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Living clinical guidelines for stroke: updates, challenges and opportunities

The Australian and New Zealand living stroke management guidelines provide timely, evidence-based updates to recommendations

ontinued growth in the number of published clinical studies has necessitated changes to the way evidence-based resources such as clinical guidelines are developed and updated. The Australian and New Zealand Clinical Guidelines for Stroke Management (https://informme.org.au/guide lines/clinical-guidelines-for-stroke-management) are based on continual evidence surveillance and timely updates to recommendations as new research is published. In this article, we outline the main updates to recommendations since the guidelines moved into

Background

Stroke is a leading cause of adult disability in Australia, with an estimated 27428 incident strokes occurring each year, or one every 19 minutes. Compared with urban areas, the incidence of stroke is 17% higher in rural communities, where access to specialist stroke care is less likely. This makes the need for easily accessible, up-to-date, evidenced-based clinical practice guidelines for stroke care essential.

The first Australian clinical guidelines for stroke were published in 2003 (acute) and 2005 (post-acute). These were updated in 2007, 2010 and most recently in 2017 following traditional methods, including endorsement by the National Health and Medical Research Council (NHMRC). In 2017, the guidelines moved from being published in a static (pdf) format, to being published online using the Making GRADE the Irresistible Choice (MAGICapp) platform (https://magicevidence.org).²

Traditional cycles of guideline updates which involve recommendations based on the best available evidence at the time of publication are problematic because new evidence can mean that recommendations quickly become outdated. In 2018, the Stroke Foundation and Cochrane Australia were awarded funding to test a model of living guidelines for stroke management. These were the first Australian living clinical guidelines and are the first and only living stroke guidelines worldwide. Subsequent living guidelines include those for diabetes,³ maternal and perinatal health,⁴ and COVID-19.5 The stroke guidelines are published online at https://informme.org.au/guidelines/clini cal-guidelines-for-stroke-management, to guide dayto-day stroke care in Australia and New Zealand.

Development

The 2017 update of the static stroke guidelines consisted of 392 individual recommendations

including practice points across eight chapters addressing 89 topics. Each topic was structured into a PICO (patient, intervention, comparator, outcome) format to address an aspect of care, for example, the use of cholesterol-lowering therapy for secondary prevention of stroke. The living stroke guidelines project commenced in July 2018. The structures in place for the 2017 static guidelines update were adapted and expanded to fit living guidelines methods. A full description of the methods is published elsewhere. a living mode in 2018, and discuss key challenges and benefits of living guidelines.

In brief, each month the results of published new studies are reviewed by the project team. Where new evidence is deemed to potentially impact one or more recommendations, the project team works with clinical experts to update evidenceto-decision frameworks (benefits and harms and certainty of evidence component) using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) method (https://gdt.grade pro.org/app/handbook/handbook.html), and draft changes to recommendations and background text. Draft changes go through a rigorous review process, culminating in submission to the NHMRC for approval (median time from initiation to submission is about 6 months). Clinical indicators collected as part of the National Stroke Audit and the Australian Stroke Clinical Registry are monitored over time to evaluate adherence to aspects of the guidelines.

The living clinical guidelines for stroke are developed in accordance with NHMRC standards, including the use of the GRADE method for recommendations. The MAGICapp platform presents the recommendations and related information in a multilayered, transparent format. MAGICapp allows users to review all previous versions of each recommendation for full transparency. Any new or updated recommendations are flagged as such within the platform for a period of 6–12 months. A summary of updates is also maintained online (https://informme.org.au/guidelines/living-guide lines-updates).

Recommendations

Since the 2017 update to the static guideline, a total of 35 new or updated recommendations have been made. Just under half (16) of the changes are new recommendations (five strong, 10 weak, and one practice point), with updates to 19 recommendations (12 without change to the direction or grade of recommendation, six upgraded strength, and one downgraded strength [from weak recommendation for to weak recommendation against]). New and updated strong recommendations are presented in the Box. All new and updated recommendations are reported in

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coralie.english@ newcastle.edu.au the Supporting Information and are described in brief below.

Acute medical and surgical management

The first living guideline recommendation, developed after the 2017 update but before the start of the funded living guidelines project, extended the time window for endovascular clot retrieval to 24 hours for specific clinical presentations. Additionally, based on results from new studies, 12-14 the recommended time window for safe administration of alteplase has been extended to 9 hours post-stroke and a new recommendation made about safe use of alteplase for stroke of unknown onset time. Both recommendations are based on favourable perfusion imaging. Two new recommendations have been made for the use of tenecteplase as an alternative to alteplase within 4.5 hours of stroke onset¹⁵ or for large vessel occlusions.¹⁶ Ticagrelor in combination with aspirin commenced within 24 hours of symptom onset and continued for the first 30 days may now be used for acute antiplatelet therapy for people with minor ischaemic stroke or transient ischaemic attack, ¹⁷ although this should be considered secondary to a strong recommendation for aspirin plus clopidogrel for the first 21 days. The recommendation for oxygen therapy has been updated to include a specific threshold (92% blood oxygen saturation on room air), above which routine use of supplemental oxygen therapy is not recommended. 18 There is a new recommendation for the use of telestroke services to assist in patient assessment and decision making for the use of thrombolysis and/or endovascular clot retrieval for people presenting to hospitals where medical specialist services are not available. 19,20 Finally, there is a new recommendation that clarifies that patients not receiving nasogastic feeding do not require head elevation and may be managed in any position.²¹

Secondary prevention

Several recommendations have been updated regarding secondary prevention. The first specifies a target of < 1.8 mmol/L for low density lipoprotein levels for people with ischaemic stroke.²² The recommendation for management of patent foramen ovale now specifies that where this is considered the likely cause of stroke, percutaneous closure should occur.²³ People who were taking antiplatelet therapy before experiencing an intracerebral haemorrhage may be safely recommenced, although the optimal timing for this is not clear.²⁴ Left atrial appendage occlusion may be considered for the management of atrial fibrillation if there is a genuine contraindication to anticoagulation.²⁵ Non-pharmacological interventions to reduce stroke risk factors include exercise training as well as individual support and counselling, and the final new recommendation suggests that people with stroke should follow a Mediterranean style diet.26

Rehabilitation

The most significant updated recommendation pertains to the use of selective serotonin reuptake inhibitors (SSRIs) to reduce disability after stroke. New

large trials^{27,28} found SSRIs did not reduce disability and were associated with a small risk of harm, and therefore are no longer recommended for routine use in this context but may still be relevant specifically to prevent or treat depression. The recommendations for management of motor weakness and difficulty standing have been updated. These updates include greater specificity in the types of training modalities that are recommended. Finally, new recommendations for specific interventions to improve memory function, and for the use of telehealth as an alternative mode of rehabilitation service delivery²⁹ have been made.

Managing complications

Due to an increase in the number of published high quality, albeit small trials, it is now recommended that acupuncture may be considered for the management of shoulder pain after stroke.³⁰ Minor changes have also been made in preventing or managing swelling in the arms or legs.

Discussion

Major updates to the guidelines over the past four years have occurred, ensuring the recommendations are current. Importantly, there have been no cases in which a recommendation for an intervention has been downgraded from a strong to a weak recommendation. Furthermore, no recommendation has been changed multiple times. Important new recommendations have been made regarding lifesaving therapy such as extension of the time window for endovascular clot retrieval and the administration of alteplase for thrombolysis.

The key benefit of living guidelines is the ability to rapidly update recommendations in response to new evidence. As a case example, results from the EXTEND trial demonstrating the safety and efficacy of thrombolysis up to 9 hours after stroke were published in May 2019, followed soon after by a systematic review and individual patient data meta-analysis. By November 2019, our updated recommendation had completed the full development, review and public consultation process and was endorsed by the NHMRC and disseminated to key end-user organisations; a total time of less than six months.

While it is hard to estimate the direct and definitive impact of rapid guideline updates, based on trial outcomes and reported patient numbers, we estimate that about 320 Australians each year may be saved from premature death or disability following a severe stroke based on the updated recommendations for endovascular clot retrieval from 6–24 hours after symptom onset (unpublished data). Rapid guideline updates as part of a living model are almost certain to have played a significant role by expediting local and state-wide system changes. Further work to quantify the impact, including the potential economic impact and return-on-investment, of the living guidelines compared with traditional guideline updates is planned. Since 2007, we have had national, standardised systems of monitoring adherence to the clinical guideline recommendations

in Australia. Specifically, these systems include the National Stroke Audit (detailed cross-sectional audits of acute care and inpatient rehabilitation every alternate year) and the Australian Stroke Clinical Registry, whereby adherence to the national acute care standards is continuously monitored, including patient outcomes 90-180 days after stroke. These data permit reliable assessment of practice change and health outcomes over time to inform economic and other impact assessments. However, preliminary findings of the independent evaluation indicate that end users of the living stroke management guidelines report have increased trust in and likelihood of accessing and following the guidelines compared with the traditional, periodically updated guideline model (Wiles L, Zurynski Y, Hibbert P, et al. Living stroke guidelines evaluation. Australian Institute of Health Innovation, 2021. Unpublished report).

Importantly, living guidelines provide currency of advice. The experience with stroke as well as other guidelines³⁻⁵ demonstrates that the rigour of the methods does not need to be compromised when living modes are adopted. The GRADE method is as appropriate for living guidelines as for traditional, periodic guidelines. NHMRC support is also vital in ensuring living guidelines continue to meet its standards.

Sustainability remains the key challenge for the living stroke guidelines. Collaboration with major stroke guideline groups in Europe and North America may improve guideline efficiency and sustainability, but although discussions have been undertaken, no formal projects have been forthcoming as only a few groups currently use the GRADE method. However, there has been strong collaboration and sharing of knowledge and experience with other national guideline groups as part of the Australian Living Evidence Consortium (https://livingevidence.org.au/). Compared with the costs of updating the stroke guidelines every five years, our initial experience indicates the living model is likely to have similar overall costs, but with the significant benefits of increased trust and use from clinicians. Ongoing, secure funding for this new model is now required for stroke along with similar guidelines for other high burden diseases.

The Australian and New Zealand living guidelines for stroke management are the first of their kind globally. A number of important changes have occurred in the guideline recommendations. Our model of continual evidence surveillance and timely updates to recommendations is feasible, but sustainability remains a challenge. Now that we have started down this road, the message from guideline end users is that a return to the old model of static updates is no longer acceptable, and ongoing long term investment in living guidelines must be prioritised.

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- 1 Deloitte Access Economics. No postcode untouched: stroke in Australia 2020. Stroke Foundation, 2020. http://maps.strokefoundation.com.au/wp-content/themes/dlstroke/downloads/No%20 Postcode%20Untouched%202020%20Final%20report.pdf (viewed Jan 2022).
- 2 MAGIC Evidence Ecosystem Foundation. https://magicevidence. org (viewed Jan 2022).
- 3 White H, Tendal B, Elliott J, et al. Breathing life into Australian diabetes clinical guidelines. *Med J Aust* 2020; 212: 250-251. https://www.mja.com.au/journal/2020/212/6/breathing-life-australian-diabetes-clinical-guidelines
- 4 Vogel JP, Dowswell T, Lewin S, et al. Developing and applying a 'living guidelines' approach to WHO recommendations on maternal and perinatal health. *BMJ Glob Health* 2019; 4: e001683.
- 5 Tendal B, Vogel JP, McDonald S, et al. Weekly updates of national living evidence-based guidelines: methods for the Australian living guidelines for care of people with COVID-19. *J Clin Epidemiol* 2021; 131: 11-21.
- 6 Hill K, English C, Campbell BCV, et al. Feasibility of national living guideline methods: the Australian Stroke Guidelines. *J Clin Epidemiol* 2021; 142: 184-193.
- 7 Hao Q, Tampi M, O'Donnell M, et al. Clopidogrel plus aspirin versus aspirin alone for acute minor ischaemic stroke or high risk transient ischaemic attack: systematic review and meta-analysis. *BMJ* 2018; 363: k5108.
- 8 Amarenco P, Kim JS, Labreuche J, et al. A comparison of two LDL cholesterol targets after ischemic stroke. N Engl J Med 2020; 382: 9.19
- 9 Turc G, Calvet D, Guérin P, et al. closure, anticoagulation, or antiplatelet therapy for cryptogenic stroke with patent foramen ovale: systematic review of randomized trials, sequential metaanalysis, and new insights from the CLOSE study. J Am Heart Assoc 2018; 7: e008356.
- 10 Dorsch S, Ada L, Alloggia D. Progressive resistance training increases strength after stroke but this may not carry over to activity: a systematic review. J Physiother 2018; 64: 84-90.
- **11** Albers GW, Marks MP, Kemp S, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med* 2018; 378: 708-718.
- 12 Ma H, Campbell BCV, Parsons MW, et al. Thrombolysis guided by perfusion imaging up to 9 hours after onset of stroke. N Engl J Med 2019; 380: 1795-1803.
- 13 Campbell BCV, Ma H, Ringleb PA, et al. Extending thrombolysis to 4-5-9 h and wake-up stroke using perfusion imaging: a systematic review and meta-analysis of individual patient data. *Lancet* 2019; 394: 139-147.

- 14 Thomalla G, Simonsen CZ, Boutitie F, et al. MRI-Guided thrombolysis for stroke with unknown time of onset. *N Engl J Med* 2018; 379: 611-662.
- 15 Huang X, MacIsaac R, Thompson JL, et al. Tenecteplase versus alteplase in stroke thrombolysis: an individual patient data meta-analysis of randomized controlled trials. *Int J Stroke* 2016; 11: 534-543.
- 16 Campbell BCV, Mitchell PJ, Churilov L, et al. Tenecteplase versus alteplase before thrombectomy for ischemic stroke. N Engl J Med 2018; 378: 1573-1582.
- 17 Johnston SC, Amarenco P, Denison H, et al. Ticagrelor and aspirin or aspirin alone in acute ischemic stroke or TIA. N Engl J Med 2020; 383: 207-217.
- 18 Chu DK, Kim LH-Y, Young PJ, et al. Mortality and morbidity in acutely ill adults treated with liberal versus conservative oxygen therapy (IOTA): a systematic review and meta-analysis. *Lancet* 2018; 391: 1693-1705.
- 19 Lazarus G, Permana AP, Nugroho SW, et al. Telestroke strategies to enhance acute stroke management in rural settings: a systematic review and meta-analysis. *Brain Behav* 2020; 10: e01787.
- 20 Bladin CF, Kim J, Bagot KL, et al. Improving acute stroke care in regional hospitals: clinical evaluation of the Victorian Stroke Telemedicine program. Med J Aust 2020; 212: 371-377. https:// www.mja.com.au/journal/2020/212/8/improving-acute-strokecare-regional-hospitals-clinical-evaluation-victorian
- 21 Anderson CS, Arima H, Lavados P, et al. Cluster-randomized, crossover trial of head positioning in acute stroke. N Engl J Med 2017; 376: 2437-2447.
- 22 Amarenco P, Kim JS, Labreuche J, et al. A comparison of two LDL cholesterol targets after ischemic stroke. N Engl J Med 2020; 382: 9.

- 23 Turc G, Calvet D, Guérin P, et al. Closure, anticoagulation, or antiplatelet therapy for cryptogenic stroke with patent foramen ovale: systematic review of randomized trials, sequential metaanalysis, and new insights from the CLOSE study. J Am Heart Assoc 2018: 7: e008356.
- 24 RESTART Collaboration. Effects of antiplatelet therapy after stroke due to intracerebral haemorrhage (RESTART): a randomised, open-label trial. *Lancet* 2019; 393: 2613-2623.
- 25 Osmancik P, Herman D, Neuzil P, et al. Left atrial appendage closure versus direct oral anticoagulants in highrisk patients with atrial fibrillation. J Am Coll Cardiol 2020; 75: 3122-3135.
- 26 English C, MacDonald-Wicks L, Patterson A, et al. The role of diet in secondary stroke prevention. *Lancet Neurol* 2021; 20: 150-160.
- 27 AFFINITY Trial Collaboration. Safety and efficacy of fluoxetine on functional outcome after acute stroke (AFFINITY): a randomised, double-blind, placebo-controlled trial. *Lancet Neurol* 2020; 19: 651-660.
- 28 EFFECTS Trial Collaboration. Safety and efficacy of fluoxetine on functional recovery after acute stroke (EFFECTS): a randomised, double-blind, placebo-controlled trial. *Lancet Neurol* 2020; 19: 661-669.
- 29 Laver KE, Adey-Wakeling Z, Crotty M, et al. Telerehabilitation services for stroke. Cochrane Database Syst Rev 2020; (1): CD010255.
- 30 Liu S, Zhang CS, Cai Y, et al. Acupuncture for post-stroke shoulderhand syndrome: a systematic review and meta-analysis. *Front* Neurol 2019; 10: 433. ■

Supporting Information

Additional Supporting Information is included with the online version of this article.