ESOC 2021

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VIRTUAL

THE VOICE OF STROKE IN EUROPE

ESO and EAN Joint Guideline

Post Stroke Cognitive Impairment

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Faculty Disclosure (TQ)

x	No, nothing to disclose
	Yes, please specify:

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The need for a guideline on cognitive impairment

- Post stroke cognitive impairment is common
- Stroke survivors and clinicians rate it as a priority
- Variation in practice across Europe
- Limited Guideline recommendations

Composition of the writing group

Diversity and representation

Chairs: Terence J Quinn (ESO), Hugh S Markus (EAN)

Module Working Group: Rose Bruffaerts (Belgium), Thomas Gattringer (Austria), Hysse Forchammer (Denmark), Emma Ghaziani (Denmark), Celine Gillebert (Belgium), Niamh Merriman (Ireland), Milija Mijalovic (Serbia), Edo Richard (Netherland), Sarah T Pendlebury (UK), Reinhold Schmidt (Austria), Yvonne Teuschl (Austria), John T O'Brien (UK), Ana Verdelho (Portugal)

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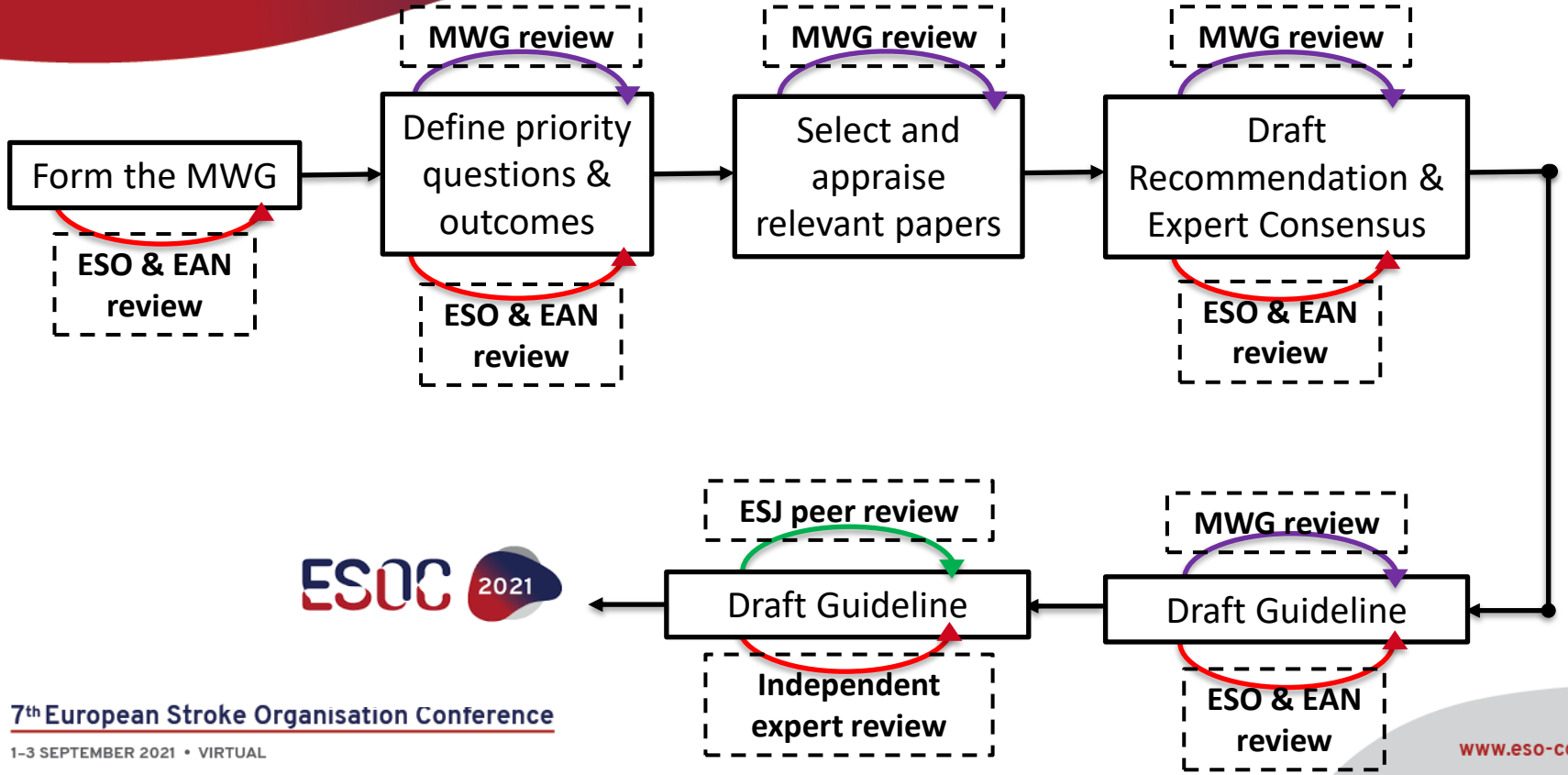
Guideline Content

Prevention	Diagnosis
Edo Richard Yvonne Teuschl, Thomas Gattringer, Melanie Hafdi	**Niamh Merriman** John T O'Brien, Celine Gillebert, Hanne Huyglier
Treatment	**Prognosis**
Ana Verdelho, Reinhold Schmidt Emma Ghaziani, Hysse Forchammer	**Sarah T Pendlebury** Milija Mijajlovic, Emily Ball, Bogna A Drozdowska, Rose Bruffaerts

Guideline Methods

- ESO Guidelines Standard Operating Procedure
- GRADE methodology
- Systematic literature search and critical appraisal
- Delphi process and consensus
- Multiple stages of internal and external review

Guideline Methods



Guideline content

- > 100 pages
- > 200 references
- 18 PICO questions with Recommendation and Expert Consensus Statements
- Highlights

Prevention

In stroke survivors, **do monitored lifestyle-based interventions** (exercise, dietary change, alcohol moderation, weight loss, smoking cessation), **alone or in combination**, compared to care as usual, prevent: future cognitive decline or dementia?

Prevention

In stroke survivors, **do monitored lifestyle-based interventions** (exercise, dietary change, alcohol moderation, weight loss, smoking cessation), **alone or in combination**, compared to care as usual, prevent: future cognitive decline or dementia?

We cannot recommend monitored lifestyle interventions solely for the prevention of post-stroke cognitive decline or dementia.

Quality of evidence: **Very Low** ⊕

Strength of recommendation: No recommendation

(This recommendation only relates to the cognitive effects of lifestyle interventions)

Prevention

In stroke survivors, does **monitored intensive management of vascular risk factors**, compared to care as usual, prevent: future cognitive decline or dementia?

Prevention

We cannot recommend intensive treatment of **blood pressure** compared to usual care solely for the prevention of post-stroke cognitive decline and dementia.

Quality of evidence: Very Low ⊕ Strength of recommendation: No recommendation

We suggest against using **dual antiplatelet therapy** compared to single antiplatelet therapy for the prevention of cognitive decline or dementia following lacunar stroke.

Quality of evidence: Very Low ⊕ Strength of recommendation: **Weak against ↓?**

We cannot recommend **intensive statin treatment** compared to usual care solely for the prevention of post-stroke cognitive decline or dementia.

Quality of evidence: Very Low ⊕ Strength of recommendation: No recommendation

Prevention

In stroke survivors, does cognitive training, compared to care as usual, prevent: future cognitive decline or dementia?

Prevention

In stroke survivors, does cognitive training, compared to care as usual, prevent: future cognitive decline or dementia?

There is continued uncertainty over the benefits and limitations of cognitive training for the prevention of cognitive decline and dementia in people living with stroke.

Quality of evidence: Very low

Strength of recommendation: No recommendation

Prevention

In people with post stroke dementia, does **stopping pharmacological management of vascular risk factors** (deprescribing), compared to continuation, prevent: future cognitive decline or improve quality of life?

Prevention

In people with post stroke dementia, does **stopping pharmacological management of vascular risk factors** (deprescribing), compared to continuation, prevent: future cognitive decline or improve quality of life?

There is continued uncertainty over the benefits and risks of continuing treatment with antihypertensive or statin medications compared to withdrawal of these medications for cognitive or quality of life outcomes in people living with post-stroke dementia.

Quality of evidence: **Very low**

Strength of recommendation: No recommendation

Prevention

In people with post stroke dementia, does **stopping pharmacological management of vascular risk factors** (deprescribing), compared to continuation, prevent: future cognitive decline or improve quality of life?

Given the beneficial effect on cardiovascular disease and no clear signal of cognitive harm, pharmacological vascular risk factor management should be continued in patients with mild to moderate post-stroke dementia.

In people with more advanced dementia, where potential harms and burden of treatment may be greater, the benefits of continuing stroke secondary prevention medications are unclear.

Pragmatic trials of deprescribing medications are needed in this group.

Diagnosis

In patients with stroke, **does routine use of cognitive screening**, compared to no routine screening, improve stroke care.

Diagnosis

In patients with stroke, **does routine use of cognitive screening**, compared to no routine screening, improve stroke care.

Due to a lack of relevant trials in patients with stroke, there is continued uncertainty over the benefits and risks of routine cognitive screening to improve stroke care.

Quality of evidence: **Very Low** ⊕

Strength of recommendation: no recommendation

(this recommendation applies only to routine screening of all patients presenting with stroke, and does not apply to clinician directed assessment)

Diagnosis

Cognitive screening should be considered as part of the comprehensive assessment of stroke survivors.

However, there are insufficient data to make recommendations around the timing, the content or the potential benefits of cognitive screening to the patient, their care-givers, and to healthcare systems.

Further studies describing the effects of routine cognitive screening following stroke are required. These studies should include acute stroke settings, should record **feasability** and **acceptability**, consider effects on **care pathways**, and describe care-giver outcomes and health economics.

Diagnosis

In patients with stroke (acute or post-acute), what is the accuracy of **Montreal Cognitive Assessment** for contemporaneous diagnosis of post-stroke cognitive impairment or dementia?

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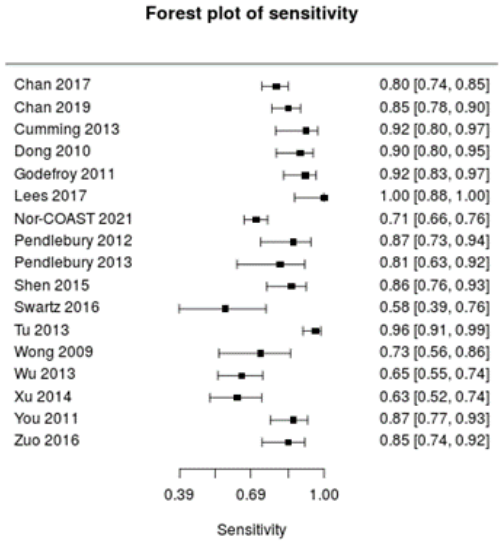

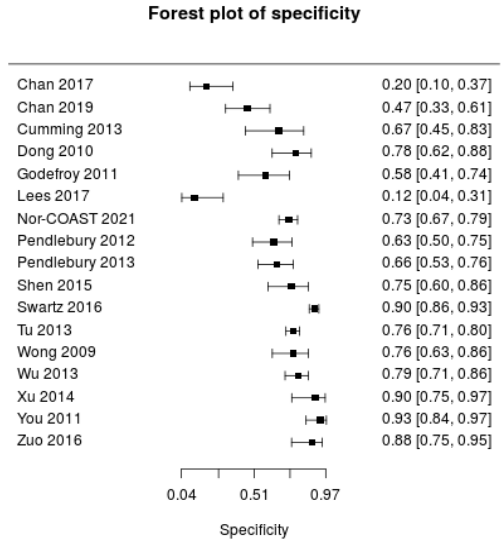

Diagnosis

In patients with stroke (acute or post-acute), what is the accuracy of **Montreal Cognitive Assessment** for contemporaneous diagnosis of post-stroke cognitive impairment or dementia?

We suggest that in post-acute stroke settings, screening of cognition using the Montreal Cognitive Assessment (MoCA) is considered, but it is not a substitute for comprehensive clinical assessment.

At the conventional threshold for test positivity, MoCA screening will detect most stroke survivors with important cognitive issues but at the cost of substantial false positives.

We suggest that a revised (lower) threshold be considered for stroke populations.

Quality of evidence: **Low** ⊕⊕ Strength of recommendation: **Weak for intervention** ↑?

Diagnosis

In patients with stroke (acute or post-acute), what is the accuracy of **Folstein's Mini-Mental State Examination** for contemporaneous diagnosis of cognitive impairment or dementia?

We suggest that in post-acute stroke settings, screening of cognition using the Mini-Mental State Examination (MMSE) is considered, but it is not a substitute for comprehensive clinical assessment.

At the conventional threshold for test positivity, MMSE screening will exclude most stroke survivors with no important cognitive issues, but at the cost of false negatives.

Quality of evidence: **Low** ⊕⊕ Strength of recommendation: **Weak for intervention** ↑?

Diagnosis (MoCA, MMSE, ACE, OCS, telephone)

There are inherent limitations to the various versions of the Addenbrookes Cognitive Examination (ACE), which all rely on intact visuospatial and language function for completion.

Consideration should be given to the development of cognition screening tools that are more acceptable and feasible for those with communication difficulties or spatial neglect.

Those utilising the ACE cognitive screening test should be trained in its administration.

Further comprehensive cognitive assessment is recommended in the event of a positive ACE test result and findings should be shared with the stroke care team.

Treatment

In people with post-stroke cognitive impairments, do **cholinesterase inhibitors and/or memantine**, compared to placebo, delay cognitive decline or progression to dementia; improve behavioural and psychological symptoms, decrease caregiver burden and/or cause adverse effects?

Treatment

In people with post-stroke cognitive impairments, do **cholinesterase inhibitors and/or memantine**, compared to placebo, delay cognitive decline or progression to dementia; improve behavioural and psychological symptoms, decrease caregiver burden and/or cause adverse effects?

In people living with post-stroke cognitive impairment there is continued uncertainty over the benefits and risks of cholinesterase inhibitors and/or memantine for cognition, behavioural and psychological symptoms, activities of daily living and caregiver burden.

Quality of evidence: **Very Low** ⊕

Strength of recommendation: No recommendation

Treatment

In people living with post stroke dementia, any beneficial effect of cholinesterase inhibitors is likely to be modest, and perhaps not clinically relevant, the risk of adverse events should also be considered.

In a predominantly vascular cognitive impairment the effect of these drugs is minimal, but many older adults with stroke have other neurodegenerative diseases that may benefit from cholinesterase inhibitors.

Stroke should not be a barrier to considering treatment with cholinesterase inhibitors if suspected concomitant Alzheimer's disease or Lewy Body dementia.

Treatment

In people with post-stroke cognitive impairments, do the **nootropics actovegin or cerebrolysin**, compared to placebo, improve cognitive decline, improve BPSD, reduce caregiver burden and/or increase adverse events.

Treatment

In people with post-stroke cognitive impairments, do the **nootropics actovegin or cerebrolysin**, compared to placebo, improve cognitive decline, improve BPSD, reduce caregiver burden and/or increase adverse events.

In people living with post-stroke cognitive impairment there is continued uncertainty over the benefits and risks of actovegin and cerebrolysin for cognition, BPSD and caregiver burden.

Quality of evidence: Very Low ⊕ Strength of recommendation: No recommendation possible

The available evidence suggests that any benefits of actovegin and cerebrolysin are likely to be modest and there is risk of serious adverse events. Considering the balance of risks and harms, we suggest against using these agents for post stroke cognitive impairment.

Treatment

In people with post-stroke cognitive impairments, does **cognitive rehabilitation (skill training or compensation strategies)** compared to no rehabilitation, delay cognitive decline or progression to dementia, improve BPSD, improve performance in activities of daily living or decrease caregiver burden?

Treatment

In people with post-stroke cognitive impairments, does **cognitive rehabilitation (skill training or compensation strategies)** compared to no rehabilitation, delay cognitive decline or progression to dementia, improve BPSD, improve performance in activities of daily living or decrease caregiver burden?

Due to a lack of robust trials, for most cognitive rehabilitation interventions, there is continued uncertainty on the benefits and limitations associated with these interventions for stroke survivors.

Quality of evidence: Very low ⊕ Strength of recommendation: no recommendation

Although many studies did not meet our inclusion criteria for this PICO, there is emerging evidence that cognitive rehabilitation, particularly compensatory strategies, in the context of individually relevant functional tasks, may be beneficial for people with post-stroke cognitive impairments.

Robust trials to support definitive recommendations for clinical practice are needed.

Prognosis

In people with a history of stroke, **do structural features on acute brain MR imaging**, predict (at least one year from index stroke event) future cognitive decline or dementia.

Prognosis

Participants: Patients with acute stroke

Prognostic factor: Acute stroke MR brain imaging

Timing of follow-up: At least 12 months from index stroke

Outcome	MRI abnormality	No of participants	Risk of bias	Quality of evidence (GRADE)
PSCI	White matter hyperintensity	Eight studies 1781 participants	High	Moderate
PSCI	Atrophy	Two studies 415 participants	High	Very low[1]
PSCI	Lesion volume	Four studies 895 participants	High	Low
PSCI	Small Vessel Disease score	Three studies 925 participants	High	Low
PSCI	Cerebral microbleeds	Four studies 980 participants	High	Very low[1]
PSCI	Perivascular spaces	Three studies 925 participants	High	Very low[1]

Prognosis

In people with a history of stroke, **do structural features on acute brain MR imaging**, predict (at least one year from index stroke event) future cognitive decline or dementia.

We suggest that in patients with acute stroke, the presence of substantial white matter hyperintensities of presumed vascular origin on acute MRI brain may help predict cognitive outcomes more than one year after stroke.

Quality of evidence: **Moderate** ⊕ Strength of recommendation: **Weak for intervention** ↑?

In patients with acute stroke there is continued uncertainty regarding the value of other MRI brain features to predict cognitive outcomes more than one year after stroke.

Quality of evidence: **Very Low** ⊕ Strength of recommendation: no recommendation

Prognosis

In people with a history of stroke, **do structural features on acute brain CT imaging**, predict (at least one year from index stroke event) future cognitive decline or dementia.

Prognosis

In people with a history of stroke, **do structural features on acute brain CT imaging**, predict (at least one year from index stroke event) future cognitive decline or dementia.

In patients with acute stroke there is continued uncertainty regarding the value of acute CT-brain imaging findings for predicting cognitive outcomes more than one year after stroke.

Quality of evidence: Very Low ⊕

Strength of recommendation: No recommendation

Prognosis

As CT is widely available and commonly used in acute stroke, a better understanding of the prognostic value of the imaging findings for future cognitive prognosis would be useful.

Further studies of the predictive value of CT-based imaging variables should use **standardized measurements** and validated tools.

Consideration needs to be given to the population included, with preferably unselected samples and low rates of attrition from cognitive follow-up.

Results of these studies need appropriate adjustments to distinguish the **added prognostic value** of CT imaging features over standard clinical factors such as age, sex and stroke severity.

Prognosis

In people with a history of stroke, do **multi-item prognostic tools** performed soon after stroke, predict future cognitive decline or dementia.

Prognosis

In people with a history of stroke, do **multi-item prognostic tools** performed soon after stroke, predict future cognitive decline or dementia.

There is continued uncertainty over the advantages and disadvantages of using multi-item prognostic tools to predict cognitive outcomes following stroke.

Quality of evidence: Very Low ⊕

Strength of recommendation: No recommendation

Conclusions

Conclusions

No evidence for anything

Few practice recommendations

Justification to disinvest or remove services

Conclusions

No evidence for anything

Few practice recommendations

Justification to disinvest or remove services

Honest synthesis of available data

Consensus statements to guide practice

Catalyst to focus attention, funding on high quality RCTs

Areas for future research

Prevention

- Low cost risk stratification tools
- Barriers & facilitators to lifestyle change
- Include cognitive outcomes in RCTs

Diagnosis

- Efficacy of routine cognitive screening
- Comparative accuracy of screening tools
- Methods and best practice for remote cognitive testing

Treatment

- RCTs of de-prescribing, nootropics, rehab
- Similarities and differences between stroke, dementia and other conditions

Prognosis

- Validation and added benefit of prediction tools
- Implementation and efficacy of prediction tools

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