Recent Advances in Stroke Outcomes Research: Contributions from Canada

Gustavo Saposnik

Knowing is not enough; we must apply.
Willing is not enough; we must do.
– Johann Wolfgang von Goethe (1749–1832)

Stroke is a devastating disease for patients, families and the healthcare system. Outcomes research can contribute with the analysis, evaluation and dissemination of the result of specific treatment, processes of care or medical procedures to improve patient outcomes. According to the Agency for Healthcare Research and Quality (2000), outcomes research "seeks to understand the end results of specific health care practices and interventions." By linking the care people get to the outcomes they experience, outcomes research can become the key to developing better ways to monitor and improve the quality of care.

Health outcomes research may include studies evaluating the effectiveness of a particular medical treatment or surgical procedure (e.g., carotid endarterectomy, mechanical devices), the impact of socioeconomic status, disparities in access to care, process measures or reimbursement policies. It is sometimes difficult to understand that an intervention in healthcare (e.g., hospital care, stroke unit admission, expertise provided by a stroke neurologist) is a treatment in itself, in much the same way as are coronary artery bypass surgery, the administration of thrombolytic therapy or the prescription of statins for stroke prevention.

The field of outcomes research has evolved over the past few years. Initially, most of the research was centred on individual patient factors influencing stroke outcomes. More recently, the study of interrelated factors affecting cost and quality of care has made healthcare providers and policy makers in the public and private sectors increasingly interested in health outcomes. Stroke outcomes research provides a more comprehensive understanding of factors influencing stroke outcomes and health policy by including the perspectives of all players (patients, families, healthcare providers, insurers, policy makers and the general public).

This brief summary highlights some recent studies in the field of stroke outcomes research completed in Canada from 2008 to 2010.

Stroke Research: The Canadian Model

The unique characteristics of Canada's healthcare system and research model have provided an opportunity to lead advances in stroke outcomes research. Universal, government-funded health coverage, lack of co-payments and availability of detailed administrative and clinical databases have fomented numerous publications. SORCan (Stroke Outcomes Research Canada Working Group [www.sorcan.ca]) is a dedicated group of investigators with expertise in the field of health system research who have played a major role in advancing this field in Canada. SORCan was created and is led by Dr. Gustavo Saposnik, an adjunct scientist at the Institute for Clinical Evaluative Sciences (ICES) in Toronto.

It is sometimes difficult to understand that an intervention in healthcare (e.g., hospital care, stroke unit admission, expertise provided by a stroke neurologist) is a treatment in itself.

Data from the Registry of the Canadian Stroke Network (RCSN) provide a rich resource to stimulate recent advances in stroke outcomes research as highlighted in key review articles (Rudd and Williams 2009; Williams and Rudd 2009). The RCSN is recognized worldwide for containing detailed demographic and clinical information and process measures, which can be linked to vital statistics and/or administrative databases. Most of the studies using registry or administrative databases are retrospective, with a defined inception cohort. To make groups comparable, different analytical strategies are usually applied, including the adjustment for potential confounders or propensity score matching.

Key Findings

Access to Care and Stroke Outcomes

Stroke-unit admission has been associated with a reduction in stroke disability and mortality (Stroke Unit Trialists'

Collaboration 2007). Unfortunately, there are few countries with utilization rates higher than 50% for the stroke population. Organized in-patient stroke care consists of a multidisciplinary approach aimed at improving stroke outcomes. It is unclear whether all patients admitted to stroke centres receive comprehensive care. Our research group (SORCan) created a risk score providing evidence that higher levels of access to specialized care (occupational therapy/physiotherapy, assessment by the stroke team and admission to a stroke unit) is associated with better stroke outcomes. This study provided evidence supporting the argument that stroke patients are best served by comprehensive and specialized in-patient care and not by individual interventions. Stroke mortality was reduced approximately 10 times (with a very low number needed to treat of five) when we compared adjusted mortality rate for the highest levels of care (organized care index 2–3) versus lowest levels of care (organized care index 0–1) (Saposnik et al. 2008a). In addition, the SORCan team found that organized care/stroke unit admission was beneficial irrespective of age and stroke subtype (i.e., large atherosclerotic disease, cardioembolism, small vessel disease) (Saposnik et al. 2009a; Smith et al. 2010).

A retrospective study from Calgary compared a cohort of stroke patients managed on general neurology/medical wards before 2001 with a similar cohort of stroke patients managed on a stroke unit after 2003. There was a four-day reduction (from 19 days to 15 days) in the average length of stay between patients on a stroke unit (n = 2,461) and patients managed on general neurology/medical wards (n = 1,567; p < .001). The adjusted odds of a length of stay of more than seven days was reduced by 30% (p < .0001) on a stroke unit compared to general neurology/medical wards (Zhu et al. 2009). Interestingly, physician expertise in stroke management was also associated with better survival after controlling for age, stroke severity, comorbidities and other factors (Saposnik et al. 2008b).

These studies provide "real-world" evidence of the effectiveness of organized stroke care, suggesting that investment in the Ontario Stroke Strategy, a health initiative of the government of Ontario, has been fruitful, not only by reducing stroke disability but also by improving survival.

Carotid imaging and time to revascularization are commonly used indicators of quality of stroke care. A study including 10,213 ischemic stroke and transient ischemic attack events admitted to participating institutions in the RCSN found that 6,270 (61%) received carotid imaging in hospital (Gladstone et al. 2009). Among those, 1,011 (16.1%) were found to have a presumed symptomatic carotid stenosis of 50–99% with only 177 (17.5%) undergoing endarterectomy within six months of the index event. The median time from index event to surgery was 30 days; only one third of patients (38 of 105) received endarterectomy within the recommended two-week target time frame. This study highlights the importance of implementing an effective system to minimize delays to diagnosis and surgical treatment for patients with symptomatic carotid stenosis.

Another study evaluated age differences in stroke quality of care and delivery of services (Saposnik et al. 2009b). Several process measures were analyzed including use of thrombolysis; dysphagia screening; admission to a stroke unit; carotid imaging; antithrombotic therapy; and warfarin for atrial fibrillation at discharge. Among 3,631 patients with ischemic stroke, 1,219 (34%) were aged 80 and older. Stroke care was similar across age groups for the primary outcome measures of thrombolysis, admission to a stroke unit, screening for dysphagia, management by a stroke team, discharge on antiplatelet therapy or discharge on warfarin for patients with atrial fibrillation. Carotid imaging was slightly lower in the oldest group. Mortality increased with age, with a 30-day risk-adjusted fatality of 7.1%, 6.5%, 8.8% and 14.8% for those aged 59 or younger, 60–69, 70–79 and 80 or older, respectively. Those aged 80 and older had a longer length of hospitalization, increased risk of pneumonia and higher disability at discharge and were less likely to be discharged home compared to those younger than 80 years of age. A similar study on sex disparities suggests that differences in stroke care are largely explained by confounding factors (Reid et al. 2008). The authors highlighted the importance of a coordinated stroke care system providing similar access to stroke care across all groups.

Influence of Pre-admission Use and Adherence to Preventive Agents on Stroke Outcomes

A study of 3,571 patients aged 66 and older discharged home from 11 tertiary care centres found that over 85% were treated with antihypertensive therapy within one year of stroke. Suboptimal adherence occurred in one third of patients receiving thiazide diuretics, 25% of those receiving angiotensin-converting enzyme inhibitor (ACEI) and 38% of those receiving an ACEI/diuretic combination (Khan et al. 2010). Using a similar design, Dowlatshahi et al. (2009) found that pre-admission treatment with aspirin and clopidogrel was associated with less severe stroke upon presentation. Pre-treatment use of antiplatelet agents did not result in increased intracerebral hemorrhage following the administration of tissue plasminogen activator (t-PA). Moreover, early administration of antithrombotics during hospitalization was associated with a substantial reduction in mortality at seven days (odds ratio [OR] 0.12; 95% CI 0.07–0.19), at 30 days (OR 0.13; 95% CI 0.08–0.21) and at one year (OR 0.29; 95% CI 0.20–0.43) after adjusting for confounders (Saposnik et al. 2008b).

Identification of New Risk Groups

Studies have shown poorer stroke outcomes for patients presenting with seizures (Burneo et al. 2010), or who develop an acute myocardial infarction (Liao et al. 2009) or gastrointestinal bleeding (O'Donnell et al. 2008). In a study including over

5,000 stroke patients, those with seizures had a higher mortality at 30 days (36.2% versus 16.8%, $p < .0001$) and at one year post-stroke (48.6% versus 27.7%, $p < .001$), longer hospitalization and greater disability at discharge ($p < .001$) (Burneo et al. 2010). In a study of 9,180 patients with acute ischemic stroke, Liao et al. (2009) found that 211 of them (2.3%) had a myocardial infarction during hospitalization. At hospital discharge, 65% of the patients with in-hospital myocardial infarction had died or were severely disabled, compared with 36% in the entire cohort. O'Donnell et al. (2008) observed similar results for stroke patients experiencing gastrointestinal hemorrhage during hospitalization (1.5%). Gastrointestinal hemorrhage was independently associated with death or severe dependence at discharge (OR 3.3; 95% CI 1.9–5.8) and mortality at six months (hazard ratio [HR] 1.5; 95% CI 1.1–2.0).

More recently, a population-based case-control study across the province of Ontario tested the hypothesis that recent immigrants, usually healthier than long-term residents but exposed to resettlement stress, would have a higher risk of stroke and less access to care (Saposnik et al. 2010b). Contrary to the expected results, the researchers found that new immigrants to Ontario have a 30% lower incident risk of stroke (HR 0.69; 95% CI 0.64–0.74) after adjusting for confounders. Similar results were observed for new immigrants admitted with heart attacks (Saposnik et al. 2010a). Both studies support the concept of the "healthy immigrant effect," moving away from the popular misconception that new immigrants are a burden on their host country's healthcare system.

Future Directions

Canada has been recognized worldwide for its effective stroke care delivery model. Unique opportunities have arisen for the integration of clinical care, research and health policy. Different research approaches (e.g., development of a risk score model, technology assessment) may contribute to the implementation of innovative models of care aimed at facilitating in- and outpatient access and improving quality of care. In 2010, the Institute of Medicine and the National Heart, Lung, and Blood Institute jointly released a report recommending that scientific organizations, development agencies, nongovernmental organizations and governments should work toward two essential goals: (1) creating environments that promote healthy lifestyle choices and help reduce the risk of chronic diseases and (2) building infrastructure and health systems with the capacity to implement programs that will effectively detect, reduce risk of and manage cardiovascular diseases. Outcomes and health services research is essential for implementation, evaluation and continuous quality improvement. Results from some recent Canadian contributions suggest that we may be going in the right direction. HQ

Acknowledgement

Dr. Saposnik is supported by a Clinician-Scientist Award from the Heart and Stroke Foundation of Ontario. The author thanks Dr. Sandra E. Black for her thoughtful comments.

Dr. Saposnik appreciates the support provided from several scientific organizations, including the Heart and Stroke Foundation of Ontario, the Canadian Institutes for Health Research (CIHR), the Ontario Stroke Network, the Connaught Foundation, the University of Toronto, St. Michael's and the Li Ka Shing Knowledge Institute.

ICES is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). The opinions, results and conclusions reported in this article are those of the authors and are independent from the funding sources. No endorsement by ICES or MOHLTC is intended or should be inferred.

References

Agency for Healthcare Research and Quality. 2000. *Outcomes Research: Fact Sheet.* Rockville, MD: Author. Retrieved June 30, 2010. <http://www.ahrq.gov/clinic/outfact.htm>.

Burneo, J.G., J. Fang, G. Saposnik and the Investigators of the Registry of the Canadian Stroke Network. 2010. "Impact of Seizures on Morbidity and Mortality after Stroke: A Canadian Multi-centre Cohort Study." *European Journal of Neurology* 17(1): 52–58.

Dowlatshahi, D., A. Hakim, J. Fang and M. Sharma. 2009. "Pre-admission Antithrombotics are Associated with Improved Outcomes following Ischaemic Stroke: A Cohort from the Registry of the Canadian Stroke Network." *International Journal of Stroke* 4(5): 328–34.

Gladstone, D.J., J. Oh, J. Fang, P. Lindsay, J.V. Tu, F.L. Silver et al. 2009. "Urgency of Carotid Endarterectomy for Secondary Stroke Prevention: Results from the Registry of the Canadian Stroke Network." *Stroke* 40(8): 2776–82.

Institute of Medicine. March 2010. *Promoting Cardiovascular Health in the Developing World: A Critical Challenge to Achieve Global Health. Consensus Report.* Washington, DC: Author. Retrieved August 9, 2010. <http://www.iom.edu/Reports/2010/Promoting-Cardiovascular-Health-in-the-Developing-World-A-Critical-Challenge-to-Achieve-Global-Health/Report-Brief-Promoting-Cardiovascular-Health-in-the-Developing-World.aspx?page=1>.

Khan, N.A., L. Yun, K. Humphries and M. Kapral. 2010. "Antihypertensive Drug Use and Adherence after Stroke: Are There Sex Differences?" *Stroke* 41(7): 1445–49.

Liao, J., M.J. O'Donnell, F.L. Silver, D. Thiruchelvam, G. Saposnik, J. Fang et al. 2009. "In-Hospital Myocardial Infarction following Acute Ischaemic Stroke: An Observational Study." *European Journal of Neurology* 16(9): 1035–40.

O'Donnell, M.J., M.K. Kapral, J. Fang, G. Saposnik, J.W. Eikelboom, W. Oczkowski et al. 2008. "Gastrointestinal Bleeding after Acute Ischemic Stroke." *Neurology* 71(9): 650–55.

Reid, J.M., D. Dai, G.J. Gubitz, M.K. Kapral, C. Christian and S.J. Phillips. 2008. "Gender Differences in Stroke Examined in a 10-Year Cohort of Patients Admitted to a Canadian Teaching Hospital." *Stroke* 39(4): 1090–95.

Rudd, A.G. and L.S. Williams. 2009. "Advances in Health Policy and Outcomes." *Stroke* 40(5): e301–04.

Saposnik, G., D.A. Redelmeier, H. Lu, E. Fuller-Thomson, E. Lonn and J.G. Ray. 2010a. "Myocardial Infarction Associated with Recency of Immigration to Ontario." *QJM* 103(4): 253–58.

Saposnik, G., D.A. Redelmeier, H. Lu, E. Lonn, E. Fuller-Thomson and J.G. Ray. 2010b. "Risk of Premature Stroke in Recent Immigrants (PRESARIO): Population-Based Matched Cohort Study." *Neurology* 74(6): 451–57.

Saposnik, G., J. Fang, M. O'Donnell, V. Hachinski, M.K. Kapral, M.D. Hill et al. 2008a. "Escalating Levels of Access to In-Hospital Care and Stroke Mortality." *Stroke* 39(9): 2522–30.

Saposnik, G., M.D. Hill, M. O'Donnell, J. Fang, V. Hachinski, M.K. Kapral et al. 2008b. "Variables Associated with 7-Day, 30-Day, and 1-Year Fatality after Ischemic Stroke." *Stroke* 39(8): 2318–24.

Saposnik, G., M.K. Kapral, S.B. Coutts, J. Fang, A.M. Demchuk, M.D. Hill et al. 2009a. "Do All Age Groups Benefit from Organized Inpatient Stroke Care?" *Stroke* 40(10): 3321–27.

Saposnik, G., S.E. Black, A. Hakim, J. Fang, J.V. Tu, M.K. Kapral et al. 2009b. "Age Disparities in Stroke Quality of Care and Delivery of Health Services." *Stroke* 40(10): 3328–35.

Smith, E., M. Kapral, K. Al-Hassan, J. Fang, D. Selchen, G. Saposnik et al. 2010. "Do All Ischemic Stroke Subtypes Benefit from Organized Inpatient Stroke Care?" *Neurology* 75(5): 456–62.

Stroke Unit Trialists' Collaboration. 2007. "Organised Inpatient (Stroke Unit) Care for Stroke." *Cochrane Database of Systematic Reviews* 4: CD000197.

Williams, L.S. and A.G. Rudd. 2009. "Advances in Health Policy and Outcomes 2009." *Stroke* 41(2): e77–80.

Zhu, H.F., N.N. Newcommon, M.E. Cooper, T.L. Green, B. Seal, G. Klein et al. 2009. "Impact of a Stroke Unit on Length of Hospital Stay and In-Hospital Case Fatality." *Stroke* 40(1): 18–23.

About the Author

Gustavo Saposnik, MD, MSc, FAHA, is the director of the Stroke Outcomes Research Unit, Division of Neurology, Department of Medicine, at St. Michael's; adjunct scientist, Institute for Clinical Evaluative Sciences (ICES); and assistant professor, Department of Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario. Dr. Saposnik can be contacted at saposnikg@smh.ca.