



## The pathway towards an effective reduction of stroke burden worldwide: teamwork

See [Policy View](#) page 674

“It is not enough to do your best; you must know what to do, and then do your best.”

*W Edwards Deming (1900–93)*

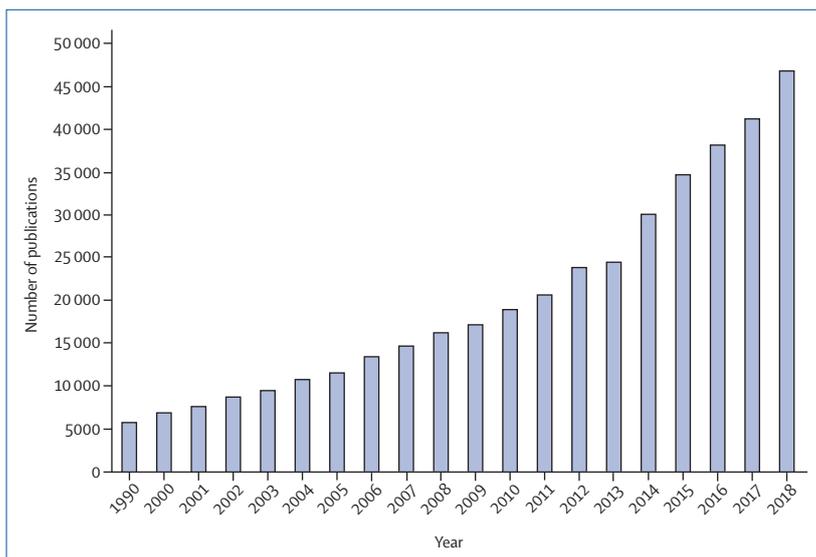
The burden of stroke in Latin American countries has been neglected for many decades; however, in the past 5 years, several initiatives have been developed to organise stroke care in this region. In *The Lancet Neurology*, Valery Feigin and colleagues<sup>1</sup> summarise the most recent initiatives to increase awareness of cardiovascular diseases and to reduce the stroke burden in these countries, while involving policy makers and governments. The stroke burden in Latin American countries, with over 5.5 million survivors of stroke in 2017, has a dramatic impact in the working force, reflected by a nearly 5.5 million stroke-related disability-adjusted life-years (DALYs).<sup>2</sup> Other unique characteristics of this region highlighted in their Policy View include the mean patient age at stroke onset (approximately 10 years younger than in North America), and the high proportion of intracerebral haemorrhage events (27%) and subarachnoid haemorrhage events (15%) compared with high-income countries (eg, North America).<sup>1</sup>

Several barriers were identified such as limited access to acute stroke care, lack of stroke prevention programmes, and scarce government support for stroke rehabilitation. Limited awareness of stroke symptoms and poor control of vascular risk factors (eg, hypertension, diabetes) are other barriers to optimal stroke care. The limited investment in stroke research is also reflected in the scientific outcomes of Latin American countries.<sup>3</sup> For example, the assessment of publications submitted to the *Stroke* journal from 2004 to 2011 showed that Latin American countries, with a relatively low gross domestic product and English proficiency scores, had lower submission and adjusted acceptance rates than European countries, Australia, and North America.<sup>3</sup>

However, we have witnessed an increasing interest in stroke in Latin American countries in the past 20 years. For example, the number of stroke publications increased more than 8-times from 1999 to 2018 (figure). These publications contribute to one of the key needs in stroke care: increasing awareness in the public sector, the scientific community, and among policy makers.

How can this Policy View advance stroke care in Latin America?<sup>2</sup> As the Latin proverb *res non-verba* (we need facts, not just words) implies, we should aim for written words and informal discussions that promptly and effectively translate into actions. The Policy View summarises the initial steps into those actions. The Declaration of Gramado, Brazil (August, 2018), illustrates the teamwork and shared commitments of this group (eg, to provide public education on stroke signs, stimulate healthy eating habits and physical activity, reduce sodium intake and alcohol use, control weight, organise the pre-hospital care to prioritise patients with stroke, and prioritise the implementation of stroke centres). The next steps of this group would be to design a roadmap towards achieving those goals.<sup>4</sup> In other words, the key question resides in how these priorities will be implemented given the disparities of necessities and resources across Latin American countries.<sup>5,6</sup>

According to Darwin’s theory, biological evolution and behavioural changes occur by short, although slow, steps.<sup>7</sup> Simple objectives should be attached to an action and a deliverable (and measurable) instrument.



**Figure: Timeline of publications of stroke research in Latin American countries**  
We searched PubMed between Jan 1, 1999, and Dec 31, 2018, for relevant publications with the search term “stroke” in the title and abstract field combined with each Latin American country, according to the primary affiliation of the corresponding author.

No simple or uniform solutions exist to improve stroke care worldwide.<sup>5</sup> Disparities among countries constitute a major barrier when evaluating the implementation of programmes to reduce the burden of stroke.

Quality improvement strategies would be an effective approach to account for differences across countries and improving patients' experiences in stroke care.<sup>8,9</sup> The US Agency for Healthcare Research and Quality recommends a sequence of steps known as the Deming cycle or Plan, Do, Study, Act (PDSA). One of its major advantages is the customisation of programmes and strategies according to each country needs and available resources.<sup>10</sup> The PDSA cycles become iterative by using the achievements as the starting point to tackle the next goal and priority.

As a result of the mentioned concepts, we should not expect simple solutions from partners working in isolation, but should work together (clinicians, researchers, policy makers, and academic institutions) towards the common UN goals of embracing country collaborations to reduce premature death caused by non-communicable diseases by improving prevention and treatment, and to promote mental health and wellbeing. We paraphrase an African proverb to highlight the impact of teamwork: "If you want to go fast, go alone. If you want to go far, go together". Physicians and policy makers have to work together towards better access and delivery of stroke care services in Latin American countries and worldwide.

Gustavo Saposnik, \*Vladimir Hachinski

Division of Neurology, Department of Medicine, and Outcomes and Decision Neuroscience Research Unit, Li Ka Shing Knowledge Institute, St. Michael's Hospital, University of Toronto, ON, Canada (GS); and Department of Clinical Neurological Sciences, Western University, London, ON N6A 5A5, Canada (VH)  
vladimir.hachinski@lhsc.on.ca

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## Immune checkpoint blockade for treating progressive multifocal leukoencephalopathy



A case series from the National Institutes of Health<sup>1</sup> and two single case-reports<sup>2,3</sup> indicate that some cases of progressive multifocal leukoencephalomyelopathy (PML) can benefit from treatment with pembrolizumab or nivolumab, which are anti-programmed death protein 1 (PD-1) checkpoint-blocking antibodies.

PML is a severe opportunistic brain infection caused by neurotropic variants of the John Cunningham (JC) virus, a ubiquitous polyoma virus latently present in up to 50% of the adult healthy population.<sup>4</sup> PML usually occurs in the setting of immunosuppression (eg, in haematopoietic malignancies and lymphoma, HIV infection, and in patients treated with immunosuppressive drugs). Neurologists have become highly alerted to PML as

it is the most common and serious complication of natalizumab, a monoclonal antibody used for treating multiple sclerosis. For natalizumab-associated PML, discontinuation of the immunosuppressive therapeutic antibody is the pragmatic first step in treating the opportunistic infection.<sup>5</sup> However, for PML associated with other conditions it is impossible to withdraw the causative agent. In such cases it would be desirable to stimulate the immune system by other means.

Immune checkpoint blockade with monoclonal antibodies has emerged as a very promising strategy for treating various malignancies. This approach also has potential for the treatment of chronic infectious diseases such as malaria, HIV infection, hepatitis B, and tuberculosis.<sup>6</sup>

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