Recommendations 2022 de l'ESO

Pr Guillaume TURC, MD, PhD, FESO

Chairman of the ESO Guideline Board

ESO Guideline Board

Guideline Board

- **Guillaume Turc, Chair (France)**
- **Terry Quinn, Co-Chair (UK)**
- Aristeidis Katsanos (Canada)
- Blanca Fuentes (Spain)
- Christian Nolte (Germany)
- Daniel Strbian (Finland)
- Diana Aguiar de Sousa (Portugal)
- Georgios Tsivgoulis (Greece)
- Linxin Li (UK)
- Sven Poli (Germany)

Workshop Subcommittee

Gian Marco De Marchis (Switzerland)
Jan Purrucker (Germany)

Publication Subcommittee

Marialuisa Zedde (Italy)
Joan Marti-Fabregas (Spain)

Recommandations publiées en 2021

Guidelines

- Thrombolyse intraveineuse
- AIT
- Infarctus malin
- Pression artérielle à la phase aiguë
- Sténose carotide
- Troubles cognitifs post-AVC
- Troubles de la déglutition post-AVC
- Dissections

Expedited Recommendation

- Bithérapie antiplaquettaire infarctus mineur / AIT

Recommandations publiées en 2022

Guidelines

- Prévention secondaire post-AVC
- AVC chez la femme
- Athérome intracrânien
- Maladie des petits vaisseaux «silencieuse»
- Détection de la FA en cas d’infarctus cryptogénique
- Anévrismes asymptomatiques
- Unités Neurovasculaires Mobiles

Expedited Recommendation

- Intérêt de la thrombolyse avant thrombectomie

Recommandations publiées en 2022

Guidelines

- Prévention secondaire post-AVC
- AVC chez la femme
- Athérome intracrânien
- Maladie des petits vaisseaux «silencieuse»
- Détection de la FA en cas d'infarctus cryptogénique
- Anévrismes asymptomatiques
- Unités Neurovasculaires Mobiles

Expedited Recommendation

- Intérêt de la thrombolyse avant thrombectomie

Méthodologie

- ESO Guideline Standard Operating Procedure
- Méthodologie GRADE
- Questions PICO
- Revue systématique de la littérature pour chaque question PICO
- Méta-analyses
- Evaluation du risque de biais
- Résumé grand public

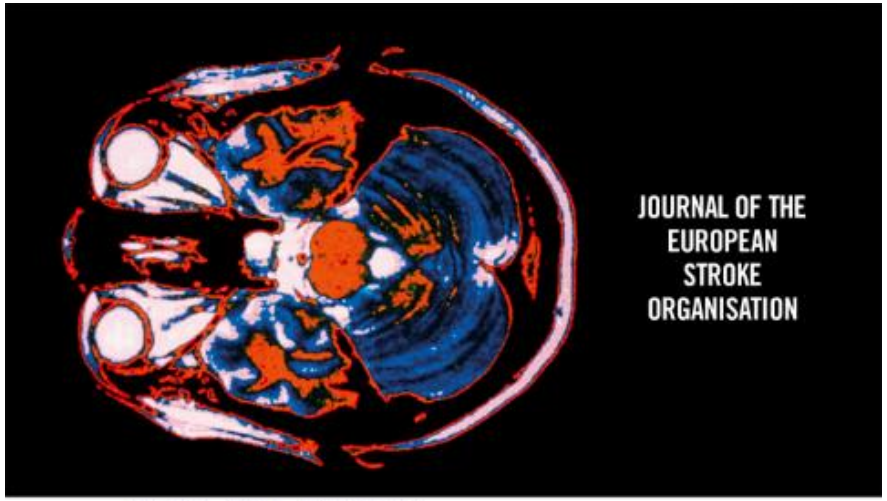
Deux types de recommendations:

a) **Evidence-based recommendations**

- Quality of Evidence: **High** ⨁⨁⨁⨁ / **Moderate** ⨁⨁⨁ / **Low** ⨁⨁ / **Very low** ⨁
- Strength of recommendation: **Strong** ↑↑ / **Weak** ↑?
  Strong ↓↓ / **Weak** ↓?

b) **Expert consensus statements** (+ vote)

Steiner et al, Eur Stroke J 2021



VOLUME 6 ISSUE 4 DECEMBER 2021

EUROPEAN STROKE JOURNAL

http://journals.sagepub.com/home/eso

Impact factor: 5,89

EUROPEAN STROKE ORGANISATION

ESMINT
European Society of Minimally Invasive Neurological Therapy

Expedited recommendation on intravenous thrombolysis before mechanical thrombectomy in patients with acute ischaemic stroke and anterior circulation large vessel occlusion

Guillaume Turc, Georgios Tsivgoulis, Heinrich Audebert, Hieronymus Boogarts, Pervinder Bhogal, Gian Marco De Marchis, Catarina Fonseca, Pooja Khatri, Mikaël Mazighi, Natalia Pérez de la Ossa, Peter Schellinger, Daniel Strbian, Danilo Toni, Philip White, William Whiteley, Andrea Zini, Wim van Zwam, and Jens Fiehler

Randomized controlled trials

Mothership, ≤4.5 hrs of symptom onset

Trial	N	Location	Non-inferiority margin	Conclusion of non inferiority
DIRECT-MT	654	China	Relative, cOR 0.80	Yes
DEVT	234	China	Absolute, 10% mRS 0-2	Yes
SKIP	204	Japan	Relative, OR 0.74 mRS 0-2	No
MR CLEAN No IV	539	Europe	Relative, cOR 0.80	No
SWIFT DIRECT	404	Europe & North America	Absolute, 12% mRS 0-2	No
DIRECT-SAFE	293	Oceania & Asia	Absolute, 10% mRS 0-2	No

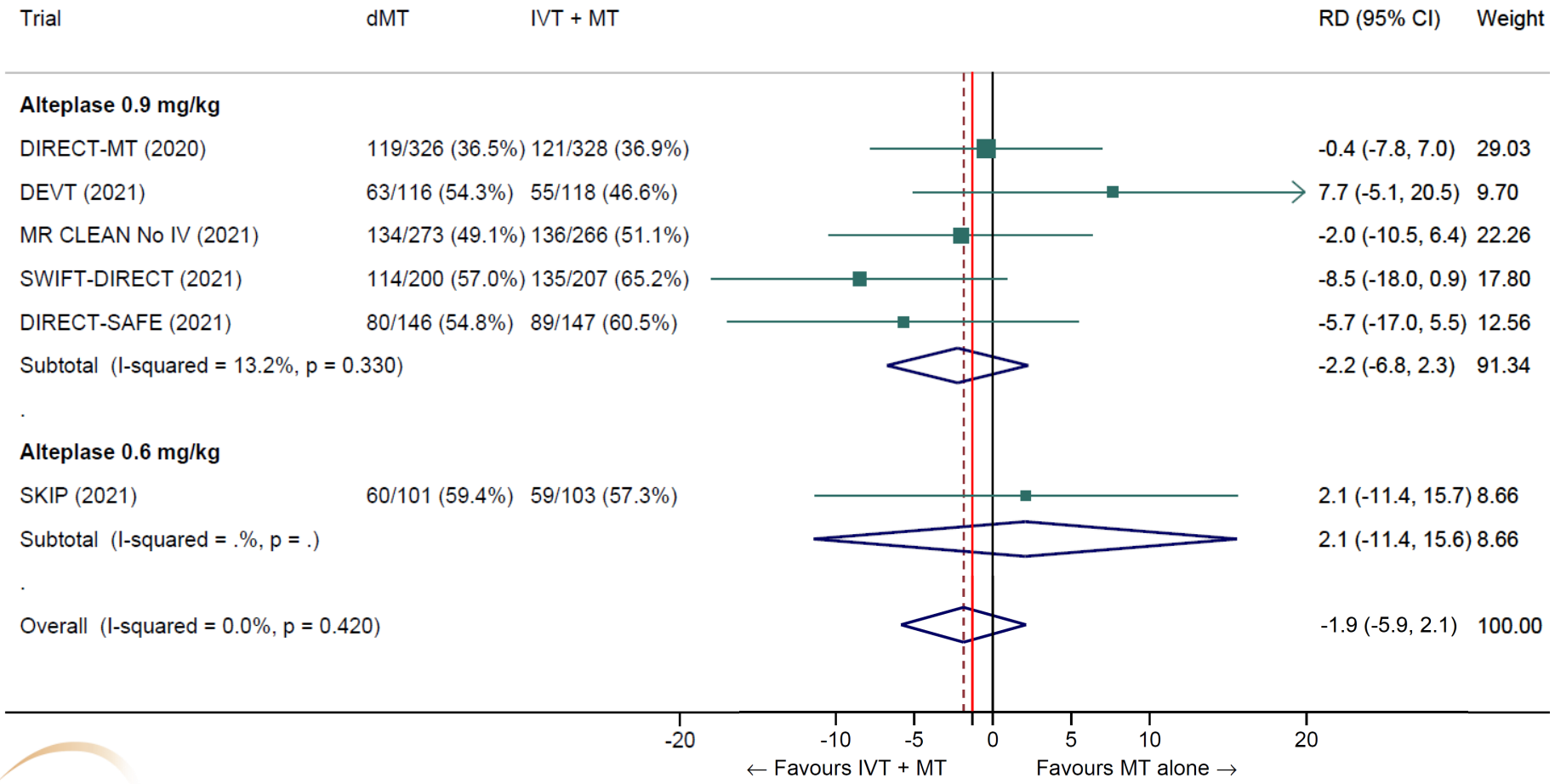
ESMINT
European Society of Minimally Invasive Neurological Therapy

Yang P et al, NEJM 2020; Zi W et al, JAMA 2021; Suzuki K et al, JAMA 2021
LeCouffe N et al, NEJM 2021; Fischer U et al, ESOC 2021; Mitchell PJ et al, WSC 2021

ESO
EUROPEAN STROKE ORGANISATION

Direct MT vs. IVT plus MT

Good functional outcome (mRS 0-2 at 90 days)



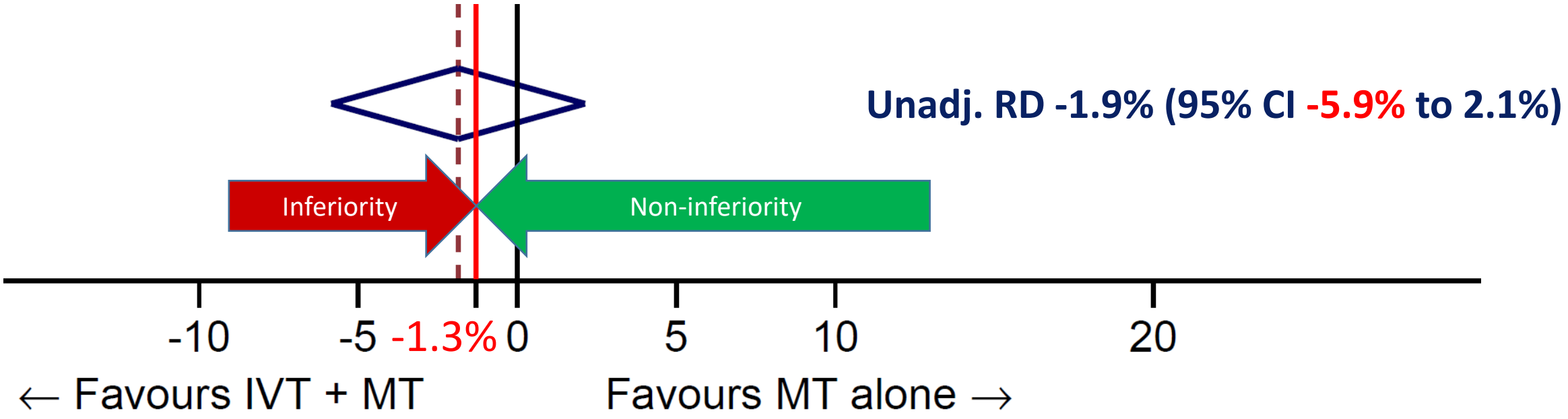
Unadj. RD -1.9% (95% CI -5.9% to 2.1%)

ESMINT
European Society of Minimally Invasive Neurological Therapy

ESO
EUROPEAN STROKE ORGANISATION

Direct MT vs. IVT plus MT

Good functional outcome (mRS 0-2 at 90 days)

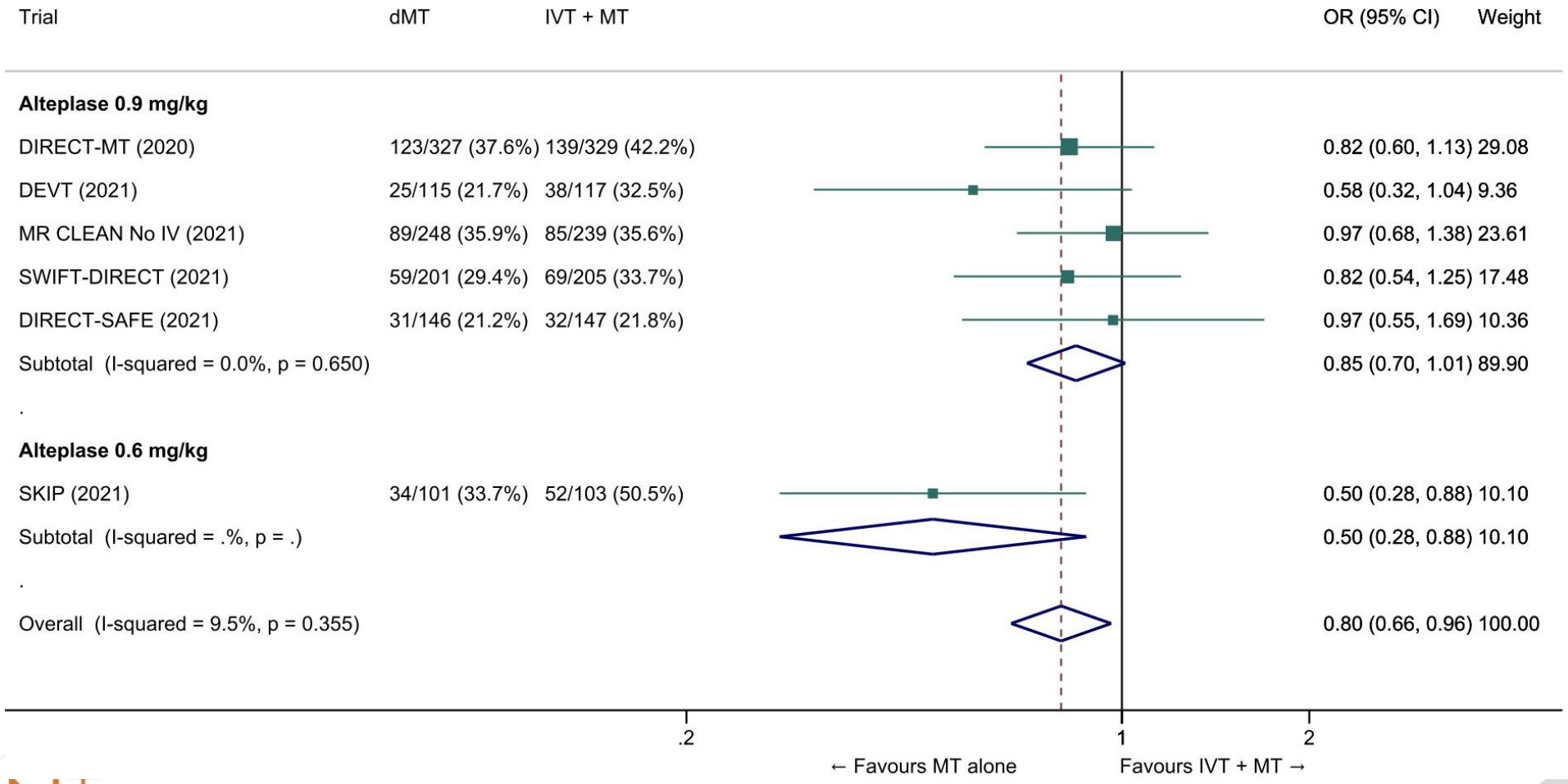


ESMINT
European Society of Minimally Invasive Neurological Therapy

ESO
EUROPEAN STROKE ORGANISATION

Direct MT vs. IVT plus MT

Any intracranial haemorrhage



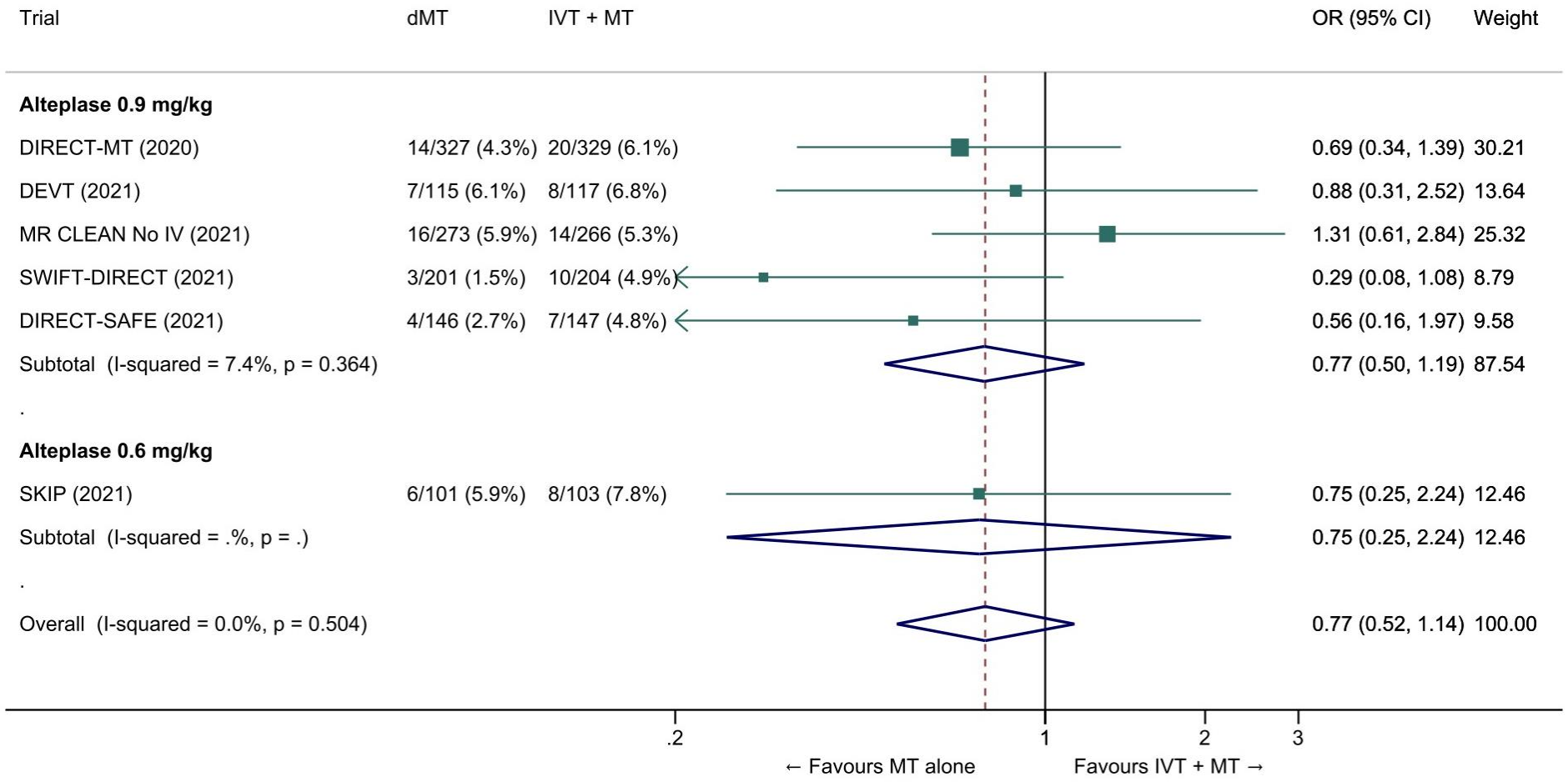
Unadj. OR 0.80 (95% CI 0.66 to 0.96)

ESMINI
European Society of Minimally Invasive Neurological Therapy

ESO
EUROPEAN STROKE ORGANISATION

Direct MT vs. IVT plus MT

Symptomatic intracranial haemorrhage



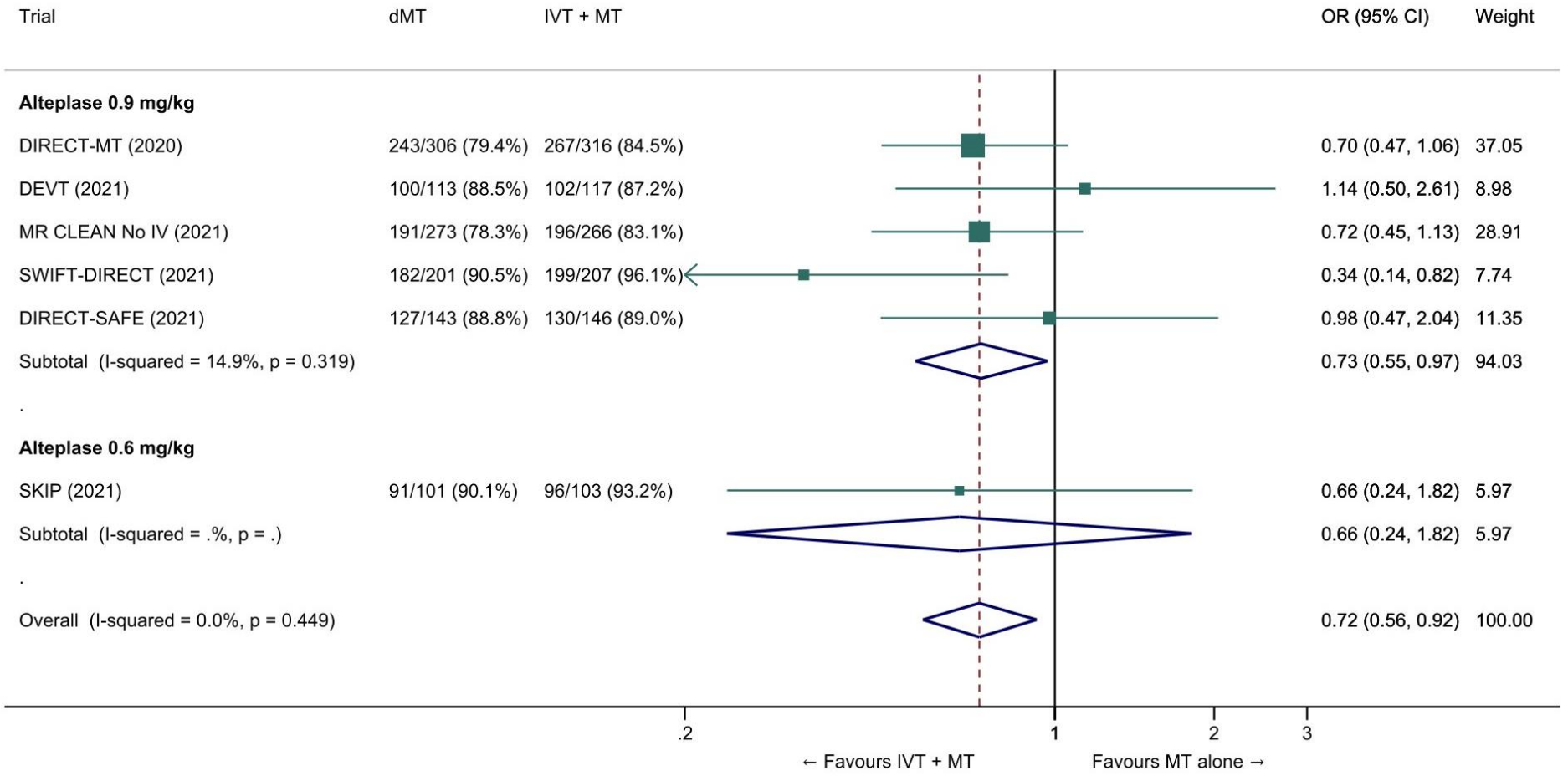
Unadj. OR 0.77 (95% CI 0.52 to 1.14)

ESMINT
European Society of Minimally Invasive Neurological Therapy

ESO
EUROPEAN STROKE ORGANISATION

Direct MT vs. IVT plus MT

Succesful reperfusion (mTICI ≥2b) at the end of the endovascular procedure



Unadj. OR 0.72 (95% CI 0.56 to 0.92)

ESMINT
European Society of Minimally Invasive Neurological Therapy

ESO
EUROPEAN STROKE ORGANISATION

Evidence-based Recommendation

Mothership, ≤4.5 hrs of symptom onset

For patients directly admitted to a thrombectomy-capable centre for an acute ischaemic stroke (≤4.5 hrs of symptom onset) with anterior circulation large vessel occlusion and who are eligible for both treatments, **we recommend intravenous thrombolysis plus mechanical thrombectomy** over mechanical thrombectomy alone.

Both treatments should be performed **as early as possible** after hospital arrival. Mechanical thrombectomy should not prevent the initiation of intravenous thrombolysis, and intravenous thrombolysis should not delay mechanical thrombectomy.

Quality of evidence: **Moderate** ⊕⊕⊕

Strength of recommendation: **Strong** ↑↑

ESMINT
European Society of Minimally Invasive Neurological Therapy

ESO
EUROPEAN STROKE ORGANISATION

Expert Consensus Statement

Mothership, wake-up stroke

For patients directly admitted to a thrombectomy-capable centre within 4.5 hours of symptom recognition after wake-up stroke caused by anterior circulation large vessel occlusion, **we suggest intravenous thrombolysis plus mechanical thrombectomy** over mechanical thrombectomy alone **in selected patients**.

The selection criteria are detailed in the corresponding European Guidelines. Notably, eligibility imaging criteria for IVT include DWI-FLAIR mismatch or perfusion core/penumbra mismatch*.

*Perfusion core/penumbra mismatch:
- Infarct core** volume < 70 ml
- and Critically hypoperfused† volume / Infarct core** volume > 1.2
- and Mismatch volume > 10 ml

** rCBF <30% (CT perfusion) or ADC < 620 $\mu m^2/s$ (Diffusion MRI)
† Tmax >6s (perfusion CT or perfusion MRI)

ESMINT
European Society of Minimally Invasive Neurological Therapy

2019 ESO-ESMINT Guidelines on mechanical thrombectomy (Turc G et al, Eur J Stroke 4(1):6-12)
2021 ESO Guidelines on intravenous thrombolysis (Berge E et al, Eur J Stroke 6(1):I-LXII)

ESO
EUROPEAN STROKE ORGANISATION

Conclusions

- Randomized trials only included:
  - Patients with anterior circulation large vessel occlusion strokes
  - Eligible for alteplase within 4.5hrs of symptom onset
  - Admitted to a thrombectomy-capable centre

- In that setting, non-inferiority of direct MT has not been demonstrated (1.3%, or even 5%)
- Therefore, in the absence of contraindication, **we recommend IVT before MT**
- **IVT should not delay MT or the transfer to a center with MT facilities**

- We also suggest IVT before MT in selected patients with wake-up stroke (expert opinion)

- These recommendations may be updated in case IPD meta-analyses disclose subgroups of ‘mothership’ patients in whom direct MT is superior to IVT + MT

ESMINT
European Society of Minimally Invasive Neurological Therapy

ESO
EUROPEAN STROKE ORGANISATION

EUROPEAN STROKE ORGANISATION

Covert Cerebral Small Vessel Disease

Joanna Wardlaw, Stephanie Debette, Hanna Jokinen, Frank-Erik De Leeuw, Leonardo Pantoni, Hugues Chabriat, Julie Staals, Fergus Doubal, Christian Enzinger, Charlotte Cordonnier, Arne Lindgren

Evidence-based Recommendations PICO 1.1 – 1.7

Does **antihypertensive treatment**, reduce ischaemic or haemorrhagic strokes (1.1), cognitive decline or dementia (1.2), dependency (1.3), death (1.4), MACE (1.5), mobility (1.6), or mood disorders (1.7)

Evidence-based Recommendation

We recommend the use of antihypertensive treatment in hypertensive ccSVD patients (≥140/90 mmHg), to prevent the extension of SVD lesions and related clinical manifestations.

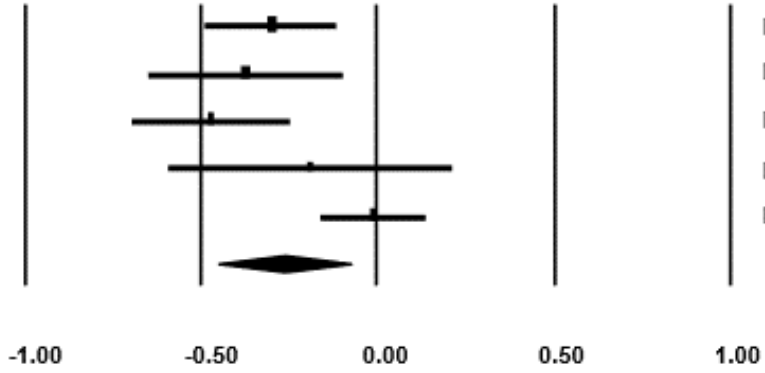
Quality of evidence: **Very low⊕**

Strength of recommendation: **Strong for intervention ↑↑**

2540 papers; 93 full text; 2 RCTs, 1 observational study: 924 participants
RCTs in primary & secondary prevention; IPD meta-analyses of observational studies; RCTs reporting WMH change meta-analysis

Effects of BP lowering in RCTs on WMH progression

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Baseline WMH Control (Mean)	Baseline WMH Intervention (Mean)	Change in WMH Control (Mean)	Change in WMH Intervention (Mean)	Comparison
SPRINT MIND	-0.300	0.097	0.009	-0.489	-0.111	-3.103	0.002	4.40	4.57	1.45	0.90	Intensive lowering vs standard lowering
INFINITY	-0.370	0.142	0.020	-0.648	-0.092	-2.606	0.009	18.50	20.50	7.40	4.20	Intensive lowering vs standard lowering
ACCORD MIND	-0.470	0.114	0.013	-0.694	-0.246	-4.110	0.000	1.80	2.04	1.16	0.67	Intensive lowering vs standard lowering
SCOPE	-0.190	0.206	0.043	-0.595	0.215	-0.921	0.357	12.40	11.30	1.86	1.31	BP lowering drug vs Placebo
Zhang2019	-0.010	0.076	0.006	-0.160	0.140	-0.131	0.896	5.09	5.35	1.40	1.24	BP lowering drug vs Placebo
	-0.262	0.098	0.010	-0.454	-0.070	-2.672	0.008					



Blue= cSVD and hypertensive study population;
Red= Diabetic study population;
Green= Hypertensive and/or high vascular risk study population

Expert Consensus Statement

Antihypertensive treatment in ccSVD

- All group members suggest that: BP should be appropriately monitored and well controlled. Provided that BP is well controlled we cannot advise any specific antihypertensive treatment.
- Most group members suggest that: For ccSVD patients, there is currently insufficient evidence to systematically advocate targeting BP levels lower than standard targets, although more intensive BP lowering than conventional BP lowering guidelines is associated with slower progression of WMH burden.
- All group members suggest that: In ccSVD patients in whom more intensive BP lowering targets are recommended for other reasons there is no strong evidence to suggest that this could be harmful.
- On current evidence the guideline group unanimously does not support systematic BP lowering in normotensive ccSVD patients.

Evidence-based Recommendations PICO 2.1 – 2.7

Does **antiplatelet treatment**, reduce ischaemic or haemorrhagic strokes (2.1), cognitive decline or dementia (2.2), dependency (2.3), death (2.4), MACE (2.5), mobility (2.6), or mood disorders (2.7)?

Evidence-based Recommendation

We suggest against antiplatelet treatment in patients with ccSVD as a means to reduce the clinical outcome events of ischaemic or haemorrhagic strokes, cognitive decline or dementia, dependency, death, MACE, mobility, or mood disorders.

Quality of evidence: **Very low⊕**

Strength of recommendation: **Weak against intervention ↓?**

1084 papers; 32 full text; 1 RCT; 83 participants
RCTs & systematic reviews in primary (eg ASPREE, n=19114) and secondary prevention; large epidemiology studies (eg WHI)

Expert Consensus Statement

Antiplatelet agents in ccSVD

Most group members agreed that:

- We advise against use of antiplatelet drugs to prevent clinical outcomes in subjects with ccSVD when no other indication for this treatment exists.
- With current available knowledge, the use of antiplatelet drugs to prevent progression of cerebral SVD may be harmful in older patients (from around ≥70 years of age) if no other indication for this treatment exists.

EUROPEAN STROKE ORGANISATION

Guideline on pharmacological interventions for long-term secondary prevention after ischaemic stroke or transient ischaemic attack

Jesse Dawson, Yannick Bejot, Louisa Christensen, Gian Marco de Marchis, Martin Dichgans, Guri Hagberg, Mirjam Heldner, Haralampos Milionis, Linxin Li, Martin Taylor-Rowan, Cristina Tiu, Alastair Webb

Evidence-based Recommendation: Blood Pressure

PICO 1: In people with a history of ischaemic stroke or TIA, does blood pressure lowering treatment compared to no blood pressure lowering treatment reduce the risk of any recurrent stroke?

Evidence-based Recommendation

In people with previous ischaemic stroke or TIA, we recommend blood pressure lowering treatment to reduce the risk of recurrent stroke.

Quality of evidence: **High** ⊕⊕⊕⊕

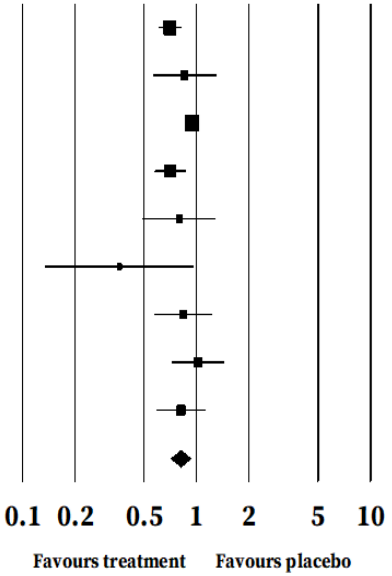
Strength of recommendation: **Strong for intervention** ↑↑

ESO
EUROPEAN STROKE ORGANISATION

Supporting Information

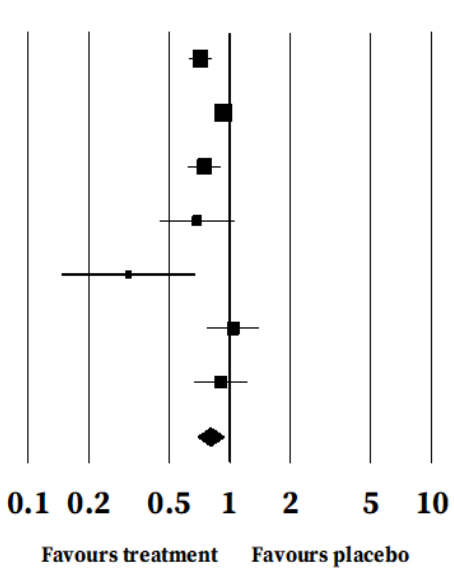
Recurrent Stroke

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
PROGRESS	0.702	0.600	0.821	-4.435	0.000
HOPE	0.852	0.557	1.305	-0.735	0.462
PROFESS	0.941	0.854	1.036	-1.241	0.215
PATS	0.706	0.571	0.872	-3.234	0.001
HSCS	0.796	0.489	1.294	-0.922	0.357
SCOPE	0.360	0.134	0.973	-2.015	0.044
DUTCH TIA	0.837	0.571	1.229	-0.906	0.365
TEST	1.013	0.711	1.445	0.072	0.942
FEVER	0.812	0.583	1.130	-1.236	0.216
	0.808	0.709	0.922	-3.173	0.002



MACE

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
PROGRESS	0.716	0.627	0.819	-4.899	0.000
PROFESS	0.928	0.858	1.005	-1.832	0.067
PATS	0.750	0.618	0.909	-2.930	0.003
HSCS	0.690	0.448	1.062	-1.685	0.092
SCOPE	0.315	0.147	0.678	-2.954	0.003
DUTCH TIA	1.039	0.767	1.407	0.246	0.806
TEST	0.902	0.664	1.224	-0.665	0.506
	0.802	0.686	0.938	-2.771	0.006



- Significant benefits for CV death (0.88, 0.78 – 0.99); NS for Death, MI, functional outcome. No data for dementia

ESO
EUROPEAN STROKE ORGANISATION

Blood Pressure

- The benefit of antihypertensive treatment in secondary prevention of stroke at mildly hypertensive levels is supported by the PROGRESS trial, in which the risk of recurrent stroke was reduced by treatment in both hypertensive and non-hypertensive populations.

Evidence-based Recommendation: Blood Pressure

PICO 3: In people with a history of ischaemic stroke or TIA starting or increasing antihypertensive therapy, does treating to a more intensive (i.e. blood pressure <130/80) versus less intensive (<140/90 mmHg) target reduce the risk of recurrent stroke?

Evidence-based Recommendation

In people with previous ischaemic stroke or TIA, we suggest aiming for a blood pressure target of <130/80 mmHg to reduce the risk of recurrent stroke.

Quality of evidence: **Moderate ⊕⊕⊕**

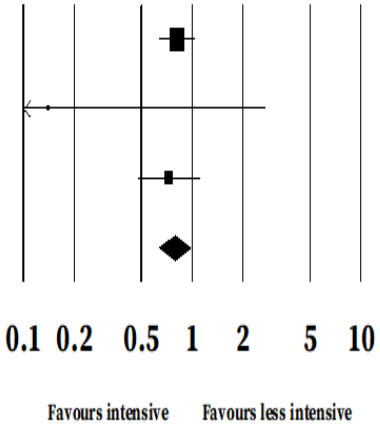
Strength of recommendation: **Weak for intervention ↑?**

ESO
EUROPEAN STROKE ORGANISATION

Supporting Information

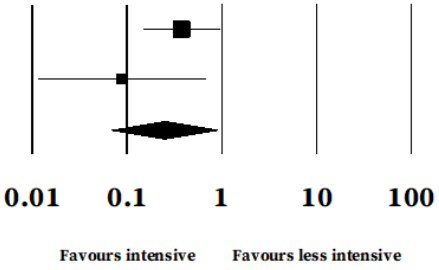
Any Stroke

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
SPS3	0.817	0.637	1.047	-1.596	0.110
PAST-BP	0.140	0.007	2.717	-1.300	0.194
RESPECT	0.730	0.474	1.123	-1.433	0.152
	0.787	0.635	0.975	-2.187	0.029



ICH

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
SPS3	0.377	0.147	0.966	-2.032	0.042
RESPECT	0.089	0.011	0.692	-2.312	0.021
	0.247	0.068	0.895	-2.129	0.033



- NS for ischaemic stroke, MACE, death, CV death, MI, functional outcome.
- Limited, heterogeneous trials, in specific populations (ie SPS3).

ESO
EUROPEAN STROKE ORGANISATION

Expert Consensus Statements: Achieving BP control

PICO 4: In people with a history of ischaemic stroke or TIA starting antihypertensive therapy, does initiation of two blood pressure lowering medications compared to monotherapy reduce the risk of recurrent stroke?

In people with ischaemic stroke or TIA, we support initiation of a combination of two blood pressure lowering drugs to reduce the risk of recurrent stroke, with consideration of monotherapy where there are potential risks of hypotension, such as in frail, elderly people and people with borderline hypertension

ESO
EUROPEAN STROKE ORGANISATION

Evidence-based Recommendation: Lipid lowering

PICO 5: In people with ischaemic stroke or TIA does use of an HMGCoA reductase inhibitor compared to no lipid-lowering therapy reduce the risk of recurrent stroke?

Evidence-based Recommendation

In people with previous ischaemic stroke or TIA we recommend use of a HMGCoA reductase inhibitor to reduce the risk of recurrent ischaemic stroke.

Quality of evidence: **High** ⨁⨁⨁⨁

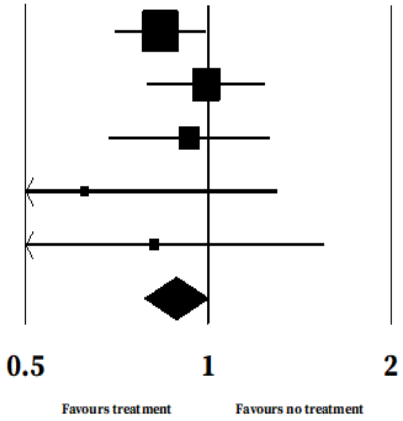
Strength of recommendation: **Strong for intervention** ↑↑

EUROPEAN STROKE ORGANISATION

Supporting Information

Recurrent Stroke

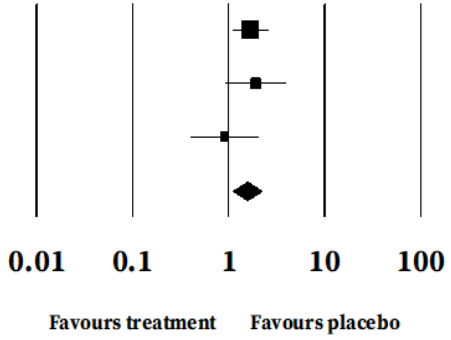
Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
SPARCL	0.834	0.700	0.993	-2.038	0.042
HPSC	0.992	0.792	1.242	-0.069	0.945
J-STARS	0.930	0.686	1.263	-0.463	0.643
CARE	0.625	0.301	1.300	-1.258	0.208
LIPID	0.814	0.428	1.550	-0.626	0.531
	0.885	0.784	0.999	-1.969	0.049



Meta Analysis

ICH

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
SPARCL	1.683	1.089	2.602	2.344	0.019
HPSC	1.919	0.922	3.992	1.743	0.081
J-STARS	0.906	0.397	2.066	-0.234	0.815
	1.552	1.090	2.210	2.437	0.015



- Significant benefits for ischaemic stroke (0.79, 0.67-0.92), MACE (0.78, 0.70-0.87); NS for Death, MI, functional outcome, dementia
- Treatment reduces 13 fewer strokes per 1000 cases, with 6 per 1000 more ICH

ESO
EUROPEAN STROKE ORGANISATION

Risk of ICH

- Our analysis showed that the risk of haemorrhagic stroke is increased with use of an HMGCoA reductase inhibitor.
- Even if this increase is real, our data show that use of an

HMGCoA reductase inhibitor may cause 6 haemorrhagic

strokes per 1000 people treated but prevent 40 major cardiovascular events.

- Participants in the SPARCL trial received atorvastatin 80 mg daily and when this is considered alongside the data for PICO question 6, we believe this is an appropriate dose for most people with ischaemic stroke or TIA

ESO
EUROPEAN STROKE ORGANISATION

Evidence-based Recommendation: Lipid lowering

PICO 6: In people with ischaemic stroke or TIA does working to an intensive cholesterol treatment target, compared to a less intensive target, reduce the risk of recurrent stroke?

Evidence-based Recommendation

In people with ischaemic stroke or TIA, we recommend aiming for an LDL cholesterol level of <1.8 mmol/l (70 mg/dl) to reduce the risk of major cardiovascular events.

Quality of evidence: **Moderate ⊕⊕⊕**

Strength of recommendation: **Strong for intervention ↑↑**

ESO
EUROPEAN STROKE ORGANISATION

Supporting Information

- Only 1 trial: Treating Stroke to Target (TST):
  - Significant reduction in MACE (HR 0.78, 95% CI 0.61 to 0.98; P=0.04).
  - Non-significant reductions in risk of stroke (HR 0.82, 95% CI 0.63 to 1.07), death, CV death etc.
  - There was a non-significant increase in intracranial haemorrhage (HR 1.38, 95% CI 0.68–2.82).
- Supported by post-hoc analyses of achieved control in other studies (SPARCL, J-STARS)

ESO
EUROPEAN STROKE ORGANISATION

Aparté

- TST eligibility criteria: atherosclerotic disease:
  - stenosis of an extracranial or intracranial cerebral artery
  - atherosclerotic plaques of the aortic arch ≥4 mm in thickness
  - known history of coronary artery disease.

- 2021 AHA Guidelines:

1	A	1. In patients with ischemic stroke with no known coronary heart disease, no major cardiac sources of embolism, and LDL cholesterol (LDL-C) >100 mg/dL, atorvastatin 80 mg daily is indicated to reduce risk of stroke recurrence.[208,209]
1	A	2. In patients with ischemic stroke or TIA and atherosclerotic disease (intracranial, carotid, aortic, or coronary), lipid-lowering therapy with a statin and also ezetimibe, if needed, to a goal LDL-C of <70 mg/dL is recommended to reduce the risk of major cardiovascular events.[210]

ESO
EUROPEAN STROKE ORGANISATION

Evidence-based Recommendation: Antithrombotics

Recommendation 1

In people with a non-cardioembolic minor ischaemic stroke (NIHSS score of 3 or less) or high-risk TIA (ABCD2 score of 4 or more) in the past 24 hours, we recommend 21-days of dual antiplatelet therapy with aspirin and clopidogrel, followed by antiplatelet monotherapy thereafter.

Quality of evidence: High ⊕⊕⊕⊕

Strength of recommendation: Strong for intervention ↑↑

Recommendation 2

In people with non-cardioembolic mild to moderate ischaemic stroke (NIHSS of 5 or less) or high-risk TIA (ABCD2 score of 6 or more or other high-risk features*) in the past 24 hours, we suggest 30-days of dual antiplatelet therapy with aspirin and ticagrelor followed by antiplatelet monotherapy thereafter.

*defined as either intracranial atherosclerotic disease or at least 50% stenosis in an internal carotid artery that could account for the presentation.

Quality of evidence: Moderate ⊕⊕⊕

Strength of recommendation: Weak for intervention ↑?

ESO
EUROPEAN STROKE ORGANISATION

Evidence-based Recommendation: Antithrombotics

PICO 9: In people with TIA and ischaemic stroke, does treatment with dual antiplatelet therapy for longer than 90 days with aspirin plus clopidogrel or aspirin plus dipyridamole, compared to a single antiplatelet, reduce the risk of recurrent stroke?

Evidence-based Recommendation

In people with previous ischaemic stroke or TIA, we recommend against use of dual antiplatelet therapy with aspirin and clopidogrel in the long-term and recommend use of single antiplatelet to reduce the risk of recurrent stroke.

Quality of evidence: **Very Low ⊕**

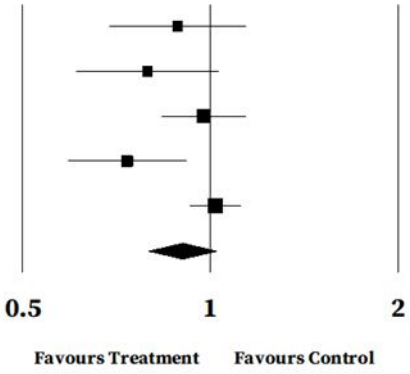
Strength of recommendation: **Weak against intervention ↓?**

ESO
EUROPEAN STROKE ORGANISATION

Supporting Information

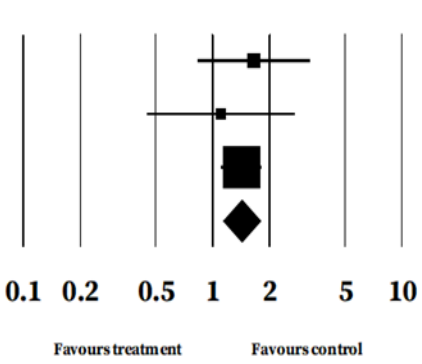
Recurrent Stroke

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
SPS3	0.888	0.689	1.144	-0.917	0.359
CHARISMA	0.794	0.610	1.033	-1.715	0.086
MATCH	0.976	0.834	1.142	-0.302	0.763
ESPS2 (aspirin)	0.737	0.591	0.918	-2.725	0.006
PROFESS	1.019	0.925	1.122	0.377	0.706
	0.903	0.797	1.022	-1.612	0.107



ICH

Study name	Hazard ratio	Lower limit	Upper limit	Z-Value	p-Value
SPS3	1.650	0.826	3.295	1.419	0.156
CHARISMA	1.110	0.450	2.739	0.226	0.821
PRoFESS	1.420	1.106	1.823	2.749	0.006
	1.421	1.132	1.784	3.026	0.002



Meta Analysis

- Non-significant reduction in recurrent stroke → NNT 8 per 1000
- Significant increase in intracerebral haemorrhage → NNH 4 per 1000

ESO
EUROPEAN STROKE ORGANISATION

Alternative Strategies: NOACs

PICO 10 Expert Consensus Statement: Low dose NOAC + Antiplatelet

The use of antiplatelet therapy combined with a low-dose direct oral anticoagulant (rivaroxaban) can be considered to optimise treatment of coronary artery disease or peripheral arterial disease in people with a history of ischaemic stroke or TIA more than one month previously. It should not be considered in people with ischaemic stroke or TIA who do not have coronary artery disease or peripheral arterial disease.

PICO 11 Evidence-based Recommendation: NOAC vs Antiplatelet in ESUS

In people with an embolic stroke of undetermined source, we suggest use of antiplatelet therapy and not a DOAC to reduce the risk of recurrent stroke.

Quality of evidence: **Low ⊕⊕**

Strength of recommendation: **Weak against intervention ↓?**

ESO
EUROPEAN STROKE ORGANISATION

Expert Consensus Statements: Diabetes

PICO 12: In people with diabetes mellitus and ischaemic stroke or TIA, does intensive control of glycated haemoglobin level (HbA1c) compared to less intensive HbA1c control reduce the risk of recurrent stroke?

Expert Consensus Statement

In people with ischaemic stroke or TIA and diabetes mellitus, we support aiming for an HbA1c level of <53mmol/mol (7%, 154 mg/dl) to reduce risk of microvascular and macrovascular complications. However, this target may need to be individualised based on duration of diabetes, age and comorbidities.

- No Secondary Prevention Evidence
- Based upon primary prevention guidance

ESO
EUROPEAN STROKE ORGANISATION

EUROPEAN STROKE ORGANISATION

European Stroke Organisation (ESO) guidelines on treatment of patients with intracranial atherosclerotic disease (ICAD)

Marios Psychogios, Elena López-Cancio, Gian Marco De Marchis, Elena Meseguer, Aristeidis Katsanos, Christine Kremer, Peter Sporns, Marialuisa Zedde, Adam Kobayashi, Jildaz Caroff, Daniel Bos, Sabrina Lémeret, Avtar Lal and Juan Arenillas

Important definitions

- **Intracranial atherosclerotic disease (ICAD)**

Atherosclerotic plaques affecting major intracranial arteries in any stage of the disease, including non-stenotic ICAD

- **Intracranial atherostenosis (ICAS)**

Atherosclerotic plaque causing a significant luminal narrowing (> 50%);

High-grade ICAS: > 70% or associated with symptoms

- **Hemodynamic compromise:**

Significant reduction of anterograde flow in the downstream arterial territory

Management of patients with symptomatic ICAD

PICO 6:

In patients with an ischemic stroke or transient ischemic attack related to a high-grade stenosis related to ICAD and without any formal indication for anticoagulation, does anticoagulant therapy, as compared to antiplatelet therapy, improve outcome?

Evidence-based Recommendation

In patients with an ischemic stroke or transient ischemic attack due to high-grade stenosis related to ICAD we recommend against oral anticoagulation over aspirin unless there is another formal indication for it.

Quality of evidence: **Moderate ⊕⊕⊕**

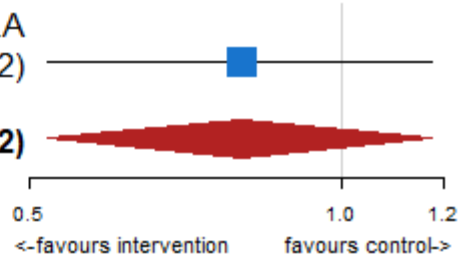
Strength of recommendation: **Strong against intervention ↓↓**

ESO
EUROPEAN STROKE ORGANISATION

Additional information PICO 6

PICO 6 - Association between anticoagulation therapy compared to antiplatelet therapy and risk of long term recurrence of IS in RCT

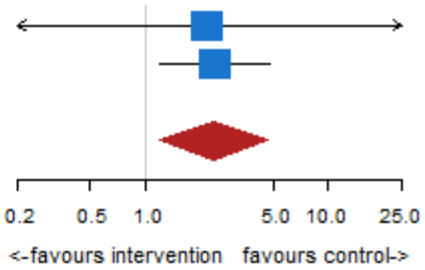
Study	*n(I)*	*N(I)*	*n(C)*	*N(C)*	*weight*	*OR(95%CI)*
Marti-Fabregas 2006	0	14	0	14	0.0%	N.A
Chimowitz 2005	49	289	57	280	100.0%	0.80 (0.52-1.22)
Total	**49**	**303**	**57**	**294**	**100.0%**	**0.80 (0.52-1.22)**



PICO 6 - Association between anticoagulation therapy compared to antiplatelet therapy and mortality in RCT

Study	*n(I)*	*N(I)*	*n(C)*	*N(C)*	*weight*	*OR(95%CI)*
Marti-Fabregas 2006	2	14	1	14	7.1%	2.17 (0.17-27.08)
Chimowitz 2005	28	289	12	280	92.9%	2.40 (1.19-4.81)
Total	**30**	**303**	**13**	**294**	**100.0%**	**2.38 (1.21-4.66)**

I^2=0%, p=0.94



- Data from two RCTs
- Effects primary driven by WASID trial
- No effect on risk of long-term recurrence of IS
- Higher risk of mortality and major bleeding
- No trials on NOACs

EUROPEAN STROKE ORGANISATION

Management of patients with symptomatic ICAD

PICO 7:

In patients with an ischemic stroke or transient ischemic attack related to intracranial stenosis related to ICAD, does dual antiplatelet therapy, as compared to single antiplatelet therapy, improve outcome?

Evidence-based Recommendation

In patients with an ischemic stroke or transient ischemic attack related to intracranial stenosis due to ICAD we suggest dual antiplatelet therapy over single antiplatelet therapy. Regarding the duration of the dual antiplatelet therapy, we refer to the expert consensus statement.

Quality of evidence: **Very low ⊕**

Strength of recommendation: **Weak for intervention ↑?**

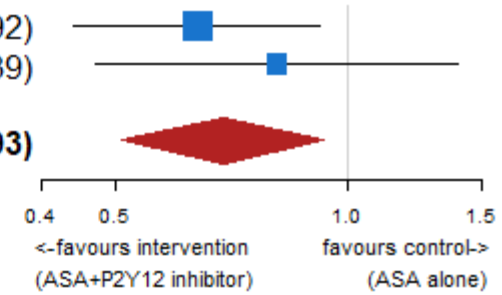
ESO
EUROPEAN STROKE ORGANISATION

Additional information PICO 7

PICO 7 - Association between aspirin + P2Y12 inhibitor intake, compared to aspirin intake alone, and risk of recurrent IS or death in RCT

Study	*n(I)*	*N(I)*	*n(C)*	*N(C)*	*weight*	*OR(95%CI)*
Amarenco 2020	53	516	85	558	68.9%	0.64 (0.44-0.92)
Liu 2015	26	231	34	250	31.1%	0.81 (0.47-1.39)
Total	**79**	**747**	**119**	**808**	**100.0%**	**0.69 (0.51-0.93)**

I^2=0%, p=0.48



- Data from subgroup analysis of 2 RCTs

- THALES:
  - aspirin + ticagrelor for 30 days
  - subgroup: Intracranial stenosis >= 30%
  - Primary endpoint: recurrent stroke or death at 30 days

- CHANCE:
  - Aspirin + clopidogrel for 21 days
  - Subgroup: Intracranial stenosis >= 50% (MRA)
  - Primary endpoint: any stroke at 90 days

ESO
EUROPEAN STROKE ORGANISATION

Expert Consensus Statement PICO 7

In patients with symptomatic ICAD, the optimal duration of DAPT is not clear according to current evidence. We suggest prolonging DAPT up to day 90 after the index event.

Voting results: 12 agree / 0 disagree

ESO
EUROPEAN STROKE ORGANISATION

Management of patients with symptomatic ICAD

PICO 8:

In patients with an ischemic stroke (IS) or transient ischemic attack (TIA) related to a high-grade stenosis due to ICAD, does angioplasty and/or stenting plus BMT, as compared to BMT alone, improve outcome?

Evidence-based Recommendation

In patients with an ischemic stroke or transient ischemic attack related to a high-grade stenosis due to ICAD, we recommend against angioplasty and/or stenting added to best medical treatment as first-line treatment.

Quality of evidence: **Low** ⊕⊕

Strength of recommendation: **Strong against intervention** ↓↓

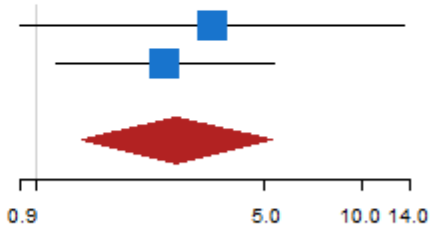
ESO
EUROPEAN STROKE ORGANISATION

Additional information PICO 8

PICO 8 - Association between angioplasty and/or stenting + BMT compared to BMT and risk of recurrent IS at 30 days in RCT

Study	*n(I)*	*N(I)*	*n(C)*	*N(C)*	*weight*	*OR(95%CI)*
Zaidat 2015	10	58	3	53	24.4%	3.47 (0.90-13.39)
Derdeyn 2014	23	224	10	227	75.6%	2.48 (1.15-5.35)
Total	**33**	**282**	**13**	**280**	**100.0%**	**2.69 (1.38-5.25)**

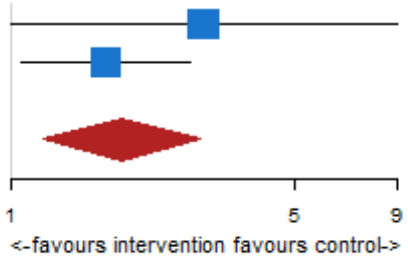
I^2=0%, p=0.67



PICO 8 - Association between angioplasty and/or stenting + BMT compared to BMT and risk of MACE in RCT

Study	*n(I)*	*N(I)*	*n(C)*	*N(C)*	*weight*	*OR (95%CI)*
Zaidat 2015	14	58	5	53	13.3%	2.99 (1.00-8.96)
Derdeyn 2014	52	224	34	227	86.7%	1.72 (1.06-2.77)
Total	**66**	**282**	**39**	**280**	**100.0%**	**1.88 (1.21-2.92)**

I^2=0%, p=0.35



- Data from two RCTs
- Effects driven by the SAMMPRIS trial (451 patients vs 112 patients)
- Both trials show worse outcomes in intervention arm
- However, new devices and more experienced interventionalists might offer more beneficial results

ESO
EUROPEAN STROKE ORGANISATION

Expert Consensus Statement PICO 8

We suggest considering endovascular treatment (angioplasty and/or stenting) as a rescue therapy in selected patients with symptomatic high-grade ICAS after clinical recurrence despite BMT.

Voting results: 11 agree / 1 disagree

EUROPEAN STROKE ORGANISATION

Management of patients with symptomatic ICAD

PICO 11:

In patients with an ischemic stroke or transient ischemic attack related to an intracranial atherostenosis, does aggressive vascular risk factor control, including lipid management, improve outcome?

Evidence-based Recommendation

In patients with an ischemic stroke or transient ischemic attack related to an intracranial atherostenosis, we suggest aggressive vascular risk factor control, including lipid management and lifestyle changes (i.e., increased physical activity), in order to improve outcomes, although uncertainty exists regarding target levels of BP and LDL in this specific population.

Quality of evidence: **Low ⊕⊕**

Strength of recommendation: **Weak for intervention ↑?**

ESO
EUROPEAN STROKE ORGANISATION

Expert Consensus Statement PICO 11

We suggest that patients with symptomatic ICAS should be considered as a very-high-risk population and target levels of LDL cholesterol should be achieved according to ESC/EAS guidelines (LDL <55 mg/dl).

Voting results: 11 agree / 1 disagree

We suggest that even in the subacute phase of stroke due to ICAS, strict BP control probably should be initiated to prevent recurrence and stenosis progression. Regarding the optimal BP target in ICAD patients, we refer the readers to ESO stroke secondary prevention guidelines, since there is no specific evidence-based recommendation for ICAD patients.

Voting results: 12 agree / 0 disagree

ESO
EUROPEAN STROKE ORGANISATION

EUROPEAN STROKE ORGANISATION

European Stroke Organisation guideline on screening for subclinical AF after stroke or TIA of undetermined origin

Marta Rubiera, Ana Aires, Kateryna Antonenko, Sabrina Lémeret, Christian Nolte, Jukka Putaala, Renate Schnabel, Anil Tuladhar, David Werring, Dena Zeraatkar, Maurizio Paciaroni

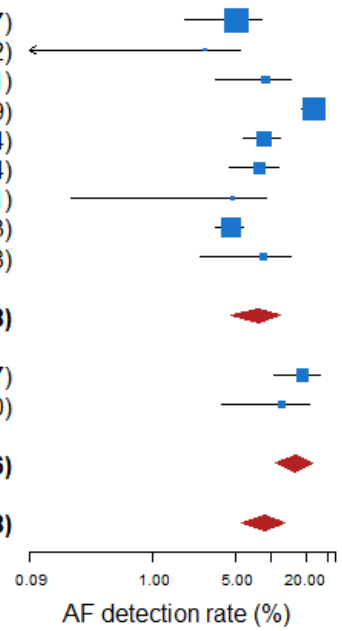
Outcome: detection of subclinical AF

Expert consensus statement

In adult patients with ischaemic stroke or TIA of undetermined origin, we suggest prolonged cardiac rhythm monitoring for AF for more than 48 hours.

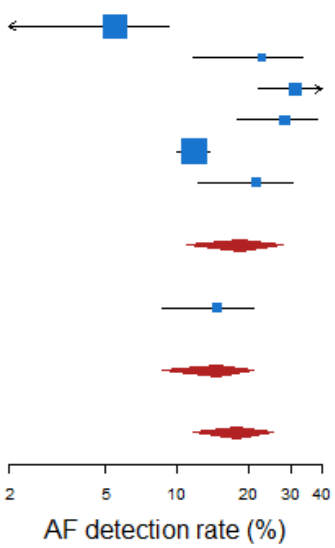
PICO 1 - AF detection rate in single arm studies (30 days follow-up)

Study	*n*	*N*	*weight*	*rate (95%CI)*
Marks 2021	9	178	9.4%	5.06% (1.84-8.27)
Chorin 2020	4	145	9.2%	2.76% (0.09-5.42)
Magnusson 2020	9	100	8.6%	9.00% (3.39-14.61)
Pagola 2020	61	264	9.8%	23.11% (18.02-28.19)
Milstein 2019	30	343	10.0%	8.75% (5.76-11.74)
Favilla 2015	18	227	9.7%	7.93% (4.41-11.44)
Kalani 2015	4	85	8.3%	4.71% (0.20-9.21)
Ziegler 2015	57	1247	10.6%	4.57% (3.41-5.73)
Gaillard 2010	7	82	8.2%	8.54% (2.49-14.58)
Total (CS or TIA)	**199**	**2671**	**83.9%**	**7.82% (4.53-11.88)**
I²=90%, p=0.00				
Jordan 2019	18	99	8.6%	18.18% (10.58-25.77)
Lumikari 2019	7	57	7.5%	12.28% (3.76-20.80)
Total (ESUS)	**25**	**156**	**16.1%**	**16.15% (10.76-22.36)**
I²=0%, p=0.35				
Total 30 days	**224**	**2827**	**100.0%**	**8.88% (5.55-12.88)**
I²=89%, p=0.00				



PICO 1 - AF detection rates in single arm studies (6 months follow-up)

Study	*n*	*N*	*weight*	*rate (95%CI)*
Chorin 2020	8	145	14.9%	5.52% (1.80-9.23)
De Angelis 2020	13	58	12.5%	22.41% (11.68-33.14)
Carrazco 2018	31	100	14.1%	31.00% (21.93-40.06)
Poli 2016	21	75	13.3%	28.00% (17.84-38.16)
Ziegler 2015	147	1247	16.8%	11.79% (10.00-13.59)
Fonseca 2013	17	80	13.5%	21.25% (12.29-30.21)
Total (CS or TIA)	**237**	**1705**	**85.2%**	**18.45% (10.92-27.37)**
I²=90%, p=0.00				
Lee 2021	20	136	14.8%	14.71% (8.75-20.66)
Total (ESUS)	**20**	**136**	**14.8%**	**14.71% (8.75-20.66)**
Total 6 months	**257**	**1841**	**100.0%**	**17.87% (11.62-25.10)**
I²=88%, p=0.00				



EUROPEAN STROKE ORGANISATION

Evidence-based Recommendations

Implantable monitoring devices compared to any non-implantable external monitoring device

PICO 3: In adult patients with ischaemic stroke or TIA of undetermined origin, do implantable monitoring devices compared to any non-implantable external monitoring device increase the detection of subclinical AF, increase the rate of anticoagulation, reduce the rate of recurrent stroke or systemic embolism, intracranial haemorrhage, any major haemorrhage, mortality and improve functional outcome?

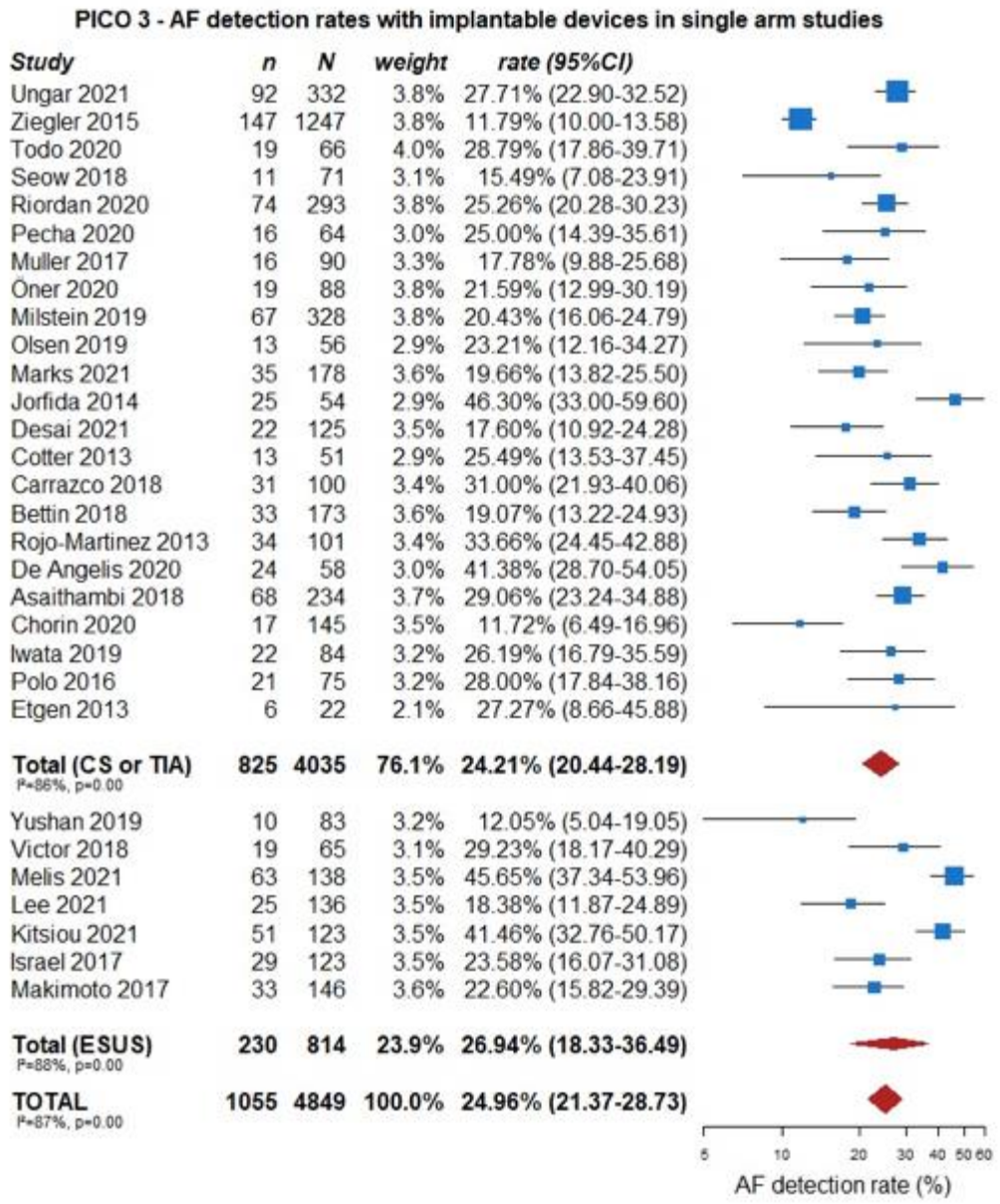
Evidence-based Recommendation

In adult patients with ischaemic stroke or TIA of undetermined origin, we suggest the use of implantable devices for cardiac monitoring instead of non-implantable devices to increase the detection of subclinical AF.

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

ESO
EUROPEAN STROKE ORGANISATION

Outcome: detection of subclinical AF



EUROPEAN STROKE ORGANISATION

Conclusions

Take Home Messages:

- ✓To maximise AF detection, clinicians should perform the longest possible cardiac rhythm monitoring, starting as soon as possible, in patients with stroke or TIA of undetermined origin.
- ✓However, RCTs are needed to determine if increased AF detection improves clinical outcomes.

ESO
EUROPEAN STROKE ORGANISATION

Recommandations en préparation

Guidelines

- Tenecteplase
- Moya-Moya
- Angéite primitive du système nerveux central
- Hémorragie intraparenchymateuse
- Hémorragie sous arachnoïdienne
- Maladie des petites artères cérébrales «symptomatique»
- FOP
- Rééducation post-AVC: déficit moteur et marche
- Rééducation post-AVC: aphasie
- Rééducation post-AVC: troubles neurovisuels
- Rééducation post-AVC: troubles cognitifs
- PRES/SVCR
- Thromboses veineuses cérébrales

…

Merci de votre attention !

https://eso-stroke.org/guidelines/eso-guideline-directory

30 guidelines

g.turc@ghu-paris.fr