuroscience, Lund University, Site Coordinator); Kjell Asplund (Department of Public Health and Clinical Medicine, Umeå University, Site Investigator).