Author	Organisation	Guideline altered?	Topic (and Recommendation if relevant)	Feedback	Actions taken
Karen Honson (individual) 11.10.20	Melbourne Health, The Royal Melbourne Hospital Neurosciences pharmacist	Noted. No further input required	Acute antithrombotic therapy Aspirin plus ticagrelor commenced within 24 hours may be used in the short term (first 30 days) in patients with minor ischaemic stroke or high-risk TIA to prevent stroke recurrence. (Johnston et al 2020 [137])	In 2018 in the USA, the FDA began approving generic brands of ticagrelor and there are now a number of different brands available in America. This is suggestive of a generic version of ticagrelor entering the Australian market at some stage. Therefore, the issue of cost-effectiveness of the use of ticagrelor for the proposed draft recommendation would be worth revisiting once a generic version of ticagrelor is available on the Australian market. Furthermore, of great interest would be further research into the use of ticagrelor in stroke patients in light of the issues of the use of clopidogrel in patients deemed to have a CYP2C19 poor metaboliser status	Noted. No change required.
Prof Helen Dewey (individual) 12.10.20	Eastern Health Clinical School, Box Hill Hospital Director of Neurosciences		Acute antithrombotic therapy Aspirin plus ticagrelor commenced within 24 hours may be used in the short term (first 30 days) in patients with minor ischaemic stroke or high-risk TIA to prevent stroke recurrence.	Not supported. I disagree with this alternative being included in the guidelines when the therapy is currently ‘off label’ and prescription would be a significant cost for the patient. There is no doubt that there is evidence for the efficacy of this therapy but these are guidelines for the Australian environment and this therapy is not generally available at this time. The guideline could be updated once the therapy is approved for use for this indication.	We acknowledge this is clearly 'off label', however, many therapies are used off-label (including clopidogrel for stroke*) and the guidelines primarily reflect evidence rather than regulatory status. Of note, the FDA have licensed ticagrelor (but not clopidogrel) for this indication. The cost differential is clearly noted in the Resource section and is one reason for the "weak" strength of recommendation. We agree that the implementation of this recommendation would be increased if generic ticagrelor is available in future. *clopidogrel + aspirin is off-label for stroke in

			(Johnston et al 2020 [137])		Australia and clopidogrel is not listed on the PBS as first line therapy for stroke.
Kate Jaques (Group) 20.20.20	QLD Statewide Stroke Clinical Network (SSCN) Multidisciplinary	NA	Decision aids in: Cholesterol targets Limb weakness and management Aspirin plus ticagrelor use in TIA and minor stroke within 24 hrs	Overall, the Queensland clinicians involved in stroke care are very happy with the updates. I can see the immense value these aids will bring in engaging with consumers and educating them regarding their choices in treatment. It would be particularly valuable to see something similar in the discharge planning guidelines, particularly for discharge medications and lifestyle change implementation.	Noted. No change required.
Kylie Jonasson (group) 22.10.20	Director-General, ACT Health Multidisciplinary	NA	All	Noted drafted updates	Noted. No change required.
Kate Jackson / NSW health (group) 28.10.20	Agency for Clinical Innovation Multidisciplinary		Acute antithrombotic therapy Aspirin plus ticagrelor commenced within 24 hours may be used in the short term (first 30 days) in patients with minor ischaemic stroke or high-risk TIA to prevent stroke recurrence. (Johnston et al 2020 [137])	In the explanation, the last sentence in the second paragraph, is unclear as the comparator and patient groups are not stated. “A previous study by Johnston et al (2016) [138] reported a non-statistical difference in the time to occurrence of stroke, MI or death within 90 days with ticagrelor alone compared to aspirin (HR 0.89, 95%CI 0.78-1.01, p=0.07). Ischaemic stroke occurred in 5.8% treated with ticagrelor vs 6.7% treated with aspirin (HR 0.87, 95%CI 0.76-1.00). Major bleeding and ICH was similar between groups. Ticagrelor is PBS listed in Australia for cardiac indications and is superior to clopidogrel in the cardiac group. However, ticagrelor is not superior to aspirin in non-thrombolysis, non-severe stroke/TIA but may be similar in bleeding risk although this study wasn't designed to show non-inferiority.”	We have rephrased the last sentence to now say: "Single-agent ticagrelor was not superior to aspirin in patients with mild stroke or high risk TIA but may have similar bleeding risk.(Johnston et al. 2016 [138])"

Kate Jackson / NSW health (group) 28.10.20	Agency for Clinical Innovation Multidisciplinary		Cholesterol lowering therapy In patients with ischaemic stroke, cholesterol lowering therapy should target LDL cholesterol < 1.8 mmol/L for secondary prevention of atherosclerotic cardiovascular disease. (Amarenco et al 2020 [112])	The “Moderate” certainty of the evidence is somewhat at odds with the wide confidence interval in the outcome table – a moderate recommendation might be more appropriate.	The overall certainty of evidence was noted as moderate mainly due to the fact that this was a single trial which unfortunately was terminated earlier than planned and further studies may change the effect estimate. This aligns with the guidelines within the GRADE handbook. While it is true the confidence intervales for recurrent stroke in particular were wide (and hence non-significant) the overall outcome of prevention of atherosclerotic CVD was significant. In GRADE we only refer to weak and strong recommendations and the working group considered a range of factors (not just the confidence in the estimates of effects) in deciding to make this a strong rather than weak recommendation. These factors included: * Clear observational data related to the relationship between LDL and stroke/CVD events * Relatively short duration of follow up (longer follow up would likely detect more events and potentially narrow the confidence intervals) * The composite outcome was positive * The current levels align to existing national targets in Australia within PBS/MBS for additional agents that may be needed to reach target * Adverse event rates are low so the balance clearly falls to desirable (lower CVD events) outcomes. Further information about GRADE and the strength of the recommendations is listed in the 'Methodology' section of each chapter.

Kate Jackson / NSW health (group) 28.10.20	Agency for Clinical Innovation Multidisciplinary		Weakness For stroke survivors with arm weakness repetitive practice using assistive technology, constraint induced movement therapy (CIMT), and robotics may be used to improve arm strength. (de Sousa et al 2018 [70]). For stroke survivors with leg weakness task specific training, repetitive practice using cycling or electrical stimulation may be used to improve leg strength. (de Sousa et al 2018 [70])	Broadly agree with this recommendation for progressive resistance training, so long as the wording of the recommendation makes it clear that the primary goal of this therapy is STRENGTHENING, and not necessarily FUNCTION. Agree with the new recommendation for repetitive training. For cycling, there were only two studies included in the subgroup analysis in the de Sousa systematic review – is this sufficient to make a recommendation? For Electrical stimulation the subgroup analysis (in de Souza) included 2 studies that included ES only on the upper limb – does removing these studies change the result of the sub-group analysis?	We agree focus on PRE is on strength and that has been reflected throughout. However, we have added this into the recommendation to ensure this is clear and the recommendation now reads: For stroke survivors with reduced strength in their arms or legs, progressive resistance training should be provided to increase strength. (Dorsch et al. 2018 [73]) Regarding cycling, there are other recommendations made on small numbers of studies and this is one important consideration as to why we only made a weak recommendation. We will continue to monitor any new evidence in this regard. Regarding electrical stimulation - while de Souza supplement does provide a breakdown in UL and LL the effects were not that different (SMD 0.37 vs 0.45) with two small studies in the UL leading to wide confidence intervals. The group didn't feel there was a reason to expect differences in FES should be different for muscles in the UL and LL and hence presented the stronger, combined effect estimates.

Kate Jackson / NSW health (group) 28.10.20	Agency for Clinical Innovation Multidisciplinary		Shoulder pain For stroke survivors with shoulder pain, electrical stimulation may be used to manage pain. (Qiu et al 2019 [87])	These shoulder recommendations seem to sit under a heading of Central Post-Stroke Pain (CPSP). It is considered that strapping intervention, and the electrical stimulation intervention are more likely to help some forms of Mechanical shoulder pain. Even if the studies were 'non-discriminatory' recommending these therapies for CPSP, we believe, inappropriate. This applies to the Practice points as well. The data for electrical stimulation to assist with pain is inadequate. The apparent improvements in pain at a mean of less than 2.0 on the visual analogue scale (VAS) could be regarded as statistically significant but not clinically significant, where a shift of at least 2.0 on the VAS is usually required. Concerns raised in relation to the rationale to include any statement re acupuncture. Not only does the degree of pain reduction not reach clinical significance, but the studies are of low quality, and there is no definition around what 'type' of acupuncture is being recommended. All the studies included in the systematic review had acupuncture in addition to normal rehabilitation – it would be good to highlight/include this. Is there a risk that identifying this by itself that a member of public would just want acupuncture?	Comment inserted to separate central pain heading from shoulder pain. Regarding electrical stimulation -the data is based on 4 studies -two of these used VAS but two others used Brief Pain Inventory 12 so the outcome is a standardised mean difference (SMD). Thus 1.89 lower SMD is a significant and clinically meaningful difference. Regarding acupuncture we agree that the evidence is weak and effects small and this is reflected in the evidence summary. However, we also agree that acupuncture should not be considered in isolation and have made changes to the recommendation and rationale to reflect this. Regarding the minimally clinical important difference (MCID) there is a lack of evidence to determine the threshold for this specific to stroke. An additional sentence has been inserted in the evidence summary to reflect this uncertainty and to also reflect in other patient populations with shoulder problems (rotator cuff disease and post shoulder arthroplasty) the MCID was found to be -1.4cm and the group felt while the effect is small it may still be worthwhile to some patients.
Hannah Paal (Group) 3.11.20	Tasmanian Stroke Clinical Network Multidisciplinary	NA	All	Nil	Noted. No change required.