Topical Review

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New Strategy to Reduce the Global Burden of Stroke

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Increasing Global Stroke Burden

The socioeconomic and health effect of stroke and other non-communicable disorders (NCDs) that share many of the same risk factors with stroke, such as heart attack, dementia, and diabetes mellitus, is huge and increasing. Collectively, NCDs account for 34.5 million deaths (66% of deaths from all causes) and 1344 million disability-adjusted life years lost worldwide in 2010. The burden of NCDs is likely to burgeon given the aging of the world’s population and the epidemiological transition currently observed in many low- to middle-income countries (LMICs). In addition, there is low awareness in the population about these NCDs and their risk factors, particularly in LMICs. These factors, coupled with underuse of strategies for primary prevention of stroke/NCDs on an individual level and the lack of accurate data on the prevalence and effect of risk factors in different countries and populations have been implicated in the ever-increasing worldwide burden of the NCDs. Of particular concern is a significant increase in the number of young adults (aged <65 years) affected by stroke, and diabetes mellitus worldwide. If these trends continue, the burden of stroke and other major NCDs will increase even faster. The increasing burden of stroke and other major NCDs provide strong support for the notion that the currently used primary prevention strategies for stroke and other major NCDs (business as usual) are not sufficiently effective. The most pertinent solution to this problem is the implementation of new, effective, widely available, and cost-effective prevention and treatment strategies to reduce the incidence and severity distribution of stroke and other major NCDs.

Issues With Population-Wide Prevention Strategies

The recent INTERSTROKE case-control study, conducted in 22 countries worldwide, provided evidence that, collectively, 10 risk factors accounted for 88.1% (99% confidence interval, 82.3%-92.2%) of the population-attributable risk for all stroke. Because many (but not all) of these risk factors are modifiable, the INTERSTROKE data suggest that interventions that reduce blood pressure, promote physical activity, smoking cessation, and a healthy diet, could substantially reduce the burden of stroke. Although a combination of population-wide and individual high-risk prevention strategies were initially advocated >30 years ago, and have since been repeatedly recommended as the most promising strategies to reduce stroke and NCDs burden, there is still no country in the world where both these prevention strategies have been implemented in full. There are major hurdles to implementing population-wide primary prevention strategies, including the need for policy and legislative changes that are often not supported by major industries (such as salt reduction in processed food, reduction of exposure to cigarette smoking, alcohol, and fast food). In addition, there are significant costs associated with the implementation of some of these strategies (eg, availability and accessibility of facilities for sport and physical activity, healthy food outlets). However, there are some regions (eg, North Karelia, Finland; Franklin County, USA; and Japan) where implementation of some elements of these preventative strategies have proven highly effective at the community level.

Global Burden of Risk Factors for Stroke

The Global Burden of Diseases 2010 studies found that the 3 leading risk factors for disease burden were high blood pressure, tobacco smoking (including second-hand smoke), and alcohol use. Moreover, these 3 risk factors were ranked in the top 3 for several low- to middle-income regions, including Central and Eastern Europe, Southern Latin America, and Central Asia. In addition, lifestyle factors, such as high sodium, low fruit diets, and physical inactivity contributed to 10% of disability-adjusted life years in 2010. These risk factors, along with the nonmodifiable factors of age, sex, and ethnicity, contribute significantly to stroke incidence. A national survey estimated the prevalence of high blood pressure in China to be 29.6%, whereas a systematic review estimated the overall prevalence in India at 29.8%. High blood pressure is the most potent risk factor for stroke and the current and rising prevalence rates of this risk factor alone will contribute significantly to stroke burden globally. Given that nearly 70% incident stroke occur in LMICs, health policies to reduce the prevalence of these risk factors is crucial.

Issues With High-Risk Prevention Strategies

High-risk prevention strategies are currently based on the identification and management of subjects with high absolute risk...
of acute cardiovascular disease (CVD) occurrence, such as in those with heart attack, stroke, and acute peripheral artery disease.27–29 This high absolute risk of CVD is usually defined as a risk of ≥15% during the next 5 years.27 This approach is valid and suitable for selecting people at high risk of acute CVD and for monitoring their progress in CVD prevention in the outpatient setting. However, in terms of effective primary stroke/ CVD prevention, there are several issues with this approach. First and foremost, although there are well-recognized management strategies for prevention of stroke, transient ischemic attack, and other NCDs,30 these strategies are primarily targeted at high-risk individuals that represent a small proportion of those who will go on to have a stroke.31,32 Given that the majority of strokes in the population occur in those with mildly elevated stroke risk, population-wide reduction strategies aimed at all levels of stroke risk would improve the effectiveness of these campaigns. In addition, clinical experience shows that an unintended consequence of risk assessment is that people who are told by a doctor they are at low (<5%) and moderate (5% to 14%) 5-year risk of CVD occurrence are not motivated enough to do anything to control their risk factors because they think they are not at high risk of CVD. Second, calculation of absolute risk based on most CVD prediction algorithms used, often requires additional laboratory tests (eg, for determination of the level of blood cholesterol or glucose). Determining the risk of stroke/CVD also usually requires a visit to a health professional or an outpatient clinic. The time and costs associated with these arrangements may be a deterrent for many individuals, particularly those who are socioeconomically disadvantaged or live in remote rural communities. Third, even in high-income countries, the use of high-risk CVD prevention strategies by medical professionals is poor27 as is the adherence of patients to the recommended medications and lifestyle for primary and secondary CVD prevention.33 Fourth, the tools that are commonly used to predict the risk of stroke/CVD34,35 are not easily accessible in multiple languages, not aimed at younger age groups (<55 years), do not account for racial/ethnic and geographical differences, or are designed for use by health professionals only. Therefore, people who do not fall into the high-risk category will not usually have access to this information, and are consequently unable to take the remedial steps necessary to minimize their likelihood of having a stroke in the future. Finally, CVD prediction algorithms used for calculating the risk are usually based on the Framingham Study34,36 and have several major limitations.37 The Framingham Study was based on a selective group of primarily white Americans aged >55 years and, therefore, the Framingham algorithm for CVD prediction may not be applicable to all populations. In addition, many risk factors recently demonstrated to be important for CVD occurrence (eg, diet, physical activity, overweight, race/ethnicity, etc.) were not included in the Framingham Study CVD prediction algorithm. These limitations have resulted in the American Heart Association and the American College of Cardiology in 2013 no longer recommending the use of the Framingham Study algorithm for individual risk prediction of coronary heart disease in the United States.38 However, the American Heart Association/ American Stroke Association still recommends the use of the Framingham stroke prediction algorithm as a risk-assessment tool for primary stroke prevention.30

**Gaps in Knowledge**

Reliable data on the frequency, distribution and determinants of stroke, and other major NCDs in most countries of the world are lacking.3,16,36 although modeling performed for the Global Burden of Disease project has provided estimates for some.3,16,17,24,38 This information is crucial for developing global and country-specific and culturally tailored evidence-based recommendations on the prevention and care of stroke and other major NCDs. In addition, although compelling evidence exists that increasing population/country-specific knowledge about stroke warning signs and risk factors can reduce stroke burden in the population,40–42 the uptake of this knowledge is poor in most countries. This poor uptake of knowledge is particularly the case in older adults (65+),7 minority ethnic groups,8–11 people with poor educational attainment,12 and rural dwellers.46 The lack of epidemiological data on stroke and other NCDs in most countries is chiefly because of the high costs associated with conducting conventional, ideal population-based studies on NCDs incidence, prevalence, and risk factors because they usually require coverage of the large study populations/areas, face-to-face contacts with study participants or postal/telephone interviews. In addition, there is often a lack of local expertise and experience to properly design and conduct such studies.

**New and Promising Strategy for Primary Stroke Prevention**

Recent advances in smartphone technologies, including high processing power, storage, constant internet connection, personalized notification methods, growing worldwide uptake, and proximity to the users, offer unique opportunities to use these technologies for improving health and enhancing research capabilities. Importantly, easily accessible and cost-effective risk-estimation systems are well suited to the developing world and other regions where access to medical facilities is limited.37 including elderly populations where smartphones are being increasingly used.47–49 A recent systematic review50 showed that mobile phone-based technology in LMICs positively affects the chronic disease management and their clinical outcomes.

There are numerous stroke and other NCDs smartphone applications (apps) currently available in the Apple Store and Google Play. There are also several smartphone-based technologies and apps that were, or are, being used in clinical trials for managing particular medical conditions and risk factors (eg, smoking cessation, depression, weight, and asthma management),51–54 with promising results. Despite this, few apps are based on evidence-based prediction algorithms, and even fewer have sufficient validity to be used for research data collection. As far as we are aware, there is no app designed to provide not only educational information but also to collect valid data to measure and reduce the burden of NCDs worldwide. In recognition of the importance of e-research NCDs initiatives, the United Nations Economic and Social Council, the International Telecommunication Union, and the World Health Organization in June 2013 launched a new mHealth initiative for improving NCDs prevention, treatment, and policy enforcement.55
To inform and support these United Nations/International Telecommunication Union/World Health Organization efforts (including World Health Organization Global NCD Action Plan for 2013–2020), to increase general awareness about stroke and its risk factors, and to improve stroke and heart attack prevention on an individual level, the National Institute for Stroke and Applied Neurosciences, The Faculty of Health and Environmental Sciences, Auckland University of Technology (AUT) in collaboration with AUT Enterprises Ltd of AUT University and The NZ Stroke Education (charitable) Trust recently developed an app called the Stroke Riskometer App (Figure 1). The Stroke Riskometer App calculates the 5-year and 10-year risk of stroke for any individual aged ≥20 years, based on their responses to a short questionnaire. Full details of the app have been described in detail elsewhere and are briefly described in Table I in the online-only Data Supplement.

The majority of these additional risk factors were identified as being important predictors of stroke by the INTERSTROKE investigators, and serve to strengthen the accuracy and reliability of the prediction algorithm used in the app. The Stroke Riskometer algorithm has been validated and found to be comparable with the Framingham and QSTROKE stroke risk prevention algorithms commonly used in medical practice. Notably, as well as absolute risk, the app also provides users with their relative risk of having a stroke compared with someone of the same age and sex who does not have any risk factors at all. We think this is a significant additional preventative strategy because it may draw the attention of those with a relatively low absolute risk to their nevertheless increased relative risk, thereby motivating them to control their risk factors. This approach has been recognized as a new paradigm in primary stroke prevention.

The app has a section to educate people about stroke warning symptoms and signs and what to do if any of these symptoms/signs occur. This section uses the face, arm, speech, time message, a strategy shown to be effective in reducing the time to hospitalization. In addition, users have an option to e-mail their stroke risk assessment results to a person of their choice and they also have an option of sharing their experience of the app.

Figure 1. Example of screenshots of Stroke Riskometer App. F.A.S.T. indicates face, arm, speech, time. Images from Stroke Riskometer Lite and Pro with permission from AUT Enterprises Limited.
using the app via social media. Preliminary evidence suggests that the app is appealing to individuals concerned because it empowers them to know and self-manage their risk and risk factors. Regular and wide use of this app could be as efficient as the conventional population-based approach because it allows identification and engagement in prevention of all individuals who are at even slightly increased risk of stroke and CVD. We also encourage health professionals to use the app in their everyday practice.

There are 2 versions of the Stroke Riskometer App, Lite and Pro. Stroke Riskometer Lite version has been endorsed by the World Stroke Organization. The World Federation of Neurology and the International Association of Neurology and Epidemiology have endorsed both versions of the Stroke Riskometer App. The smartphone-based platform means that the potential reach of this app is enormous. With ≈1.75 billion people in the world owning smartphones,59 people across the globe will have easy access to their stroke risk and risk factors in their own language. Prediction of stroke risk can also be performed for family members, such as parents (who may not own a Smartphone), using one device. To be accessible to as many people as possible, the Stroke Riskometer App is being translated into 11 most commonly spoken languages (Mandarin, Hindi, Spanish, Russian, Arabic, Bengali, Portuguese, Malay, French, German, and Japanese; Table II in the online-only Data Supplement lists the editors of the translated versions) covering >160 countries (≈5.6 billion people).

New Promising Approach to Epidemiological Research of NCDs

We think that the Stroke Riskometer App represents an important tool in spreading awareness about stroke, its risk factors and how to tackle them, and, if leveraged correctly, could also represent a significant breakthrough as a method of conducting epidemiological research in NCDs internationally. The mobile app-based platform provides a cost-effective means to collect data from potential study participants on a global scale that is not possible with conventional (and costly) prospective population-based research methods. The latest update to the Stroke Riskometer App includes a research section that allows users to participate in a cross-sectional study followed by a longitudinal cohort study (initially >12 months, and with the potential to extend follow-up during a longer timeframe). The study will be conducted in 5 phases as outlined in Table.

Table. Phases of the Reducing the International Burden of Stroke Using Mobile Technology Study

<table>
<thead>
<tr>
<th>Phase Year</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>2015–2016</td>
<td>To evaluate the prevalence of stroke, heart attack, type 2 diabetes mellitus, traumatic brain injury, and dementia and their risk factors in different countries and demographic groups worldwide</td>
</tr>
<tr>
<td>2016–2017</td>
<td>To determine an etiologic role of lifestyle, environmental, sociodemographic, and pathophysiological factors in the occurrence of stroke, heart attack, type 2 diabetes mellitus, and dementia, with an emphasis on modifiable risk factors, with assessments initially conducted at 12 mo follow-up</td>
</tr>
<tr>
<td>2018</td>
<td>To develop specific algorithms (and associated Apps) for prediction of stroke, heart attack, type 2 diabetes mellitus, and dementia for specific countries/populations</td>
</tr>
<tr>
<td>2019–2024</td>
<td>To develop and test an randomized controlled trial setting culturally appropriate smartphone-based interventions (namely cognitive-behavioural) for primary prevention of stroke, heart attack, type 2 diabetes mellitus, and dementia</td>
</tr>
<tr>
<td>2025</td>
<td>To update/Improve country-specific Apps for primary NCDs prevention</td>
</tr>
</tbody>
</table>

NCD indicates noncommunicable disorder.

The Stroke Riskometer is also available in a Website format to offer the users many options to access and use the assessment tool and participate in the research study. The Website is also available commercially to governments and other organizations, such as hospitals, health and wellness clinics, and stroke foundations internationally, to allow integration of the assessment into their daily practice. The Auckland University of Technology Ethics Committee has approved the RIBURST study (reference number 14/201).

We also plan to use our findings for individual risk prediction (using the spiking neural network approach) of stroke, and other NCDs.64 Promoting participation in the Stroke Riskometer–based studies will have at least 2 major benefits. First, it could provide unprecedented patient-generated evidence about the frequency, prevalence and determinants of stroke, heart attack, dementia, and diabetes mellitus, in various countries and populations worldwide. This will serve to fill the gap in knowledge about these NCDs in many countries of the world, especially in LMIC. Second, it will allow the research team to evaluate the accuracy of the algorithm, and the research data collected will facilitate further fine-tuning to improve the prediction formula for stroke, as well as for heart attack, dementia, and diabetes mellitus. On the basis of this information, future versions of the app will have greater accuracy in calculating the risk of stroke and other major NCDs, such as for specific countries/regions and ethnic/racial groups. One additional outcome of such studies could be an improvement in the overall management of stroke risk factors by practicing health professionals and in the time to achieve management goals. In addition, the intention is to share information collected from different countries with local and regional collaborators to contribute to suitable action plans to tackle the burden of NCDs in their country/regions. We also intend to work with regional collaborators to analyze and disseminate local and regional findings to assist with tackling the significant cost and burden associated with stroke and other major NCDs. To ensure participant privacy, all data will be
stored on secure, encrypted servers. In addition, identifying details (such as names and e-mail addresses) will be stored in a separate database from the survey results (linked by a randomly generated unique identifier). All participants will have to consent to participating in the RIBURST study before any personal data are collected and stored by the researchers. For users not participating in the study, results may be saved locally on their devices, but there is no identifiable information stored within the app in these scenarios.

There are several potential limitations of the RIBURST study. One potential limitation is the question of the validity and accuracy of the recall-based responses, which is an important consideration in all self-reported research. To ensure the data collected for this research project is accurate, validation studies are planned where a random subset of participants across several countries will be approached for permission to cross-reference submitted responses with medical records. For consenting study participants in those countries, self-reported information on risk factors, health conditions, and NCDs outcomes (new NCDs events) for accuracy will be cross-checked with relevant information from the local national databases, general practitioner records or proven reliable household surveys\(^2\) for validation (subject to additional ethics approvals from participating countries). A representation of the sample demographic characteristics to the country concerned will be ascertained, and only data from reasonably representative samples will be included in the analysis. We also acknowledge that our app, as any other app, has limitations that may limit its use in certain individuals (eg, people with severe disabilities, dementia, or visual deficit). However, our intention was to develop an app that could be used by the majority of the population, including people in LMICs.

This will allow generalization of the validated data to the whole population across various countries. Other limitations include the limited access to smartphones of the most socioeconomically disadvantaged groups and people with disabilities who may have difficulties using the app (including those who became disabled during the study), stopped using the app or died during the study. However, smartphones have become less expensive and thus more accessible to some socioeconomically disadvantaged groups.

Quality control measures and statistical modeling techniques are being developed to minimize selection bias and impute missing follow-up information. For example, study participants are encouraged to provide an alternative contact person’s e-mail address and if the study participant is not contactable or cannot complete the follow-up questionnaires for various reasons their alternative contact individual will be contacted and asked to complete the questionnaire for the study participant.

In summary, stroke and other major NCDs continue to be one of the most important health concerns on a global scale. Current prevention and intervention techniques are not effective enough in targeting individuals at low or moderate risk of stroke, these being the groups in whom the majority of strokes occur. New effective and affordable primary prevention strategies to reduce the burden of stroke and other major NCDs are urgently needed on a global scale. The Stroke Riskometer App uses the rapidly growing smartphone platform to provide individualized stroke risk assessments. It will be used to inform and educate a significant proportion of the global population about their risk of stroke and how to reduce it, and is likely to contribute to reducing the burden of stroke and other NCDs worldwide.

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**Figure 2.** Map showing countries covered by the Reducing the International Burden of Stroke Using Mobile Technology Study (Remain to be Finalized).
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Disclosures

Coauthors from the Auckland University of Technology (R. Bhattacharjee, P. Parmar, T. Hussein, M. Purohit, Drs Feigin, Krishnamurthi, Theadom, Hume, Abbott, Rush, Kasabov, Crezze, and Friellieck) declare that funds resulting from the sale of the professional version of the Stroke Riskometer App will be used for further research and education for stroke prevention. Dr Theadom, as a coinvestigator of incidence of stroke study in New Zealand, has received a research grant from Health Research Council. Dr Wang has received funding from the Wellington Trust. Dr Saposnik has received a grant from the Heart and Stroke Foundation of Canada and is supported by the Distinguished clinician Scientific Award. Dr Mensah has received funding for research from the National Institutes of Health. Dr Hankey received honoraria from Bayer, Medscape, and the heart.org for his involvement in their symposia/educational program. The other authors report no conflicts.

References


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RIBURST Study Collaboration Writing Group

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### Supplemental Table I. Summary of Stroke Riskometer App content

<table>
<thead>
<tr>
<th>App sections and components</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Assess</strong></td>
<td>This is the main assessment section of the app. Users complete questions about age, sex, ethnicity, blood pressure, waist/hip circumference, medical history, medication and lifestyle factors. They are then provided with their 5 and 10 year risk of stroke (absolute risk and relative risk compared to people their age and sex with no risk factors). The Manage component of this section provides users with a list of their risk factors, and in the Pro version they are provided explanations about these factors and how to minimise their impact. Pro users and study participants can also save and track their results in this section.</td>
</tr>
<tr>
<td><strong>Research</strong></td>
<td>The Research section contains the information about the RIBURST study. The Participant information sheet and consent form are contained in this section and users need to register/log-in to submit information from here.</td>
</tr>
<tr>
<td><strong>Video</strong></td>
<td>Users of the Lite version can see a video about the Stroke Riskometer and how to use it from this section. Pro users also have access to informational videos about what a stroke is, what causes stroke, smoking and diet.</td>
</tr>
<tr>
<td><strong>F.A.S.T.</strong></td>
<td>This section informs users about how to easily detect the signs and symptoms of stroke, and what to do if they need to take action.</td>
</tr>
<tr>
<td><strong>About</strong></td>
<td>This section gives users more information about how to use the app, more information about the app and acknowledges the team involved with the development of the app.</td>
</tr>
</tbody>
</table>

### Supplemental Table II. Editors and countries of non-English versions of the Stroke Riskometer™ App

<table>
<thead>
<tr>
<th>Language</th>
<th>Name and affiliations of Editors of the translated Apps</th>
<th>Country or countries where this language is official or national</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mandarin</td>
<td>Prof. Hua Fu, Fudan University, Shanghai; Prof. Wenzhi Wang, Beijing Neurosurgical Institute, Beijing; People’s Republic of China</td>
<td>China, Singapore, Taiwan</td>
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<tr>
<td>Hindi</td>
<td>Prof. Man Mohan Mehndiratta, Janakpuri Super Speciality Hospital, New Delhi; Prof. Jeyaraj Durai Pandian, Christian Medical College, Ludhiana, Punjab; Dr Sanjeev Gupta, Banarsidas Chandiwala Institute of Physiotherapy, Kalkaji, New Delhi; Dr Vasantha Padma, AIIMS New Delhi, India</td>
<td>Fiji, India, Nepal</td>
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<td>Spanish</td>
<td>Assoc. Prof. Gustavo Saposnik, University of Toronto, Canada</td>
<td>CARIBBEAN: Cuba, Dominican Republic, Puerto Rico, CENTRAL AFRICA: Equatorial Guinea, CENTRAL AMERICA: Colombia, Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama, EUROPE: Spain, NORTH AMERICA: Mexico, SOUTH AMERICA: Argentina, Bolivia, Chile, Ecuador, Paraguay, Peru, Uruguay, Venezuela</td>
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<td>Russian</td>
<td>Prof. Michael Piradov, Prof. Yuri Varakin and Dr Michael Kravchenko, Research Center of Neurology, Moscow, Russia</td>
<td>Abkhazia, Belarus, Kazakhstan, Kyrgyzstan, Moldavia, Russia, South Ossetia, Tajikistan, Ukraine</td>
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<td>Language</td>
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<td>Arabic</td>
<td>Prof. Mohammed Saadah, University of Emirates, United Arab Emirates</td>
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<td>Bengali</td>
<td>Prof. D.K. Mandal, Founder President of Stroke Foundation of Bengal; Dr. A. Shobhanna, Secretary of Stroke Foundation of Bengal and Consultant in Stroke &amp; Critical Care Medicine at the Institute of Neurosciences, Kolkata</td>
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<td>Portuguese</td>
<td>Prof. António Freire Gonçalves, Centro Hospitalar e Universitário de Coimbra, Praceta; Prof. Mota Pinto, 3000-075 Coimbra; Prof. Manuel Correia, Hospital de Santo António, Largo Prof. Abel Salazar, Porto; Dr. Teresa Pinho e Melo, Hospital de Santa Maria, Av. Prof. Egas Moniz, 1169-024 Lisboa, Portugal</td>
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<tr>
<td>Brazilian</td>
<td>Prof. Norberto Cabral, Joinville Stroke Registry, University of Joinville Region; Dr Sheila C.O. Martins, Brazilian Ministry of Health Advisor, Hospital de Clínicas de Porto Alegre, Hospital Moinhos de Vento; Prof. Luis E. T. A. Furtado, Universidade Federal do Ceará, Sobral, Brazil</td>
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<td>Malay</td>
<td>Prof Datin Dr Norlinah Mohamed Ibrahim, Dr Ramesh Sahathevan and Dr Wan Nur Nafisah Wan Yahya, UKM Medical Center, Kuala Lumpur, Malaysia</td>
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<td>French</td>
<td>Prof. Maurice Giroud, University Hospital of Dijon, and University of Burgundy; Dr Yannick Béjot and Prof. Yves Cottin, University of Burgundy, Dijon, France</td>
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<td>German</td>
<td>Prof. Werner Hacke, Ruprecht Karl University Heidelberg, Germany; Prof. Michael Brains, Danube University Krems, Vienna, Austria</td>
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<td>Japanese</td>
<td>Chief Doctor Yoshihiro Kokubo, National Cerebral and Cardiovascular Center, Osaka, Japan</td>
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