SITS International

Report 2018
Dear Reader,

SITS started as an internet based registry for intravenous thrombolysis already in 1996. In 2002 it was given a broader international role when European Union authorities requested that all patients treated with thrombolysis should be registered in SITS for a period of three years.

Today, over 230 000 patient files are included from more than 75 countries. 75 scientific reports have been published/accepted for publication in international peer-reviewed journals based on SITS data, and many abstracts have been presented at different stroke conferences. This year, several abstracts based on SITS data have been submitted for presentation at ESOC 2019 in Milan, Italy.

With endovascular thrombectomy and direct oral anticoagulants revolutionising stroke care in recent years, SITS has enabled registration of data from patients who have received these and other modern therapies. SITS had recently completed its first trial, SITS-OPEN using the same electronic case record forms but separated from the registry. The SITS-OPEN trial results are under preparation for publication.

This year SITS has launched a new data entry protocol for intracerebral and intraventricular haemorrhage. The SITS ICH-IVH Registry has a new layout and we hope the data entry process will be easier in this format. We invite all current SITS centres to actively participate in the new registry.

In recent years, we have received requests to reduce the number of variables in our data entry protocols. We have initiated a project to address this in the IV thrombolysis and thrombectomy protocols and plan to have the reduction implemented as soon as possible.

With this annual report we give an overview of the registry data, ongoing and planned activities, and a list of our publications. We take the opportunity to acknowledge the contributions of more than 320 authors involved in SITS publications. National, regional, and local coordinators, and users at participating centres are also acknowledged in this report. We thank our Scientific Committee members (previous and current) who oversee scientific activities within SITS and contribute their expert knowledge. We also pass on our thanks to all patients participating in the registry. Last but not least, we are grateful to our team members at the SITS Coordination Office who have been involved in the preparation of this report.

Kind regards,

Nils Wahlgren
SITS Chairman (1996-2018)

Niaz Ahmed
SITS Chairman (2019-)
SITS Scientific Committee Members

Prof. Nils Wahlgren, Sweden (Chairman, until January 2019)
Associate Prof. Niaz Ahmed, Sweden (Chairman, from February 2019)
Prof. Valeria Caso, Italy
Prof. Gary A. Ford, United Kingdom
Prof. Kennedy R. Lees, United Kingdom
Prof. Danilo Toni, Italy
Prof. Christine Roffe, United Kingdom
Prof. Adam Kobayashi
Prof. Gergios Tsivgoulis
Prof. Peter Ringleb, Germany

Previous members of the Scientific Committee

Prof. Antoni Davalos, Spain
Prof. Cesare Fieschi, Italy
Prof. Lawrence Ka Sing Wang, Hong Kong
Prof. Markku Kaste, Finland
Prof. Martin Grond, Germany
Prof. Michael Hennerici, Germany
Prof. Risto Roine, Finland
Associate Prof. Robert Mikulik, Czech Republic
Prof. Turgut Tatlisumak, Finland
Prof. Vincent Larrue, France
Prof. Werner Hacke, Germany

Current SITS Coordination Team Members

Assoc. Prof. Niaz Ahmed, MD, PhD, Chairman from February 2019
Prof. Nils Wahlgren, MD, PhD, FESO, Chairman until January 2019
Charlotte Lahnborg Alme, PhD, COO - Chief Operating Officer
Michael V. Mazya, MD, PhD, FESO, Network and Research Executive
Tiago Moreira, MD, PhD, Research Executive
Johan Lundberg, MSc, Project Leader for Registry Development
Isa Ek, Executive and Network Coordinator Assistant
Shayer Rizvi, MSc, User Services and IT Manager
Linda Ekström, Research nurse
Charith Cooray, MD, PhD, SITS researcher
Irene Escudero, MD, visiting researcher, Sevilla, Spain
Writing / working group of this report
Michael V. Mazya
Niaz Ahmed
Nils Wahlgren
Charlotte Lahnborg Alme
Isa Ek
Johan Lundberg
Shayer Rizvi
<table>
<thead>
<tr>
<th>Contents</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Background and purpose</td>
<td>6</td>
</tr>
<tr>
<td>Support and Funding</td>
<td>6</td>
</tr>
<tr>
<td>SITS Studies</td>
<td>7</td>
</tr>
<tr>
<td>SITS Registries / Data entry forms / Protocols</td>
<td>11</td>
</tr>
<tr>
<td>SITS World Map</td>
<td>13</td>
</tr>
<tr>
<td>Current countries in SITS</td>
<td>14</td>
</tr>
<tr>
<td>General SITS data overview</td>
<td>15</td>
</tr>
<tr>
<td>SITS Thrombolysis Registry</td>
<td>17</td>
</tr>
<tr>
<td>SITS Thrombectomy Registry</td>
<td>22</td>
</tr>
<tr>
<td>SITS General Stroke Registry</td>
<td>24</td>
</tr>
<tr>
<td>SITS-EAST</td>
<td>25</td>
</tr>
<tr>
<td>SIECV-SITS</td>
<td>26</td>
</tr>
<tr>
<td>SITS-MENA</td>
<td>27</td>
</tr>
<tr>
<td>SITS Award 2018</td>
<td>28</td>
</tr>
<tr>
<td>What is new in SITS – current and future</td>
<td>30</td>
</tr>
<tr>
<td>SITS Publications</td>
<td>32</td>
</tr>
<tr>
<td>Appendix</td>
<td>39</td>
</tr>
</tbody>
</table>
Background and purpose

SITS (Safe Implementation of Treatment in Stroke) is a non-profit, research-driven, independent, international collaboration. It is an initiative by the medical profession to assure excellence in acute treatment and secondary prevention of stroke, as well as to facilitate clinical trials.

SITS started in 1996 as an initiative by participants in the European-Australian randomised stroke thrombolysis studies (ECASS). In 2002, the European Medicines Agency (then EMEA, currently EMA) endorsed SITS as the registry for follow-up on thrombolysis treatment in acute ischemic stroke. SITS has since developed its services to enable follow-up of other evidence-based treatments in acute stroke such as thrombectomy, as well as secondary prevention.

The purpose of this report is to demonstrate how the registry has developed since 2002 with updated data since the previous report of 2017, and summarize how SITS has contributed to the body of knowledge on modern stroke treatment. The time span of the presented data is December 2002 – December 2018, illustrating the growth of SITS over 16 years. 75 scientific articles based on SITS data have been published/are accepted for publication in peer reviewed journals since 2002, with over 320 co-authors. This would not have been possible without the dedicated efforts of SITS national, regional, and local coordinators, as well as local users.

The SITS network is expanding. Almost 1200 stroke centres in more than 75 countries on five continents have contributed with data to the registry. This makes SITS one of the world’s largest stroke treatment databases and networks, with participation of many leading stroke experts.

Support and Funding

SITS is financed directly and indirectly by grants from Karolinska Institutet, Stockholm County Council, the Swedish Heart and Lung Foundation, the Swedish Order of St. John, Friends of Karolinska Institutet, and private donors, as well as from an unrestricted sponsorship from Boehringer-Ingelheim.

SITS has previously received grants from the European Union Framework 7, the European Union Public Health Authority and Ferrer Internacional.
SITS has recently completed studies supported by EVER Pharma, as well as in collaboration with Karolinska Institutet, supported by the Swedish Heart and Lung Foundation, Stryker, Covidien, Phenox, and Codman. SITS is currently conducting studies supported by Boehringer-Ingelheim.
SITS Studies
Completed Studies

SITS-MOST
An open, prospective, non-randomised observational study of safety and efficacy of treatment with intravenous rt-PA within 3 hours of onset of acute ischaemic stroke, based on the SITS International Stroke Thrombolysis Register. Performed in European Union countries.

SITS-NEW
An observational study of safety and efficacy of intravenous rt-PA within 3 hours of symptom onset in acute ischaemic stroke patients, according to the Summary of Product Characteristics (SPC) of the countries involved. Performed in India, People’s Republic of China, Singapore and South Korea.

SITS-UTMOST
A prospective, post-approval registry study of intravenous rt-PA (0.9 mg/kg) up to 4.5 hours after symptom onset in acute ischaemic stroke patients. The study has been completed and the main results were published in the European Stroke Journal in 2016.

SITS-OPEN
An international, multicentre, prospective, controlled, blinded evaluation study of safety and efficacy of thrombectomy in acute occlusive stroke. The SITS-OPEN trial results are under preparation for publication.

SITS TBY Study
A retrospective and prospective registry study of implementation of thrombectomy in routine clinical practice. The primary results were presented at ESOC 2018 and the manuscript is in its final stage for submission. Two main secondary result papers are also under preparation for submission.

Ongoing Studies / Projects

SITS AF Study 1
A retrospective and prospective study to identify the safest and most effective time point for initiation of oral anticoagulation (OAC) following ischaemic stroke of different severity in patients with atrial fibrillation.

SITS AF Study 2
A retrospective and prospective study to investigate the type, timing, safety and reasons for choice of acute interventions in patients taking direct OACs or warfarin prior to stroke onset. This study shall also evaluate the use of idarucizumab in patients on dabigatran suffering acute stroke.
Intracerebral Haemorrhage (ICH-IVH) Registry and Network
Intracerebral haemorrhage is the most devastating form of stroke, with 30-day mortality reaching 50% and half of the survivors suffering from severe disability. With emerging treatments, new diagnostic techniques and updated management guidelines for ICH, there is a need for a large international collaborative registry to enable better follow-up, care quality assurance, and research studies in this field. The SITS ICH-IVH Registry and Network will become a valuable tool for clinicians and researchers striving to improve outcomes in the most severely afflicted stroke patients. We will soon establish an executive committee for the SITS ICH-IVH Registry. Initial data collection will go on for 2 years before analysis for the first publication will be performed. Top recruiting centre coordinators will be invited to join as co-authors and all participating centres will be acknowledged as collaborators.

SITS IVT >80 years Study
A prospective, post-approval registry of intravenous rt-PA (0.9 mg/kg) in acute ischaemic stroke patients over 80 years within the SITS-ISTR Registry. Although IVT in patients >80 years has been used off-label in many countries, the use of IVT in patients >80 years will probably increase further after approval. The SITS-ISTR provides an instrument for continuous monitoring of thrombolysis treatment in stroke, and provides a technical platform for the SITS->80 years post-approval study. At least 1000 patients from approximately 60 European sites are planned to be registered in this prospective study.

SITS Fertile Woman Study
A retrospective and prospective study of intravenous rt-PA (0.9 mg/kg) given up to 4.5 hours after symptom onset in female acute ischaemic stroke patients, aged between 13 and 50 years, with particular focus on pregnancy and menstruation.

SITS Collaborative Project ESO-Angels
The European Stroke Organisation (ESO) is currently implementing a Europe-wide project aiming to stimulate high quality in stroke management by awarding excellent performance in key quality factors such as high proportion of ischaemic stroke patients undergoing reperfusion treatment, door-to-needle time, and proportion of patients treated in stroke units. Based on requests from numerous SITS users, we created the SITS-Quality Registry (SITS-QR) which can be used by SITS centers, including those participating in the ESO-Angels Award Program or the Angels Program outside ESO member countries.
Planned Projects

SITS-TEST
The SITS Tenecteplase in Ischemic Stroke Monitoring Study (SITS-TEST): In the SITS IVT registry, it is now possible to enter whether tenecteplase is used as IVT therapy in acute ischemic stroke. SITS is planning an observational study of safety and outcome of intravenous tenecteplase in acute stroke in routine clinical use.

SITS IVT Pediatric Study
Until recently, IVT with alteplase was not approved in patients with acute ischaemic stroke aged under 18 years. Based on observational data, regulatory authorities in several countries have now approved use of IVT with alteplase in patients 16-17 years, if other Summary of Product Criteria (SmPC) are fulfilled. SITS will perform a monitoring study of IVT in patients with acute ischaemic stroke aged 16-17 years. The study protocol and Swedish ethics committee application is under preparation. We will contact all SITS centers to participate in this study. We encourage interested centres to inform their paediatric department about the upcoming study.

SITS Seizure Study
A prospective study of seizures in acute stroke patients treated with intravenous rt-PA (0.9 mg/kg) up to 4.5 hours after symptom onset.

SITS IVT Wake-up Stroke Study
SITS has published one article on IVT in patients with unknown stroke symptom onset. However, the main weakness of the study was missing data on whether the unknown onset time was due to wake-up stroke, the last known well time being known, or truly unknown timepoints. Relevant variables have been added to the registry and data collection is ongoing. Top recruiting centre coordinators will be invited to join as co-authors.

SITS Low-dose IVT Study
In many Asian countries, 0.6 mg/kg bodyweight IVT thrombolysis is given instead of 0.9 mg/kg. Although the ENCHANTED trial did not show noninferiority of low-dose alteplase compared to standard-dose alteplase with respect to death and disability at 90 days, significantly fewer symptomatic intracerebral haemorrhages with low-dose alteplase occurred. SITS has now added the option to specify the alteplase dose and data collection is ongoing.

Data Completeness and High Quality Data Entry Project
SITS has started a pilot project to identify causes for incomplete data entry and ways to assist centres to complete and enter high quality data in the SITS registry. National and Local Coordinators will receive reports on data completeness at centers in their respective countries, in
order to inform initiatives for improvement. The SITS-EAST Coordination Committee has agreed to start the project in SITS-EAST centres as a pilot project. The project will later be extended to SITS on a global level.
SITS Registries / Data entry forms / Protocols

A range of SITS data entry forms allow centres to collect data on patients receiving treatments during the acute stroke phase, care quality parameters and long-term outcomes.

SITS protocols are electronic forms that are automatically enabled in the registry depending on the chosen acute phase intervention. SITS protocols can also be downloaded as Case Record Forms in PDF format on the SITS website.

Current Registries / Data entry forms / Protocols

Thrombolysis Registry (IVT data entry form) - suitable for all stroke patients treated with IV thrombolysis.
- **Intravenous Thrombolysis Protocol, standard version (IVTP-s)** - protocol for registering stroke patients treated with IV thrombolysis.
- **Intravenous Thrombolysis Protocol, minimal version (IVTP-m)** - protocol for registering all stroke patients treated with IV thrombolysis. The minimal version omits certain variables at various time points, making the protocol less extensive compared to IVTP-s.

General Stroke Registry (APP-S and APP-m data entry forms) - suitable for any stroke and TIA patients who have not received IV thrombolysis or thrombectomy or for centres which do not use the IV thrombolysis or thrombectomy registries.
- **All Patients Protocol, standard version (APP-s)** - protocol for registering stroke and TIA patients who have not been treated with IV thrombolysis or thrombectomy or for centres which do not use the IV thrombolysis or thrombectomy registries.
- **All Patients Protocol, minimal version (APP-m)** - protocol for registering stroke and TIA patients who have not been treated with IV thrombolysis or thrombectomy. The minimal version omits certain baseline and imaging variables, 2- and 24-hour follow-up.

Thrombectomy Registry (TBY or Bridge Protocol: IVT + TBY data entry form) - suitable for all stroke patients treated with thrombectomy.
- **Thrombectomy Protocol (TBYP)** - protocol for registering stroke patients treated with thrombectomy without prior treatment with IV thrombolysis.
- **Bridging Protocol: IVT + Thrombectomy** - protocol for registering patients who initially receive intravenous thrombolysis and are subsequently treated with thrombectomy.
Atrial Fibrillation and Oral Anticoagulation in Acute Stroke and TIA Registry - suitable for all patients admitted to hospital with an acute ischemic stroke or TIA, diagnosed with atrial fibrillation. The registry provides additional data entry options for details surrounding atrial fibrillation and the use of oral anticoagulation for secondary stroke prevention.

SITS Quality Registry (SITS-QR) – suitable for some SITS centres, which prefer a short and simple stroke care quality registry protocol completed in 5 minutes. Can be used by centres in western European countries participating in the ESO-Angels Award Program or the Angels Program outside ESO member countries.

SITS Intracerebral Haemorrhage Registry (SITS ICH-IVH) – suitable for all stroke patients suffering intracerebral haemorrhage and/or intraventricular haemorrhage. The layout and data entry form for the SITS ICH-IVH Registry is different than the traditional SITS registry data entry form. Our aim with the new layout is to simplify data entry.
SITS World Map
## Current countries in SITS

<table>
<thead>
<tr>
<th>Country</th>
<th>Country</th>
<th>Country</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albania</td>
<td>Estonia</td>
<td>Libya</td>
<td>Russian Federation</td>
</tr>
<tr>
<td>Algeria</td>
<td>Finland</td>
<td>Lithuania</td>
<td>Saudi Arabia</td>
</tr>
<tr>
<td>Argentina</td>
<td>France</td>
<td>Rep of Macedonia</td>
<td>Serbia*</td>
</tr>
<tr>
<td>Australia</td>
<td>Germany</td>
<td>Malta*</td>
<td>Singapore</td>
</tr>
<tr>
<td>Austria</td>
<td>Georgia*</td>
<td>Mexico</td>
<td>Slovakia</td>
</tr>
<tr>
<td>Belarus*</td>
<td>Greece</td>
<td>Rep of Moldova</td>
<td>Slovenia</td>
</tr>
<tr>
<td>Belgium</td>
<td>Guatemala</td>
<td>Morocco</td>
<td>Spain</td>
</tr>
<tr>
<td>Bolivia</td>
<td>Honduras</td>
<td>Netherlands</td>
<td>Sri Lanka</td>
</tr>
<tr>
<td>Bosnia and Herzegovina</td>
<td>Hong Kong</td>
<td>New Zealand</td>
<td>Sweden</td>
</tr>
<tr>
<td>Brazil</td>
<td>Hungary</td>
<td>Nicaragua</td>
<td>Switzerland</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>Iceland</td>
<td>Nigeria*</td>
<td>Thailand</td>
</tr>
<tr>
<td>Chile</td>
<td>India</td>
<td>Norway</td>
<td>Tunisia</td>
</tr>
<tr>
<td>China</td>
<td>Iran</td>
<td>Oman</td>
<td>Turkey</td>
</tr>
<tr>
<td>Colombia</td>
<td>Ireland</td>
<td>Pakistan*</td>
<td>Ukraine</td>
</tr>
<tr>
<td>Costa Rica</td>
<td>Israel</td>
<td>Panama</td>
<td>United Arab Emirates</td>
</tr>
<tr>
<td>Croatia</td>
<td>Italy</td>
<td>Paraguay</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>Japan</td>
<td>Peru</td>
<td>Uruguay</td>
</tr>
<tr>
<td>Denmark</td>
<td>Kazakhstan</td>
<td>Philippines</td>
<td>Venezuela</td>
</tr>
<tr>
<td>Dominican Rep</td>
<td>Rep of Korea</td>
<td>Poland</td>
<td>Vietnam</td>
</tr>
<tr>
<td>Ecuador</td>
<td>Kuwait*</td>
<td>Portugal</td>
<td></td>
</tr>
<tr>
<td>Egypt</td>
<td>Kyrgyzstan</td>
<td>Qatar</td>
<td></td>
</tr>
<tr>
<td>El Salvador</td>
<td>Lebanon</td>
<td>Romania</td>
<td></td>
</tr>
</tbody>
</table>

* Not yet recruiting patients
General SITS data overview

Data presented in this general overview is based on all patient files entered in the SITS registries between December 25, 2002 and December 31, 2018. Patient recruitment is calculated using files with both confirmed and unconfirmed data.

Figure 1. Cumulative patient recruitment in SITS

Table 1. Top 20 recruiting countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Patients</th>
<th>Country</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Italy</td>
<td>47453</td>
<td>Spain</td>
<td>4636</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>31601</td>
<td>Finland</td>
<td>4085</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>25680</td>
<td>Australia</td>
<td>4050</td>
</tr>
<tr>
<td>Sweden</td>
<td>10249</td>
<td>Russian Federation</td>
<td>3901</td>
</tr>
<tr>
<td>Germany</td>
<td>7233</td>
<td>Estonia</td>
<td>3782</td>
</tr>
<tr>
<td>Poland</td>
<td>6901</td>
<td>Egypt</td>
<td>3517</td>
</tr>
<tr>
<td>India</td>
<td>6451</td>
<td>Iran</td>
<td>3401</td>
</tr>
<tr>
<td>Belgium</td>
<td>6060</td>
<td>Tunisia</td>
<td>3189</td>
</tr>
<tr>
<td>Slovakia</td>
<td>5789</td>
<td>Lithuania</td>
<td>3071</td>
</tr>
<tr>
<td>Portugal</td>
<td>5139</td>
<td>Bulgaria</td>
<td>3036</td>
</tr>
</tbody>
</table>
Table 2. Number of patients registered using SITS data entry forms / protocols

<table>
<thead>
<tr>
<th>Country</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVT standard</td>
<td>159889</td>
</tr>
<tr>
<td>IVT minimal</td>
<td>6066</td>
</tr>
<tr>
<td>APP minimal</td>
<td>41773</td>
</tr>
<tr>
<td>APP standard</td>
<td>6307</td>
</tr>
<tr>
<td>Thrombectomy + IVT</td>
<td>4355</td>
</tr>
<tr>
<td>Thrombectomy</td>
<td>7634</td>
</tr>
</tbody>
</table>
SITS Thrombolysis Registry

Data based on all patient files entered between December 25, 2002 and December 31, 2018 using the standard and minimal SITS IV Thrombolysis protocols. Patient recruitment is calculated using files with both confirmed and unconfirmed data.

Figure 2. Cumulative and annual registration of patients using IV thrombolysis protocols
Figure 3. Change in median age per year during the last 12 years in patients with acute ischaemic stroke treated with IV thrombolysis

Figure 4. Change in median NIHSS score per year during the last 12 years in patients with acute ischaemic stroke treated with IV thrombolysis
Figure 5. Change in median time logistics in minutes in IV thrombolysis treated patients - Onset to Door (OTD), Onset to Treatment (OTT) and Door to Needle (DTN)

Outcome data

Intracerebral haemorrhage in patients treated with IV thrombolysis

Table 4. Proportions of patients with intracerebral haemorrhage

<table>
<thead>
<tr>
<th>ICH</th>
<th>Proportion</th>
<th>SICH</th>
<th>Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>HI1</td>
<td>4.5%</td>
<td>SITS-MOST</td>
<td>1.7%</td>
</tr>
<tr>
<td>HI2</td>
<td>3.1%</td>
<td>ECASS II</td>
<td>4.5%</td>
</tr>
<tr>
<td>PH1</td>
<td>2.6%</td>
<td>NINDS</td>
<td>6.3%</td>
</tr>
<tr>
<td>PH2</td>
<td>2.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHr1</td>
<td>1.9%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHr2</td>
<td>1.0%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In this table, we present the frequency of intracerebral haemorrhage (ICH) of various types, and of symptomatic intracerebral haemorrhage (SICH) by three definitions, in patients treated with IV thrombolysis.
ICH Definitions

Haemorrhagic infarction type 1 (HI1): small petechiae along the margins of the infarct.
Haemorrhagic infarction type 2 (HI2): confluent petechiae within the infarcted area without space-occupying effect.
Parenchymal haemorrhage type 1 (PH1): local, or intra-ischemic confluent hematoma in ≤ 30% of the infarcted area with at the most some slight space-occupying effect.
Parenchymal haemorrhage type 2 (PH2): local, or intra-ischemic confluent hematoma >30% of the infarcted area with a substantial space-occupying effect.
Remote parenchymal haemorrhage type 1 (PHr1): small to medium sized hematoma located remote from the infarct(s), with mild space occupying effect.
Remote parenchymal haemorrhage type 2 (PHr2): large confluent hematoma in an area remote from the actual infarct(s), with substantial space occupying effect.

SICH Definitions

SICH per SITS-MOST: Local or remote parenchymal haemorrhage type 2 on the 22-36 h post-treatment imaging scan, combined with a neurologic deterioration of 4 points or more compared to baseline NIHSS or the lowest NIHSS value between baseline and 24 h or death within 24 h. Type 2 indicates a hematoma exceeding 30% of the infarct, with substantial space-occupying effect.

SICH per ECASS II: Any haemorrhage with neurologic deterioration as indicated by an increase in NIHSS ≥4 compared to baseline or the lowest value within 7 days, or any haemorrhage leading to death.

SICH per NINDS: Any intracerebral haemorrhage on any post-treatment imaging scans combined with any decline in neurologic status as measured by NIHSS between baseline and 7d.
Figure 6. Outcome at 3 months in IV thrombolysis treated patients

Data show the distribution of patients on the modified Rankin Scale (mRS) as assessed at three months after the acute stroke.

Table 5. Outcome at 3 months in IV thrombolysis treated patients

<table>
<thead>
<tr>
<th>Outcome within 3 months</th>
<th>Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent outcome (mRS 0-1)</td>
<td>41%</td>
</tr>
<tr>
<td>Functional independence (mRS 0-2)</td>
<td>56%</td>
</tr>
<tr>
<td>Death</td>
<td>17%</td>
</tr>
</tbody>
</table>
SITS Thrombectomy Registry

Data based on all patient files entered between December 25, 2002 and December 31, 2018 using the SITS protocols for thrombectomy and bridging of thrombectomy with IV thrombolysis. Patient recruitment is calculated using files with both confirmed and unconfirmed data. Data collection using the thrombectomy protocols is ongoing and will be used in upcoming studies.

Figure 7. Annual registration of patients using thrombectomy protocols
Table 6. Patient recruitment by country, thrombectomy protocols

<table>
<thead>
<tr>
<th>Country</th>
<th>Patients</th>
<th>Country</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Czech Republic</td>
<td>3045</td>
<td>Germany</td>
<td>87</td>
</tr>
<tr>
<td>Italy</td>
<td>2300</td>
<td>Greece</td>
<td>47</td>
</tr>
<tr>
<td>Portugal</td>
<td>1000</td>
<td>United Arab Emirates</td>
<td>47</td>
</tr>
<tr>
<td>Slovakia</td>
<td>812</td>
<td>Norway</td>
<td>36</td>
</tr>
<tr>
<td>Finland</td>
<td>746</td>
<td>Thailand</td>
<td>28</td>
</tr>
<tr>
<td>Sweden</td>
<td>719</td>
<td>Hungary</td>
<td>21</td>
</tr>
<tr>
<td>Lithuania</td>
<td>650</td>
<td>Egypt</td>
<td>21</td>
</tr>
<tr>
<td>Spain</td>
<td>554</td>
<td>Slovenia</td>
<td>21</td>
</tr>
<tr>
<td>Belgium</td>
<td>501</td>
<td>Japan</td>
<td>18</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>462</td>
<td>Brazil</td>
<td>4</td>
</tr>
<tr>
<td>Estonia</td>
<td>414</td>
<td>Croatia</td>
<td>3</td>
</tr>
<tr>
<td>Poland</td>
<td>202</td>
<td>Morocco</td>
<td>2</td>
</tr>
<tr>
<td>Turkey</td>
<td>160</td>
<td>Australia</td>
<td>1</td>
</tr>
<tr>
<td>India</td>
<td>88</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
SITS General Stroke Registry

The SITS general registry is aimed at registering all stroke and TIA patients. Recruitment numbers presented are based on patient files with confirmed and unconfirmed data entered until December 31, 2018.

Figure 8. Cumulative and annual recruitment

Table 7. Top 30 recruiting countries, general stroke protocols

<table>
<thead>
<tr>
<th>Country</th>
<th>Patients</th>
<th>Country</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>5659</td>
<td>Argentina</td>
<td>1130</td>
</tr>
<tr>
<td>Tunisia</td>
<td>3187</td>
<td>Qatar</td>
<td>1128</td>
</tr>
<tr>
<td>Egypt</td>
<td>3074</td>
<td>Turkey</td>
<td>1079</td>
</tr>
<tr>
<td>Russian Federation</td>
<td>2966</td>
<td>Australia</td>
<td>1012</td>
</tr>
<tr>
<td>Italy</td>
<td>2537</td>
<td>Mexico</td>
<td>988</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>2428</td>
<td>Morocco</td>
<td>917</td>
</tr>
<tr>
<td>Peru</td>
<td>2283</td>
<td>Moldova, Republic of</td>
<td>759</td>
</tr>
<tr>
<td>Venezuela</td>
<td>2059</td>
<td>Sri Lanka</td>
<td>742</td>
</tr>
<tr>
<td>Iran</td>
<td>1884</td>
<td>Poland</td>
<td>708</td>
</tr>
<tr>
<td>Belgium</td>
<td>1644</td>
<td>Thailand</td>
<td>668</td>
</tr>
<tr>
<td>United Arab Emirates</td>
<td>1504</td>
<td>Slovakia</td>
<td>498</td>
</tr>
<tr>
<td>Brazil</td>
<td>1459</td>
<td>Czech Republic</td>
<td>497</td>
</tr>
<tr>
<td>Chile</td>
<td>1419</td>
<td>Dominican Republic</td>
<td>449</td>
</tr>
<tr>
<td>Sweden</td>
<td>1244</td>
<td>Ecuador</td>
<td>418</td>
</tr>
<tr>
<td>Kyrgyzstan</td>
<td>1241</td>
<td>Germany</td>
<td>393</td>
</tr>
</tbody>
</table>
SITS-EAST

SITS–EAST is a regional network in Central and Eastern Europe. It started as a study of implementation of evidence-based stroke therapy supported by the SITS International Registry. The registry was initiated in autumn 2007 with the support of a European Union grant. It is now an ongoing registry for the documentation and statistical evaluation of stroke management in Eastern Europe. During 2018, the SITS EAST Coordination Committee initiated the project of data completeness and high quality data entry. The Committee consists of Janika Körv – Estonia, Adam Kobayashi – Polen, Geogios Tsivgoulis – Greece and Zuzana Gdovinova – Slovakia.

Participating countries*:
Albania, Bulgaria, Croatia, Czech Republic, Estonia, Greece, Hungary, Kazakhstan, Kyrgyzstan, Lithuania, Macedonia, Moldova, Poland, Romania, Russian Federation, Slovakia, Slovenia, Turkey, Ukraine.
*See the Appendix for participating centres.

Figure 9. Annual recruitment, SITS-EAST – all protocols
Table 8. Number of patients registered using SITS protocols in SITS-EAST

<table>
<thead>
<tr>
<th>Data entry forms</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVT Protocols</td>
<td>52198</td>
</tr>
<tr>
<td>APP Protocols</td>
<td>10858</td>
</tr>
<tr>
<td>Thrombectomy Protocols</td>
<td>5375</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>68431</strong></td>
</tr>
</tbody>
</table>

SIECV-SITS

The SIECV-SITS registry was initiated through a joint venture by Sociedad Iberoamericana de Enfermedades Cerebrovasculares (SIECV) and SITS. The SIECV-SITS Stroke Registry is a database for documentation and statistical evaluation of stroke management in Central and Latin America. Recruitment numbers presented are based on patient files with confirmed and unconfirmed data, entered until December 31, 2018. Since 2018, Sheila Martins is appointed International Regional Coordinator for SIECV-SITS.

Participating countries*:
Argentina, Bolivia, Brazil, Chile, Colombia, Costa Rica, Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Uruguay, Venezuela.
*See the Appendix for participating centres.

Table 9. Number of patients registered using SITS protocols in SIECV-SITS

<table>
<thead>
<tr>
<th>Data entry forms</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>APP Protocols</td>
<td>10594</td>
</tr>
<tr>
<td>IVT Protocols</td>
<td>1118</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>11712</strong></td>
</tr>
</tbody>
</table>
SITS-MENA

The SITS-MENA Registry was initiated in 2013 as part of the SITS Regional Network in the Middle East and North Africa. Several countries and centres in the Regional Network are also participating in a prospective observational study of ischemic stroke in the region. Recruitment numbers presented are based on patient files with confirmed and unconfirmed data, entered until December 31, 2018. Since 2018, Suhail Alrukn functions as the International Regional Coordinator for the SITS MENA region and Foad Abd-Allah as the International Regional Coordinator for SITS Sub-Saharan Africa.

Participating countries*:
Algeria, Egypt, Iran, Lebanon, Libya, Morocco, Oman, Qatar, Saudi Arabia, Tunisia, United Arab Emirates
*See the Appendix for participating centres.

Figure 10. Cumulative and annual recruitment, SITS-MENA – all protocols
Table 10. Number of patients registered using SITS protocols in SITS-MENA

<table>
<thead>
<tr>
<th>Data entry forms</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>APP Protocols</td>
<td>11965</td>
</tr>
<tr>
<td>IVT Protocols</td>
<td>2921</td>
</tr>
<tr>
<td>Thrombectomy Protocols</td>
<td>70</td>
</tr>
<tr>
<td>Total</td>
<td>14956</td>
</tr>
</tbody>
</table>

SITS Award 2018

For the first time, SITS has awarded the top 20 centres fulfilling the highest standards of data collection into the SITS Registry over the last two years. The award is in keeping with our mission - to assure excellence in acute treatment and secondary prevention of stroke, as well as to facilitate clinical research. We invited the top centers in each category to receive their SITS 2018 award and diploma at the ESO-Karolinska Stroke Update Conference in Stockholm, November 11-13.

From the left: Niaz Ahmed (current SITS chair) and Nils Wahlgren (past SITS chair) handing out the SITS award to winners of the TBY protocol: Ana Paiva Nunes from Sao Jose Hospital in Portugal, Longest Time in the Registry: Jonathan Leempoel representing Andre Peeters from CHU St. Luc, Belgium (1st place, could not attend), IVT protocol (2 awards): Angela Welch from South Glasgow University Hospital, UK and Janika Körv, Tartu University Hospital, Estonia. Award winners for the APP protocol could not attend the meeting.
The following centres received a diploma as the 2018 top centre in SITS using the IVT/TBY/APP protocol / the SITS Registry for the longest time period:

**IVT protocol Award Winners**
1. South Glasgow University Hospital – UNITED KINGDOM
   LC: Azmil Abdul-Rahim & Angela Welch
2. Tartu University Hospital – ESTONIA
   LC: Janika Körv
3. Republican Vilnius University Hospital – LITHUANIA
   LC: Aleksandras Vilionskis
4. University Hospital of Heidelberg – GERMANY
   LC: Peter Ringleb
5. Krajska Nemocnice Liberec – CZECH REPUBLIC
   LC: Lubomir Jurak
6. Azienda Ospedaliera Universitaria di Modena – ITALY
   LC: Andrea Zini
7. FN u sv Anny v Brne – CZECH REPUBLIC
   LC: Lenka Kouřilová
8. Hamad General Hospital – QATAR
   LC: Naveed Akhtar

**TBY protocol Award Winners**
1. Hospital Sao Jose – PORTUGAL
   LC: Ana Paiva Nunes
2. FN Ostrava – CZECH REPUBLIC
   LC: Eva Hurtikova
3. Azienda Ospedaliera Universitaria di Modena – ITALY
   LC: Andrea Zini
4. North Estonia Medical Centre – ESTONIA
   LC: Viiu-Mariika Rand
5. CHU St. Luc – Woluwe – BELGIUM
   LC: Andre Peeters

**APP protocol Award Winners**
1. Naberezhnye Chelny BSMP Tatarstan – RUSSLAND
   LC: Shamil Musin
2. Hamad General Hospital – QATAR
   LC: Naveed Akhtar
3. Bishkek City Civil Clinic 1 – KYRGYSTAN
   LC: Inna Lutsenko

**Longest Time Period in SITS Registry**
1. University Hospital of Heidelberg – GERMANY
   LC: Peter Ringleb
2. CHU St. Luc – Woluwe – BELGIUM
   LC: Andre Peeters
What is new in SITS – current and future

The number of centres and countries participating in SITS has increased since 2018. Patient input to the registry has continued to reach all time high levels. We believe this is a strong indicator that SITS remains highly relevant for centres treating acute stroke patients worldwide.

SITS is increasingly focusing on data quality and completeness. In collaboration with SITS National Coordinators, we have started a pilot project with SITS-EAST countries and this work will continue in the future on a global level.

Since 2018, SITS has also started to award centres with top recruitment and a high level of data completeness. In November, at the ESO-KSU meeting in Stockholm, SITS presented the SITS award for the first time to top centers in several categories. We will continue to publish lists online every 6 months with top 50 SITS centers in each category. With this, we aim to stimulate recruitment and data quality in the SITS registry.

SITS implemented a thrombectomy registry in 2013 and a strong increase in patient recruitment was seen in both 2017 and 2018. The primary and main secondary results of the SITS thrombectomy registry are being analysed and will be submitted for publication during 2019. We encourage SITS centres to submit project proposals for further analysis of the thrombectomy dataset.

Additional new data entry options related to IV thrombolysis treatment appeared in April 2018. The option to record tenecteplase treatment in SITS thrombolysis data entry forms has been added. This does not constitute a recommendation of off-label use, but rather an emphasis on the importance of monitoring safety and outcomes if SITS centres choose to use tenecteplase for stroke treatment. Collection of sufficient amount of data will enable scientific comparison of tenecteplase with alteplase in a future study.

Recruitment from the SITS-MENA (Middle East and North Africa) network has seen strong progress. Selected centres from the SITS-MENA countries have participated in a two-year prospective observational study of demographics, risk factors and treatments in stroke patients. The results of the study have been accepted for publication in the International Journal of Stroke. A manuscript of a
prospective observational study of IV thrombolysis treatment in the region is currently in late stages of preparation.

A renewal of the SITS regional network in Latin America has recently been started, and we look forward to increased participation by new and old SITS centers. A manuscript describing the results of the first SIECV-SITS observational study has recently been submitted for peer-review and we hope for increased activity in the region following the publication.

In 2014, we developed a new online reporting tool for descriptive patient statistics. With this tool, SITS users can select and obtain pre-designed reports, where standard variables are already chosen, or create custom-made reports. The output can be downloaded either as raw data presented in an excel file structured on an individual patient level, or as a summary with calculated descriptive statistics.

SITS is currently working on reducing the amount of data entry in the SITS registry. A working group is set up for this purpose. Prof. Danilo Toni, the National Coordinator for Italy, is engaged in this project together with colleagues from Italy, to suggest removal of variables currently considered as low priority. The reduction of entry options in the case report forms will be implemented during 2019.

The SITS ICH-IVH Registry, a new data entry form with a new layout is planned to launch in May. We invite all SITS Local Coordinators to activate and try the ICH data entry form at their center.

Our intention with this report is to give the reader an update on SITS patient and centre recruitment status, as well as ongoing and planned activities since the publication of the first SITS International Report in 2014. We plan to publish the next report in spring 2020. We would be delighted to receive feedback on the current issue, as well as suggestions for future report contents. Any views and ideas on all matters concerning SITS are warmly welcomed by the International Coordinating Office.
SITS Publications

75. Charith Cooray, Michael Mazya, Robert Mikulik, Jurak Lubomir, Miroslav Brozman, Peter Ringleb, Anand Dixit, Danilo Toni, Niaz Ahmed. Safety and outcome of intravenous thrombolysis in acute ischaemic stroke patients on prophylactic doses of low-molecular-weight heparins at stroke onset. Stroke. Accepted for publication 7 March 2019


73. Marius Matusevicius, Maurizio Paciaroni, Valeria Caso, Matteo Bottai, Dheeraj Khurana, Mario de Bastos, Sheila Cristina Ouriques Martins, Yakup Krespi, Charith Cooray, Danilo Toni, Niaz Ahmed. Outcome after intravenous thrombolysis in patients with acute lacunar stroke, an observational study based on SITS international registry (Accepted for publication in International Journal of Stroke, January 2019)


anterior vessel occlusion-Results from SITS-ISTR. (Stroke, In press December 2016)


36. Kharitonova TV, Castillo J, Wahlgren N; SITS investigators. Importance of


Appendix

List with centres contributing with data to the SITS Registry between December 25, 2002 and December 31, 2018.